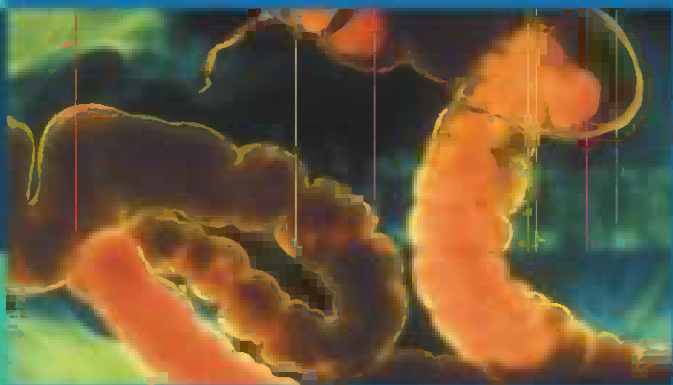


David E. Beck • Patricia L. Roberts • John L. Rombeau
Michael J. Stamos • Steven D. Wexner



The ASCRS Manual of Colon and Rectal Surgery



Springer

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Preface

This manual is abstracted from and is a companion to the American Society of Colon and Rectal Surgeons' (ASCRS) *ASCRS Textbook of Colon and Rectal Surgery*, Wolff BG, Fleshman JW, Beck DE, Pemberton JH, Wexner SD, eds. New York: Springer; 2007. It is yet another resource representing ASCRS's ongoing major commitment to education. The purpose of the *ASCRS Manual of Colon and Rectal Surgery* is to provide a "user friendly", pocket resource for the busy medical student, resident, private clinician, nurse practitioner, physician's assistant and others caring for patients with colorectal surgical diseases.

The ASCRS Manual is intended to provide succinct, clinically relevant information for daily patient care and to stimulate the reader to seek more extensive information in the ASCRS Textbook. Each chapter in the manual has been abstracted, edited and reviewed by the textbook authors and manual editors. Many diagrams, figures and algorithms from the textbook have been retained inasmuch as they have been found to be helpful in daily patient care. Moreover, other textual content has been purposely excluded from the manual including discussions of research trials, step-by-step technical descriptions of operations, operative techniques, and various figures, x-rays, and patient photos which did not transcribe well to the manual format. The manual will also serve as a bridge to create future electronic links between our journal (*Diseases of the Colon and Rectum*) and the ASCRS Textbook.

Readers of the ASCRS Manual are strongly encouraged to consult the ASCRS Textbook for in-depth discussions, clarification of content and appropriate citings of references. It is hoped that the reader will find the manual to be a practical and clinically relevant resource for the daily care of colorectal surgical patients.

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1. Anatomy and Embryology of the Colon, Rectum, and Anus

A. Anatomy

Anus and Rectum

Anal Canal Structure, Anus, and Anal Verge

- The anus or anal orifice is an anteroposterior cutaneous slit, that along with the anal canal remains virtually closed at rest, as a result of tonic circumferential contraction of the sphincters and the presence of anal cushions.
- The edge of the anal orifice, the anal verge or margin (anocutaneous line of Hilton), marks the lowermost edge of the anal canal and is sometimes the level of reference for measurements taken during sigmoidoscopy.
- Others favor the dentate line as a landmark because it is more precise. The difference between the anal verge and the dentate line is usually 1–2 cm.
- The epithelium distal to the anal verge acquires hair follicles, glands, including apocrine glands, and other features of normal skin, and is the source of perianal hidradenitis suppurativa, (inflammation of the apocrine glands).

Anatomic Vs. Surgical Anal Canal

- Two definitions are found describing the anal canal (Fig. 1.1)
- The “anatomic” or “embryologic” anal canal is only 2.0 cm long, extending from the anal verge to the dentate line, the level that corresponds to the proctodeal membrane. The “surgical” or “functional” anal canal is longer, extending for approximately 4.0 cm (in men) from the anal verge to the anorectal ring (levator ani).

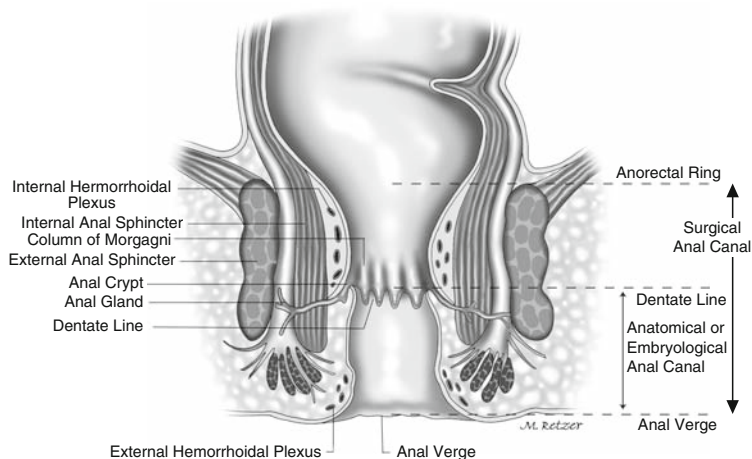


Fig. 1.1. Anal canal.

- The anorectal ring is at the level of the distal end of the ampullary part of the rectum and forms the anorectal angle, and the beginning of a region of higher intraluminal pressure. Therefore, this definition correlates with digital, manometric, and sonographic examinations.

Anatomic Relations of the Anal Canal

- Posteriorly, the anal canal is related to the coccyx and anteriorly to the perineal body and the lowest part of the posterior vaginal wall in the female, and to the urethra in the male. The ischium and the ischiorectal fossa are situated on either side. The fossa ischiorectal contains fat and the inferior rectal vessels and nerves, which cross it to enter the wall of the anal canal.

Muscles of the Anal Canal

- The muscular component of the mechanism of continence can be stratified into three functional groups: lateral compression from the pubococcygeus, circumferential closure from the internal and external anal sphincter, and angulation from the puborectalis (Fig. 1.2).

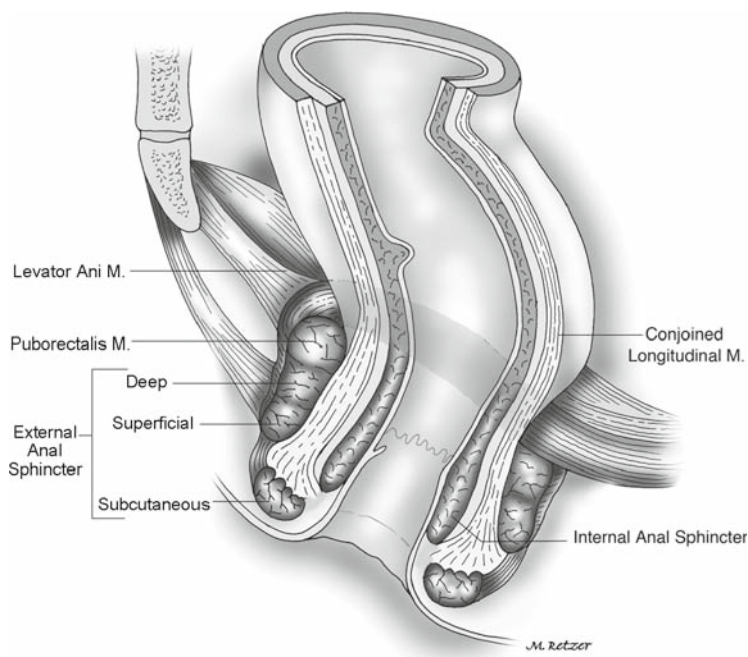


Fig. 1.2. Muscles of the anal canal.

Internal Anal Sphincter

- The internal anal sphincter represents the distal 2.5- to 4.0-cm condensation of the circular muscle layer of the rectum. As a consequence of both intrinsic myogenic and extrinsic autonomic neurogenic properties, the internal anal sphincter is a smooth muscle in a state of continuous maximal contraction, and represents a natural barrier to the involuntary loss of stool and gas.
- The lower rounded edge of the internal anal sphincter can be felt on physical examination, about 1.2 cm distal to the dentate line. The groove between the internal and external anal sphincter, the intersphincteric sulcus, can be visualized or easily palpated.
- Endosonographically, the internal anal sphincter is a 2- to 3-mm-thick circular band and shows a uniform hypoechogenicity.

External Anal Sphincter

- The external anal sphincter is the elliptical cylinder of striated muscle that envelops the entire length of the inner tube of smooth muscle, but it ends slightly more distal than the internal anal sphincter.
- The deepest part of the external anal sphincter is intimately related to the puborectalis muscle, which can actually be considered a component of both the levator ani and the external anal sphincter muscle complexes.
- Endosonographically, the puborectalis and the external anal sphincter, despite their mixed linear echogenicity, are both predominantly hyperechogenic, with a mean thickness of 6 mm (range, 5–8 mm).
- In the male, the upper half of the external anal sphincter is enveloped anteriorly by the conjoined longitudinal muscle, whereas the lower half is crossed by it.
- In the female, the entire external anal sphincter is encapsulated by a mixture of fibers derived from both longitudinal and internal anal sphincter muscles.
- The automatic continence mechanism is formed by the resting tone, maintained by the internal anal sphincter, magnified by voluntary, reflex, and resting external anal sphincter contractile activities.
- In response to conditions of threatened incontinence, such as increased intraabdominal pressure and rectal distension, the external anal sphincter and puborectalis reflexively and voluntarily contract further to prevent fecal leakage.
- The external anal sphincter and the pelvic floor muscles, unlike other skeletal muscles, which are usually inactive at rest, maintain unconscious resting electrical tone through a reflex arc at the cauda equina level.

Conjoined Longitudinal Muscle

- Whereas the inner circular layer of the rectum gives rise to the internal anal sphincter, the outer longitudinal layer, at the level of the anorectal ring, mixes with fibers of the levator ani muscle to form the conjoined longitudinal muscle. This muscle descends between the internal and external anal sphincter, and ultimately some of its fibers, referred to as the corrugator cutis

ani muscle, traverse the lowermost part of the external anal sphincter to insert into the perianal skin.

- Possible functions of the conjoined longitudinal muscle include attaching the anorectum to the pelvis and acting as a skeleton that supports and binds the internal and external sphincter complex together.

Epithelium of the Anal Canal

- The lining of the anal canal consists of an upper mucosal (endoderm) and a lower cutaneous (ectoderm) segment (Fig. 1.1).
- The dentate (pectinate) line is the “saw-toothed” junction between these two distinct origins of venous and lymphatic drainage, nerve supply, and epithelial lining. Above this level, the intestine is innervated by the sympathetic and parasympathetic systems, with venous, arterial, and lymphatic drainage to and from the hypogastric vessels. Distal to the dentate line, the anal canal is innervated by the somatic nervous system, with blood supply and drainage from the inferior hemorrhoidal system. These differences are important when the classification and treatment of hemorrhoids are considered.
- The pectinate or dentate line corresponds to a line of anal valves that represent remnants of the proctodeal membrane. Above each valve, there is a little pocket known as an anal sinus or crypt. These crypts are connected to a variable number of glands, in average 6 (range, 3–12).
- More than one gland may open into the same crypt, whereas half the crypts have no communication.
- The anal gland ducts, in an outward and downward route, enter the submucosa; two-thirds enter the internal anal sphincter, and half of them terminate in the intersphincteric plane. Obstruction of these ducts, presumably by accumulation of foreign material in the crypts, may lead to perianal abscesses and fistulas.
- Cephalad to the dentate line, 8–14 longitudinal folds, known as the rectal columns (columns of Morgagni), have their bases connected in pairs to each valve at the dentate line.
- At the lower end of the columns are the anal papillae. The mucosa in the area of the columns consists of several layers of cuboidal cells and has a deep purple color because of the underlying internal hemorrhoidal plexus. This 0.5- to 1.0-cm strip of mucosa above the dentate line is known as the anal transition or

cloacogenic zone. Cephalad to this area, the epithelium changes to a single layer of columnar cells and macroscopically acquires the characteristic pink color of the rectal mucosa.

- The cutaneous part of the anal canal consists of modified squamous epithelium that is thin, smooth, pale, stretched, and devoid of hair and glands.

Rectum

- Both proximal and distal limits of the rectum are controversial: the rectosigmoid junction is considered to be at the level of the third sacral vertebra by anatomists but at the sacral promontory by surgeons, and likewise, the distal limit is regarded to be the muscular anorectal ring by surgeons and the dentate line by anatomists.
- The rectum measures 12–15 cm in length and has three lateral curves: the upper and lower are convex to the right and the middle is convex to the left. These curves correspond intraluminally to the folds or valves of Houston. The two left-sided folds are usually noted at 7–8 cm and at 12–13 cm, respectively, and the one on the right is generally at 9–11 cm. The middle valve (Kohlrausch's plica) is the most consistent in presence and location and corresponds to the level of the anterior peritoneal reflection.
- Although the rectal valves do not contain all muscle wall layers from a clinical point of view, they are a good location for performing a rectal biopsies, because they are readily accessible with minimal risk for perforation.
- The rectum is characterized by its wide, easily distensible lumen, and the absence of taeniae, epiploic appendices, haustra, or a well-defined mesentery.
- The word "mesorectum" has gained widespread popularity among surgeons to address the perirectal areolar tissue, which is thicker posteriorly, containing terminal branches of the inferior mesenteric artery and enclosed by the fascia propria.
- The "mesorectum" may be a metastatic site for a rectal cancer and is removed during surgery for rectal cancer without neurologic sequelae, because no functionally significant nerves pass through it.
- The upper third of the rectum is anteriorly and laterally invested by peritoneum; the middle third is covered by peritoneum on

its anterior aspect only. Finally, the lower third of the rectum is entirely extraperitoneal, because the anterior peritoneal reflection occurs at 9.0–7.0 cm from the anal verge in men and at 7.5–5.0 cm from the anal verge in women.

Anatomic Relations of the Rectum

- The rectum occupies the sacral concavity and ends 2–3 cm anteroinferiorly from the tip of the coccyx. At this point, it angulates backward sharply to pass through the levators and becomes the anal canal. Anteriorly, in women, the rectum is closely related to the uterine cervix and posterior vaginal wall; in men, it lies behind the bladder, vas deferens, seminal vesicles, and prostate. Posterior to the rectum lie the median sacral vessels and the roots of the sacral nerve plexus.

Fascial Relationships of the Rectum

- The parietal endopelvic fascia lines the walls and floor of the pelvis and continues on the internal organs as a visceral pelvic fascia (Fig. 1.3a, b).
- The lateral ligaments or stalks of the rectum are distal condensations of the pelvic fascia that form a roughly triangular structure with a base on the lateral pelvic wall and an apex attached to the lateral aspect of the rectum.
- The lateral stalks are comprised essentially of connective tissue and nerves, and the middle rectal artery does not traverse them. Branches, however, course through in approximately 25% of cases. Consequently, division of the lateral stalks during rectal mobilization is associated with a 25% risk for bleeding.
- One theoretical concern in ligation of the stalks is leaving behind lateral mesorectal tissue, which may limit adequate lateral or mesorectal margins during cancer surgery.
- The presacral fascia is a thickened part of the parietal endopelvic fascia that covers the concavity of the sacrum and coccyx, nerves, the middle sacral artery, and presacral veins. Operative dissection deep to the presacral fascia may cause troublesome bleeding from the underlying presacral veins.
- Presacral hemorrhage occurs as frequently as 4.6–7.0% of resections for rectal neoplasms, and despite its venous nature, can be life threatening. This is a consequence of two factors: the difficulty in securing control because of retraction of the

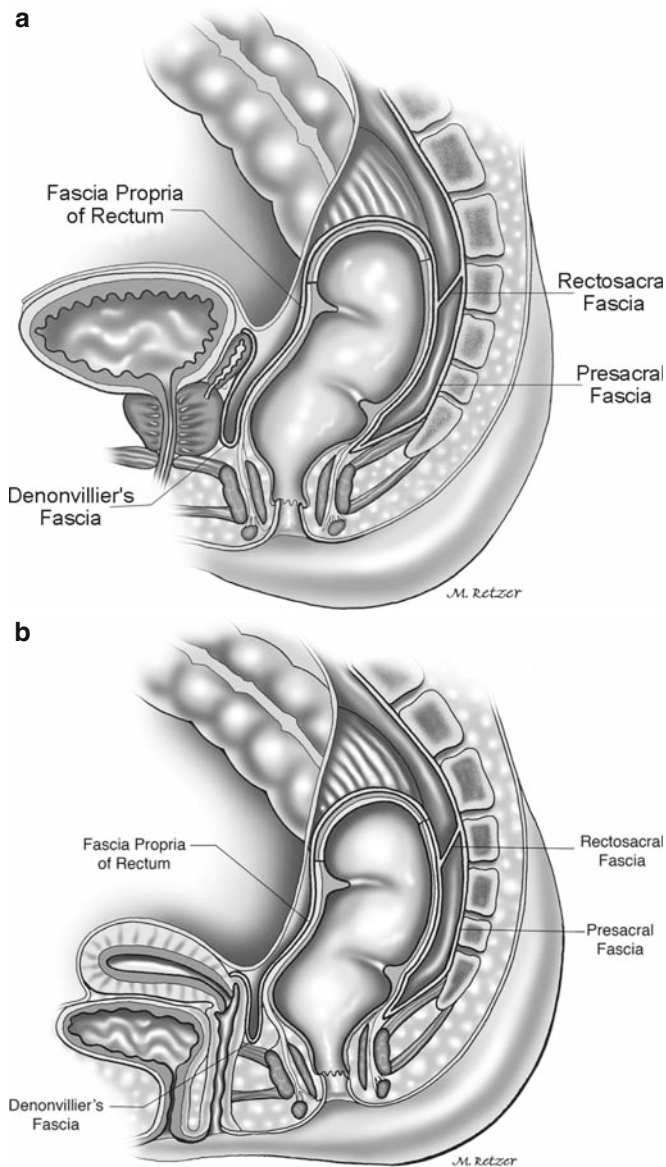


Fig. 1.3. Fascial relationships of the rectum: (a) male, (b) female.

vascular stump into the sacral foramen and the high hydrostatic pressure of the presacral venous system.

- The rectosacral fascia is an anteroinferiorly directed thick fascial reflection from the presacral fascia at the S-4 level to the fascia propria of the rectum just above the anorectal ring. The rectosacral fascia, classically known as the fascia of Waldeyer, is an important landmark during posterior rectal dissection.
- The visceral pelvic fascia of Denonvilliers is a tough fascial investment that separates the extraperitoneal rectum anteriorly from the prostate and seminal vesicles or vagina.

Urogenital Considerations

- Identification of the ureters is advisable to avoid injury to their abdominal or pelvic portions during colorectal operations. On both sides, the ureters rest on the psoas muscle in their inferomedial course; they are crossed obliquely by the spermatic vessels anteriorly and the genitofemoral nerve posteriorly. In its pelvic portion, the ureter crosses the pelvic brim in front of or a little lateral to the bifurcation of the common iliac artery, and descends abruptly between the peritoneum and the internal iliac artery.
- In the female, as the ureter traverses the posterior layer of the broad ligament and the parametrium close to the side of the neck of the uterus and upper part of the vagina, it is enveloped by the vesical and vaginal venous plexuses and is crossed above and lateromedially by the uterine artery.

Arterial Supply of the Rectum and Anal Canal

- The superior hemorrhoidal artery is the continuation of the inferior mesenteric artery, once it crosses the left iliac vessels. The artery descends in the sigmoid mesocolon to the level of S-3 and then to the posterior aspect of the rectum. In 80% of cases, it bifurcates into right, usually wider, and left terminal branches; multiple branches are present in 17%. These divisions, once within the submucosa of the rectum, run straight downward to supply the lower rectum and the anal canal.
- The superior and inferior hemorrhoidal arteries represent the major blood supply to the anorectum. In addition, it is also supplied by the internal iliac arteries.

- The contribution of the middle hemorrhoidal artery varies with the size of the superior hemorrhoidal artery; this may explain its controversial anatomy. Some authors report absence of the middle hemorrhoidal artery in 40–88% whereas others identify it in 94–100% of specimens.
- The middle hemorrhoidal artery is more prone to be injured during low anterior resection, when anterolateral dissection of the rectum is performed close to the pelvic floor and the prostate and seminal vesicles or upper part of the vagina are being separated.
- The anorectum has a profuse intramural anastomotic network, which probably accounts for the fact that division of both superior and middle hemorrhoidal arteries does not result in necrosis of the rectum.
- The paired inferior hemorrhoidal arteries are branches of the internal pudendal artery, which in turn is a branch of the internal iliac artery.

Venous Drainage and Lymphatic Drainage of the Rectum and Anal Canal

- The anorectum also drains, via middle and inferior hemorrhoidal veins, to the internal iliac vein and then to the inferior vena cava.
- The external hemorrhoidal plexus, situated subcutaneously around the anal canal below the dentate line, constitutes when dilated the external hemorrhoids.
- The internal hemorrhoidal plexus is situated submucosally, around the upper anal canal and above the dentate line. The internal hemorrhoids originate from this plexus.
- Lymph from the upper two-thirds of the rectum drains exclusively upward to the inferior mesenteric nodes and then to the paraaortic nodes.
- Lymphatic drainage from the lower third of the rectum occurs not only cephalad, along the superior hemorrhoidal and inferior mesentery arteries, but also laterally, along the middle hemorrhoidal vessels to the internal iliac nodes.
- In the anal canal, the dentate line is the landmark for two different systems of lymphatic drainage: above, to the inferior mesenteric and internal iliac nodes, and below, along the inferior

rectal lymphatics to the superficial inguinal nodes, or less frequently along the inferior hemorrhoidal artery.

- In the female, drainage at 5 cm above the anal verge in the lymphatic may also spread to the posterior vaginal wall, uterus, cervix, broad ligament, fallopian tubes, ovaries, and cul-de-sac, and at 10 cm above the anal verge, spread seems to occur only to the broad ligament and cul-de-sac.

Innervation of the Rectum and Anal Canal

- Innervation of the Rectum
 - The sympathetic supply of the rectum and the left colon arises from L-1, L-2, and L-3 (Fig. 1.4a, b).
 - Two main hypogastric nerves, on either side of the rectum, carry sympathetic innervation from the hypogastric plexus to the pelvic plexus.
 - The parasympathetic fibers to the rectum and anal canal emerge through the sacral foramen and are called the nervi erigentes (S-2, S-3, and S-4).
 - The periprostatic plexus, a subdivision of the pelvic plexus situated on Denonvilliers' fascia, supplies the prostate, seminal vesicles, corpora cavernosa, vas deferens, urethra, ejaculatory ducts, and bulbourethral glands.
 - Sexual function is regulated by cerebrospinal, sympathetic, and parasympathetic components. Erection of the penis is mediated by both parasympathetic (arteriolar vasodilatation) and sympathetic inflow (inhibition of vasoconstriction).
 - All pelvic nerves lie in the plane between the peritoneum and the endopelvic fascia and are in danger of injury during rectal dissection. Permanent bladder paresis occurs in 7–59% of patients after abdominoperineal resection of the rectum; the incidence of impotence is reported to range from 15 to 45%, and that of ejaculatory dysfunction from 32 to 42%. The overall incidence of sexual dysfunction after proctectomy has been reported to reach 100% when wide dissection is performed for malignant disease.
 - Dissections performed for benign conditions are undertaken closer to the bowel wall, thus reducing the possibility of nerve injury.

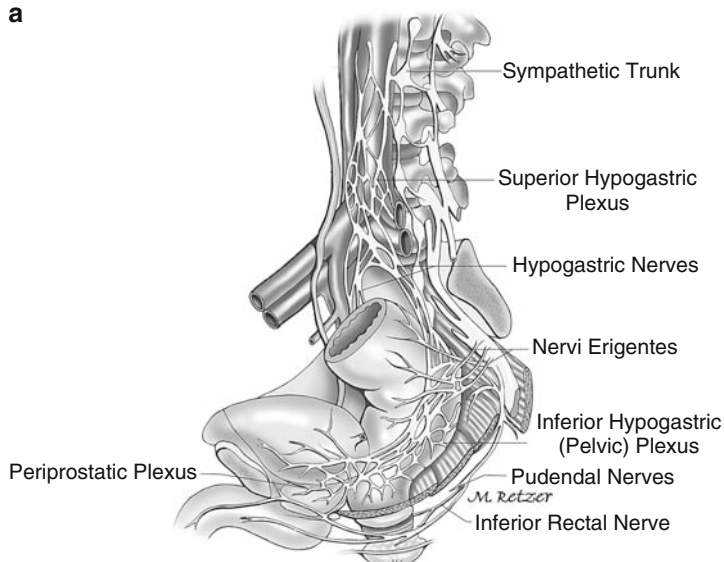
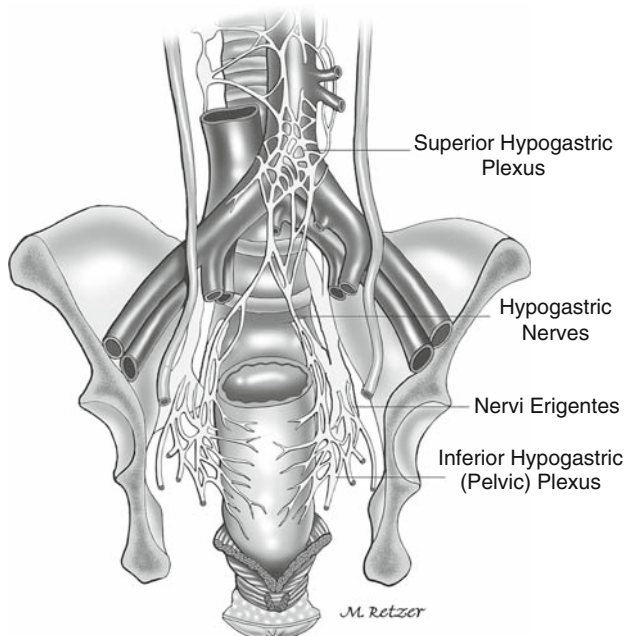
a**b**

Fig. 1.4. (a, b) Innervation of the colon, rectum, and anal canal.

- Trauma to the autonomic nerves may occur at several points. During high ligation of the inferior mesenteric artery, close to the aorta, the sympathetic preaortic nerves may be injured.
- Division of both superior hypogastric plexus and hypogastric nerves may occur also during dissection at the level of the sacral promontory or in the presacral region. In such circumstances, sympathetic denervation with intact nervi erigentes results in retrograde ejaculation and bladder dysfunction.
- The nervi erigentes are located in the posterolateral aspect of the pelvis, and at the point of fusion with the sympathetic nerves are closely related to the middle hemorrhoidal artery. Injury to these nerves will completely abolish erectile function.
- The pelvic plexus may be damaged either by excessive traction on the rectum, particularly laterally, or during division of the lateral stalks when this is performed close to the lateral pelvic wall.
- Finally, dissection near the seminal vesicles and prostate may damage the periprostatic plexus, leading to a mixed parasympathetic and sympathetic injury. This can result in erectile impotence as well as a flaccid, neurogenic bladder.
- Sexual complications after rectal surgery are readily evident in men but are probably underdiagnosed in women.
- Anal Canal
 - The internal anal sphincter is supplied by sympathetic (L-5) and parasympathetic nerves (S-2, S-3, and S-4) following the same route as the nerves to the rectum.
 - The external anal sphincter is innervated on each side by the inferior rectal branch of the pudendal nerve (S-2 and S-3) and by the perineal branch of S-4. Despite the fact that the puborectalis and external anal sphincter have somewhat different innervations, these muscles seem to act as an indivisible unit.
 - After unilateral transection of a pudendal nerve, external anal sphincter function is still preserved because of the crossover of the fibers at the spinal cord level.
 - Anal sensation is carried in the inferior rectal branch of the pudendal nerve and is thought to have a role in maintenance of anal continence.

Anorectal Spaces

- The potential spaces of clinical significance in close relation to the anal canal and rectum include: ischiorectal, perianal, intersphincteric, submucosal, superficial postanal, deep postanal, supralelevator, and retrorectal spaces (Fig. 1.5a, b).
- The ischiorectal fossa is subdivided by a thin horizontal fascia into two spaces: the perianal and ischiorectal.
- The perianal space surrounds the lower part of the anal canal and contains the external hemorrhoidal plexus, the subcutaneous part of the external anal sphincter, the lowest part of the internal anal sphincter, and fibers of the longitudinal muscle. This space is the typical site of anal hematomas, perianal abscesses, and anal fistula tracts.
- The intersphincteric space is a potential space between the internal and external anal sphincters. It is important in the genesis of perianal abscess, because most of the anal glands end $\square$ in this space.
- The submucous space is situated between the internal anal sphincter and the mucocutaneous lining of the anal canal. This space contains the internal hemorrhoidal plexus and the muscularis submucosae ani. It is continuous with the submucous layer of the rectum, and, inferiorly, it ends at the level of the dentate line.
- The superficial postanal space is interposed between the anococcygeal ligament and the skin. The deep postanal space, also known as the retro-sphincteric space of Courtney, is situated between the anococcygeal ligament and the anococcygeal raphe. Both postanal spaces communicate posteriorly with the ischiorectal fossa and are the sites of horseshoe abscesses.
- The supralelevator spaces are situated between the peritoneum superiorly and the levator ani inferiorly.
- Supralelevator abscesses may occur as a result of upward extension of a cryptoglandular infection or develop from a pelvic origin.
- The retrorectal space is located between the fascia propria of the rectum anteriorly and the presacral fascia posteriorly. The retrorectal space is a site for embryologic remnants and rare presacral tumors.

Pelvic Floor Musculature

- The muscles within the pelvis can be divided into three categories (1) the anal sphincter complex; (2) pelvic floor muscles; and (3) muscles that line the sidewalls of the osseous pelvis.

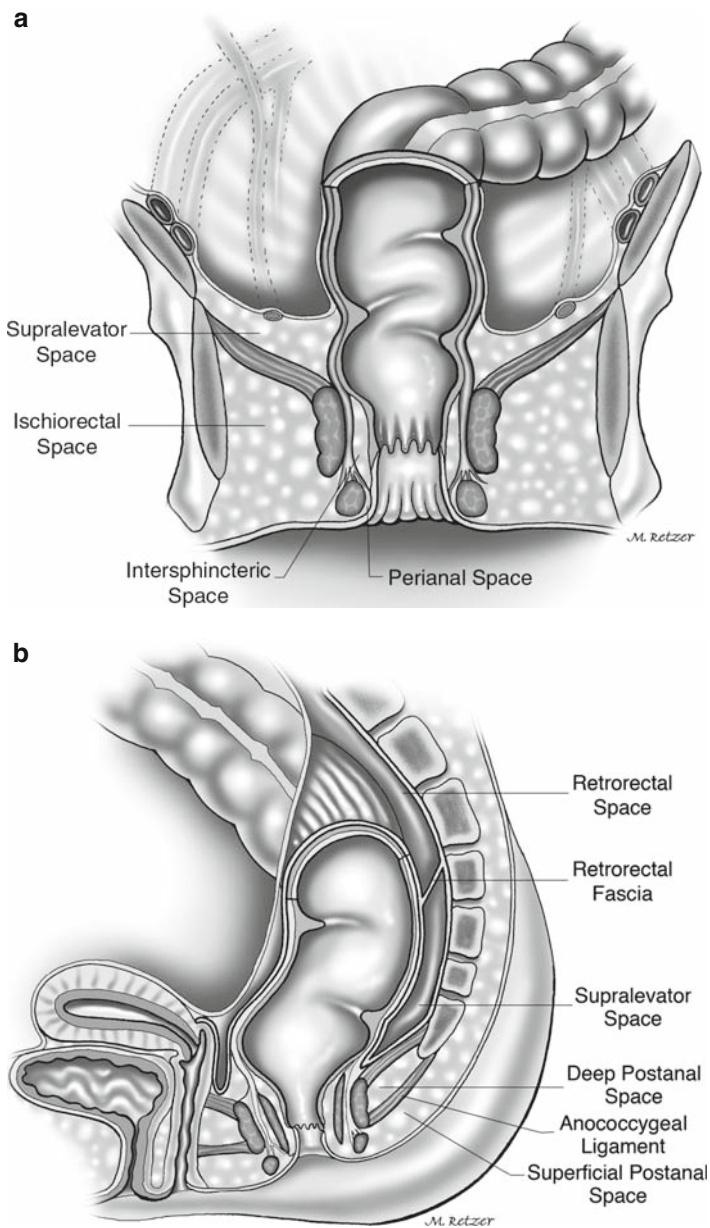


Fig. 1.5. Para-anal and pararectal spaces. (a) Frontal view. (b) Lateral view.

Levator Ani

- The levator ani muscle, or pelvic diaphragm, is the major component of the pelvic floor. It is a pair of broad, symmetric sheets composed of three striated muscles: ileococcygeus, pubococcygeus, and puborectalis (Fig. 1.6a, b).
- The pelvic floor is “incomplete” in the midline where the lower rectum, urethra, and either the dorsal vein of the penis in men,

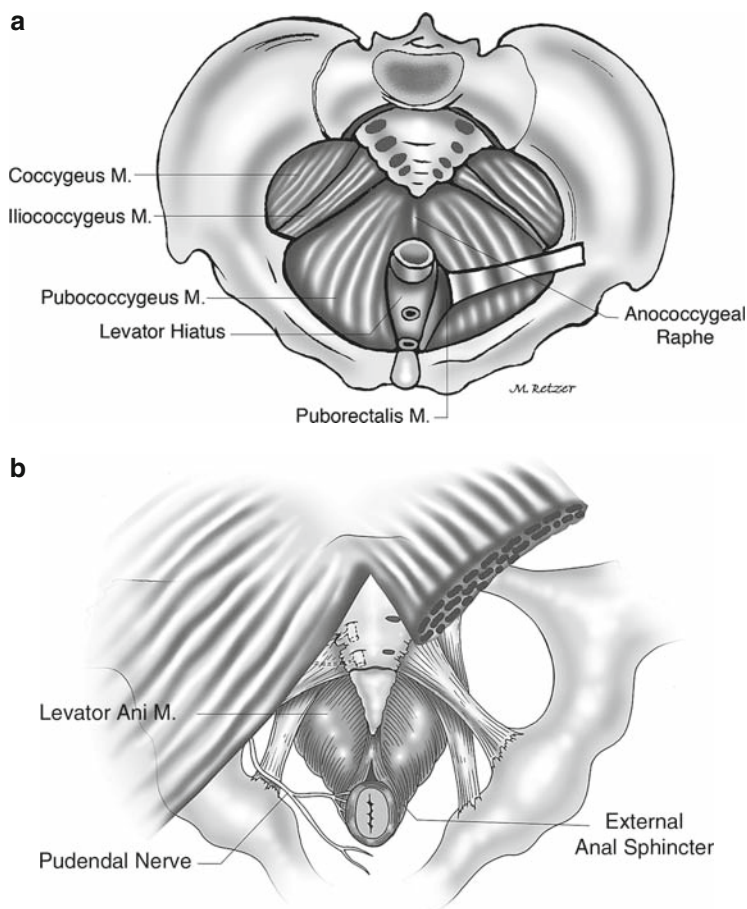


Fig. 1.6. Levator ani muscle. (a) Superior. (b) Inferior surface.

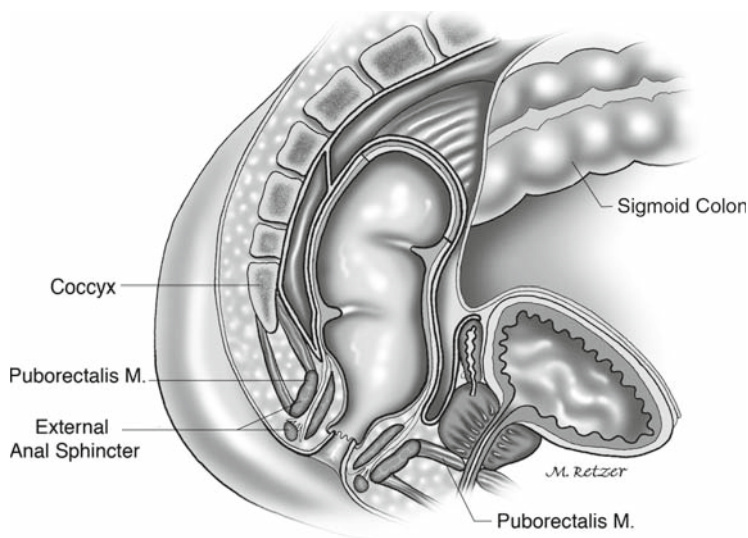


Fig. 1.7. The anteriorly directed pull of the puborectalis contributes to the angulation between the rectum and anal canal, the anorectal angle.

or the vagina in women, pass through it. This defect is called the levator hiatus and consists of an elliptic space situated between the two pubococcygeus muscles.

- The puborectalis muscle is a strong, U-shaped loop of striated muscle that slings the anorectal junction to the posterior aspect of the pubis (Fig. 1.7).

The Anorectal Ring and the Anorectal Angle

- Two anatomic structures of the junction of the rectum and anal canal are related to the puborectalis muscle: the anorectal ring and the anorectal angle. The anorectal ring, a term coined by Milligan and Morgan, is a strong muscular ring that represents the upper end of the sphincter, more precisely the puborectalis, and the upper border of the internal anal sphincter, around the anorectal junction.
- It is of clinical relevance, because division of this structure during surgery for abscesses or fistula inevitably results in fecal incontinence.

- The anorectal angle is thought to be the result of the anatomic configuration of the U-shaped sling of puborectalis muscle around the anorectal junction. Whereas the anal sphincters are responsible for closure of the anal canal to retain gas and liquid stool, the puborectalis muscle and the anorectal angle are designed to maintain gross fecal continence.

Colon

General Considerations

- Named from the Greek koluein (“to retard”), the colon is variable in length, averaging approximately 150 cm, which corresponds to one-quarter the length of the small intestine.
- Its diameter can be substantially augmented by distension, it gradually decreases from 7.5 cm at the cecum to 2.5 cm at the sigmoid.
- Anatomic differences between the small and large intestines include position, caliber, degree of fixation, and, in the colon, the presence of three distinct characteristics: the taeniae coli, the haustra, and the appendices epiploicae.
- The three taeniae coli, anterior (taenia libera), posteromedial (taenia mesocolica), and posterolateral (taenia omentalis), represent bands of the outer longitudinal coat of muscle that traverse the colon from the base of the appendix to the recto-sigmoid junction, where they merge.
- The haustra or haustral sacculations are outpouchings of bowel wall between the taeniae; they are caused by the relative shortness of the taeniae, about one-sixth shorter than the length of the bowel wall. The haustra are separated by the plicae semilunares or crescentic folds of the bowel wall, which give the colon its characteristic radiographic appearance when filled with air or barium.
- The appendices epiploicae are small appendages of fat that protrude from the serosal aspect of the colon.

Cecum

- The cecum is the sacculated segment (Latin caecus, “blind”) of the large bowel that projects downward as a 6- to 8-cm blind pouch below the entrance of the ileum.

- Usually situated in the right iliac fossa, the cecum is almost entirely, or at least in its lower half, invested with peritoneum.
- The ileum terminates in the posteromedial aspect of the cecum.
- A circular sphincter, the ileocecal sphincter, originates from a slight thickening of the muscular layer of the terminal ileum. A competent ileocecal valve is related to the critical closed-loop type of colonic obstruction. However, ileocecal competence is not always demonstrated on barium enema studies. Instead of preventing reflux of colonic contents into the ileum, the ileocecal valve regulates ileal emptying. The ileocecal sphincter seems to relax in response to the entrance of food into the stomach. As in the gastroesophageal junction, extrasphincteric factors such as the ileocecal angulation apparently have a role in the prevention of reflux from the colon to the ileum.

Appendix

- The vermiform appendix is an elongated diverticulum that arises from the posteromedial aspect of the cecum about 3.0 cm below the ileocecal junction. Its length varies from 2 to 20 cm (mean, 8–10 cm), and it is approximately 5 mm in diameter.
- The appendix, because of its great mobility, may occupy a variety of positions, possibly at different times in the same individual. It has been estimated that in 85–95% of cases, the appendix lies posteromedial on the cecum toward the ileum, but other positions include retrocecal, pelvic, subcecal, pre-ileal and retroileal.
- The confluence of the three taeniae is a useful guide in locating the base of the appendix.

Ascending Colon

- The ascending colon is approximately 15 cm long. It ascends, from the level of the ileocecal junction to the right colic or hepatic flexure, laterally to the psoas muscle and anteriorly to the iliacus, the quadratus lumborum, and the lower pole of the right kidney.
- The ascending colon is covered with peritoneum anteriorly and on both sides.
- Like the descending colon on its posterior surface, the ascending colon is devoid of peritoneum, which is instead replaced by an areolar tissue (fascia of Toldt). In the lateral peritoneal

reflection, this process is represented by the white line of Toldt, which is more evident at the descending-sigmoid junction. This line serves as a guide for the surgeon when the ascending, descending, or sigmoid colon is mobilized.

- At the visceral surface of the right lobe of the liver and lateral to the gallbladder, the ascending colon turns sharply medially and slightly caudad and ventrally to form the right colic (hepatic) flexure.

Transverse Colon

- The transverse colon is approximately 45 cm long, the longest segment of the large bowel. It crosses the abdomen, with an inferior curve immediately caudad to the greater curvature of the stomach. The transverse colon is relatively fixed at each flexure, and, in between, it is suspended by a 10- to 15-cm-wide area which provides variable mobility; the nadir of the transverse colon may reach the hypogastrium.
- The transverse colon is completely invested with peritoneum, but the greater omentum is fused on its anterosuperior aspect. The left colic or splenic flexure is situated beneath the lower angle of the spleen and firmly attached to the diaphragm by the phrenocolic ligament, which also forms a shelf to support the spleen. Because of the risk for hemorrhage, mobilization of the splenic flexure should be approached with great care, preceded by dissection upward along the descending colon and medially to laterally along the transverse colon toward the splenic flexure. This flexure, when compared with the hepatic flexure, is more acute, higher, and more deeply situated.

Descending Colon

- The descending colon courses downward from the splenic flexure to the brim of the true pelvis, a distance of approximately 25 cm.
- The descending colon is narrower and more dorsally situated than the ascending colon.

Sigmoid Colon

- The sigmoid colon is commonly a 35- to 40-cm-long, mobile, omega-shaped loop completely invested by peritoneum; however, it varies greatly in length and configuration.

- The rectosigmoid junction has been frequently regarded by surgeons as an indistinct zone, a region comprising the last 5–8 cm of sigmoid and the uppermost 5 cm of the rectum.

Blood Supply

- The superior and inferior mesenteric arteries nourish the entire large intestine, and the limit between the two territories is the junction between the proximal two-thirds and the distal third of the transverse colon. This represents the embryologic division between the midgut and the hindgut.
- The superior mesenteric artery originates from the aorta behind the superior border of the pancreas at L-1 and supplies the cecum, appendix, ascending colon, and most of the transverse colon.
- From its right side arises the colic branches: middle, right, and ileocolic arteries. The ileocolic, the most constant of these vessels, bifurcates into a superior or ascending branch, which communicates with the descending branch of the right colic artery, and an inferior or descending branch, which gives off the anterior cecal, posterior cecal, and appendicular and ileal divisions.
- The right colic artery may also arise from the ileocolic or middle colic arteries and is absent in 2–18% of specimens. It supplies the ascending colon and hepatic flexure through its ascending and descending branches, both of them joining with neighboring vessels to contribute to the marginal artery.
- The middle colic artery is the highest of the three colic branches of the superior mesenteric artery, arising close to the inferior border of the pancreas. Its right branch supplies the right transverse colon and hepatic flexure, anastomosing with the ascending branch of the right colic artery. Its left branch supplies the distal half of the transverse colon.
 - Anatomic variations of this artery include absence in 4–20% of cases and the presence of an accessory middle colic artery in 10%; the middle colic artery can be the main supply to the splenic flexure in about 33% of cases.
- The inferior mesenteric artery originates from the left anterior surface of the aorta, 3–4 cm above its bifurcation at the level of L2-3, and runs downward and to the left to enter the pelvis. Within the abdomen, the inferior mesenteric artery branches into the left colic artery and two to six sigmoidal arteries.

- The left colic artery, the highest branch of the inferior mesenteric artery, bifurcates into an ascending branch, which runs upward to the splenic flexure to contribute to the arcade of Riolan, and a descending branch, which supplies most of the descending colon.
- The marginal artery terminates within the arcade of sigmoidal arteries. The superior hemorrhoidal artery is the continuation of the inferior mesenteric artery, once it crosses the left iliac vessels.
- The venous drainage of the large intestine basically follows its arterial supply. Blood from the right colon, via the superior mesenteric vein, and from left colon and rectum, via the inferior mesenteric vein, reaches the intrahepatic capillary bed through the portal vein.

Collateral Circulation

- The central anastomotic artery connecting all colonic mesenteric branches, also known as the marginal artery of Drummond. Discontinuity of the marginal artery has been shown at the lower ascending colon, and especially at the left colic flexure and the sigmoid colon. This potential hypovascularity is a source of concern during colonic resection.
- The splenic flexure comprises the watershed between midgut and hindgut supplies (Griffiths' critical point); this anastomosis is of variable magnitude, and it may be absent in about 50% of cases. For this reason, ischemic colitis usually affects or is most severe near the splenic flexure.
- The meandering mesenteric artery is a thick and tortuous vessel that makes a crucial communication between the middle colic artery and the ascending branch of the left colic artery, especially in advanced atherosclerotic disease. The presence of the meandering mesenteric artery indicates severe stenosis of either the superior mesenteric artery (retrograde flow) or inferior mesenteric artery (antegrade flow).

Lymphatic Drainage

- The submucous and subserous layers of the colon and rectum have a rich network of lymphatic plexuses, which drain into an extramural system of lymph channels and follow their vascular supply.

- Colorectal lymph nodes are classically divided into four groups: epiploic, paracolic, intermediate, and principal. The epiploic group lies on the bowel wall under the peritoneum and in the appendices epiploicae; they are more numerous in the sigmoid and are known in the rectum as the nodules of Gerota. The lymphatic drainage from all parts of the colon follows its vascular supply. The paracolic nodes are situated along the marginal artery and on the arcades; they are considered to have the most numerous filters. The intermediate nodes are situated on the primary colic vessels, and the main or principal nodes on the superior and inferior mesenteric vessels.
- The lymph then drains to the cisterna chyli via the paraaortic chain of nodes. Colorectal carcinoma staging systems are based on the neoplastic involvement of these various lymph node groups.

Innervation

- The sympathetic and parasympathetic components of the autonomic innervation of the large intestine closely follow the blood supply.
- The sympathetic supply of the right colon originates from the lower six thoracic segments. These thoracic splanchnic nerves reach the celiac, preaortic, and superior mesenteric ganglia, where they synapse.
- The parasympathetic supply comes from the right (posterior) vagus nerve and celiac plexus. The fibers travel along the superior mesenteric artery, and finally synapse with cells in the autonomic plexuses within the bowel wall.

B. Embryology

Anus and Rectum

- The distal colon, rectum, and the anal canal above the dentate line are all derived from the hindgut. Therefore, this segment is supplied by the hindgut (inferior mesenteric) artery, with corresponding venous and lymphatic drainage. Its parasympathetic outflow comes from S-2, S-3, and S-4 via splanchnic nerves.

- The dentate line marks the fusion between endodermal and ectodermal tubes, where the terminal portion of the hindgut or cloaca fuses with the proctodeum, an ingrowth from the anal pit.
- The cloaca originates at the portion of the rectum below the pubococcygeal line, whereas the hindgut originates above it.
- The cloacal part of the anal canal, which has both endodermal and ectodermal elements, forms the anal transitional zone after breakdown of the anal membrane.
- The sphincters apparently migrate during their development; the external sphincter grows cephalad and the internal sphincter moves caudally. Concomitantly, the longitudinal muscle descends into the intersphincteric plane.

Anorectal Malformations

- The anorectal malformations can be traced to developmental arrest at various stages of normal maturation.
- Associated anomalies, most frequently skeleton and urinary defects, may occur in up to 70%.
- There is evidence for familial occurrence of anorectal defects; the estimated risk in a family of a second occurrence of some form of imperforate anus is up to 50 times the normal chance.
- The proposed classification systems for the congenital malformations of the anorectal region are usually either incomplete or complex. The most comprehensive system has been proposed by Gough and Santulli, and takes into consideration whether the rectum terminates above (anorectal defects) or below (anal defects) the puborectalis sling (Table 1.1).

Anal Defects

Anal Stenosis

- Some degree of stricture of the rectum is present in 25–39% of infants, and only about 25% of these will show some degree of disordered evacuation.

Membranous Atresia

- This defect, also known as “covered anus” is very rare. It is characterized by presence of a thin membrane of skin between the blind end of the anal canal and the surface.

Table 1.1. Classification of anorectal malformations.

A. Anal defects (“low” defects)
1. Anal stenosis
2. Membranous atresia (rare)
3. Anal agenesis
(a) Without fistula
(b) With fistula (ectopic anus)
B. Anorectal defects (“high” defects)
1. Anorectal agenesis
(a) Without fistula
(b) With fistula
2. Rectal atresia (“high” atresia)
C. Persistent cloaca
1. Rectal duplication
2. Developmental cysts

Anal Agenesis

- The rectum extends below the puborectalis and ends, either blindly, or more often, in an ectopic opening or fistula to the perineum anteriorly, to the vulva, or urethra.

Anorectal Defects

Anorectal Agenesis

- Anorectal agenesis more often affects males and represents the most common type of “imperforate anus.” The rectum ends well above the surface, the anus is represented by a dimple, and the anal sphincter is usually normal.
- In most cases, there is a fistula or fibrous remnant connecting the rectal ending to the urethra or vagina.

Rectal Atresia or “High Atresia”

- Although considered clinically as an anorectal defect, embryologically this is the most caudal type of atresia of the large intestine. The rectum and anal canal are separated from each other by an atretic portion.

Persistent Cloaca

- This is a rare condition that occurs only in female infants.

Colon and Small Bowel

- The normal embryologic process of rotation of the intestinal tract includes three stages.

First Stage: Physiologic Herniation of the Primitive Digestive Tube

- The first stage of rotation begins between the sixth and eighth weeks of intrauterine life, when the primitive intestinal tube elongates on its mesenteric around the superior mesenteric artery and bulges through the umbilical cord as a temporary physiologic herniation.
- The anomalies of this stage are rare and include situs inversus, inverted duodenum, and extroversion of the cloaca.

Second Stage: Return of the Midgut to the Abdomen

- During this stage, the midgut loop returns to the peritoneal cavity from the umbilical herniation, and simultaneously rotates 180° counterclockwise around the pedicle formed by the mesenteric root.
- Anomalies of the second stage are relatively more common than the ones originated from the first stage and include non-rotation, malrotation, reversed rotation, internal hernia, and omphalocele.

Third Stage: Fixation of the Midgut

- The third stage of gut rotation starts after return of the gut to the peritoneal cavity and ends at birth. The cecum, initially in the upper abdomen, descends, migrating to the right lower quadrant, as counterclockwise rotation continues to 270°.
- After completion of the sequential rotation of the gastrointestinal tract, in the latter weeks of the first trimester, the process of fixation initiates.
- Anomalies of this stage are common and include mobile cecum, subhepatic or undescended cecum, hyperdescent of the cecum, and persistent colonic mesentery.
- The midgut progresses below the major pancreatic papilla to form the small intestine, the ascending colon, and the proximal two-thirds of the transverse colon. This segment is supplied by the midgut (superior mesenteric) artery, with corresponding venous and lymphatic drainage.

- The distal colon (distal third of the transverse colon), the rectum, and the anal canal above the dentate line are all derived from the hindgut. Therefore, this segment is supplied by the hindgut (inferior mesenteric) artery, with corresponding venous and lymphatic drainage. Its parasympathetic outflow comes from S-2, S-3, and S-4 via splanchnic nerves.

Abnormalities of Rotation

Nonrotation

- In this condition, the midgut loop returns to the peritoneal cavity without the process of rotation, and, consequently, the entire small bowel locates on the right side of the abdomen, and the left colon is on the left side.
- This condition may be entirely asymptomatic and constitute a finding at laparotomies. However, it may complicate with volvulus affecting the entire small bowel. The twist of the entire midgut loop on its pedicle can occur, usually at the level of the duodenojejunal junction and the midtransverse colon, because of the defective fixation of the mesenteric root.

Malrotation

- In malrotation, the cecum fails to complete the 360° rotation around the superior mesenteric, and does not complete the migration process. As a result of this failure in the migration process, the malrotated cecum locates in the right upper quadrant and is fixed by lateral bands or adhesions. These bands can overlie the distal part of the duodenum and cause extrinsic compression.

Reversed Rotation

- In this condition, the midgut rotates clockwise instead of counterclockwise; consequently, the transverse colon locates posteriorly and the duodenum anteriorly, in relation to the mesenteric artery.

Omphalocele

- Omphalocele is the retention of the midgut in the umbilical sac as a result of failure of the gut to return to the peritoneal cavity.

Incomplete Attachment of Cecum and Mesentery

- In normal conditions, the cecum is almost entirely, or at least in its lower half, invested with peritoneum. However, its mobility is usually limited by a small mesocecum. In approximately 5% of individuals, the peritoneal covering is absent posteriorly; it then rests directly on the iliacus and psoas major muscles.
- Alternatively, an abnormally mobile cecum-ascending colon, resulting from an anomaly of fixation, can be found in 10–22% of individuals. In this case, a long mesentery is present, and the cecum may assume varied positions. This lack of fixation may predispose to the development of volvulus.

Internal Hernias Around Ligament of Treitz

- Both internal hernias and congenital obstructive bands or adhesions are causes of congenital bowel obstruction, and result from an anomaly during the process of fixation.
- Retroperitoneal hernias can occur in any intraperitoneal fossae, particularly paraduodenal, paracecal, and intersigmoid. The most common internal hernias resulting from abnormal fixation of the colon are right and left paraduodenal hernias.

Other Congenital Malformations of the Colon and Small Intestine

Proximal Colon Duplications

- Duplication of the colon comprises three general groups of congenital abnormalities: mesenteric cysts, diverticula, and long colon duplication.
 - Mesenteric cysts lie in the mesentery of the colon or behind the rectum, may be separable or inseparable from the bowel wall, and usually present, as the size increases, either as a palpable mass or intestinal obstruction.
 - Diverticula are blind ending pouches of variable lengths and arise either from the mesenteric or the antimesenteric border of the bowel. They may have heterotopic gastric mucosa or pancreatic-type tissue.
 - Long colon duplication or tubular duplication of the colon is the rarest form of duplication. Frequently it involves the entire colon and rectum. Often, there is an association of pelvic genitourinary anomalies.

Meckel's Diverticulum

- Meckel's diverticulum is a remnant of the vitelline or omphalomesenteric duct, arising from the antimesenteric border of the terminal ileum, usually within 50 cm of the ileocecal valve.
- Associated abnormalities include persistence of a fibrous band connecting the diverticulum to the umbilicus or a patent omphalomesenteric duct, presence of ectopic mucosa or aberrant pancreatic tissue (in more than half of asymptomatic diverticula), and herniation of the diverticulum in an indirect inguinal hernia (Littre's hernia).
- In most people, Meckel's diverticulum is asymptomatic, and according to autopsy series, it exists in 1–3% of the general population.
- Surgical complications are more frequent in infants and children and include hemorrhage from ectopic gastric mucosa, intestinal obstruction resulting from associated congenital bands or ileocolic intussusception, diverticulitis, perforation, and umbilical discharge from a patent omphalomesenteric duct.

Atresia of the Colon

- Colonic atresia is a rare cause of intestinal obstruction; it represents only 5% of all forms of gastrointestinal atresia. It is probably caused by a vascular accident occurring during intra-uterine life.

Hirschsprung's Disease

- This disease results from the absence of ganglion cells in the myenteric plexus of the colon caused by interruption of migration of neuroenteric cells from the neural crest before they reach the rectum.
- The physiologic obstruction, more insidious than an anatomic atresia, results in proximal dilation and hypertrophy of the colon above.
- The extent of the aganglionosis is variable. The internal anal sphincter is involved in all cases, and the entire rectum in most cases.
- The disease is more common in males and its severity is related to the length of the aganglionic segment. Although most patients reach surgery before they are a year old, many are older, and a few reach adulthood.

2. Physiology: Colonic

A. Colonic Function

Salvage, Metabolism, and Storage

- Even though the majority of our food undergoes digestion in the stomach and small intestine, the colon still has a major role in digestion. It processes certain starches and proteins, which are resistant to digestion and absorption in the foregut.
- The large quantity of heterogeneous bacteria in the colon is responsible for fermentation – the process by which these starches and proteins are broken down and energy is produced.
- There are more than 400 different species of bacteria, the majority of which are anaerobes. The bacteria feed upon mucous, residual proteins, and primarily complex carbohydrates that enter the colon.
- During fermentation of complex carbohydrates, short-chain fatty acids (SCFAs) are produced. More than 95% of SCFAs are produced and absorbed within the colon. The principle ones are acetate, propionate, and butyrate. This process for the most part occurs in the right and proximal transverse colon.
- Protein residue, which reaches the colon is also fermented by anaerobic bacteria. Proteins are fermented in the left colon. Proteins are broken down into SCFAs, branched chain fatty acids, and ammonia, amines, phenols, and indoles. Part of these metabolites become a nitrogen source for bacterial growth.
- Dietary fat is probably not absorbed to any degree in the colon.
- The colonic mucosa is unable to nourish itself from the bloodstream. Therefore, the nutrient requirements are met from the luminal contents.

- Butyrate (produced in the least amount) is important as the primary energy source for the colonocyte. Butyrate may also have a major role in cell proliferation and differentiation as well as being important in absorption of water and salt from the colon.
- The proximal colon acts as a reservoir and the distal colonic segments mainly act as a conduit.
- Even after right colon resection, the transverse colon can adapt to store colonic contents nearly as efficiently as the right colon.
- In addition, the haustral segmentation of the colon facilitates mixing, retention of luminal material, and formation of solid stool.

Transport of Electrolytes

- The colon is extremely efficient at conserving sodium and water. Normally the colon is presented 1–2 L of water daily. It efficiently absorbs 90% such that approximately 100–150 mL of fluid is eliminated in the stool. When challenged, it can increase the absorption to 5–6 L daily.
- When the ileal flow of fluid and electrolytes exceeds the capacity of the colon, diarrhea will result.
- Under normal conditions, the colon absorbs sodium and chloride and secretes bicarbonate and potassium.
- Sodium is actively absorbed against a concentration and electrical gradient. This concept is extremely important for the colon's ability to conserve sodium.
- Aldosterone is secreted by the adrenal gland in response to sodium depletion and dehydration. Aldosterone enhances fluid and sodium absorption in the colon.
- SCFAs produced in the colon are the principle anions. They also stimulate sodium absorption.
- Chloride is exchanged for bicarbonate, which is secreted into the lumen to neutralize organic acids that are produced. This occurs at the luminal border of the mucosal cells.
- Potassium movement, overall, is believed to be passive as a result of the active absorption of sodium. There is evidence that active potassium secretion occurs in the distal colon. This secretion combined with potassium in bacteria and colonic mucous in stool may explain the relatively high concentration of potassium, 50–90 mmol/L, in stool.

- The colon secretes urea into the lumen. The urea is metabolized to ammonia. The majority is absorbed passively.
- Absorption of water and salt occurs primarily in the ascending and transverse colon. Active transport of sodium creates an osmotic gradient and the water passively follows.
- The surface cells in the colon seem to be responsible for absorption whereas the crypt cells are involved with fluid secretion.

B. Colonic Motility

Methodology for Determining Motility

- Stool frequency has been shown to correlate poorly with colorectal transit time. Early studies used barium but lacked the ability to give precise measurement of colonic motility.

Marker

- Radiopaque markers orally ingested and followed sequentially through the intestinal tract via plain X-rays is one of the first methods used to actually measure transit time. This test is still used frequently to evaluate patients with severe constipation looking for slow transit through the colon.
 - One method calls for a capsule with 24 markers to be ingested and an X-ray obtained on day 5. This reflects the transit time of the entire gut. On day 5, 80% (17) of the markers should be expelled. Other methods utilize x-rays on days 1–5, days 1, 3 and 5 or 3 and 5.
- Total colonic transit time is 30.7 (SD 3.0) hours for men and 38.3 (SD 2.9) hours for women.

Scintigraphy

- ¹¹¹In-labeled radioisotope is ingested. The coating dissolves in the distal ileum and the radioactive material passes into the colon.
- Segmental transit is usually calculated for the right, left, and rectosigmoid regions of the colon.

Recording Techniques of Colonic Motility

- Most techniques that record colonic motility using some form of colonic manometry still remain in the researcher's domain and have not been assimilated into the clinical armamentarium for the caregiver.

Peristalsis

- Peristalsis is the waves of alternate contraction and relaxation of the muscles of the intestinal tube, which propels contents.
- It is difficult to precisely define colonic contractions, pressure waves, and electrical events because no standard terminology or definitions exist.
- Contractile events are divided as (1) segmental contractions that are either single contractions or bursts of contractions, either rhythmic or arrhythmic contractions; (2) propagated contractions – low-amplitude propagated contraction (LAPC) (long spike bursts) and high-amplitude propagated contraction (HAPC) (migrating long spike bursts).
- The main function of HAPCs is to move large amounts of colonic contents toward the anus. They usually occur upon awakening, during the day, and after meals. They are usually associated with abdominal sensation and defecatory stimulation (or defecation).
- The majority of the colonic motility is represented by segmental contractions. This allows slow transit and the opportunity for the luminal contents to maximally come in contact with the mucosal surface.

Cellular Basis for Motility

- Cells important for movement in the colon include the circular muscle, longitudinal muscle, and interstitial cells of Cajal (ICC).
- All electrical activity in the human colon is dependent on stimulation by stretch or chemical mediation. Critical volumes of distention are needed for propulsion. Fiber may augment this degree of stretch.
- ICC are the pacemaker cells of the gut that have a central role in regulation of intestinal motility. These are mesenchymal cells, which form a three-dimensional network, placed between and in smooth muscle layers. They are also in close association

with elements of the enteric nervous system. They are electrically active and create ion currents for pacemaker function.

Characteristics of Colonic Motility in Health

- Using 24-h manometry, it has been found that the colon is continually active. There is a well-established circadian rhythm with marked diminution of pressure activity at night.
- Immediately after waking, there is a threefold increase in colonic pressure activity. This may account for bowel patterns in some individuals who move their bowels after awakening in the morning.
- Colonic pressure activity also increases after meals, which in one study lasted for up to 2 h after a meal.
- Stress can influence gut function. One study found that psychological stress induced prolonged propagated contractions without appreciable autonomic response. These contractions propagated across several areas of the colon. The motor activity persisted after the stressor ceased.
- The right colon and transverse colon are major sites of storage of solid stool. Solid residue remains in the right colon for extended periods allowing for mixing. There is also considerable variability among individuals as far as right colon transit.
- After eating, the proximal colon has an immediate increase in tonic contraction. There is also increased tone in the distal colon, but this is less pronounced than the one on the right.
- Well before the ingested food reaches the colon, there is an increase in colonic motility and tone. This is known as the gastrocolic reflex.

C. Defecation and Colonic Sensation

- The process of defecation seems to involve the entire colon. It has been shown to begin up to an hour before stool elimination – a preexpulsive phase.
- Scintigraphic studies have also shown that the right colon can also be emptied during one episode of defecation.
- A second component begins approximately 15 min before stool expulsion. Propagating sequences during this time are associated with an increasing sensation of an urge to defecate.

- Colonic sensation is complicated and poorly understood. The colon has no specialized sensory end organs.
- Modulation of visceral sensation occurs through several methods.
 - The first allows for enteroenteric reflexes that are mediated in the spinal cord to alter smooth muscle tone thereby increasing or decreasing the activation of the nerve endings in the gut or mesentery.
 - Another method involves direct central modulation of pain.
 - A further method explains “referred pain.” When the overlap of input appears more recognized by higher central brain forces from somatic input, referred pain may occur. The input is actually occurring in the visceral structure, but is perceived to be from the somatic structure. It is of note that when pain is referred it is usually to a structure that developed from the same embryonic dermatome.
 - Visceral sensation can relay information via collaterals to the reticular formation and thalamus. This can induce changes in affect, appetite, pulse, and blood pressure through autonomic, hypothalamic, and limbic system connections.

D. Disturbances in Colonic Physiology

Physiology of Constipation

- Constipation refers to stools that are infrequent or hard to pass (or both).
- There may be dietary, pharmacologic, systemic, or local causes.
- Constipation may be seen more frequently in sedentary people.
- Idiopathic slow transit constipation involves a measurable delayed movement of material through the colon. These patients are not helped (in fact may be made worse) with increased dietary fiber. They seem to have altered colonic motor response to eating and impaired or decreased HAPCs of the colon. This leads to reduced or absent colonic propulsive activity.
- Irritable bowel syndrome (IBS) can manifest with multiple forms. It usually is characterized as altered bowel habits and pain directly related to the altered bowel habits. In one form,

constipation can be the predominant feature. This may encompass about 30% of the IBS population and traditionally overwhelmingly affects women. This group of patients can show an overlap with those having slow transit constipation, but may have a normal transit study.

Obstructed Defecation

- Obstructed defecation usually results from abnormalities in pelvic function vs. colonic function.
- Typically this problem is associated with failure of the puborectalis to relax with defecation, rectocele, perineal descent, or other pelvic- and rectal-associated issues. Failure of the rectum to evacuate may lead to marker studies which also show marker collection in the left colon. This may also be associated with colonic total inertia.

Ogilvie's Syndrome

- Ogilvie's syndrome is also known as acute colonic pseudoobstruction.
- The pathophysiology is not clearly understood.
- Based on evidence from pharmacologic studies there seems to be an imbalance of autonomic innervation to the gut. The parasympathetic nerves, which are responsible for stimulating gut motility, have decreased function or input and the sympathetic nerves, which are inhibitory, increase their input.
- Because of the law of Laplace, the cecum can be the site of extreme dilatation (it requires the smallest amount of pressure to increase in size and therefore increase the wall tension).
- Treatment has focused on ruling out a distal obstruction with a Gastrografin enema and if needed colonoscopic decompression.
- Pharmacologic treatment with neostigmine has been successful. This drug is a cholinesterase inhibitor that allows more available acetylcholine for neurotransmission in the parasympathetic system (excitatory) to promote contractility. Due to potential side effects, this drug is administered with cardiac monitoring in an intensive care setting.

Irritable Bowel Syndrome

- As stated previously, IBS is characterized by altered bowel habits associated with pain. Besides the constipation-predominant type described above, there can be a diarrhea-predominant type and a mixed type.
- If IBS is found in men it tends to be more diarrhea-predominant type.
- Treatment is based on the nature and severity of symptoms. Education, reassurance, and dietary modification (elimination of foods that aggravate the problem and either adding or reducing fiber) are the first steps.
- For those who do not respond, medication is considered. Antispasmodics (anticholinergic) medication is considered for those with pain and bloating that is especially aggravated by meals.
- Low-dose tricyclic antidepressants may be considered when the pain is more constant and perhaps disabling.
- Considering specific types, no good pharmacologic research is available for the mixed-type IBS patients. However, for the diarrhea prone, 5-HT₃ antagonists have been found to be effective.

E. Implications of Colonic Physiology for the Surgeon

- Recognizing the innervation and differences in embryologic development may be important in colon resections when considering nerve preservation, blood flow, and resection margins.
- Resection of all or a portion of the colon can have profound ramifications for the patient. It is the surgeon's responsibility to understand the physiologic possibilities, recognize, and manage the outcome. For instance, this may be important for patients with a new ileostomy who may need counseling regarding fluids and increased salt intake to compensate for the colon, which has been resected.
- In the colon, many metabolic processes can be influenced by food components. Prebiotics are "non-digestible food ingredients that beneficially affect the host by selectively stimulating

the growth and/or activity of one or a limited number of bacteria in the colon, that can improve the host health.”

- Probiotics are “a live microbial feed supplement which beneficially affects the host by improving its intestinal microfloral balance.”
- Currently, probiotics may be used in cases of disturbed microbial balance, such as antibiotic-associated diarrhea, to lessen the risk and duration.

3. Anal Physiology

A. Introduction

- Normal bowel continence is a complex process that involves the coordinated interaction between multiple different neuronal pathways and the pelvic and perineal musculature.
- Complicating this are multiple other factors that have a role in normal regulation such as systemic disease, emotional effects, bowel motility, stool consistency, evacuation efficiency, pelvic floor stability, and sphincter integrity.
- Anorectal physiology testing allows evaluation of the patient with pelvic floor complaints using techniques such as manometry, endoanal ultrasound, electrophysiologic studies, and defecography, all of which help to elucidate anorectal structures and function.

B. Pelvic Floor Muscles

- The pelvic floor consists of a striated muscular sheet through which viscera pass. This striated muscle, the paired levator ani muscles, is actually subdivided into four muscles defined by the area of attachment on the pubic bone.
- The components of the levator ani are therefore named the pubococcygeus, ileococcygeus, and ischiococcygeus. The pubococcygeus is further subdivided to include the puborectalis.
- Between the urogenital viscera and the anal canal lies the perineal body. The perineal body consists of the superficial and deep transverse perinei muscles and the ventral extension

of the external sphincter muscle to a tendinous intersection with the bulbocavernosus muscle.

- The fourth sacral nerve innervates the levator ani muscles.
- The rectal smooth muscle consists of an outer muscularis mucosa, inner circular muscle, and outer longitudinal layer. The inner circular muscle forms the valves of Houston proximally and distally extends down into the anal canal becoming the internal anal sphincter (IAS).
- The outer longitudinal layer surrounds the sigmoid colon coalescing proximally into thicker bands called taenia coli.
 - The terminal fibers extend to skin as the corrugation cutaneous ani muscles.

C. Reflexes

- There are a great number of reflexes that end with the name "... anal reflex."
- Consequently, there are several ways that one can assess the integrity of neurologic connection through or around the spinal chord.

Cutaneous-Anal Reflex

- The cutaneous-anal reflex is a brief contraction of the anal sphincter in response to pricking or scratching the perianal skin. This is a spinal reflex that requires intact S4 sensory and motor nerve roots.
- If a cauda equina lesion is present, this reflex will usually be absent.
- From a practical standpoint, this is a sacral reflex that can be interrogated during physical examination by simply scratching the perianal skin with visualization of contraction of the subcutaneous anal sphincter. The response to perianal scratch fatigues rapidly so it is important to test this as the first part of the sphincter examination.

Cough Reflex

- The cough-anal reflex contributes to the maintenance of urinary and fecal continence during sudden increases in intraabdominal pressure as might also be seen with laughing, shouting, or heavy lifting.

- The reflex is preserved in paraplegic patients with lesions above the lumbar spine but it is lost if the trauma involves the lumbar spine or with cauda equine lesions.

Bulbocavernosus Reflex

- The bulbocavernosus reflex is pelvic floor contraction elicited by squeezing the glans penis or clitoris.
- The bulbocavernosus reflex latency will be prolonged by various disorders affecting the S2–S4 segments of the spinal chord.

Rectoanal Inhibitory Reflex

- The rectoanal inhibitory reflex (RAIR) represents the relaxation of the IAS in response to distension of the rectum.
- It is believed that this permits fecal material or flatus to come into contact with specialized sensory receptors in the upper anal canal. This sampling process, the sampling reflex, creates an awareness of the presence of stool and a sense of the nature of the material present.
- It is believed that this process of IAS relaxation with content sampling is instrumental in the discrimination of gas from stool and the ability to pass them independently.
- The degree to which IAS relaxation occurs seems to be related to the volume of rectal distension more so in incontinent patients than in constipated or healthy control patients.
- Lower thresholds for the RAIR have been found to be associated with favorable response to biofeedback therapy in patients with fecal incontinence for formed stool.
- The RAIR is primarily dependent on intrinsic nerve innervation in that it is preserved even after the rectum has been isolated from extrinsic influences, following transection of hypogastric nerves and the presence of spinal chord lesions.
- The reflex is destroyed in Hirschsprung's disease when myenteric ganglion are absent. In addition, the reflex is lost after circumferential myotomy and after generous lateral internal sphincterotomy.
- The RAIR seems to be nearly abolished in the early postoperative period after low anterior resection for cancer.
- In a study involving 46 patients, O'Riordain et al. found that the RAIR that had been present in 93% of patients preoperatively was only present in 18% 10 days after low anterior resection.

However, at 6–12 months, the RAIR was intact in 21% of patients and this increased to 85% after 2 years.

- Loss of RAIR is often a consequence of restorative proctocolectomy.
- Saigusa et al. found that the RAIR was present in only 53% of double-stapled ileal pouch anal anastomosis patients at a mean of 23 months after closure of the ileostomy. Preservation of the RAIR correlated with less nocturnal soiling.
- Disturbances in the RAIR seem to be involved in the incontinence that is associated with systemic sclerosis.

Rectoanal Excitatory Reflex

- The rectoanal excitatory reflex (RAER), or inflation reflex, is the contraction of the EAS in response to rectal distension.
- Rectal distension sensation is likely transmitted along the S2, S3, and S4 parasympathetic fibers through the pelvic splanchnic nerves. However, on the motor side, a pudendal nerve block abolishes the excitatory reflex suggesting that pudendal neuropathy may interfere with the RAER.

D. Mechanical Factors of Continence and Defecation

Anorectal Angle and Flap Valve

- As a part of the pelvic floor musculature, the puborectalis arises from the pubic bone and passes horizontally and posteriorly around the rectum as the most medial portion of the levator ani muscle. This forms a U-shaped sling around the rectum near its anatomic junction with the anus, pulling the rectum anteriorly, and giving rise to the so-called anorectal angle.
- There are differences of opinion as to whether the puborectalis and anorectal angle are truly important in maintaining continence. Unlike the fine control of the external and internal sphincter muscles, the puborectalis sling is believed to be more involved with gross fecal continence.
- Parks postulated a mechanism by which this takes place. As intraabdominal pressure is increased – such as with sneezing, coughing, or straining – and the force is transmitted across the anterior wall of the rectum at the anorectal angle. The underlying

mucosa is opposed against the upper anal canal, creating a flap-valve mechanism that prevents stool from passing to the lower anal canal and preserving continence.

- Yet other authors have disputed this flap-valve mechanism and downplayed the role and reliability of measuring the anorectal angle.
- Furthermore, quantifying the anorectal angle and relating that to patient symptoms has resulted in mixed views.

Reservoir

- As an additional part of the continence mechanism, the rectum must be able to function as a temporary storage site for liquid and solid stool. With passage of the fecal stream into the rectum, the pliable rectal walls are able to distend and delay the defecation sequence until an appropriate time.
- This process relies both on rectal innervation to sense and tolerate the increasing volume of stool (capacity), as well as maintain a relatively low and constant pressure with increases in volume (compliance). Extremes of either of these components can lead to fecal incontinence through decreased accommodation or overflow states.
- Although decreased compliance has been demonstrated more often in patients with fecal incontinence, it has also been shown to occur as a normal consequence of aging.
- Furthermore, after low anterior resection for cancer, those patients with resultant lower rectal compliance and lower rectal volume tolerability (capacity) have been associated with higher rates of fecal incontinence.

Normal Defecation

- The process begins with movement of gas, liquid, or solid contents into the rectum. Distention of the rectum leads to stimulation of pressure receptors located on the puborectalis muscle and in the pelvic floor muscles, which in turn stimulate the RAIR. The IAS relaxes allowing sampling of contents.
- If defecation is to be deferred, voluntary contraction of the EAS and levator ani muscles occurs and the rectum accommodates with relaxation after an initial increase in pressure.

- When the anal canal is deemed to have solid contents and a decision to defecate is made, the glottis closes, pelvic floor muscles contract, and diaphragm and abdominal wall muscles contract, all increasing abdominal pressure. The puborectalis muscle relaxes, resulting in straightening of the anorectal angle, and the pelvic floor descends slightly. The EAS relaxes and anal canal contents are evacuated.
- Upon normal complete evacuation, the pelvic floor rises and sphincters contract once more in a “closing reflex.”

E. Pathologic Conditions

Incontinence

- Incontinence is the inability to defer the passage of gas, liquid, or solid stool until a desired time.
- Numerous alterations in anorectal physiology can lead to incontinence and many patients have more than one deficit. Structural defects in the IAS or EAS muscles occur because of obstetric injury, trauma, or anorectal surgery.
- The keyhole deformity is a groove in the anal canal allowing the seepage of stool or mucus. Originally described as a complication after the posterior midline fissurectomy or fistulotomy, it can also occur with lateral IAS defects.
- Intact sphincter muscles with impaired neurologic function, because of pudendal nerve damage or systemic disorders such as diabetes, can also result in incontinence, especially if the impaired sphincter is further stressed by diarrhea or irritable bowel syndrome.
- Abnormal rectal sensation can lead to incontinence in two ways. Conditions such as proctitis caused by inflammation or radiation can result in hyperacute sensation. The rectum fails to accommodate and the reservoir function is impaired leading to urgency and frequency stooling.
- Fragmentation of stools is often described by patients after low anterior resection, particularly if the pelvis has been radiated as in the case of adjuvant therapy for the treatment of rectal cancer.
- In the case of blunted sensation, because of a large rectocele, megarectum, or neurogenic disorders, the rectum becomes over-distended and overflow incontinence occurs.

- Perineal descent may be a predictor of incontinence among patients with denervation of both the external sphincter and the puborectalis, and in patients with impaired anal sensation. Among patients with constipation, perineal descent and straining at stool may predict future fecal incontinence.

Obstructed Defecation

Rectocele

- A rectocele is defined as greater than 2 cm of rectal wall out-pouching or bowing while straining, and can precede or accompany rectal intussusception.
- The rectocele can prevent passage of stool both by obstructing the anal orifice and by acting as a diverticulum to sequester stool.
- Patients with rectoceles often complain of the need for frequent sequential episodes of defecation, and even for manual compression or splinting of the anterior perineum or posterior vagina in order to completely evacuate.
- Patients may experience incontinence with relaxation, leading to reduction of the rectocele and return of the sequestered stool to the lower rectum.

Dyskinetic Puborectalis

- Dyskinetic puborectalis, paradoxical puborectalis, nonrelaxing puborectalis, and anismus are terms that describe the absence of normal relaxation of pelvic floor muscles during defecation, resulting in rectal outlet obstruction.
- Once diagnosed, dyskinetic puborectalis is usually treated with biofeedback and bowel management.
- Patients who fail conservative treatment have been offered botulinum toxin injections into the puborectalis muscle with limited success.

F. Continence

- The dynamic interaction of the aforementioned anatomy and physiology ensures continence. It does not follow that a deficit in any one area ensures incontinence.

- Even profound deficits do not necessarily lead to incontinence if stool consistency is solid, whereas minor deficits can easily lead to incontinence of gas.
- To determine and treat abnormal fecal continence requires a systematic approach focusing on identifying the specific deficits present, applying appropriate testing to elucidate anal physiology and anatomy, and then directing therapy accordingly.

4. Physiologic Testing

A. Introduction

- Physiologic testing is used to assess pelvic floor and anorectal disorders.
- These physiologic tests are performed in conjunction with a history, diary of the disorder, physical examination, endoscopy, and imaging studies.
- Physiologic tests have provided or confirmed a diagnosis in 75% of patients with constipation, 66% of patients with incontinence, and 42% of patients with chronic anorectal pain.
- Commercial equipment is available which produces reproducible results.
- However, the lack of validated normal values for healthy patients of both sexes and all ages remains a major problem.
- Physiologic testing includes several tests which complement each other. No single test contributes the data necessary to analyze disorders of the pelvic floor.
- Unfortunately, many patients have diseases or disorders that are of multifactorial pathophysiologies which produce several abnormal results, that are difficult to interpret.

B. Manometry

- Manometry is a technique for measuring pressures in the rectum and anus, and pressures and reflexes elicited by voluntary actions or by local stimuli.
- Interpretation of data, requires comparison to a range of normals by sex and age (which is often lacking).

Indications

- First, manometry is used for evaluation of incontinence. A sphincter defect can be located and quantified.
- Second, constipation, mainly outlet obstruction type, is investigated to determine whether abnormal pressures exist. The loss of the rectoanal inhibitory reflex (RAIR) suggests Hirschsprung's disease.
- Third, some anorectal pain syndromes are associated with abnormal pressures within the sphincter mechanism.
- Fourth, the study is conducted to establish a baseline when an anorectal or pelvic floor procedure is contemplated. For example, if biofeedback or a surgical procedure is to be used for incontinence or constipation, a pre- and postprocedure study provides the means to quantify a change.

Equipment

- The equipment consists of several essential components: the probe, the transducers, the recorder, and the hydraulic pump for water infusion methods.

Probes

- The most popular type is the water-perfusion probe, which is relatively inexpensive, durable, and easy to use.
- The solid-state catheter is expensive and fragile, but it gives the most accurate, reproducible results.

Hydraulic Water-Perfusion Machines

- The water-perfusion machine is a key part of the water-perfusion method. The water is driven through each of the individual channels in the tube at a chosen rate; the water perfuses through the holes near the tip and thus is exposed to pressure changes.

Transducers

- The mechanical water pressure is changed to electrical signals in the transducer.

Amplifier/Recorder

- Many recording devices are available, but computerized systems with small amplifiers and recorders are preferable.
- Software has been designed to give chart, table, and graph printouts. An attached monitor is a useful way to observe the tracings as the procedure progresses.

Technique of Manometry

Initial Considerations

- The study is performed with focus on the distal 5 cm, which is the segment that contains the sphincter muscles.
- The internal sphincter and the external sphincter may be analyzed based on the portions of pressure represented by the resting tone and the squeeze pressure.

Preparation

- The preparation is a simple small, tap-water enema or commercially prepared enema to empty stool from the rectum and anus before coming for the examination.

Calibration

- The calibration record should be saved with the actual procedure recording to validate the measurements.

Resting Pressure

- The probe is introduced higher than the 5-cm level and left in place for 5 min to permit the temperature to equalize to body temperature and the sphincter mechanism to relax to a baseline.
- There is usually a stepwise increase in pressure as the sensors progress distally (Fig. 4.1). As the sensor leaves the sphincter mechanism, the pressure will drop to zero.

Squeeze Pressure

- The probe is reinserted to at least the 6-cm level and reoriented. The probe is again removed at 1-cm increments. The patient is

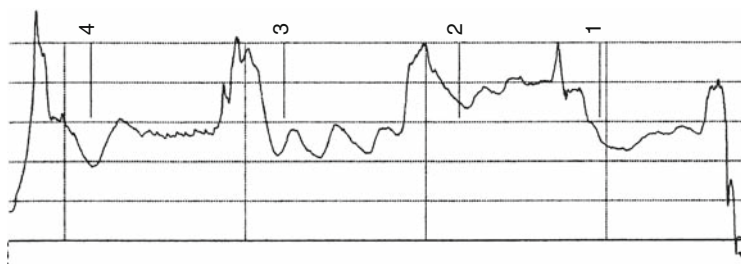


Fig. 4.1. Normal tracing of resting tone in one quadrant on the manometry probe. The scale is 100 mm Hg. The pressure progressively increases from the 4-cm level to 2-cm level with a small decrease in pressure at the 1-cm level, and then to zero as the probe exits.



Fig. 4.2. Normal tracing of voluntary squeeze in one quadrant on the manometry probe. The scale is 100 mm Hg. The squeeze essentially doubles the resting pressure.

instructed to squeeze the sphincter muscles as if to stop a bowel movement and hold the squeeze for 3 s (Fig. 4.2). The patient is also instructed to avoid using accessory muscles, especially the gluteals.

Squeeze-Duration Study

- The probe is positioned in the site of the highest pressure in the anal canal. The high pressure zone is the length of the anal canal with resting pressures at least 30% higher than rectal pressure. The patient is instructed to squeeze and hold the

squeeze for 45 s as the recording is made. Some investigators perform this maneuver once and others do two or three runs and average the results.

- This study is also termed sphincter endurance.

Reflexes

- The probe is again positioned in the high pressure zone in the anal canal to observe for the RAIR. Then 10 cc of air is injected into the balloon and the pressures are observed for 10 s. Then air is inflated into the balloon at 20-, 30-, 40-, 50-, and 60-cc increments (Fig. 4.3).
- The recording normally shows a relaxation from the baseline, which verifies the intact reflex from the stimulated rectal wall to the internal sphincter.

Strain Maneuver

- The probe is positioned in the high pressure zone. The patient is instructed to bear down as if to defecate for at least 5 s.
- The pressure is normally reduced for a few seconds similar to the RAIR (Fig. 4.4). This maneuver is repeated after a 30-s rest. The result is obtained by averaging the total runs. To appreciate what is happening to the sphincter, the rectal pressure is measured at the same time with the rectal balloon, which corresponds to the increased abdominal pressure.

Rectal Sensation

- The balloon is inflated in 10-cc increments until the patient senses the balloon. The first sensation is normally at or before 20-cc inflation.

Compliance

- Having recorded the first rectal sensation, the balloon is inflated slowly in 50-cc increments. The patient will feel a point at which there is a strong urge to defecate. This is recorded. At a further point, the patient will experience a discomfort, which is recorded as the maximal tolerated volume.
- In the normal-sized rectum, this will be 200–250 cc (Fig. 4.5).

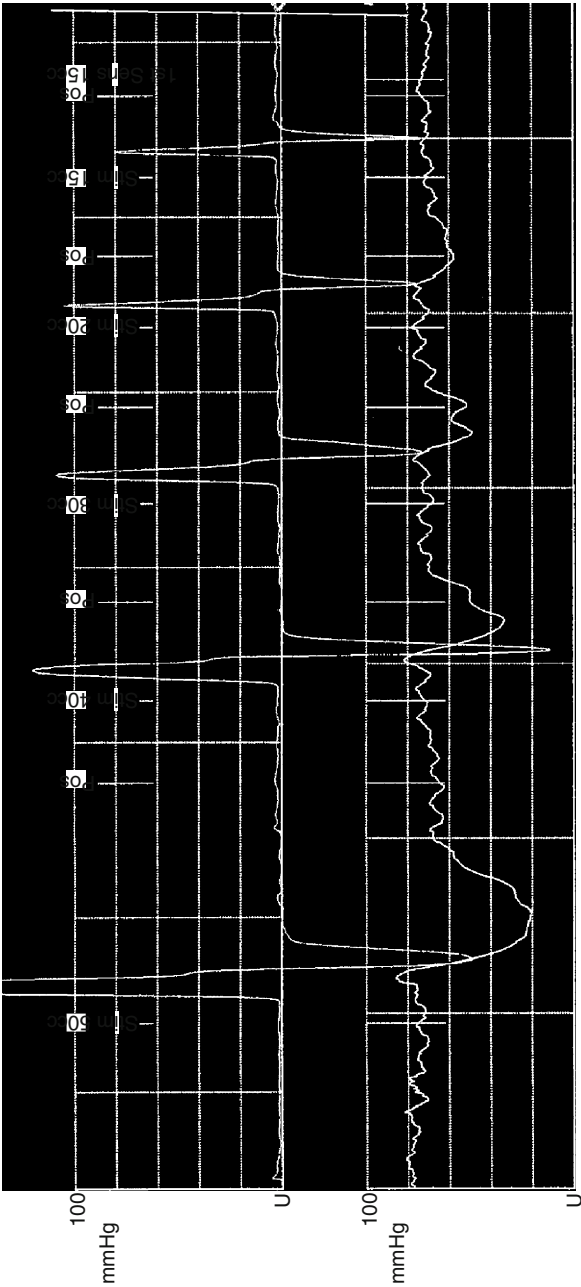


Fig. 4.3. Normal RAI in one quadrant on the manometry probe. The scale is 100 mm Hg.

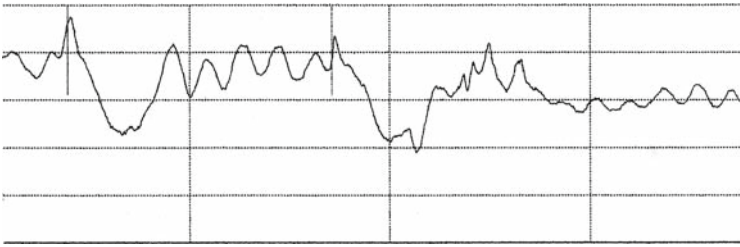


Fig. 4.4. Normal strain maneuver. A relaxation occurs.

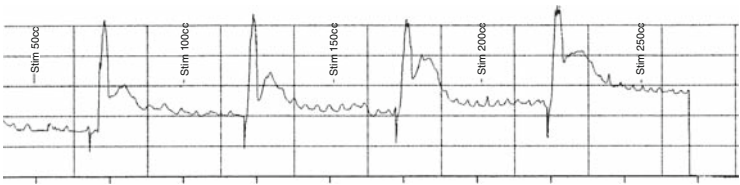


Fig. 4.5. Normal compliance in one quadrant on the manometry probe. The patient reports the insufflation causing the first sensation, the first urge, and the last tolerable volume.

Interpretation

Normals

- In the anal canal there are subtle differences in the upper, middle, and distal segments.
- Overall, men and young patients have higher pressures. However, there is overlap of normal measurements by sex and age.
- The resting pressure has contributions from both the internal and external sphincters, with the internal sphincter providing 75–80% of the total.
- The squeeze pressure is derived dominantly from the voluntary external sphincter.

Interpretation of Resting Pressure

- The resting pressure is the pressure in the high pressure zone at rest after a period of stabilization. Seventy-five to eighty percent of the resting pressure is a measure of the internal sphincter tone.

- For women, the resting pressure is approximately 52 mm Hg (range, 39–65). For men, the resting pressure is approximately 59 mm Hg (range, 47–71).
- Sometimes a normal patient may have low pressures, but does not have a complaint if the stool is well formed. However, a patient may have “normal” pressures, but yet complains of incontinence. These measurements cannot be interpreted alone, but must be analyzed in the context of the history and other measurements.
- Low resting pressures are usually seen in patients who have the chief complaint of incontinence (Fig. 4.6).
- Patients who have low pressures may not be good candidates for a surgery that will leave them with a poorly formed or liquid stool, such as total colectomy with ileorectal anastomosis or proctocolectomy with ileal pouch to anal anastomosis; these patients might be better served with a permanent ileostomy.
- High basal pressures may be associated with anorectal pain.
- Some patients have spastic sphincters, which may be associated with outlet obstruction.
- Patients with anal fissure have a spastic internal sphincter with high pressure measurements as part of the pathophysiology. These patients may be candidates for lateral internal sphincterotomy. Pharmacologic relaxation may be achieved in lieu of surgery. Relaxation of internal sphincter spasm can be achieved by 10 mg of sublingual nitroglycerine. Topical 0.2% nifedipine or 0.2% nitroglycerine applied to the anoderm relaxes the underlying muscle.

Interpretation of Squeeze Pressure

- The maximum voluntary pressure is the highest pressure recorded above the zero baseline at any level of the anal canal during maximum squeeze effort by the patient.
- The squeeze pressure is the pressure increment above resting pressure after voluntary squeeze contraction and is a calculated value that is the difference between the maximum voluntary pressure and the resting pressure at the same level of the anal canal.
- The squeeze pressure is mainly a measure of the external sphincter. For women, the squeeze pressure is approximately 128 mm Hg (range, 83–173). For men, the squeeze pressure is approximately 228 mm Hg (range, 190–266).

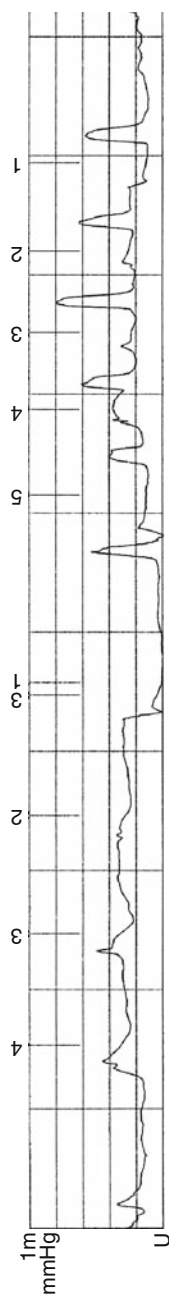


Fig. 4.6. Low resting and voluntary squeeze pressures in an incontinent patient.

- The squeeze pressure is examined as a total squeeze pressure, which includes the resting pressure plus the squeeze, and as a maximum squeeze pressure, which is the squeeze pressure minus the resting pressure.
- A low squeeze pressure may be associated with sphincter injury or nerve damage from surgery, especially anal fistula surgery, obstetric trauma, or other anorectal trauma (Fig. 4.6).
- High squeeze pressure is found in those patients who have pelvic floor spasm (anismus), often associated with anorectal pain. These same patients are unable to relax the sphincter when asked to bear down as if to defecate.

Interpretation of Squeeze Duration

- The sphincter duration is the length of time the patient can maintain a squeeze pressure above the resting pressure.
- The duration of squeeze should be >30 s at >50% of maximum squeeze pressure. When patients are unable to maintain a squeeze, they may be incontinent.

Interpretation of Reflex Studies

- The RAIR is the transient decrease in resting anal pressure by >25% of basal pressure in response to rapid inflation of a rectal balloon, with subsequent return to baseline.
- The decrease in pressure during the RAIR test is a measure of the internal sphincter relaxation.
- This reflex may be present even with central nervous system disorders; however, disease that interferes with the peripheral nerves or ganglion cells of the myenteric plexus or fibrosis of the internal anal sphincter may interfere with a measurable reflex relaxation.
- The presence of a normal RAIR rules out Hirschsprung's disease (Fig. 4.7).
- The cough reflex is the pressure increment above resting pressure after a cough, and is a calculated value that is the difference between the maximum pressure recorded during cough and the resting pressure at the same level in the anal canal.
- The cough reflex, also equated with a Valsalva reflex, is a rectal reflex to counter a sudden abdominal pressure increase.

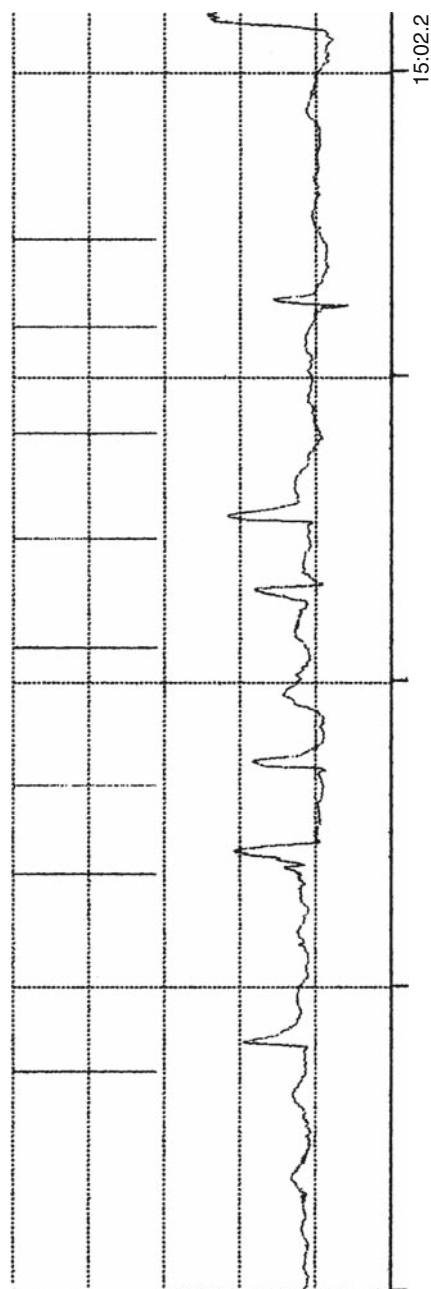


Fig. 4.7. Absent rectoanal reflex (RAIR), consistent with Hirschsprung's disease. Each spike is an insufflation, but no RAIR follows.

- This reflex may be abolished if there is a disruption of nerves in the cauda equina, sacral nerves, pudendal nerves, or peripheral nerves, but is maintained if nerves higher than the sacrum are injured.

Interpretation of Strain Maneuver

- The ability to defecate requires both anal relaxation and abdominal compression.
- Low abdominal pressures may be seen when there is central nervous system disruption or skeletal muscle disorders that prevent abdominal compression. Very high abdominal compression occurs when the anal sphincter does not relax, permitting high, recurrent pressures to be exerted on the pelvic floor.
- The failure for the sphincter to relax appropriately is termed anismus or paradoxical pelvic floor contraction (Fig. 4.8).
- The failure to relax has been found in sexually abused patients and in neurologic disorders where inhibitory pathways are ablated.

Interpretation of Rectal Sensation

- The sensory threshold is the minimum rectal volume perceived by a patient. A normal value for perception of rectal distention is approximately 15-mL (range, 9–25) inflation.
- Poor or absent sensation portends a poor response to biofeedback. The inability to sense suggests neural impairment, which may be

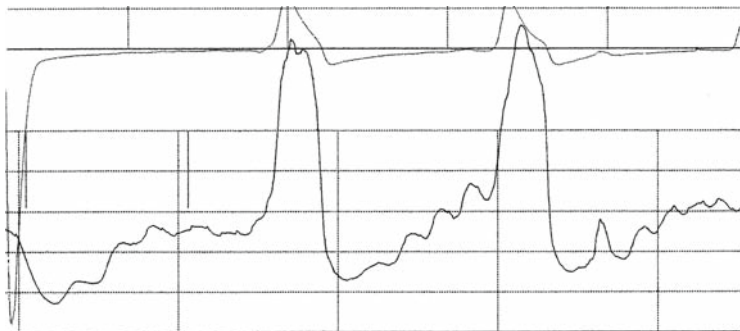


Fig. 4.8. Paradoxical increase in sphincter pressure during the strain maneuver, rather than a relaxation, is consistent with anismus.

related to a primary or secondary disorder, such as diabetes or amyloidosis. Constipated patients who have severe straining may progressively lose their ability to sense rectal fullness. Hypersensitivity may be evident in patients who have inflammatory bowel diseases, or have irritable bowel syndrome.

Interpretation of Compliance

- The urge sensation is the volume associated with the initial urge to defecate.
- The maximum tolerated volume is the volume at which the patient experiences discomfort and an intense desire to defecate. The maximal tolerable volume and pain threshold are reduced in patients who have a fixed, noncompliant rectal wall. For example, patients who have had proctectomy, fibrosis caused by ischemia, or fibrosis caused by inflammatory bowel disease will have lower maximal tolerable volumes and lower pain thresholds.
- A low tolerable volume may indicate rectal hypersensitivity and irritability. Increased compliance may be found in the megarectum. Decreased compliance caused by rectal reservoir reduction will result in fecal frequency and urgency with possible incontinence.

C. Defecography

- Defecography is a dynamic fluoroscopic examination performed with rectal contrast to study the anatomy and function of the anorectum and pelvic floor during defecation.
- The specific points to be analyzed may be captured on still radiographs, but cineradiography provides a better look at the potential pathophysiologies that may influence and perhaps interfere with successful and normal evacuations.

Indication

- The use of defecography is indicated as part of the evaluation of a patient who has an outlet obstruction type of constipation.

Equipment

Chair and Cushion

- A defecography chair, which has a standard-shaped toilet seat, fits onto the footboard of the table.

Contrast System

- High density, barium paste (Anatrast E-Z-EM, Westbury, NY; or Evacupaste) is introduced into the rectum.
- A tampon soaked in barium may be used to outline the vagina.

Technique

Preparation

- The bowel may be studied with or without preparation.

Introduction of Contrast

- The clinician will have decided which sites require contrast based on the clinical history. The rectum, vagina, bladder, colon, small bowel, perineal skin, and/or peritoneum may be marked with contrast material.
- If an enterocele is suspected, the patient should take 240 cc of diluted liquid barium orally 1 h before the procedure.

Imaging

- The patient is asked to be seated on the defecography chair (toilet), which is adjacent to the radiography table which has been erected to an upright 90-° angle.
- It is important to remember that patients sometimes are quite embarrassed and intimidated by the mechanisms of this study; abnormal defecation dynamics may be nothing more than inability to defecate caused by embarrassment.

Interpretation

- Having the study as cinedefecography allows repeated viewing of points where abnormality is suspected.

- The findings include the anorectal angle, perineal descent, efficiency of emptying, and possibly rectocele, enterocele/sigmoidocele, anismus, and intussusception. There is an overlap of symptomatic and asymptomatic patients, so that the findings must be correlated with the clinical symptoms and signs.

Anorectal Angle

- The anorectal angle is the proctographic angle between the mid-axial longitudinal axis of the rectum and the anal canal. The videofecography can be reviewed to see that the puborectalis muscle relaxes appropriately. The anorectal angle decreases during squeezing and increases during defecation and straining.
- The resting anorectal angle ranges from 90 to 110°. During squeeze, the angle becomes more acute in the range of 75–90°. On evacuation, the angle becomes obtuse in the range of 110–180°.

Perineal Descent

- Perineal descent is the caudad movement of the pelvic floor with straining. A baseline is a line drawn from the tip of the coccyx to the underside of the pubis, the pubococcygeal line. The descent and ascent can be measured from this line.
- Normally the pelvic floor will rise during squeezing and lower during straining and evacuation.
- The pelvic floor should not rise or fall more than 4 cm from the pubococcygeal line. If there is greater descent, it suggests a decreased muscle tone, which is most often the result of pudendal nerve injury. This finding is usually associated with other mechanical abnormalities.

Anal Canal Length

- During maximal strain to evacuate, the width of the anal canal should not exceed 2.5 cm. Wider openings suggest an incompetent muscle and possible incontinence.

Efficiency of Emptying

- Normally the rectum should empty completely, but 90% is the lower limit of normal. If an ileal pouch is being examined, 60% evacuation is the lower limit of normal.

Rectocele

- A rectocele is a bulging of the rectum into the posterior wall of the vagina and is the most common finding in defecography.
- A rectocele is much better defined by defecography than by clinical examination, giving better measurements of the size and adequacy of emptying. Generally a rectocele that is <3 cm is not of consequence.
- Even large rectoceles must be associated with outlet obstruction symptoms to be considered pathologic. Most of these patients find that pressing upon the bulge of the rectocele aids them in evacuation.
- The best time to recognize a rectocele is during maximal straining to evacuate. The postevacuation film may show barium trapped in the rectocele.

Enterocoele/Sigmoidocoele

- Enterocoele is a protrusion of the peritoneum between the rectum and vagina containing small intestine.
- A sigmoidocoele (pouch of Douglas descent) is a protrusion of the peritoneum between the rectum and vagina that contains sigmoid colon.
- It is abnormal for bowel to descend below the upper rectum, and it is abnormal for a space to be present of >2 cm between the rectum and vagina.

Anismus

- Anismus is a nonrelaxing puborectalis or levator muscle complex, which is seen as a fixed anorectal angle with a puborectalis indentation in the face of straining down or evacuation.
- The patient with anismus complains of severe straining to evacuate, and sometimes pain.
- If the act of defecation is timed, patients with anismus take >30 s to empty, starting when the anal canal begins to open. Normally evacuation takes 10 s after the anal canal starts to open. In addition, the anal canal width is narrow.

Intussusception/Prolapse

- The rectum may be seen to prolapse or intussuscept during straining or evacuation. The intussusception or prolapse can be

characterized as upper, mid, or lower rectal, and the origin can be described as anterior or posterior.

Megarectum

- This diagnosis is a combination of a large diameter of the rectum and incomplete emptying.
- The measurement of the width of the rectum at the level of the distal sacrum >9 cm suggests megarectum.

Incontinence

- During the procedure, incontinent patients may not be able to hold the barium in the rectum, and it can be seen to run out of the anal canal before the instruction to defecate is given. Incontinence is often associated with other pathology.

D. Balloon Expulsion Test

- The balloon expulsion test measures the ability of the patient to expel a balloon inflated with 50–60 mL of water or air.
- Patients with outlet obstruction are not able to pass this balloon readily. The problem is that some patients may pass the balloon, but have undetected outlet obstruction. Conversely, patients with outlet obstruction may call upon compensatory mechanisms to pass the balloon.

E. Anal Ultrasound

- Anal ultrasound is used to look for anatomic abnormality of the anal sphincters. See Chapter 7 for images of anal ultrasounds. Ultrasound has replaced EMG as the best means to define an injury.

Indication

- Work-up of incontinence.
- A suspected defect in the sphincter mechanism
- An obstetric injury is readily seen the ability to find the defect approaches 100%.

Equipment

- The most commonly used ultrasound machine displays a 360° image using a mechanically rotating transducer on a hand probe. The 10-MHz transducer provides the clearest images.

Technique

- Preparation is a small enema. Sedation is not necessary.
- The probe is introduced blindly to the point where the transducer is in the rectum. Images are made in the upper, middle, and distal anus.

Interpretation

- Bartram describes six ultrasonographic layers in the anal canal (1) a hyperechoic layer that is the interface of the cone with the tissues; (2) a hypoechoic layer that represents the mucosa; (3) a hyperechoic layer that represents the submucosa; (4) a hypoechoic layer that is the internal anal sphincter; (5) a hyperechoic layer that represents the intersphincteric plane and the longitudinal muscle; and (6) a layer of mixed echogenicity representing the external anal sphincter (see Fig. 7.1)

Incontinence

- A thin muscle suggests primary degeneration of the internal sphincter. After lateral internal sphincterotomy, a distal defect can be seen in the internal sphincter. Obstetric trauma may extend into the transverse perineus muscle, the external sphincter, or completely down through the internal sphincter. The injury blurs out portions of the normal rings of tissue described above.

F. Magnetic Resonance Imaging

- Identification of the anal and rectal structures is fairly easy on MRI because the perirectal fat shows a high degree of contrast when compared with the musculature.
- Indications for MRI examination are primarily sepsis, trauma, congenital abnormalities, and tumor.

- There is a significant change in T1 and T2 weighted imaging associated with infection. This change produces high soft tissue contrast and enables abscess and fistulous tracks to be demonstrated.
- Sensitivity of MRI using the body coil can be as high as 89% in identifying fistulas, but demonstration of site of internal opening and differentiation of various muscle layers is not always possible.
- Muscular anatomy is seen so well that MRI has become useful in the evaluation of anal trauma. When compared with endorectal ultrasound, endoanal coil MRI is superior in identifying the outer aspect of the external sphincter muscle.
- Studies have shown endoanal MRI to be comparable to endoanal ultrasound for identifying defects and/or thinning of the internal sphincter. MRI, however, may also show thinning of the external sphincter and puborectalis, which are not easily seen on endoanal ultrasound. This may represent atrophy in the pelvic musculature. Atrophy may correlate with a poor result after sphincter repair.
- Determination of atrophy on endoanal MRI may help in predicting the outcome after sphincteroplasty.
- Congenital abnormalities of the anus and rectum can be delineated by MRI examination.
- MRI can be used to identify sphincter involvement by rectal tumors.
- Distance from the distal aspect of the tumor to the levator muscle can be accurately assessed before surgical planning. Because of the length of the endorectal coil, visualization of the musculature of the sphincter up to 2 cm above the levator ani only is seen.
- Visualization of depth of invasion by tumor can be done by manipulation of contrast with the use of T2 weighted images.
- Defecatory problems may also be evaluated by MRI.
- MRI is able to demonstrate peritoneoceles, cystoceles, perineal descent, and prolapse during evacuation.

G. EMG of the Anal Sphincter

- EMG is used primarily in evaluating fecal incontinence, by assessing the motor unit.

- EMG may also be used to “map” specific anatomic sphincter defects. This mapping technique has largely been replaced by anal ultrasonography, which is simple, accurate, and painless.

Concentric Needle EMG

- Concentric needle EMG focuses on different motor unit characteristics. A concentric needle electrode will record muscle contractions as motor unit potentials (MUPs). A single MUP is caused by depolarization of the muscle from a single motor unit.
- Polyphasic potentials (four or more phases) have been reported in up to 25% of normal external anal sphincter muscles. Polyphasic potentials of short duration occur in myopathic disorders and those with long duration correlate with histologic evidence of regeneration in denervated muscle.
- Concentric needle EMG can be of particular value in the diagnosis of specific neurologic problems, including conditions of the cone and cauda equina, sacral roots, pudendal nerve, and for differential diagnosis of the various types of multisystemic atrophy.
- Normal amplitude of the MUP is $<600\ \mu\text{V}$ and duration is $<6\ \text{ms}$.

Single Fiber EMG

- Single fiber EMG electrodes are used because the area of measurement is so small each fiber generates a single spike.
- In normal circumstances, only a few muscle fibers from a single motor unit are within the recording area of a single fiber electrode. In reinnervated muscle, the numbers of fibers belonging to a single motor unit increase, thereby increasing action potentials are recorded at the electrode.
- Criteria for pudendal nerve damage in single fiber EMG are the presence of an increased fiber density, increase of MUP duration and amplitude at rest, decrease of the number of MUPs during maximum contraction, and presence of “jitter and blocking” phenomena.

Surface Electrodes

- Surface EMG electrodes are generally used to document anal sphincter activity at rest, strain, and squeeze.
- When compared with proctography, both needle EMG and surface EMG have a low positive predictive value, but they have

high negative predictive values. Therefore, EMG alone is not optimal for diagnosing the presence of nonrelaxing puborectalis. Surface electrodes avoid the pain of needle EMG.

- Biofeedback training is often done using surface electrodes. This may be done for fecal incontinence or for difficulties with evacuation, particularly if paradoxical sphincter contraction is present.
- Normal patients demonstrated no evidence of paradoxical activity.

Pudendal Nerve Terminal Motor Latency

- The pudendal nerve originates from S2, S3, S4 nerve roots and travels along the lateral pelvic wall down to near the ischial spine where it exits the pelvis to supply the external anal sphincter and the periurethral muscles through its terminal perineal branch.
- Prolongation in the pudendal nerve conduction indicates injury to the pudendal nerve sheath that results in focal demyelination with resultant slowing of conduction.
- A normal PNTML does not exclude partial damage. However, when unilaterally or bilaterally severely prolonged, PNTML has been shown to affect results after sphincter repair.

H. Evaluation of Transit

- The time it takes for food to travel through the digestive tract is known as bowel transit time. Gastric emptying, small bowel transit, and colonic transit may be studied.
- Transit is dependent on diet and varies greatly from person to person. For this reason, a dietary history and bowel evacuation history should be obtained in conjunction with any transit testing. Dietary history can be evaluated for fiber, fat, and calorie intake.

Colonic Transit

- Evaluation of constipation and pelvic problems may require determination of colonic transit times in order to assist in treatment. Transit may be measured by radiopaque markers or radionuclide techniques.
- Colonic transit is most easily measured by use of a marker test. The patient ingests a capsule containing radiopaque markers, which are then followed through the colon by abdominal radiographs.

- In the most simplified colon transit technique, the patient takes one marker capsule which contains 24 markers on day 0. On day 5, a supine abdominal film is taken to determine the number and position of remaining markers. If five or fewer markers are remaining, the patient has normal colonic transit. If more than five markers are present, then the pattern of residual markers is noted. Diffuse scattering throughout the colon would suggest colonic inertia or decreased motility. If the markers are present in the rectosigmoid region, then the presence of pelvic outlet problems should be considered. Variations of the test use x-rays on day 1–5, 1, 3, and 5, and 3 and 5.
- Average normal transit is 11.3 h, 11.3 h, and 12.4 h for the right, left, and rectosigmoid colon, respectively. Normal total transit averages 35 h.
- Stool weight has been shown to correlate with transit time in constipated patients.

Radionuclide Transit

- Transit may be measured by radionuclide gamma scintigraphic techniques. Radiographic and scintigraphic methods correlate well. The major advantage of scintigraphy is that 24–48 h of scanning is needed compared with 5–7 days for marker test completion.

Small Bowel Transit

- Small intestinal transit should be evaluated before surgical treatment of constipation because the patient may have a global motility problem.
- Small bowel transit may be measured by breath hydrogen analysis. Hydrogen breath analysis depends on the presence of bacteria in the large intestine to metabolize lactulose. Up to 25% of the population cannot metabolize the sugar because they lack certain bacterial strains in the colon.
- A meal of lactulose and beans is ingested and hydrogen breath analysis is undertaken. Fermentation of the meal occurs when the substrate reaches the colon. The fermentation process releases hydrogen gas that is absorbed and excreted by the lungs. Time to a 20-ppm increase in hydrogen in the breath correlates with small bowel transit. Some conditions such as

low colonic pH, bacterial overgrowth, or antibiotic administration may interfere with the use of this test for small bowel transit.

- Small bowel transit may also be determined by scintigraphic techniques. These techniques have the advantage of also measuring gastric emptying. Scintigraphy has a tendency toward slightly shorter transit times, but this is probably not clinically significant.
- Radiation exposure with scintigraphy is highest for the colon and can be reduced by the administration of laxatives after the procedure.

5. Diagnostic Evaluations: Endoscopy: Rigid, Flexible Complications

A. Anoscopy

- Anoscopy is the examination of the anal canal. The lower part of the rectal mucosa, upper anal mucosa, anoderm, dentate line, internal and external hemorrhoids can be seen through this examination.
- There are basically two types of anosscopes: beveled type such as the Buie or Hirschman scope (Fig. 5.1) and the lighted Welch–Allen scope (Fig 5.2) that uses the same light source as the rigid proctosigmoidoscope.
- Another type is the side-opening Vernon-David scope with Hirschman handle (Fig. 5.3).
- The Hinkel–James anoscope (Fig.5.4) is much longer than the Vernon-David scope and is suitable for patients with deep buttock cheeks.

Indications

- Any anal and perianal diseases or conditions require a full examination of the anal canal. These include anal fissures, anal fistulas, anal Crohn's disease, anal tumors, hemorrhoids, anal condyloma, bright red rectal bleeding, and pruritus ani.
- Anoscopy is frequently used in conjunction with colonoscopy, flexible sigmoidoscopy, and rigid proctosigmoidoscopy as part of the examination.



Fig. 5.1. Buie anoscope.



Fig. 5.2. Lighted Welch – Allen anoscope.



Fig. 5.3. Vernon-David with Hirschman handle anoscope.



Fig. 5.4. Hinkel – James anoscope.

Contraindications

- Patients who have severe anal pain such as an acute anal fissure or a perianal or intersphincteric abscess may not tolerate the examination. In general, if a patient can tolerate a digital examination, anoscopy can usually be done. A 2% lidocaine jelly should be used in patients with anal pain. Anal stricture or severe anal stenosis is another contraindication.

Preparation

- No preparation is required.

Positioning

- A prone jackknife position gives the best exposure. An alternative is a left lateral recumbent position.

Technique

- Inspection of the anal area should always precede any other examination and, for this, good lighting is essential.
- Skin tags, excoriation, and change in color or thickness of the anal verge and perianal skin can be detected quickly.
- A scarred, patulous, or irregularly shaped anus may give clues to the cause of anal incontinence. Particularly in multiparous women, the anal verge may be pushed down quite far during straining – a feature of the descending perineum syndrome.
- The next step is to do a digital examination. The index finger should be well lubricated with a lubricant jelly, and the finger pressed on the anal aperture to “warn” the patient. Then the finger should be gradually inserted and swept all around the anal canal to detect any mass or induration. In men, the prostate should be felt. In women, the posterior vaginal wall should be pushed anteriorly to detect any evidence of a rectocele.
- Anal tone, whether tight or loose, can be easily estimated. A stricture or narrowing from scarring or a defect in the internal or external sphincters from a previous operation can be felt.
- A fibrous cord or induration in the anal area and the anal canal may indicate a fistulous tract.

- Persistence of a gaping anus indicates an abnormal reflex pathway in the thoracolumbar region frequently seen in paraplegic patients.
- In persons with good anal function voluntary contraction of the muscles produces a squeeze of the muscle on the examining finger and the finger is pulled forward by the puborectalis muscle.
- Insertion of the anoscope should always be done with the obturator in place. The obturator is removed during examination and reinserted to rotate the instrument to another area. However, if the beveled type of endoscope is used, the endoscope can be rotated all around without having to reinsert the obturator.
- The examination table need not be tipped down more than 10–15° if an inverted (jackknife) position is used.
- During examination, the patient is asked to strain with the anoscope sliding out to detect any prolapse of the rectal mucosa and the anal cushion. Excoriation, metaplastic changes, and friable mucosa indicate a prolapsed hemorrhoid.
- A biopsy of the anal canal can be performed with an anoscope or a rigid proctosigmoidoscope.

Complications

- Anal tear, especially at the posterior midline, can occur in patients with anal stenosis.

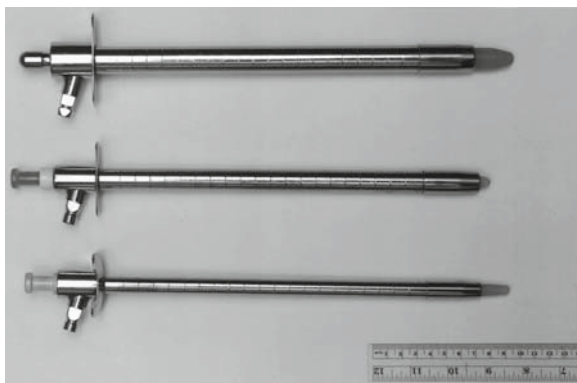


Fig. 5.5. Rigid proctosigmoidoscope. *Top*, 19 mm × 25 cm; *middle*, 15 mm × 25 cm; *bottom*, 11 mm × 25 cm.

B. Rigid Proctosigmoidoscope

- Three sizes of rigid proctosigmoidoscope are available (Fig.5.5).
- A 19mm × 25cm scope is the standard size for a general examination and for polypectomy or electrocoagulation.
- A 15mm × 25cm endoscope is a good size for general examinations. It is much better tolerated by the patient, causing less spasm of the rectum and, thus, minimal air insufflation, yet enables as adequate an examination as the standard-size endoscope.
- An 11mm × 25cm endoscope should be available for examining the patient who has anal or rectal stricture, such as Crohn's disease.
- Some physicians and surgeons prefer a disposable standard-size rigid proctosigmoidoscope for routine examination.

Indications

- Rigid proctosigmoidoscopy has largely been replaced by flexible sigmoidoscopy, but remains useful. One advantage is that blood clots or stool can easily be washed out. In a patient with massive gastrointestinal bleeding, a rigid proctosigmoidoscopy is the first line of examination to rule out an anorectal source of bleeding.
- A rigid proctosigmoidoscopy is used when an abnormality of the anal canal and rectum is suspected such as nonspecific proctitis, radiation proctitis, anorectal ulcer, anorectal neoplasm, infectious proctitis, and anorectal Crohn's disease.
- Rigid proctosigmoidoscopy is also useful to identify the precise site and size of rectal neoplasm.

Contraindications

- Patients with severe anal pain from an acute fissure, thrombosed external hemorrhoids, and perianal abscess may not allow an examination. The examination should be postponed until the area is healed or sedation is available.
- Anal stricture that will not allow the passage of the smallest size rigid proctosigmoidoscope.
- Patients with acute abdomen or a rectal or sigmoid anastomosis less than 2 weeks postoperatively requires special judgement.

Preparation

- Two phosphate enemas should be given within 2h of the examination. This is not necessary in a patient who has diarrhea or active bleeding. Sedation is unnecessary.

Positioning

- A prone jackknife is the position of choice. However, a left lateral position also gives an adequate examination and should be used in conditions such as pregnancy, severe hypertension, retinal detachment or postoperative eye surgery, apprehensive patients or if moveable examination table is not available.

Technique

- Although a standard proctosigmoidoscope is 25cm in length, the average distance that the scope can be passed is 20 cm. In men, the scope can be passed to 21–25cm half of the time, and in women, it can be passed that distance one-third of the time.
- Rigid proctosigmoidoscopy is suitable to examine the rectum and, in some patients, the distal sigmoid colon.
- When properly performed, rigid proctosigmoidoscopy should produce no pain or only mild discomfort. Most patients are fearful of the examination because of past bad experience with the procedure or from what they have heard. A few words of reassurance are often helpful.
- Air insufflation is limited to the amount necessary to open the lumen.
- It is usually necessary to insufflate a small amount of air for good visualization of the lumen.
- The length of insertion should be measured from the anal verge without stretching the bowel wall.
- If a lesion is seen, the size, appearance, location, and level must be recorded. If a biopsy is performed, the location, level, number of biopsies, and whether electrocoagulation is necessary should be noted.
- During the entire procedure, suction and water irrigation should be available.

Complications

- If not careful, the tip of the endoscope can tear the mucosa; a small or moderate amount of bleeding may occur. Abdominal pain and distention can occur from excessive air insufflation.
- Perforation from diagnostic rigid proctosigmoidoscopy is extremely rare.

C. Flexible Sigmoidoscopy

- The present-day flexible sigmoidoscope contains fiberoptic light bundles and a videochip at the tip of the endoscope. This videochip transmits the image through the processing unit to the monitor.
- The flexible videosigmoidoscope is 60 cm in functional length (Fig. 5.6). The entire sigmoid colon can be reached by the flexible sigmoidoscope in 45–85% of cases and, in a few, the splenic flexure can also be visualized.
- For selective screening examination, flexible sigmoidoscopy has a 3–6 times greater yield than does rigid proctosigmoidoscopy in detecting colonic and rectal abnormalities, especially neoplasms.



Fig. 5.6. Flexible videosigmoidoscope.

Indications

- In acute diarrhea, flexible sigmoidoscopy can be used to rule out *Clostridium difficile* colitis, acute bacterial colitis, amebic colitis, and ischemic colitis particularly after aortic aneurysm repair.
- Flexible sigmoidoscopy is also an excellent tool to examine bright red rectal bleeding to detect its cause such as nonspecific proctitis, radiation proctitis, anorectal Crohn's disease, rectal ulcer, and also anorectal neoplasm.

Contraindications

- Patients with severe anal pain from anal diseases may not tolerate the insertion of the scope. This also applies to anorectal stricture and colorectal anastomosis less than 2 weeks postoperatively.
- Other relative contraindications include acute sigmoid diverticulitis, toxic colitis, and patients with an acute abdomen.

Preparation

- Bowel preparation with two Fleet enemas given within 1–2 h of examination is adequate. The patient may eat normally. Patients with diarrhea do not require the enemas.

Positioning

- Left lateral recumbent or prone jackknife.

Technique

- Sedation is unnecessary.
- The key to success is insertion under direct vision with short withdrawals and advancements of the endoscope or a to-and-fro movement, together with rotating the instrument clockwise and/or counterclockwise as needed.
- Use of air insufflation should be kept to a minimum.
- If a lesion is detected and proved by biopsy to be a neoplasm, a complete colonic investigation is indicated, ideally by total colonoscopy.

- A polyp up to 8 mm in size can be sampled with coagulation (hot) biopsy forceps or biopsied and electrocoagulated. To prevent possible explosion, because of hydrogen or methane gas in the lumen, air should be exchanged in the colon and rectum with repeated insufflation and suction. Larger polyps should often be reserved for colonoscopic and polypectomy.

Complications

- Excessive air insufflation can cause acute abdominal distention and abdominal pain. This is best corrected by reinsertion of the endoscope and aspiration of air. Rough and improper techniques can cause perforation and other injuries.
- The most common site of perforation in flexible sigmoidoscopy is in the distal sigmoid colon where it is angulated from the relatively fixed rectum at promontory of the sacrum.

D. Ileoscopy

- Examination of the small intestine via an ileostomy can be performed using a rigid proctosigmoidoscope or a flexible sigmoidoscope.

Indications

- Indications for endoscopy of the terminal ileum are few. Most of the time it is to rule out recurrent Crohn's disease or to find an abnormality in patients with high ileostomy output.

Contraindications

- Stricture of the stoma.

Preparation

- Bowel preparation is not required, but it is helpful if the patient has been on a clear liquid diet for 1 day. Sedation is not required.

Positioning

- Supine.

Technique

- The well-lubricated rigid scope is introduced directly into the ileostomy. The terminal ileum is quite active with frequent spasm. It requires more air insufflation than scoping the rectum. The distance traversed by the endoscope is usually limited to 12–15 cm. In patients with a large para-ileostomy hernia, the endoscope may usually not be passed beyond 10 cm.
- Flexible sigmoidoscopy is much easier to perform. The angulation of the small bowel can be straightened by push, pull, and rotation of the scope. A moderate amount of air insufflation is usually required.

Complications

- The small bowel has thin walls and requires gentle maneuvering of the endoscope. Perforation can easily occur. If an angle cannot be straightened, the procedure should be terminated.

E. Pouchoscopy

Ileoanal Pouch

- Examination of the ileoanal pouch is best performed using a flexible sigmoidoscope although a rigid proctoscope can also be used.
- The endoscope can be used to examine the entire pouch and the terminal ileum proximal to the pouch.

Indications

- Examination of the pouch is indicated for patients with bleeding from the pouch, diarrhea, recent onset of fecal incontinence, obstructive symptoms, pouchitis, for surveillance follow-up examination to exclude neoplastic changes, and to rule out Crohn's disease.

Contraindications

- Severe anal or anastomotic stricture.

Preparation

- The patient is prepared by taking clear liquids for 1 day or administered a small enema before the examination. Sedation is not required.

Positioning

- Left lateral recumbent.

Technique

- The examination starts with a digital examination to evaluate the anal canal and the anal anastomosis. If there is a stricture, it should first be gently dilated with a finger or with Hegar dilators.
- The examiner should evaluate the mucosa of the pouch and anal canal for any edema of the mucosa, granularity, mucosal bleeding, contact bleeding, erosion, fibrin exudate, pattern of mucosal ulceration, plaque, and mass. Abnormal mucosa should be biopsied with cold biopsy forceps.

Complications

- Tear of the anal canal can occur if there is stricture of the anus or anastomosis. Traumatic injury from the scope may cause moderate bleeding but it usually stops spontaneously. A perforation can occur from instrumentation or a biopsy.

F. Colonoscopy

Indications

- Indications for diagnostic colonoscopy include: the evaluation of virtually all symptoms associated with potential benign or malignant, acute, or chronic diseases of the colorectum; for resolution of abnormalities seen on other imaging modalities; for investigating otherwise unexplained symptoms such as anemia; the evaluation of chronic and acute bleeding per annum; for screening and surveillance of patients at high risk for colon adenomas or carcinoma; and localization of nonpalpable lesions at open or laparoscopic operation.
- It is also increasingly possible to combine diagnostic colonoscopy and other imaging techniques such as ultrasound.

Contraindications

- Absolute contraindications are suspected bowel perforation, established peritonitis, or fulminant colitis.
- Relative contraindications include suspected ischemia, acute colitis, or recent anastomosis. In either of these instance an experienced examiner may safely perform a limited examination.

Preparation

- Several organizations have prepared and published guidelines for credentialing the individual who is permitted to perform colonoscopy in an institutional setting and, in some institutions, Credentials Committees can grant privileges.
- Although there is some controversy involving requirements for specific numbers of procedures during training, all recommendations include the following elements: background knowledge of anatomy, physiology, and pathology of the colon as well as familiarity with instruments and accessories used in endoscopy; some formal training; and quality assurance practices.
- Equipment for resuscitation should be available and individuals qualified to perform cardiopulmonary resuscitation should be present in the area where colonoscopy is performed.
- The necessity for qualified assistance during the performance of the procedure and for monitoring the patient's condition cannot be overstated.
- Obtaining informed consent is an opportunity for discussing with the patient elements of the past and present medical history, especially medications and operative procedures, which may expose psychological concerns or the need to modify preparation, add prophylactic antibiotics, or change medication, timing, and dosage.
- It is necessary to point out the potential hazards of colonoscopy, noting aspects of the process that might cause discomfort but it is also important to give reassurance that although the risk of complication is low the examiner is prepared for prompt management.
- The American Heart Association and the American Society of Colon and Rectal Surgeons have issued joint guidelines stating that antibiotic prophylaxis is not needed for endoscopic procedures.
- Thorough mechanical preparation of the colon is absolutely essential for efficient, safe, and complete endoscopic examination.

In addition, should perforation occur, the empty colon certainly poses less risk of significant peritoneal contamination.

- There are various forms of mechanical preparation possible but the most thorough and safest current regimen involves the use of polyethylene glycol electrolyte lavage solutions.
- Other forms of preparation that are sometimes used involve ingestion of a saline cathartic (usually sodium phosphate or magnesium citrate) as well as enemas. With the latter, there is more concern about electrolyte imbalance especially in patients taking diuretic medications chronically or those with renal insufficiency.

Monitoring

- Although the use of pulse oximetry and intermittent monitoring of blood pressure as well as electrocardiography (if clinically indicated) have now become standard procedures, it is important for the assistant as well as the endoscopist to be aware of any changes in the patient's level of awareness, respiration, and abdominal distention.

Bleeding Prophylaxis

- Although bleeding is rarely associated with diagnostic colonoscopy, there are concerns about bleeding at or after colonoscopy, if biopsy or polypectomy are contemplated, and this has led to modification of anticoagulation regimens and cessation of drugs that might alter platelet function.

Technique

- With the patient in the left lateral recumbent position, the examination is initiated by thoroughly inspecting the perianal area for fissures, fistulae, hemorrhoids, condylomata, and rarer conditions such as melanoma, Bowen's disease, extramammary Paget's disease, squamous and anal gland carcinomas.
- The main objective on insertion of the instrument is to reach the most proximal point desired in as expeditiously a manner as possible, leaving detailed inspection until the process of withdrawal of the endoscope.
- It is dangerous to proceed with introduction of the endoscope without knowing at all times the location of the lumen.

- One of the earliest challenges to insertion is advancing the instrument into the descending colon.
- Having entered the descending colon with the sigmoid shortened and “straight,” it is usually quite easy to advance to and around the splenic flexure.
- The hepatic is often a more complicated flexure than is the splenic and one may wander a while before entering the distal ascending colon.
- It is important to be fully cognizant of the vagaries of endoscopic anatomy in order to confirm cecal intubation – by visualization of the appendiceal orifice and the ileocecal valve
- On withdrawal of the instrument, one has to be sure that the entire mucosa is visualized.

Normal Endoscopic Anatomy

- On insertion it is important to first recognize the three rectal valves of Houston because the relationship of a lesion to them will have great relevance if surgical intervention is to be contemplated.
- Diverticula may be seen throughout the intraperitoneal colon but rarely below the peritoneal reflection.
- The descending colon, being fixed along the white line of Toldt, will often present a long straight “tunnel view.”
- More common in the sigmoid colon, diverticula may be seen throughout the length of the large intestine. Their orifices may be so wide that they may be mistaken for the bowel lumen. In any one field of view, the diverticulum will of course be at right angles to the lumen (Fig. 5.7).
- The transverse colon, on insertion, being suspended by the three taenia coli presents the appearance of an equilateral triangle (the so-called “cathedral ceiling” appearance).
- The ileocecal valve is usually recognized as an eccentric bulge with a sometimes visible umbilication. Because there is more adipose tissue in it, the appearance is often a yellowish color compared with the pink of the rest of the colon.
- It is important to intubate proximal to the valve because the true caput of the colon may be at a variable distance from the ileocecal valve. As the three taenia come together at the caput (often appearing like the branches of a tree or a crow’s foot), the appendiceal orifice is usually recognized, even in the patient who has undergone previous appendectomy.

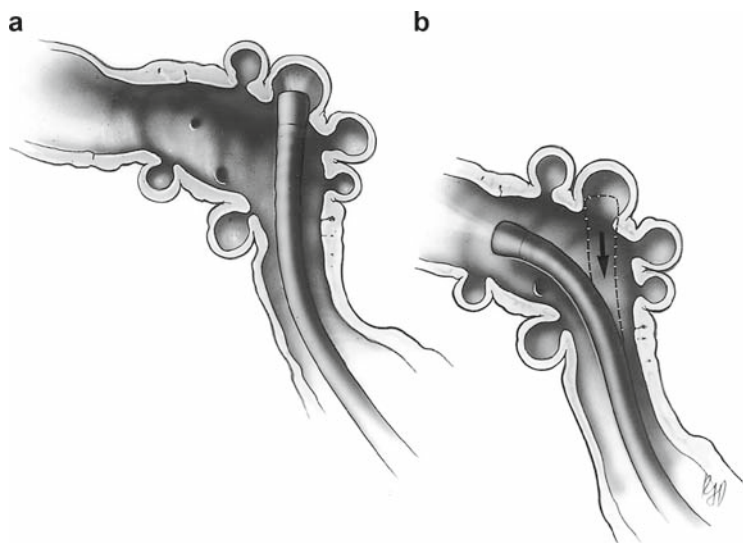


Fig. 5.7. Finding lumen in diverticulosis.

Abnormal Findings

- Exophytic lesions are the easiest to visualize and recognize at colonoscopy, the most common being adenocarcinoma.
- All polypoid lesions of the colon may be visualized at colonoscopy and virtually all have distinguishing characteristics. Several are submucosal (lymphoid hyperplasia, stromal tumors, lipomas, carcinoids, endometriomas, hemangiomas, neurofibromas, lymphoma). Some, being of no clinical consequence, require only recognition (lymphoid hyperplasia, lipoma).
- In addition to lesions that protrude, there are numerous inflammatory or degenerative conditions that have a recognizable endoscopic appearance and many can be safely sampled if necessary. These include the various colitides (bacterial, viral, ulcerative, granulomatous), ischemia, radiation proctopathy (formerly called 'proctitis') and melanosis coli.
- Areas of angiodysplasia (vascular ectasias, arteriovenous malformations) can be recognized on diagnostic colonoscopy but must be distinguished from bruises created from instrumentation or even preparation.

- The endoscopist has to recognize colonic anatomy disturbed by previous operation and therefore has to be familiar with the variety of intestinal anastomoses performed.
- Areas of stenosis and stricture may be encountered secondary to benign conditions (previous resection and anastomosis, diverticulitis, colitis, radiation injury) or malignancy.
- The manner in which the nature of a lesion is established at diagnostic colonoscopy will vary. A tiny sessile lesion (for example, a diminutive polyp) may be removed in its entirety with the biopsy forceps for pathologic examination. A pedunculated lesion suspected of being a benign adenoma may be removed at the time of diagnostic examination by snare polypectomy. A sessile lesion suspected of being a carcinoma or villous adenoma may be biopsied at one or more sites or even partially removed with a snare and cautery to obtain a satisfactory specimen.
- A stricture may be sampled for possible malignant cells by advancing a cytology brush into the stricture ahead of the colonoscope (Fig. 5.8). Malignant cells may thus be harvested even though the stricture cannot be traversed with the endoscope.

Complications

- Although colonoscopy is, in general, a safe procedure, it is invasive and adverse events do occur.

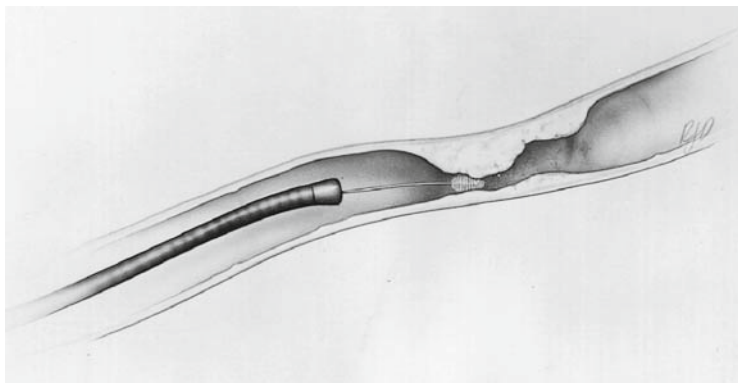


Fig. 5.8. Cytology through stricture.

- The most common serious complication of diagnostic colonoscopy is perforation with a reported incidence of 0.03–0.65% and a mortality of 0.01–0.02%.
- Other reported complications include abdominal distension, dehydration, respiratory depression, vasovagal reaction, thrombophlebitis, incarcerated hernia, splenic capsular tear and subcutaneous and/or mediastinal emphysema, and equipment failure.
- In diagnostic colonoscopy, perforation may be caused by the instrument itself, traction on a fixed segment of colon, or over-insufflation of a segment, especially a closed loop as may occur in patients with multiple strictures (inflammatory bowel disease) or as a consequence of prior radiation therapy or with hernia incarceration.
- Perforation during diagnostic colonoscopy tends to be detected earlier than when it is from instrumental causes. Perforation from therapeutic procedures is frequently related to thermal injury and is often delayed.
- The management of perforation after colonoscopy remains controversial. There is universal agreement that perforation with generalized peritonitis demands an operation. However, some believe that if the onset of symptoms is delayed, signs are localized, and the patient is not septic (even with the demonstration of pneumoperitoneum) that nonoperative management may be appropriate.
- Safe diagnostic colonoscopy is related to training, skill, and experience. Avoidance of perforation may be best achieved by avoidance of dehydration and oversedation; discontinuation of the procedure if the preparation is poor; avoiding forceful instrument insertion; recognition of vulnerable bowel (inflammation, ischemia, narrowing, fixation); careful identification and avoidance of diverticular ostia; avoidance of bowing of the instrument; awareness of fixation from pelvic adhesions or tumor extending through and beyond the colon wall; ensuring that abdominal and inguinal hernias remain reduced; avoiding over-insufflation; and looping in the splenic flexure region.
- If perforation occurs, early diagnosis ensures efficient management. Undue and sustained pain (especially shoulder discomfort), absence of liver dullness on percussion, demonstration of pneumoperitoneum on upright chest film, and subcutaneous emphysema all help in making the diagnosis.

- Surgical intervention is favored by most surgeons for early recognized perforation at diagnostic colonoscopy. However, patients with either a delayed perforation or one that has remained localized without symptoms or signs of diffuse peritonitis are candidates for nonoperative management with close observation.
- With early surgical intervention for a mechanical perforation, primary closure with or without a protective proximal stoma, if technically feasible, is desirable. However, the surgeon must use good judgment in assessment of factors such as adequacy of tissue perfusion, degree of spillage, and colon tissue free of inflammation.

6. Diagnostic Evaluations: Radiology, Nuclear Scans, PET, CT Colography

A. Plain Films

- Controversy exists over the number of views or films needed to adequately examine the abdomen. Classical teaching recommends three views consisting of a supine abdomen, upright or lateral decubitus abdomen, and upright chest.
- Plain films do not offer as much anatomic detail as the cross-sectional imaging modalities, but they remain highly sensitive and specific when there is suspicion of a bowel obstruction or a perforated viscus. Other useful indications for plain films include longitudinal examination of megacolon, identification of foreign bodies, check positions of drains or catheters, and evaluation of associated skeletal diseases.

Intestinal Obstruction

Small Bowel Obstruction

- Abdominal plain films have been shown to be diagnostic in 50–66% of cases with approximately a 20% false-negative rate.
- The radiographic diagnosis of an SBO depends on the intraluminal gas pattern projected upon the plain film. A normal gas pattern is defined as small amounts of gas distributed throughout the small and large bowel without bowel distention (<2.5 cm in diameter).
- Air-fluid levels, which are the dependent layering of fluid and air within a dilated loop of intestine when viewed in the upright position, are common radiographic findings of

an SBO. A complete or high-grade SBO is characterized by dilated loops of small bowel, air-fluid levels, and absence of colonic gas (Fig. 6.1a, b).

- Generally, the more dilated loops of intestine present, the more distal the obstruction is located.
- If the diagnosis is uncertain clinically and radiographically, then a follow-up study with either computed tomography (CT) or small bowel contrast study is warranted.
- Plain films do not reliably differentiate a simple obstruction from a strangulating obstruction. Findings considered to be high risk for vascular compromise include complete bowel obstruction, extensive mucosal thickening or edema, pneumatosis, portal venous gas, or a closed loop obstruction.

Large Bowel Obstruction

Cancer

- Typically the colon will be distended up to the point of obstruction with a paucity of distal gas. If the ileocecal valve (ICV) is competent, the cecum can be markedly dilated and there may be little dilation of the small bowel.
- Once the cecal diameter reaches >12cm, it is generally agreed that the risk of impending perforation is high.
- If a colonic obstruction is suspected, the diagnosis can be confirmed with a water-soluble contrast enema.

Pseudoobstruction

- Dr. Ogilvie first described acute colonic pseudoobstruction in 1948, which is a condition characterized by massive dilation of the colon with no evidence of mechanical obstruction.
- Radiographically, it is characterized by marked dilation of the cecum, ascending colon, and transverse colon. The descending colon and rectum are infrequently dilated.
- If the diagnosis is in question, it can be confirmed by a water-soluble enema, where there should be free flow of contrast into the cecum with no evidence of obstruction.

Colonic Volvulus

- Plain films are able to diagnose sigmoid volvulus in 75% of the cases.

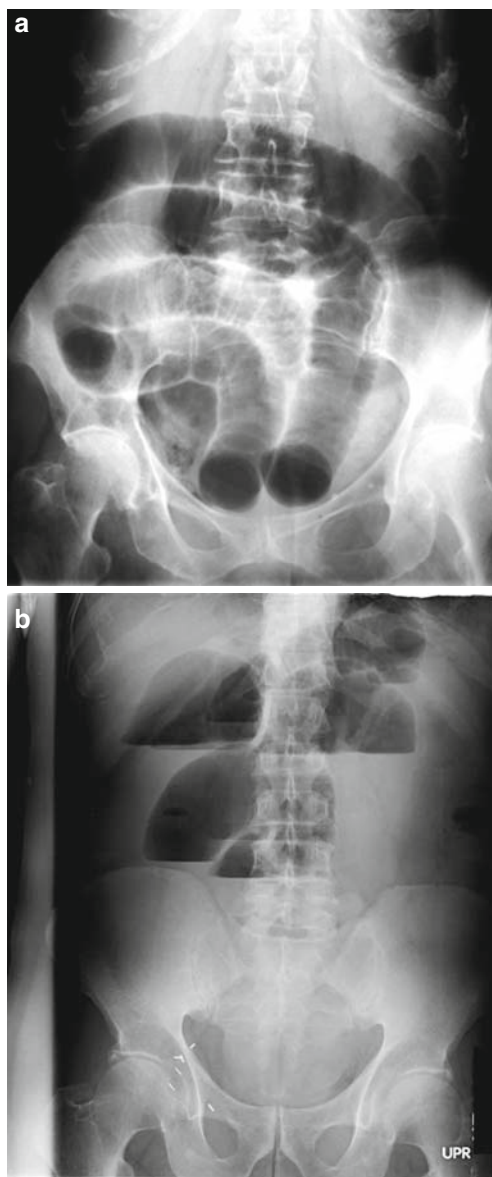


Fig. 6.1. (a) Plain film of SBO dilated loops, ladder. (b) SBO air-fluid levels.

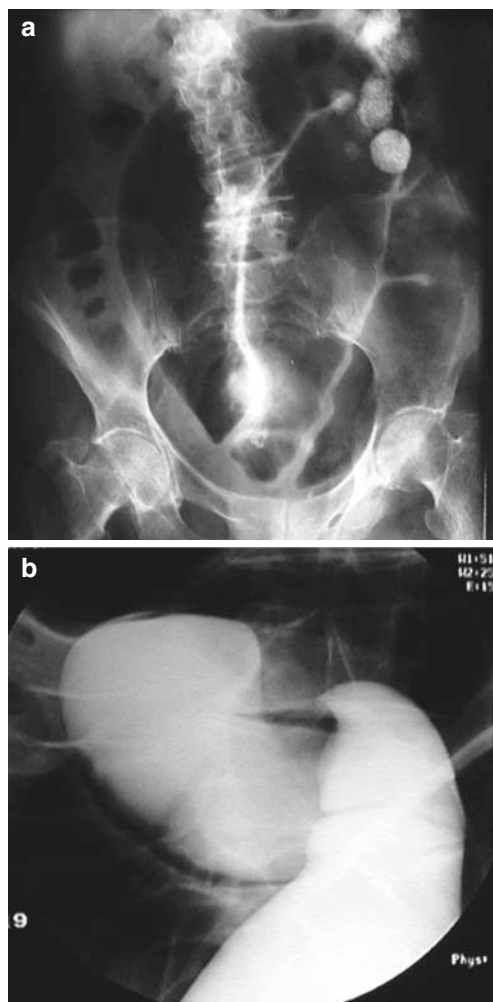


Fig. 6.2. (a) Plain film of sigmoid volvulus. (b) Contrast enema of sigmoid volvulus.

- The classic plain film findings include a dilated, U-shaped loop of colon that is projected toward the right upper quadrant. This characteristic finding has also been called the “bent inner tube” sign (Fig. 6.2a).
- If the diagnosis cannot be made with plain films, a water-soluble contrast enema will provide the diagnosis. Gentle instillation of contrast will demonstrate a smooth, tapered

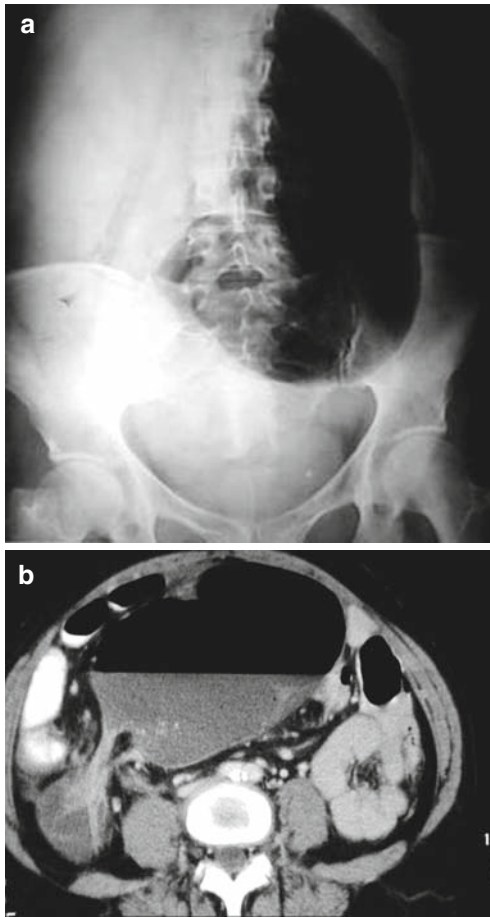


Fig. 6.3. (a) Plain film of cecal volvulus. (b) CT of cecal volvulus.

point of obstruction at the rectosigmoid junction known as a “bird’s beak” (Fig. 6.2b).

- The diagnosis of rotational cecal volvulus can be made with plain films 75% of the time.
 - Classically, the medially placed ICV indents the dilated cecum giving it the characteristic “coffee bean” or “kidney” shape (Fig. 6.3a, b).
 - The “bascule” type volvulus produces a sharp, flat cut off of retrograde contrast as the mobile, redundant cecum

flips up medially into the upper abdomen, causing a dilated cecum and small bowel on plain films.

Pneumoperitoneum

- The upright chest film is the most sensitive view for identifying free air under the diaphragm.
- The left lateral decubitus film is also fairly sensitive for patients who are unable to be transported or stand.
- The most common plain film finding is the accumulation of air under the right hemidiaphragm (Fig. 6.4a, b).
- If there is any question about the diagnosis, the films should be repeated in another position or a CT should be obtained, which is the most sensitive study to detect free air.

Colitis

- Plain films can give information regarding the condition of the mucosa, extent of colonic involvement, presence of perforation, evidence of bowel infarction, severity of colitis, and presence of associated ileus or obstruction.
- Thumbprinting is a sign for bowel wall and mucosal edema associated with most causes of acute colitis.
- An ominous sign is the presence of massively dilated segment of colon associated with bowel wall thickening and thumbprinting (Fig. 6.5). This is diagnostic for toxic megacolon when associated with the clinical findings of leukocytosis, severe abdominal tenderness, and hemodynamic instability.
- Examining five characteristics can provide considerable data regarding the severity and extent of the Crohn's or ulcerative colitis (UC).
 - First, the extent of solid colonic fecal material gives a general sense of the extent of disease. Solid stool in the right and transverse colon indicates left-sided colitis, and absence of solid stool anywhere in the colon suggests pancolitis.
 - Second, examining the mucosal contours can help determine which segments of the colon are involved. Normally, the mucosal edge is smooth with sharp, narrow haustral markings. In the presence of active or longstanding inflammatory bowel disease (IBD), the mucosal contours are altered. The mucosal edge becomes blurred and has a granular appearance because of inflammation and ulceration.

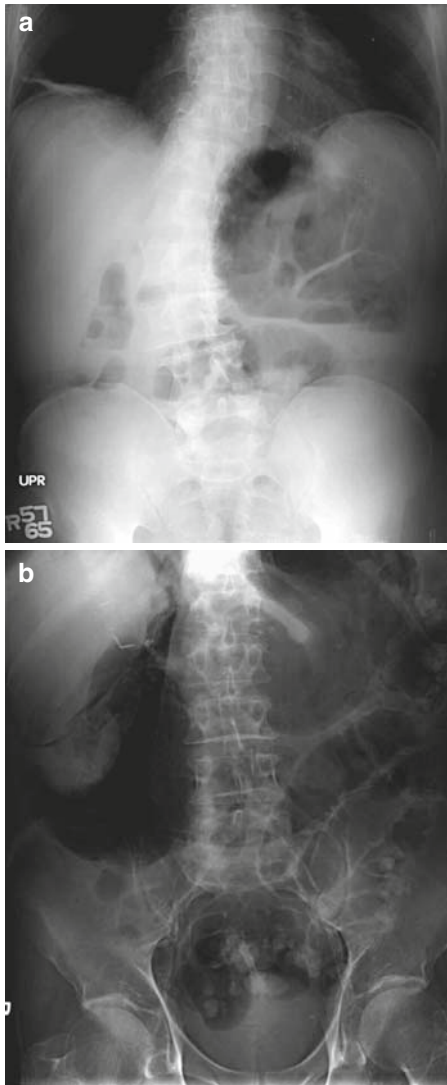


Fig. 6.4. (a) Plain film of intraperitoneal free air under diaphragm. (b) Plain film of free air under liver edge.

Depending on the extent of ulceration, the haustral markings may appear thick or be absent all together.

- Third, the character of the haustral markings provides information regarding the severity of disease. The haustral

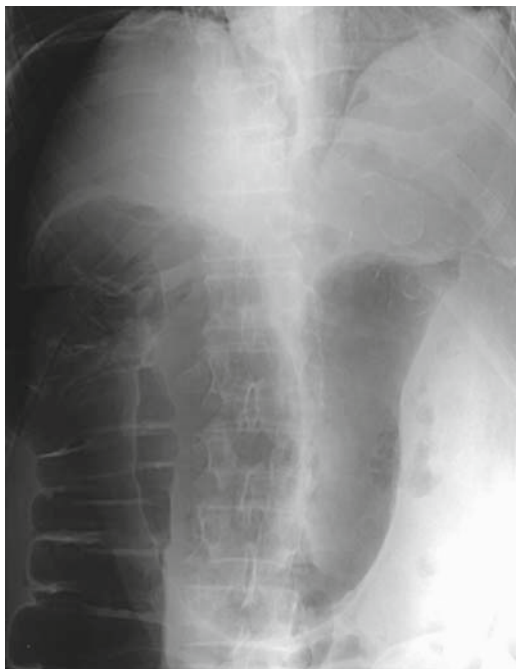


Fig. 6.5. Plain film of colitis with megacolon.

clefts are normally narrow with sharp angulation from the mucosal edge and are closely spaced. As the colitis progresses, the haustra become thicker, the angulation with the mucosal edge becomes blunted, and they are spaced farther apart. The haustra begin to disappear as the mucosal ulcerations progress.

- Fourth, the diameter of the colon can indicate the severity and chronicity of the disease. A markedly dilated (>5 cm) colon with thumbprinting and bowel wall edema is concerning for toxic megacolon. At the other end of the spectrum, a chronic, “burned out” colon takes on a tubular, narrowed appearance (Fig. 6.6). This is more characteristic of UC than Crohn’s disease.
- Finally, the thickness of the wall becomes thicker over time in patients with IBD. The distribution of the bowel wall thickening provides clues as to the extent of colonic involvement. Plain films are also able to provide infor-



Fig. 6.6. Plain film of chronic burned out colitis.

mation regarding the extraintestinal manifestations of IBD. Abnormalities of the skeletal system such as sacroiliitis, ankylosing spondylitis, and osteopenia secondary to chronic steroid use can be seen.

- Another manifestation of colitis is pneumatosis where gas has accumulated within the wall of the intestine. This may be a relatively benign process such as pneumatosis cystoides intestinalis or it may represent the very grave situation of bowel infarction.

B. Contrast Studies

Contrast Enemas

- Barium studies of the colon are designed for the detection of mucosal and intramural lesions.
- With the widespread use and availability of colonoscopy, the role of single or double contrast barium studies has diminished.

- The advantages of barium as a contrast medium are its ability to coat and adhere to the mucosa.
- The indications for a barium study include screening and diagnosis of mucosal disease processes in the elective setting.
- The exposure of barium to the peritoneal cavity results in an intense inflammatory response that has a mortality rate of approximately 50%. Therefore, the use of barium should be avoided in urgent situations such as studying the integrity of an anastomosis, evaluating a large bowel obstruction, examining acute colitis, or when there is concern for bowel perforation. In these situations, a water-soluble contrast agent should be used.
- Indications for a water-soluble study include evaluating the integrity of a colonic anastomosis, evaluating colonic obstruction, the preoperative evaluation of the colon for evidence of gross pathology, delineating colonic fistulas, and therapeutic enema for fecal impaction. The peritoneal cavity tolerates exposure of water-soluble contrast with very little reaction and, therefore, it is the contrast agent of choice in urgent situations.

Cancer and Polyps

- The most common reason for ordering an air contrast barium enema is for the screening and diagnosis of neoplastic lesions of the colon and rectum, especially when screening for colorectal cancer in conjunction with flexible sigmoidoscopy, when colonoscopy is not possible.
- A barium enema can detect up to 90% of polyps and cancers that are >1cm in size, but sensitivity decreases to 50% for lesions <1cm in size.
- The size of the lesion is the most helpful indicator of malignancy, with lesions >2cm having a 50% chance of invasive cancer.
- Sessile lesions when viewed in face take on a “bowlers hat” appearance that project into the lumen (Fig. 6.7).
- Characteristic findings implicating a malignant lesion include destruction and irregularity of the overlying mucosa with shelf-like, overhanging borders, and there is a sharp transition from normal mucosa into the annular lesion.
- Benign strictures from ischemic colitis, diverticulitis, anastomotic strictures, or Crohn’s disease, in contrast, tend to have smooth, tapering borders.



Fig. 6.7. ACE of polyp or early cancer.

- If a large bowel obstruction is suspected, barium should be avoided and a water-soluble contrast agent should be used, and only a single column contrast study is needed to define the pathology.
- A completely obstructing lesion will have an abrupt cutoff of contrast at the level of the lesion. There will be shouldering or evidence of mucosal destruction at the point of obstruction. If the lesion permits some contrast to flow past the lesion, a “string sign” may be seen (Fig. 6.8). This will be seen as a thin line of contrast extending from the column of contrast at the level of the obstruction. There is an abrupt cutoff of normal mucosa to a shouldering, overhanging lesion. The “string” of contrast will show irregular, destroyed mucosa along the length of the lesion.

Polyposis Syndromes: Familial Adenomatous Polyposis, Peutz-Jeghers, Juvenile Polyposis

- It is not possible to distinguish between the sporadic adenomatous polyps and these polyposis syndromes using contrast studies.



Fig. 6.8. Contrast enema of apple-core cancer string sign.

Ulcerative Colitis

- Barium enema is used (1) to confirm the diagnosis of UC and differentiate it from Crohn's disease, (2) to assess the extent and severity of disease, and (3) for surveillance of the disease and its complications.
- Radiographically, this appears as blunting or complete loss of the haustral markings, a narrow tubular appearance to the colon, and loss of the redundant course of the sigmoid and transverse colon (Fig. 6.9).
- Barium contrast studies are also able to detect other colonic complications of UC such as adenomatous polyps and cancers.

Crohn's Disease

- Contrast studies help differentiate Crohn's disease from UC, define the severity and extent of the colitis, and identify complications of the disease.



Fig. 6.9. Contrast enema of chronic UC.

- Contrast enemas are better than colonoscopy at identifying and characterizing fistulas, strictures, and the distribution of disease.
- Aphthous ulcerations are the earliest mucosal lesions seen in Crohn's disease. Barium accumulates within the lesions and they appear as small, shallow, or punctate collections with a surrounding radiolucent halo (Fig. 6.10a). These lesions occur more frequently in the colon than the small intestine, and they help to distinguish Crohn's disease from UC.
- The transmural nature of the inflammation allows the ulcerations to extend into the musculature of the bowel wall and even lead to fistulization. The result is deep longitudinal and transverse fissuring with edematous mucosa in between that gives the colon a cobblestone appearance. Barium deposits in the deep fissures and appear as multiple irregular white stripes (Fig. 6.10b).

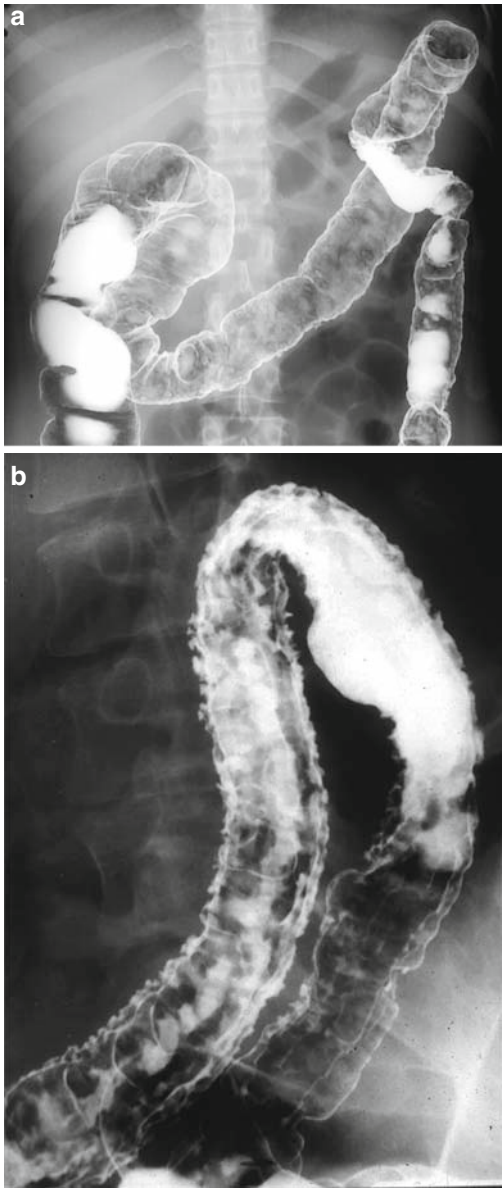


Fig. 6.10. (a) Contrast enema of Crohn's disease showing ulcers. (b) Contrast enema of Crohn's with fissures, and long linear ulcers.



Fig. 6.11. Contrast enema of Crohn's disease showing a stricture.

- Also, the identification of skip lesions or areas of normal mucosa in between areas of active colitis distinguish Crohn's disease from UC.
- Another significant feature of Crohn's disease is the development of strictures. Crohn's strictures are a result of transmural fibrosis. Radiographically, the strictures are asymmetric, have irregular borders, and are not circumferential (they are centered on the mesenteric edge) (Fig. 6.11).

Diverticulitis

- Air contrast barium enemas are more sensitive than single contrast studies at detecting diverticula because of better colonic distension and mucosal detail.
- Diverticula can be distinguished from polyps and small cancers because they project away from the lumen as compared with neoplasms that project into the lumen.

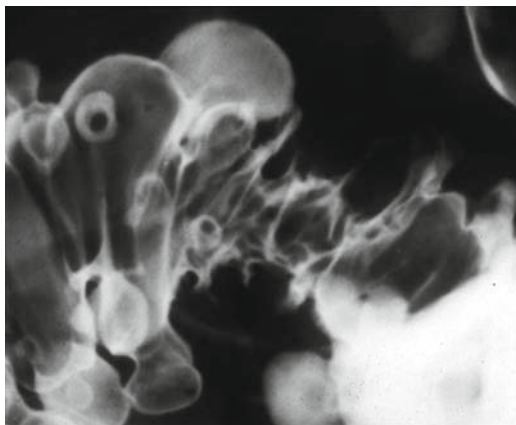


Fig. 6.12. Air contrast enema of severe diverticulosis.

- The combination of a shortened, thickened colon and extensive diverticula can disrupt the symmetric appearance of the haustral clefts, giving the mucosal outline an irregular zigzag appearance (Fig. 6.12).
- In the acute setting, a water-soluble contrast agent should be used rather than barium to avoid the highly morbid case of barium peritonitis.

Submucosal and Extracolonic Lesions

Lipoma

- On double contrast barium enema, lipomas can appear as a submucosal mass or a polypoid lesion.
- Lipomas are soft and pliable, so during fluoroscopic examination, compression can change the configuration of the lesion; this is called the “pillow sign.”

Lymphoma

- There are three basic radiographic morphologies that primary colonic lymphomas can demonstrate.
 - First, they can appear as discrete polypoid lesions.
 - Second, the mass can infiltrate the mesentery resulting in cavitation of the lesion into the mesentery.
 - Finally, disseminated lymphoma appears as multiple, long segments of nodular, narrowed colon.

Endometriosis

- The findings on barium enema in the patient with endometriosis are consistent with an extracolonic process, because the mucosa remains smooth and intact. Scarring occurs on the serosal surface which contracts the serosa causing the normal mucosa to bunch into what is called mucosal pleating.

Colonic Intussusception

- The classic appearance of an intussusception on contrast enema is the spring coil appearance or crescent sign.

Anastomotic Assessment

- Contrast enema studies are frequently used postoperatively to examine a colocolic, colorectal, coloanal, or ileal-anal anastomosis. The studies are used to evaluate for anastomotic leak in a septic patient, before closure of a diverting stoma, or to rule out an anastomotic stricture in patients with defecation difficulties.
- When testing the integrity of an anastomosis, a water-soluble contrast agent should be used.
- In the early postoperative period when evaluating for an anastomotic leak, water-soluble contrast enema is more sensitive than CT with rectal contrast.
- Radiographic findings of an anastomotic dehiscence include the extravasation of contrast freely into the peritoneal cavity or into a contained cavity (Fig. 6.13a, b).
- Finally, the postevacuation films are the most important because they identify any residual contrast outside of the lumen, which may be the only finding that a leak is present.

Small Bowel Series and Enteroclysis

- Radiologic studies of the small bowel are often used to finish an examination of the GI tract for the sake of completeness.
- Indications for small bowel studies include unexplained GI bleeding, evaluation for small bowel tumors, SBO, Crohn's disease, and malabsorption.
- Barium follow-through and enteroclysis are the principle methods for examining the small bowel. During a small bowel follow through (SBFT), the patient drinks a large volume of dilute

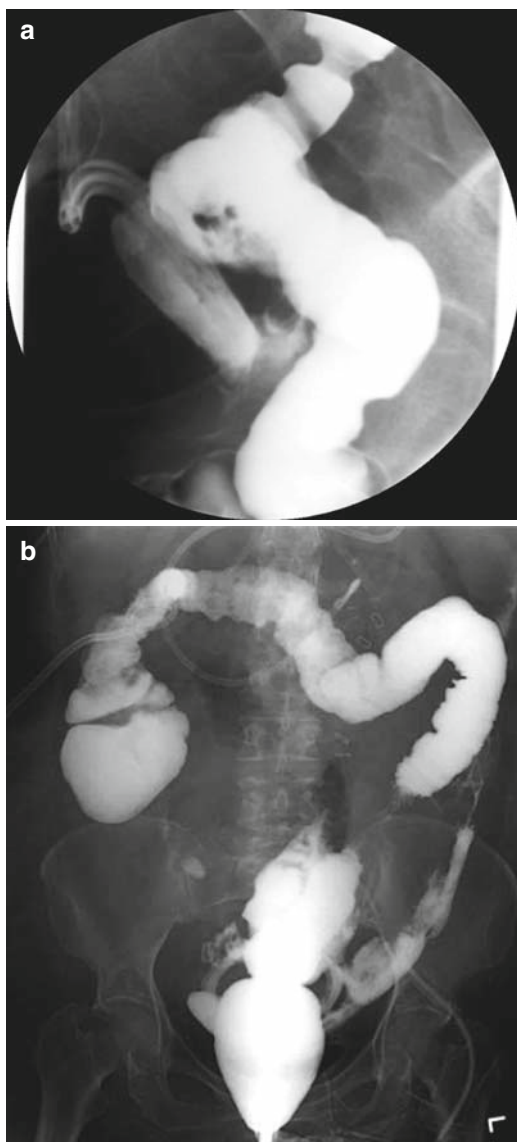


Fig. 6.13. (a) Contrast enema showing a contained anastomotic leak. (b) Contrast enema showing a free-flowing leak.

barium. The radiologist follows the flow of contrast through the small bowel with the use of fluoroscopy and spot films.

- During enteroclysis, the contrast and methylcellulose are administered through a small tube passed into the duodenum. This allows for rapid instillation of barium into the small bowel allowing for better distention and visualization. Advantages over SBFT include better filling and distention of the bowel and decreased study time. The major disadvantages are the placement of the nasoduodenal tube, the relatively high radiation dose, and hyperosmotic nature of the methylcellulose.
- Normal transit time for the small bowel can vary widely but is generally defined as 90–120 min.

Crohn's Disease

- Barium studies of the small bowel are essential for staging the severity and extent of bowel involvement in patients with Crohn's disease.
- Indications for the studies include routine surveillance of known small bowel disease, assessing the severity of disease during a flare, defining the disease distribution for a new diagnosis, preoperative assessment, and to assist in the differentiation between Crohn's disease and UC.
- The radiographic appearance of Crohn's disease depends on the severity of disease and its distribution. Early or mild Crohn's disease is characterized by thickened, irregular mucosal folds, a coarse villous pattern of the mucosa, and aphthous ulcers (Fig. 6.14a).
- Chronic or severe inflammation causes further distortion and disruption of the plicae circularis and enlargement, deepening, and coalescence of the aphthous ulcerations. The ulcers are classically located on the mesenteric border of the lumen, which is fairly specific to Crohn's disease.
- Advanced disease is characterized by transmural inflammation that can be seen radiographically as deep, long linear ulcers, sawtoothed nodularity of the mucosa, cobblestoning, severe thickening of the bowel wall, luminal narrowing, and the complications of the disease.
- Inflammation of the submucosa and subserosa allows for the deep, knife-like clefts to burrow into the bowel wall. These clefts and fissures begin to merge into a longitudinal and transverse network of ulcerations. Between the ulcers remain pieces

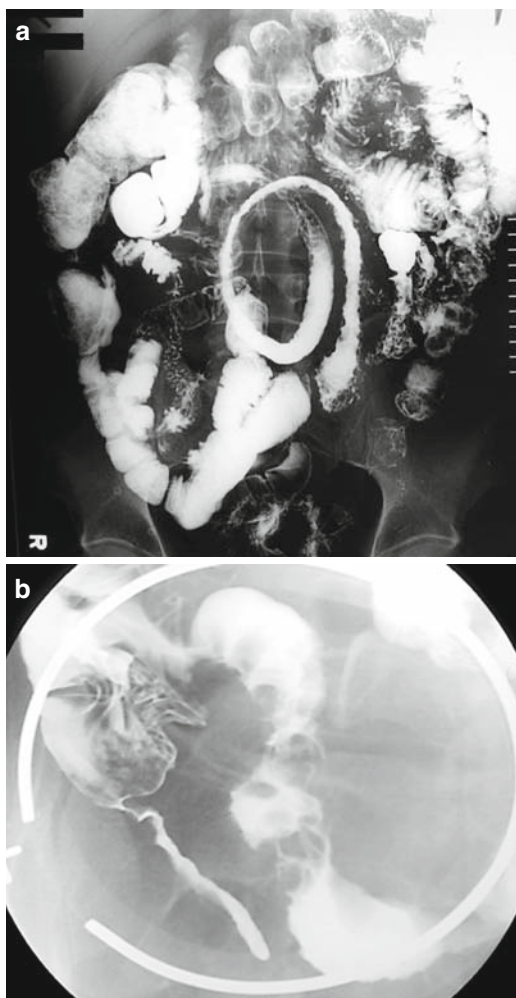


Fig. 6.14. (a) Small bowel series showing TI Crohn's disease strictures. (b) SBFT showing cobblestoning.

of relatively uninflamed mucosa. This produces a sharp, saw-tooth nodularity of the mucosal edge, and ultimately develops a cobblestone pattern (Fig. 6.14b). Barium fills the clefts and fissures and does not cling to the relatively spared mucosa in

between, which is the basis for the cobblestone pattern. As these islands of residual mucosa attempt to regenerate, they heap up and branch giving rise to pseudopolyps.

- Barium studies are more sensitive at identifying fistulas than endoscopy.

Small Bowel Obstruction

- When the diagnosis is uncertain and the clinical circumstances support further testing, contrast studies of the small bowel can be very useful.
- Specific indications for either SBFT or enteroclysis include equivocal plain films, unclear etiology, early postoperative obstructions, or when preoperative localization of the site of obstruction is important.
- Traditional SBFT is the preferred technique for assessing the presence of partial SBO.
- Lesions intrinsic to the small bowel can also be elucidated.
 - Primary adenocarcinomas of the small bowel are more common in the proximal bowel and occur with decreasing frequency more distal along the small intestine.
 - Carcinoid tumors typically occur in the terminal ileum and start as submucosal lesions.

C. Computed Tomography

- The benefit of cross-sectional imaging is the detailed imaging and resolution of the hollow viscus and solid organs. Accurate interpretation requires optimal opacification of the GI tract and vascular structures.
- If pelvic or rectal pathology is being evaluated, the contrast may also be administered per rectum at the time the scan is being performed.
- Intravenous (IV) contrast agents typically are iodinated so it is important to take a thorough history of allergies. The contrast is administered as a bolus at the time of the examination.
- CT scans are usually ordered for the staging of colorectal cancer, evaluation of abdominal complaints, and evaluation of postoperative complications.

Colorectal Cancer

- An abdominal and pelvic CT is the most common method for staging colorectal cancer before definitive surgical resection.
- The aims of the CT scan are to (1) evaluate the liver for distant metastatic disease, (2) evaluate for regional lymphadenopathy, especially in rectal cancer, where nodes may have been missed during a transrectal ultrasound, and (3) assess for the presence of intraperitoneal disease.
- CT is also used to follow colorectal cancer patients longitudinally for the development of recurrent disease. It is most effective when used to evaluate patients who have symptoms concerning for recurrent disease or have a rising carcinoembryonic antigen (CEA) level.
- There are no strong data to support its use in routine surveillance for detecting metastasis in the absence of symptoms or rising CEA.
- The majority of colorectal metastases are hypovascular and show up as hypodense lesions during the portal venous stage because the majority of metastatic lesions derive their blood supply from the arterial system. During the portal venous phase, contrast enhances the hepatic parenchyma and portal veins and the metastatic lesions do not enhance (Fig. 6.15).

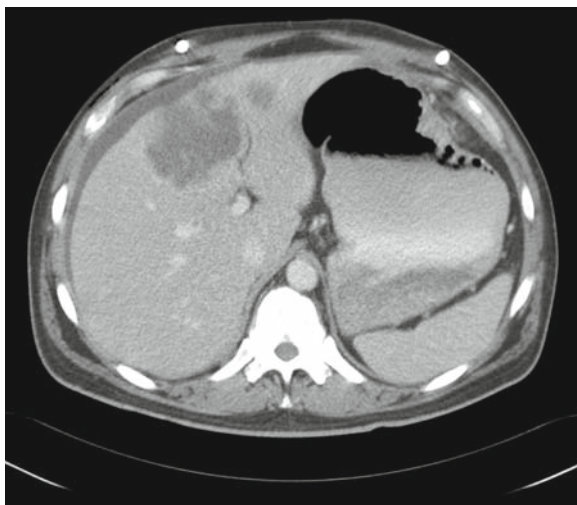


Fig. 6.15. CT scan showing liver metastasis.

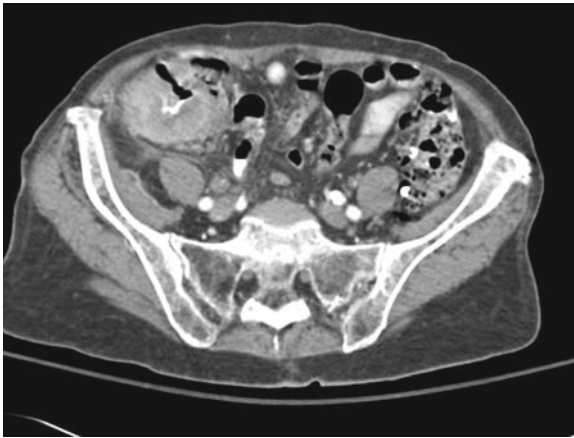


Fig. 6.16. CT scan showing primary lesion and adenopathy.

- Common liver lesions that need to be differentiated from colorectal metastasis include simple cysts, hepatic adenomas, primary liver tumors, hemangiomas, and focal nodular hyperplasia.
- Colorectal metastases typically are round, well-circumscribed lesions that are fairly homogeneous in density, which is consistent with solid tissue.
- The accuracy of CT for the detection and differentiation of liver lesions is greatest for lesions $>1\text{cm}$.
- Other advantages of the CT scans include the ability to detect regional adenopathy and to assess the relationship of the primary tumor to adjacent structures (Fig. 6.16).
- Typically, nodes $>1\text{cm}$ in size are concerning for metastatic disease.

Diverticulitis

- The most common CT findings associated with diverticulitis are pericolonic/mesenteric inflammation (98%), diverticula (84%), colonic wall thickening (70%), and abscess (47%).
- When the inflammatory response is centered on a portion of colon that is thickened ($>5\text{mm}$), the diagnosis of diverticulitis is confirmed.
- Often, the inflammatory process can be extensive, producing a phlegmon in the absence of an organized abscess (Fig. 6.17).

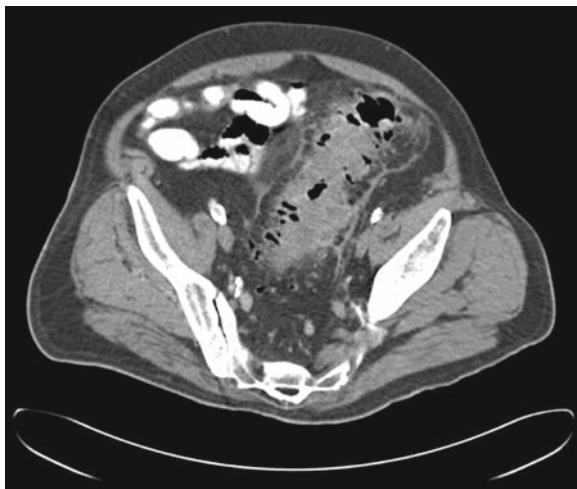


Fig. 6.17. CT scan showing uncomplicated diverticulitis.

- The presence or absence of diverticula does not impact the radiographic diagnosis.
- When the thickness of the colon wall is $>5\text{mm}$, it is considered abnormal. The wall thickening may be circumferential or just localized to the segment adjacent to the inflammation.
- Abscess formation is the most common complication of diverticulitis. An abscess appears as a fluid collection typically near the area of diverticulitis (Fig. 6.18).
- Often, oral and IV contrast are needed to distinguish an abscess from adjacent loops of intestine. When the surrounding loops of bowel are able to be opacified with oral contrast and the rim of the abscess is enhanced with IV contrast, the accuracy of diagnosing an abscess is maximized.
- A colovesical fistula is the most common fistula associated with diverticulitis, and a CT scan is the most sensitive for the detection of such a fistula.
- Air within a bladder that has not been instrumented is diagnostic for an enterovesical fistula (Fig. 6.19).

Crohn's Disease

- A CT scan is used in two general situations during the management of Crohn's disease. First, a CT is obtained to evaluate a

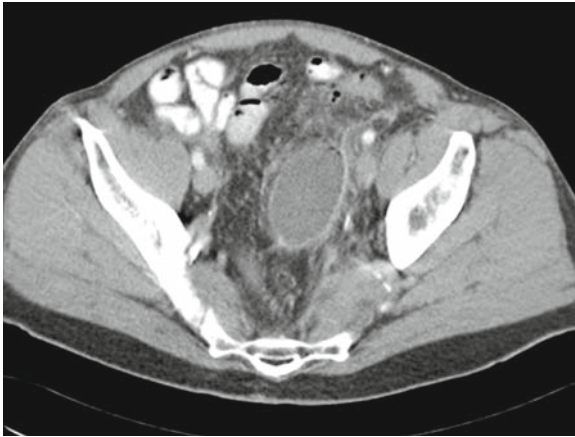


Fig. 6.18. CT scan showing a diverticular abscess.

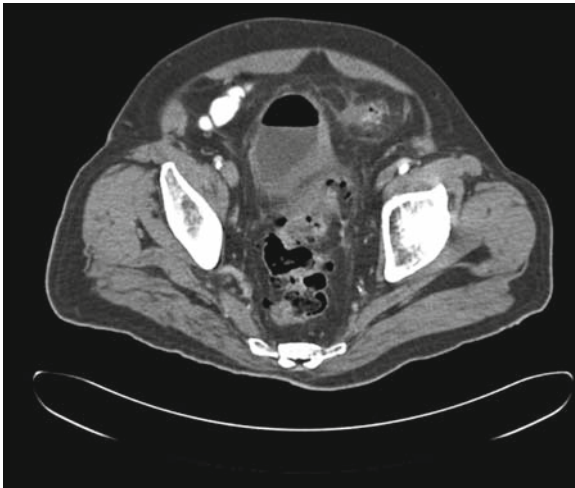


Fig. 6.19. CT scan demonstrating a colovesical fistula.

patient with new onset abdominal pain, and findings consistent with Crohn's disease are incidentally found. Second, a CT scan is obtained to evaluate for complications in a patient that is known to have Crohn's disease.

- The most common findings associated with Crohn's disease are bowel wall thickening, peri-intestinal inflammation, and



Fig. 6.20. (a) CT scan showing Terminal Ileum (TI) Crohn's disease with abscess. (b) CT scan showing Crohn's colitis.

regional lymphadenopathy. The bowel wall can reach 11–13mm in thickness, which can be either symmetric or asymmetric.

- The halo sign, which is a low-attenuation ring caused by submucosal deposition of fat between the enhancing mucosa and bowel musculature, is a common finding associated with Crohn's disease (Fig. 6.20a).
- There are many features that help to distinguish Crohn's disease from other inflammatory diseases of the GI tract.
 - First, Crohn's disease is usually found to involve the terminal ileum and right colon.
 - Second, there may be skip lesions. For example, multiple segments of small bowel and/or colon may be involved (Fig. 6.20b).
 - Third, the presence of mesenteric adenopathy suggests Crohn's or UC, but is not specific for IBD.

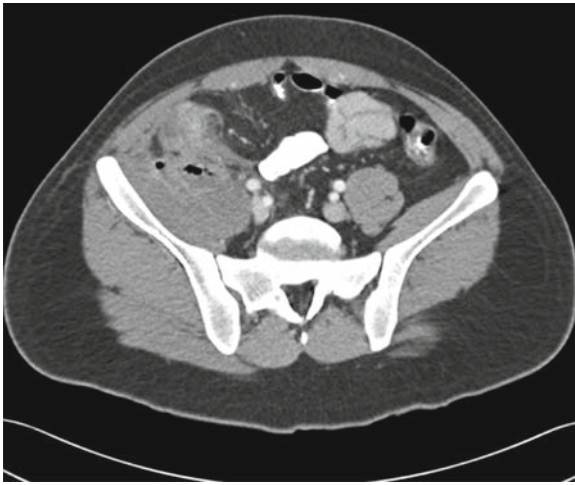


Fig. 6.21. CT scan showing a psoas abscess related to Crohn's disease.

- Finally, the presence of complications such as abscess, fistula, or perforation points to a diagnosis of Crohn's disease.
- Abscesses can be located between intestinal loops, within the mesentery, in the psoas muscle, pelvic sidewall, and subcutaneous tissues (Fig. 6.21).
- Fistulas from the diseased segment of bowel to the bladder, skin, vagina, or normal bowel can also be delineated on CT.

Small Bowel Obstruction

- CT has the advantages of being able to identify the site of obstruction, cause of obstruction, and it can provide information regarding vascular compromise of the bowel.
- Indications when a CT scan is particularly helpful include (1) a patient with no prior surgery, (2) a patient with equivocal plain films and an uncertain diagnosis, and (3) a patient with known intraabdominal pathology such as Crohn's disease or cancer.
- Oral contrast is not always necessary and should be avoided in patients with a high-grade or complete bowel obstruction. The intraluminal fluid often distends the bowel and acts as a natural contrast agent.
- The low-density intestinal fluid also extenuates the enhancement of the bowel wall after the administration of IV contrast, which can provide information regarding the flow of blood of the bowel.

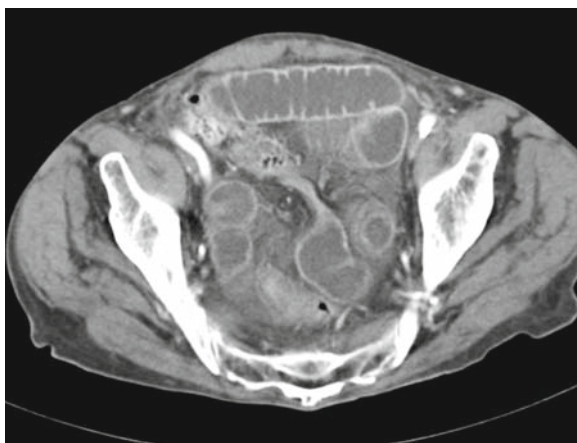


Fig. 6.22. CT scan showing a simple SBO.

- The diagnostic criteria of an SBO by CT are based on the presence of dilated proximal small bowel ($>2.5\text{cm}$) and collapsed distal bowel. When a transition between dilated and collapsed bowel is identified, then the diagnosis is confirmed (Fig. 6.22).
- But when a transition point is not identified, it is difficult to distinguish between an SBO and adynamic ileus.
- The presence of “small bowel feces,” which is gas bubbles mixed within particulate matter, in the dilated bowel is a reliable indicator of an SBO.
- When there is a sharp transition from dilated to decompressed bowel in the absence of other findings, this is highly suggestive of an SBO secondary to adhesions.
- CT does an excellent job identifying hernias such as inguinal, umbilical, incisional, or more of the atypical types. Often these hernias contain bowel but not all are obstructing. Clues indicating obstruction include dilate bowel going into the hernia and collapsed bowel exiting the hernia, oral contrast proximal to the hernia and no contrast distal to the hernia, and a localized inflammatory process surrounding the hernia, particularly in the subcutaneous tissues (Fig. 6.23).
- Another common extrinsic cause of obstruction is recurrent cancer. A CT scan is often able to demonstrate a mass at the site of obstruction and may also provide evidence of more widespread peritoneal disease.

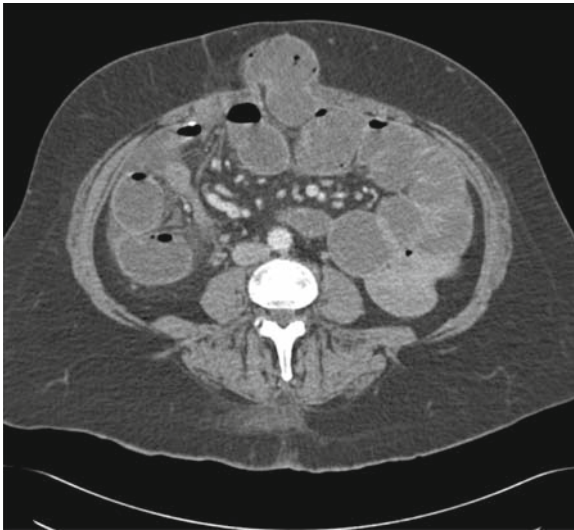


Fig. 6.23. CT scan showing an incarcerated hernia.

- Thickened, congested bowel with increased attenuation at the site of obstruction associated with engorgement of the mesenteric vasculature is concerning for strangulation.
- Other findings of ischemia include lack of enhancement after IV contrast administration or the presence of ascites.
- The presence of pneumatosis and portal venous gas are the more ominous signs of intestinal ischemia.

Postoperative Evaluation

- It is typically used to evaluate a patient with abdominal pain, fevers, leukocytosis, or persistent ileus in the postoperative period.
- The yield of a CT scan is greatest when it is obtained 5 days or more after surgery. Before postoperative day 5, it is difficult to differentiate normal postoperative intraperitoneal free air or fluid from air or fluid that represents a leak from a hollow viscus or infected fluid.
- Findings highly suggestive of an anastomotic leak include an inappropriate volume of free air or fluid in the abdomen.
- The presence of extraluminal oral contrast confirms a perforation of a hollow viscus.

- The presence of localized fluid and air around an anastomosis are concerning for a leak but must be taken in context to the postoperative period and the condition of the patient.
- Water-soluble enemas are more sensitive than a CT with rectal contrast at detecting a colorectal anastomotic leak.
- An abscess is defined as an organized fluid collection with or without air that has an enhancing rim.
- CT is very good at distinguishing between an ileus and a mechanical bowel obstruction, which is an important distinction in the perioperative period.

Other Colitides

- The CT findings are very similar for all inflammatory processes of the colon. However, their clinical presentations are different, so combining the presenting signs and symptoms with the distribution of CT findings will usually lead to the correct diagnosis.
- Ischemic colitis is the most common vascular abnormality of the colon.
- The colitis may be segmental or diffuse, typically occurring in the watershed areas of the right colon, splenic flexure, and rectosigmoid. CT findings consist of thickened, edematous colon in these areas (Fig. 6.24). The typical “thumbprinting” in the colonic mucosa can be seen on CT scan as well as plain films.

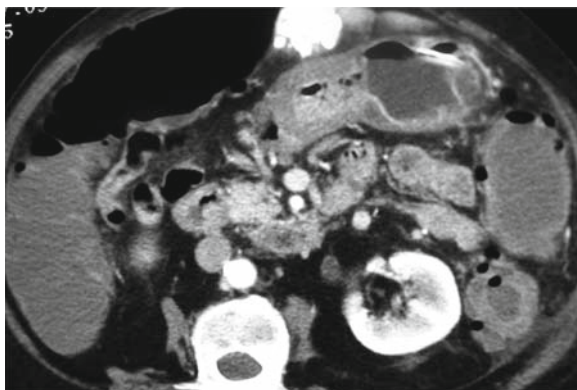


Fig. 6.24. CT scan of ischemic colitis.



Fig. 6.25. CT scan of pseudomembranous colitis.

- The presence of pancolitis also tends to suggest pseudomembranous colitis versus other colitides (Fig. 6.25).

D. Radionuclide Imaging

- Radionuclide imaging studies base their imaging on physiology rather than anatomy, and have a wide spectrum of use in clinical medicine.
- Radionuclide imaging studies are widely used in the diagnosis of lower GI bleeding. The principle is that the intravascular tracer will be extravasated into the bowel lumen during active bleeding.
- Technetium ^{99m}Tc is the radionuclide used in bleeding scans. This radiopharmaceutical can label colloid or red blood cells for scanning purposes.

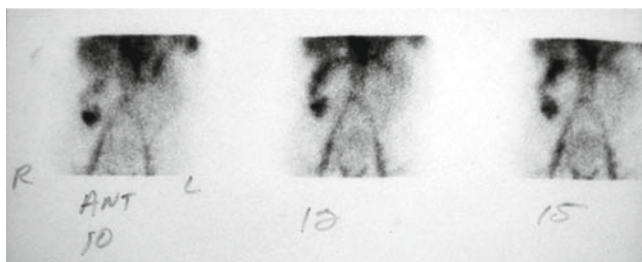


Fig. 6.26. ^{99m}Tc -tagged red blood cell study shows early blood pool activity within the ascending colon in this patient with bleeding after a recent polypectomy.

- Most centers prefer to use tagged red blood cells because lower GI bleeds are characteristically intermittent and the opportunity to identify the active bleeding sight lasts only a few minutes with labeled colloid.
- Focal areas of increased activity identified within the lumen of the bowel indicate that active bleeding occurred during this acquisition period (Fig. 6.26). A positive scan may localize the region of bowel that contains the bleeding site, but may not accurately localize the specific site, if the bleeding is slow or intermittent.
- Bleeding scans have greater prognostic value than diagnostic value when the tracer is only seen on delayed images.
- The accuracy for localizing the actual bleeding site increases if the extravasation of tracer is identified within the first 15–30min. The longer it takes the tracer to accumulate, the less likely the bleeding site will be accurately identified by angiography.
- Bleeding scans are more sensitive than angiograms in the detection of lower GI bleeding. The required rates of bleeding for detection are lower for bleeding scans (0.1–0.2mL/min) than for angiograms (0.5mL/min). The early (within 3min) detection of intraluminal tracer indicates a high likelihood of successful arteriographic localization of the bleeding site. For this reason, some interventional radiologists require a positive scan before performing angiography.
- If the patient is hemodynamically unstable and rapidly bleeding, some centers may prefer to go directly to arteriograms because the time involved in pretest preparation for tagged red blood scans may be too lengthy.

E. Arteriography

- The arteriogram is a useful diagnostic and therapeutic modality in the treatment of active lower GI bleeding. If a radionuclide scan is performed and localizes the site of bleeding, a selective angiogram can then be performed.
- For bleeding localized to the left colon on tagged RBC study, the inferior mesenteric artery is selected first. The superior mesenteric artery is selected first for those bleeds that occur in the right colon. If the bleeding site is not identified after injection of both the superior and inferior mesenteric arteries, a celiac run is performed looking for an upper intestinal bleeding source.
- Active bleeding can be diagnosed by the accumulation of contrast in the arterial phase that persists through the venous phase (Fig. 6.27).
- Bleeding needs to occur at a higher rate for a positive angiogram (0.5mL/min) than for nuclear imaging (0.1–0.2mL/min).
- Diverticulosis and vascular ectasias are presumed to be the leading cause of lower GI bleeding in most patients. Diverticular bleeds appear as a blush of contrast contained within a

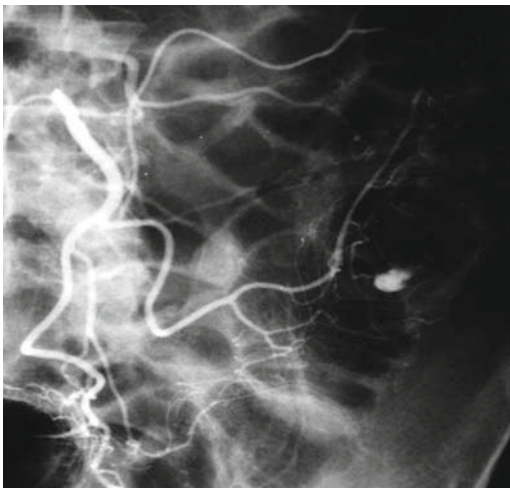


Fig. 6.27. Mesenteric angiogram shows pooling of contrast in the sigmoid colon in this patient with surgically proven diverticular bleeding.

diverticulum. Vascular ectasias often occur in the right colon and appear as small vascular clusters, a blush in the wall of the colon and early opacification of a draining vein.

- Postpolypectomy bleeding has been diagnosed and treated with angiography. A rapid blush of dye occurs at the site of bleeding and often stops with direct infusion of vasopressin or embolization (Fig. 6.28).
- Acute mesenteric ischemia is one of the most common intestinal disease processes for which arteriography is used for diagnosis and treatment.
- Acute mesenteric ischemia can be either nonocclusive or occlusive. The typical early angiographic images show diffuse vasoconstriction of mesenteric arterial branches and decreased parenchymal vascularity (Fig. 6.29).
- The diagnostic percutaneous catheter can be used to treat the mesenteric phase of constriction with IV glucagon or intraarterial infusion of the papaverine in an intensive care unit setting.
- An arteriogram is the most useful diagnostic examination for patients in whom one has a high clinical suspicion of acute occlusive mesenteric ischemia.
- A superior mesenteric artery embolus typically lodges just proximal or distal to the take off of the middle colic artery and is seen as a meniscus at the site of occlusion and blockage of contrast (Fig. 6.30).

F. CT Colonography

- CT colonography is rapidly developing as a noninvasive total colonic examination for the detection of colon polyps and cancers.
- This technique uses volumetric data acquired by helical CT scanners and workstations which use two- and three-dimensional images to evaluate data.
- Although the colon is evaluated in a noninvasive way, a bowel preparation is still required the day before the examination to eliminate formed fecal matter. Air insufflation is done via a small tube placed within the rectum to distend the bowel and to minimize folds within the colonic wall.

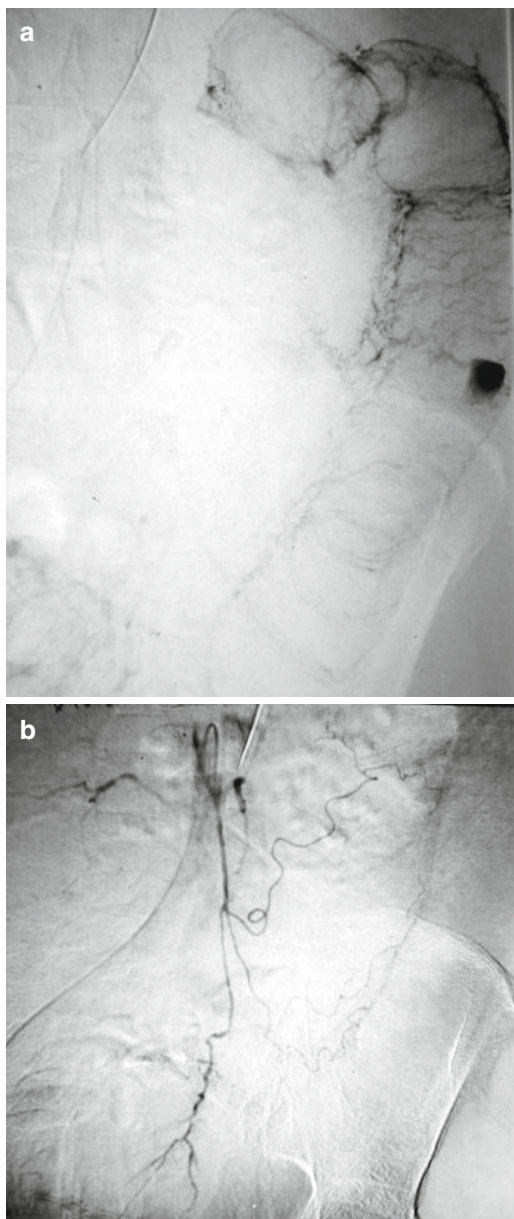


Fig. 6.28. Mesenteric angiogram shows extravasation of contrast A indicating an acute bleed that was successfully treated after infusion of pitressin B.



Fig. 6.29. Mesenteric angiogram shows vasoconstriction and pruning of the superior mesenteric artery and its branches in this patient who presented with mesenteric ischemia secondary to severe hypotension.

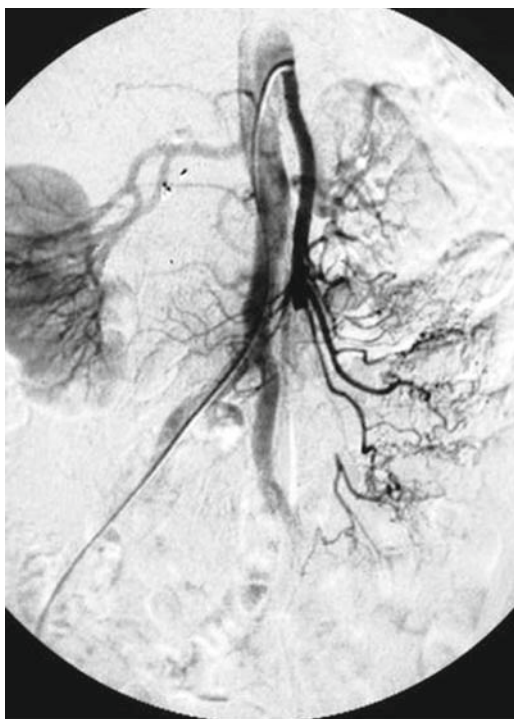


Fig. 6.30. Mesenteric angiogram shows a large filling defect within the proximal superior mesenteric artery consistent with an embolism in this patient with ischemic bowel.

- Several studies have compared CT colonography to colonoscopy for high- and low-risk patients. The sensitivity of this technique per individual patient ranges from 75 to 100% and the specificity ranges from 72 to 100%.
- In randomized, controlled trials, the specificity is greater for polyps larger than 1cm than for polyps larger than 5mm.
- The main limitation of CT colonography has been distinguishing polypoid tissue from fecal matter and the detection of flat lesions.
- Currently, most centers are using CT colonography for those patients who have had incomplete colonoscopies or who cannot undergo colonoscopy for medical reasons.

G. Positron Emission Tomography (PET)

- This technique uses [18F] 2-fluoro-2-deoxy-D-glucose (FDG) which is a radiopharmaceutical glucose analog to measure increased glucose uptake and metabolism in rapidly dividing cells. Malignant and other rapidly dividing cells that have a high metabolic rate will take up FDG for use as a glucose substrate.
- The imaging technique of PET utilizes differences in uptake of FDG in malignant versus benign cells. The intracellular accumulation concentrates the radiopharmaceutical analog, which appears “bright” upon imaging (Fig. 6.31).
- FDG PET has been used to evaluate metastatic disease and to improve staging accuracy (Fig. 6.32). This technique images the whole body and is more sensitive than CT for the detection of hepatic and extrahepatic colorectal cancer metastases and the detection of local recurrence. The reported sensitivities for PET detection of liver metastases range from 89 to 95% and for extrahepatic metastases 87–92%.
- The use of FDG PET versus CT or MRI is based on the premise that functional differences in tumor appear before size changes.
- A positive FDG PET scan in the setting of no inflammation would indicate a local recurrence of a rectal cancer.
- Furthermore, detection of small extrapelvic metastases is more accurate using FDG PET than CT or MRI.
- Thus, the use of FDG PET for staging or recurrent cancers may help plan or avoid expensive and possibly more morbid surgical procedures.

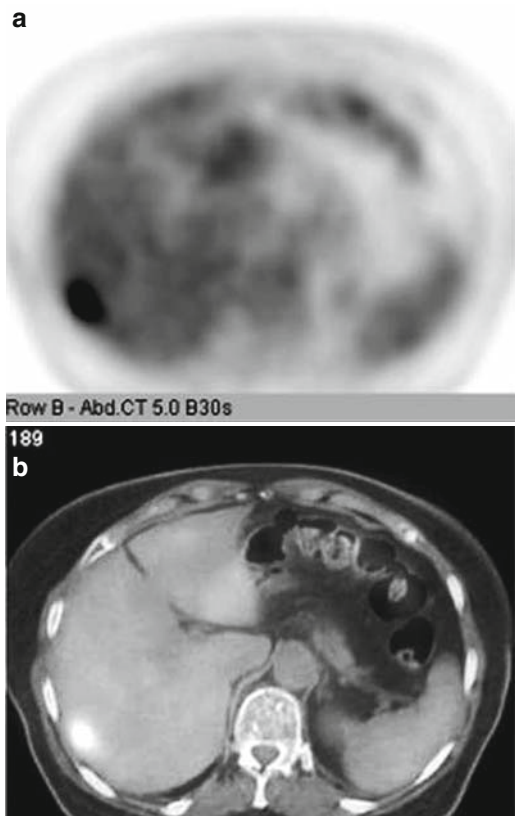


Fig. 6.31. Axial attenuation corrected PET image A and fusion PET CT image B show an area of intense FDG uptake in the right hepatic lobe consistent with hepatic metastatic disease in this patient with cecal adenocarcinoma.

- The cellular glucose metabolism is also increased in inflammation as the increased uptake of FDG can be seen in leukocytes and macrophages. Inflammatory processes such as diverticulitis and pneumonia can lead to false-positive readings thus making it imperative to correlate positive PET findings with the clinical picture and conventional radiologic evaluation.
- Detection of metastatic disease is dependent on the size and degree of metabolic activity. Limited spatial resolution may lead to false-negative readings for small, <1-cm lesions.

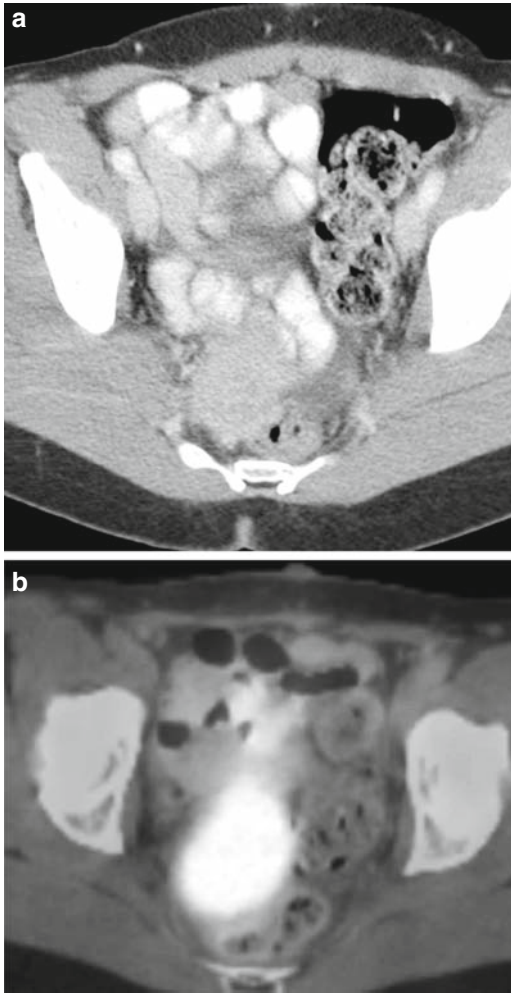


Fig. 6.32. CT scan in a patient who had prior rectal resection for carcinoma shows soft tissue mass in the surgical bed of the perirectal fat A. Follow-up PET examination B shows intense FDG uptake within this soft tissue mass consistent with recurrence.

- Adenocarcinomas with a high mucinous content may result in false-negative readings because of the low cellularity of these cancers.

- The routine use of FDG PET for primary cancers is more problematic. Although the risks and radiation doses are low and the technique is noninvasive, the cost per scan is very high.
- Current CMS (HCFA) recommendations for reimbursed PET imaging in colorectal cancer include (1) evaluation of patients with a question of recurrent disease as indicated by rising CEA, (2) evaluation of resectability, and (3) evaluation of patients with locally advanced disease to determine unresectability on the basis of metastasis when the operation is a large otherwise debilitating procedure.

H. Magnetic Resonance Imaging (MRI)

- This technique relies on the difference in tissue contrast or signal intensity. High signal intensity appears white on the image whereas low signal intensity is dark.
- T^1 and T^2 refer to specific tissue properties that describe the way protons behave after being excited by a radiofrequency pulse in a strong magnetic field.
- The specific parameters chosen to acquire an image on an MR magnetic system determine whether an image is T^1 or T^2 weighted.
- Structures containing water appear black on T^1 -rated images and structures containing fluid (cysts or gallbladder) are white on T^2 -weighted images.
- Unlike CT scans, iodinated contrast is not used for the performance of these scans. The contrast agents that have been developed can be used in patients with renal insufficiencies, and those with iodinated contrast allergic reaction.
- The risk from MRI is attributed to the interaction between the strong magnetic field and certain implantable devices such as cardiac pacemakers, cerebral aneurysms clips, and cochlear implants.
- MRI has evolved to be better than CT for tissue characterization and evaluation of tissues planes within the pelvis.
- The layers of the bowel wall can be visualized easily for evaluation of rectal cancers.
- Contrast enhancement improves the correlation with histologic stage.
- MRI more accurately predicts the circumferential resection margin (Fig. 6.33).

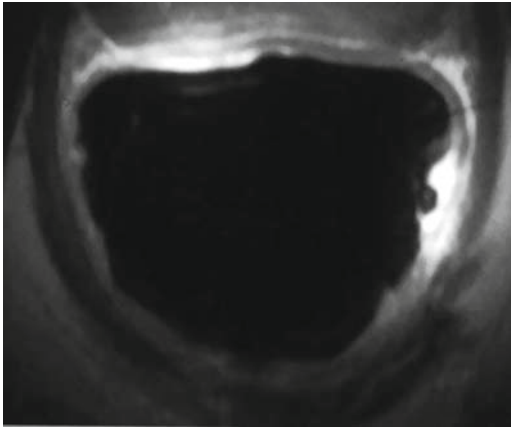


Fig. 6.33. Endorectal MRI examination shows an ulcerated plaque-like cancer arising from the mucosa and extending to the first muscular layer of the muscularis propria.

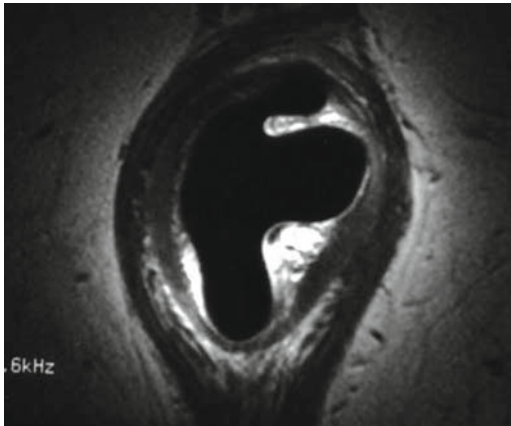


Fig. 6.34. Endoanal MRI image demonstrates a nondisrupted (normal) signal of the internal and external sphincter.

- The anal sphincter and pelvic anatomy have been imaged with MR using an internal coil (Fig. 6.34). The internal sphincter has higher signal intensity than the external sphincter. Pelvic muscle morphology, sphincter injuries, and abscesses can be identified.

7. Endoluminal Ultrasound

A. Introduction

- Endorectal ultrasound (ERUS) has evolved into the best imaging modality for accurate staging of rectal neoplasms. The accurate determination of tumor penetration depth and regional lymph node status has become critical to guiding subsequent treatment of rectal malignancies.
- In addition, endoanal ultrasound (EAUS) has become invaluable in the diagnostic workup of fecal incontinence and anorectal suppurative conditions.
- The goal of preoperatively staging the rectal lesion is an accurate evaluation of the primary tumor, which includes the depth of tumor penetration and an evaluation of regional lymph node disease.
- ERUS accomplishes these goals using an intraluminal high-frequency sonographic transducer via a handheld rotating probe to accurately image the rectal wall and adjacent structures. For this reason, ERUS has become the preferred method used to stage the patient with rectal cancer.

Equipment and Technique

- Equipment used for endoluminal ultrasonography includes a handheld endocavitary probe with rotating transducer which acquires a 360°- image.
- Because of its superior near-image clarity, the 10-MHz transducer is preferred.
- Rectal imaging requires a latex balloon covering the transducer for acoustic contact.

- The balloon is instilled with water allowing the ultrasound signals to easily pass through the water to image the rectum. The water instilled distends the rectum allowing the balloon to maintain contact with the rectal wall without separation, preventing any distortion of the image by the interposition of nonconductive air between the probe and the rectal wall.
- Patients receive one or two phosphosoda enemas to cleanse the rectum before examination.
- A digital rectal and proctoscopic examination is performed to assess the tumor size, appearance, location, and distance from the anal verge.
- A wide-bore ESI proctoscope (Electrosurgical Instrument Company, Rochester, NY) is inserted into the rectum to examine the rectum and lesion of interest. Optimally, the proctoscope is advanced proximal to the lesion to facilitate complete examination of the tumor by the transducer. The wide-bore ESI proctoscope permits passage of the ultrasound probe through the proctoscope to facilitate positioning of the probe above the lesion. This facilitates complete imaging of the lesion from its most proximal to distal extent as well as the proximal mesorectum, which may harbor involved lymph nodes.
- After correct positioning of the wide-bore ESI proctoscope, the ultrasound probe with latex balloon is lubricated and passed through the proctoscope to its full extent.
- The latex balloon is filled with 30–60 mL of water providing an optimal acoustic environment surrounding the rotating transducer.
- The evaluation of the lesion occurs on the basis of real-time imaging intermittently capturing still images that are representative of the lesion being studied.

Image Interpretation

- On most ERUS images, a series of five distinct layers can be identified in the rectal wall. They consist of three hyperechoic (white) layers separated by two hypoechoic (black) layers.
- It is this five-layer model that we continue to use today (Fig. 7.1). The five layers from the center to the periphery consist of the following:
 - First hyperechoic layer: Interface between the balloon and the rectal mucosal surface

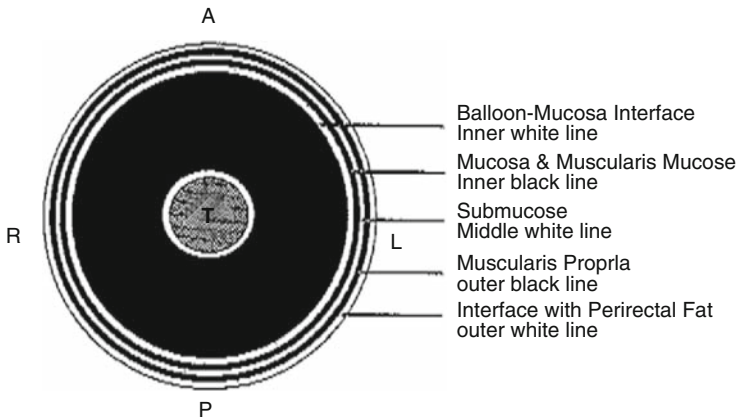


Fig. 7.1. Five-layer anatomic model of an ERUS scan. Three hyperechoic (*white*) layers and two hypoechoic (*black*) layers are visualized. A anterior; L left; P posterior; R right; T transducer.

- Second hypoechoic layer: Mucosa and muscularis mucosa
- Third hyperechoic layer: Submucosa
- Fourth hypoechoic layer: Muscularis propria
- Fifth hyperechoic layer: Interface between the muscularis propria and perirectal fat
- Occasionally, a seven-ring model may be visualized when the muscularis propria is observed as two black rings separated by a white ring (Fig. 7.2). This model represents the inner circular and outer longitudinal muscle layers as hyperechoic (black) rings separated by a hypoechoic (white) interface.

Assessment of Rectal Neoplasms

Depth of Invasion

- Ultrasound staging classification (uTNM) is presented in Table 7.1. The depth of invasion is classified as follows: uT0 lesions are benign, noninvasive lesions confined to the mucosa; uT1 lesions indicate an invasive lesion confined to the mucosa and submucosa; uT2 lesions penetrate but are confined to the muscularis propria; uT3 lesions penetrate the entire bowel wall and invade the perirectal fat; and a uT4 lesions penetrate a contiguous organ (i.e., uterus, vagina, cervix, bladder, prostate, seminal vesicles) or the pelvic sidewall or sacrum.

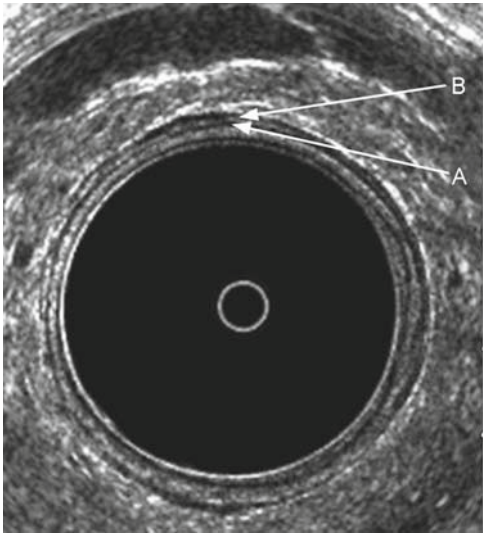


Fig. 7.2. This endorectal ultrasonography image depicts the typical five layers of the rectal wall. Seven layers are depicted anteriorly, where an interface can be seen between the inner circular (A) and outer longitudinal (B) muscle layers of the muscularis propria.

Table 7.1. Ultrasound staging classification (uTNM) for rectal cancer.

uT0	Noninvasive lesion confined to the mucosa
uT1	Tumor confined to the mucosa and submucosa
uT2	Tumor penetrates into but not through the muscularis propria
uT3	Tumor extends into the perirectal fat
uT4	Tumor involves an adjacent organ
uN0	No evidence of lymph node metastasis
uN1	Evidence of lymph node metastasis

uT0 Lesions

- uT0 lesions are benign, noninvasive lesions confined to the rectal mucosa. Sonographically, the mucosal layer (inner black band) is expanded with an intact submucosa (middle white, hyper-echoic line) (Fig. 7.3).
- The accuracy of ERUS is probably highest for T0 lesions.
- Because of the frequent misdiagnosis of rectal adenomas by biopsy and the subsequent finding of invasive cancer in the final pathologic specimen after transanal excision, Worrell et al. conducted

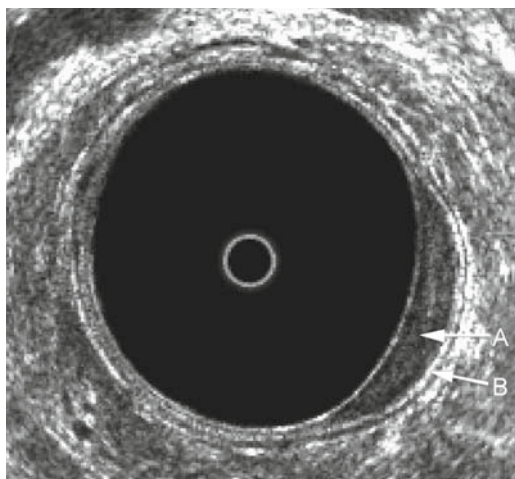


Fig. 7.3. This image demonstrates a benign uT0 lesion in the left posterolateral aspect of the rectum. There is an expansion of the inner black line that represents the mucosa (A), but the submucosa (B) is seen to be completely intact.

a systematic literature review to assess the utility of ERUS in the assessment of rectal villous adenomas comparing the diagnosis by biopsy alone with diagnosis by a combination of biopsy and ERUS. This meta-analysis revealed that, of 258 biopsy-negative rectal adenomas, 24% had focal carcinoma on final histopathology and that ERUS correctly detected the cancer in 81%.

uT1 Lesions

- uT1 lesions are early invasive cancers. uT1 lesions have invaded the mucosa and submucosa without penetrating into the muscularis propria.
- Sonographically this is characterized by an irregular middle white line (submucosa) without alteration of the outer black line (muscularis propria) (Fig. 7.4).
- Irregularities are indicated by a thickening or stippling of the submucosal layer but there must not be a distinct break in the submucosal layer. A distinct break in the submucosal (middle white line) layer indicates invasion of the muscularis propria, hence a T2 lesion.
- Local transanal excision is an acceptable treatment method for selected T1 lesions highlighting the need for accurate staging

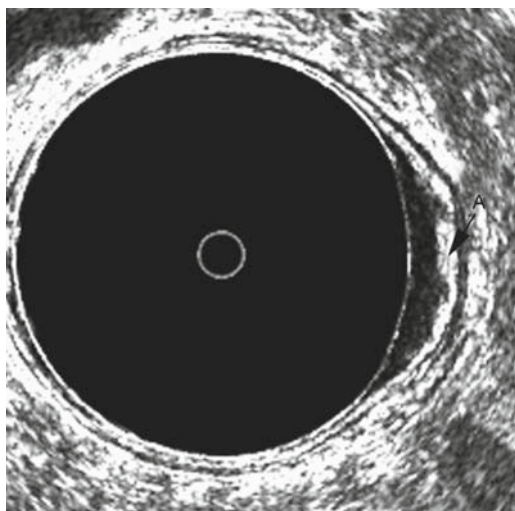


Fig. 7.4. This image depicts a uT1 cancer in the left lateral wall of the rectum. The middle white line or submucosa is irregular and somewhat thickened (A), but not completely disrupted.

of these cancers. Criteria for the use of local therapies to treat early rectal cancers have been described and include tumor size less than 4 cm, involvement less than one-third of the rectal circumference, location less than 8 cm from the anal verge, well- to moderately well-differentiated histology, absence of lymphatic or vascular invasion, and no involvement of perirectal lymph nodes.

uT2 Lesions

- uT2 lesions penetrate into the muscularis propria (second hypoechoic, black line) but are confined to the rectal wall.
- Sonographically the hallmark finding is a distinct break in the submucosal layer. Characteristically, there is an expansion of the muscularis propria (outer black line) but the interface between the muscularis propria and the perirectal fat (the outermost white line) remains intact.
- “Deep” uT2 lesions have significant expansion of the muscularis propria (outer black line) and may appear to scallop the outer aspect of the muscularis propria but preserve the interface with the perirectal fat. An example of a uT2 lesion is illustrated in Fig. 7.5.

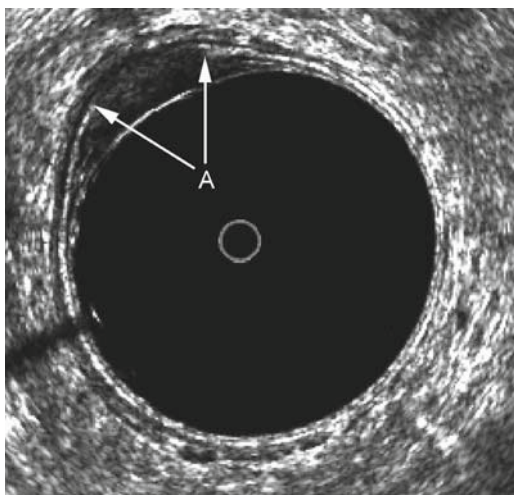


Fig. 7.5. A uT2 lesion is identified in this image, in the right anterior location. The hallmark of a uT2 lesion, as seen on endorectal ultrasonography, is the distinct break (A) in the submucosa (the *middle white line*) as seen in this image.

uT3 Lesions

- uT3 lesions penetrate the full thickness of the muscularis propria and into the perirectal fat. Contiguous structures are not involved.
- The sonographic appearance reveals disruption of the submucosa, thickening of the muscularis propria, and disruption of the outer hyperechoic, white line indicating penetration into the perirectal fat (Fig. 7.6).
- The recognition of perirectal fat invasion is an important determinant in the preoperative evaluation of the rectal cancer patient. Because of the high incidence of lymph node metastases (30–50%), local therapy cannot be recommended for these patients, who are usually candidates for preoperative radiation and chemotherapy followed by surgery.

uT4 Lesions

- uT4 lesions are locally invasive into contiguous structures such as the uterus, vagina, cervix, bladder, prostate and seminal vesicles, or involve the pelvic sidewall or sacrum. They are clinically fixed and tethered.

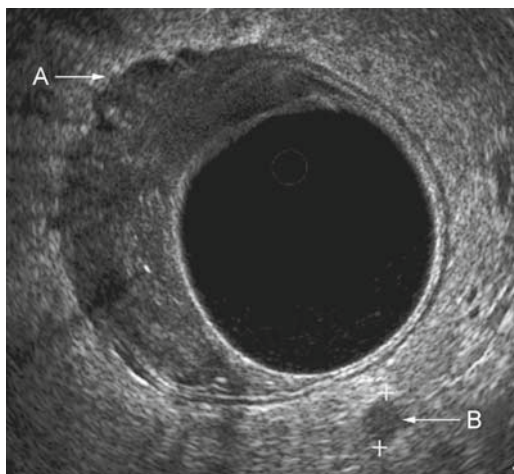


Fig. 7.6. This image demonstrates a uT3N1 lesion. The tumor disrupts all layers of the rectal wall, with extensions evident into the perirectal fat (A). A lymph node (B) is identified in the left posterior location within the mesorectum.

- Sonographically, there is loss of the normal hyperechoic interface between the tumor and adjacent organ (Fig. 7.7).
- Therapy of a T4 lesion usually requires preoperative radiation and chemotherapy followed by surgical resection of the rectal cancer and involved adjacent organ. The overall prognosis is poor, with less than half of patients resected for cure.
- Preoperative radiation and chemoradiation therapy can shrink the tumor for increased resectability and decreased local recurrence. ERUS provides the means to preoperatively identify those lesions with T4 involvement to adequately plan the patient's treatment.

Nodal Involvement

- ERUS is able to detect metastatic lymph nodes in the mesorectum. Unfortunately, the accuracy of detecting involved lymph nodes is less than the accuracy in determining the depth of invasion.
- The accuracy of ERUS in detecting lymph node metastases ranges from 50 to 88%.
- ERUS determination of metastatic lymph nodes is certainly more accurate than clinical (digital) evaluation as well as other imaging modalities including CT and conventional magnetic

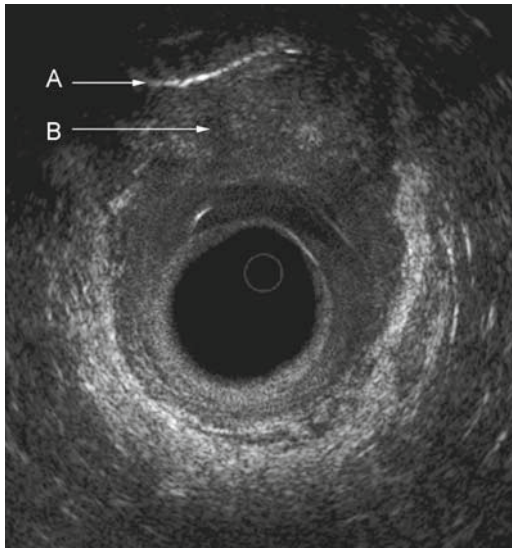


Fig. 7.7. This image identifies a T4 lesion in the distal rectum and upper anal canal extending to the vagina. The curved white line (A) seen anteriorly represents the examiner's finger in the vagina, and the hypoechoic anterior tumor (B) can be seen to extend into the vagina.

resonance imaging (MRI). However, phased array MRI and endorectal coil MRI are comparable to ERUS in lymph node assessment.

- Undetectable or benign-appearing lymph nodes are classified as uN0.
- Malignant-appearing lymph nodes are classified as uN1.
- Normal, nonenlarged lymph nodes are usually not detectable by ERUS.
- Inflamed, enlarged lymph nodes appear hyperechoic with irregular borders.
- Lymph nodes suspicious for malignancy include larger, round, hypoechoic lymph nodes with an irregular contour. ERUS findings consistent with metastatic lymph nodes are demonstrated in Fig. 7.8.
- Hypoechoic lymph nodes greater than 5 mm are highly suspicious for metastases. Involved lymph nodes are usually found adjacent to the primary tumor or within the proximal mesorectum.
- Statistically, the incidence of metastatic disease increases as lymph node size increases.

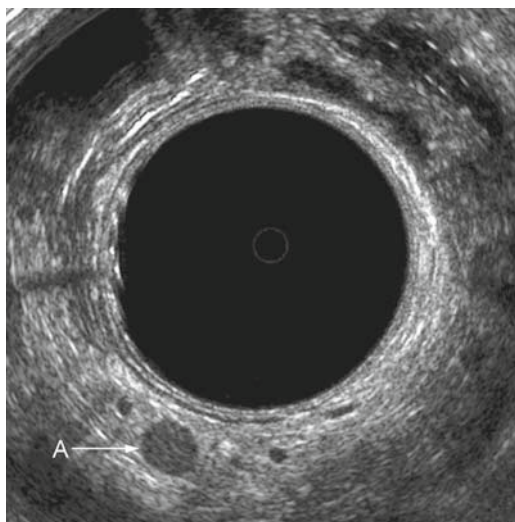


Fig. 7.8. This image demonstrates a typical metastatic lymph node (A), which is round and hypoechoic.

- Four nodal patterns are seen with differing probabilities of being involved with metastatic disease:
 - Nonvisible lymph nodes on ultrasound have a low probability of harboring lymph node metastases.
 - Hyperechoic lymph nodes with nonsharply delineated boundaries are more often benign resulting from inflammatory changes.
 - Hypoechoic lymph nodes larger than 5 mm are highly suggestive of lymph node metastases.
 - Mixed echogenic lymph nodes larger than 5 mm are difficult to classify but should be considered malignant.
- Accurate lymph node staging of rectal cancers by ERUS relies on the experience of the examiner.
- False-negative results are also problematic in interpreting nodal involvement on ERUS. Lymph nodes harboring micrometastases are difficult to detect. Grossly malignant lymph nodes may be present outside the range of the ultrasound probe and remain undetectable. This may be the case of lateral pelvic lymph nodes such as the obturator nodes as well as those within the mesorectum beyond the proximal extent of the rigid probe.

Accuracy of Ultrasound in the Diagnosis of Rectal Cancer

- The accuracy of ERUS for tumor depth of invasion has been reported in the range of 69–94% (Table 7.2).
- Overstaging has been reported in approximately 10% of patients and is believed to be the result of peritumoral inflammation beyond the leading edge of the tumor.
- Understaging for depth of wall invasion has been reported to be approximately 5% and is considerably more serious than overstaging because inadequate management may result.
- Detection of lymph node metastases with ERUS has been less accurate, ranging from 61% to 83% in reported series (Table 7.2).
- There is a significant learning curve associated with the performance and interpretation of ERUS. Accuracy rates have been demonstrated to improve significantly with experience.

Table 7.2. Accuracy of ERUS in the staging of rectal cancer.

Author	Year	n	Accuracy (%) T stage	Accuracy (%) N stage
Hildebrandt and Feifel	1985	25	92	n/a
Romano et al.	1985	23	87	n/a
Hildebrandt et al.	1986	76	88	74
Holdsworth et al.	1988	36	86	61
Beynon et al.	1989	100	93	83
Dershaw et al.	1990	32	75	72
Glaser et al.	1990	86	88	79
Glaser et al.	1990	110	94	80
Jochem et al.	1990	50	80	73
Milsom and Graffner	1990	52	83	83
Orrom et al.	1990	77	75	82
Katsura et al.	1992	112	92	n/a
Herzog et al.	1993	118	89	80
Sentovich et al.	1993	24	79	73
Deen et al.	1995	209	82	77
Adams et al.	1999	70	74	83
Garcia-Aguilar et al.	2002	545	69	64
Marusch et al.	2002	422	63	n/a
Manger and Stroh	2004	357	77	75

ERUS is highly operator dependent and thus accuracy is dependent on the experience and expertise of the examiner.

- Postbiopsy and postsurgical changes, hemorrhage, and bulky or pedunculated tumors can cause changes in the ultrasound image significantly affecting the accuracy of the ERUS interpretation.
- The accuracy of ERUS after neoadjuvant therapy is decreased. Radiation therapy can significantly downstage tumors and may in fact leave no residual tumor within the pathologic specimen. In fact, up to 24% of patients treated with preoperative radiation therapy have a complete pathologic response with no evidence of residual tumor.
- Radiation therapy can cause tissue edema and fibrosis of the rectal lesion making ERUS interpretation difficult. One cannot accurately distinguish radiation-induced changes from residual tumor. For these reasons, reevaluation of rectal lesions with ERUS after radiation therapy is inaccurate, unreliable, and not recommended.

Postoperative Follow-Up

- Even with newer adjuvant therapies available, surgical resection remains the best chance of cure for the patient with isolated local recurrence.
- When used in combination with a digital rectal examination and endoscopic surveillance, ERUS may significantly improve the sensitivity of detecting recurrent lesions. ERUS may improve the ability to diagnose recurrent neoplasm by as much as 30%.
- Although local recurrence occurs intraluminally at the anastomosis, locally recurrent tumor usually occurs from extrarectal tumor that invades through the rectum, often at the level of an anastomosis.
- Recurrent tumor appears as a circumscribed hypoechoic lesion in the para-anastomotic tissues with all or a portion of the rectal wall intact on the inner, luminal aspect (Fig. 7.9).
- Because ERUS cannot establish that a lesion is malignant with absolute certainty, a biopsy of suspicious lesions is recommended to confirm recurrent disease. Biopsies may be performed by ultrasound-guided biopsy or computed tomography scan-guided biopsy.

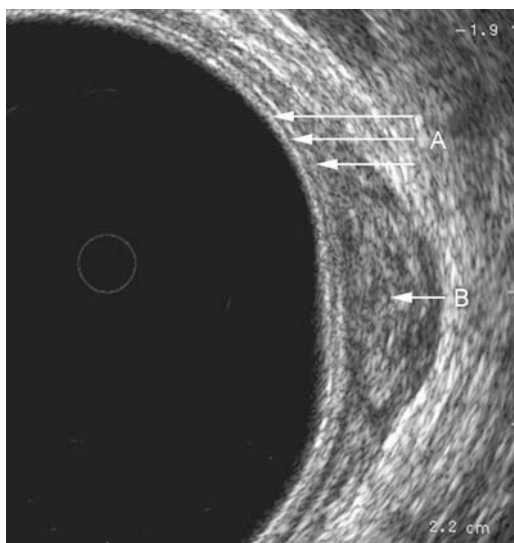


Fig. 7.9. This image demonstrates a recurrent rectal cancer. It is located in the left lateral rectal wall. Note the intact inner three lines (A) on the ultrasound image, indicating no involvement of the mucosa or submucosa but an obvious abnormality at the level of the muscularis propria (B), representing the recurrence.

B. Endoanal Ultrasound

- EAUS is useful in the evaluation of the anal canal in both benign and malignant disease.
- The anal sphincter anatomy can be clearly identified detecting abnormalities in the external and/or internal sphincter.
- EAUS is routinely used in the evaluation of fecal incontinence and may be particularly useful in the evaluation of complex perianal abscesses and fistulas.
- EAUS is also useful in the evaluation of anal canal neoplasms accurately staging these lesions.

Equipment and Technique

- The equipment used for EAUS is similar to that used for ERUS.
- In place of the latex balloon, a translucent plastic cap (B-K type WA0453) is placed over the transducer to maintain contact

with the anal canal. The plastic cap is again filled with water to provide the acoustic medium.

- The examination technique for EAUS is similar to that of ERUS.
- Certain instances of complex anorectal sepsis may be painful and require examination under anesthesia to adequately image the patient with EAUS.

Image Interpretation

- Normal anal canal anatomy is well visualized with EAUS.
- The ultrasonographic anatomy of the anal canal is generally divided into three levels: the upper, mid, and distal anal canal. Each level has a different appearance on EAUS.
- The upper anal canal is illustrated in Fig. 7.10. The puborectalis is an important landmark delineating the upper anal canal. The puborectalis is imaged as a horseshoe-shaped mixed-echogenic structure forming the lateral and posterior portion of the upper anal canal.
- The mid anal canal is illustrated in Fig. 7.11. Within the mid anal canal, the internal anal sphincter is represented by a hypoechoic band surrounded by the hyperechoic external anal sphincter. Between the transducer and the internal anal sphincter is an additional hyperechoic ring of variable thickness representing the epithelial, hemorrhoidal, and submucosal tissues.
- Perineal body measurements can be made at the level of the mid anal canal (Fig. 7.12).
- With the probe positioned within the mid anal canal, the right index finger is placed within the vagina against the rectovaginal septum and ultrasound probe. The distance between the hyperechoic ultrasound reflection of the finger and the inner aspect of the internal anal sphincter may be measured and represents the perineal body thickness.
- Normal measurements for perineal body thickness range from 10 to 15 mm, with a lower limit of normal considered to be approximately 8 mm. This measurement is useful in the evaluation of women with fecal incontinence from anterior sphincter defects.
- The distal anal canal is illustrated in Fig. 7.13. The distal anal canal is defined as the point where the internal anal sphincter is no longer seen. Only the hyperechoic external anal sphincter and surrounding soft tissues are visualized.

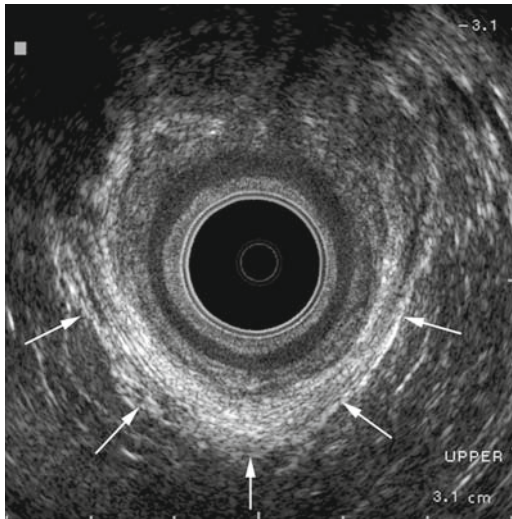


Fig. 7.10. This image represents the ultrasound appearance of the upper anal canal at the level of the puborectalis, which can be seen as the hyperechoic U-shaped structure seen posteriorly and laterally (*arrows*) in this image.

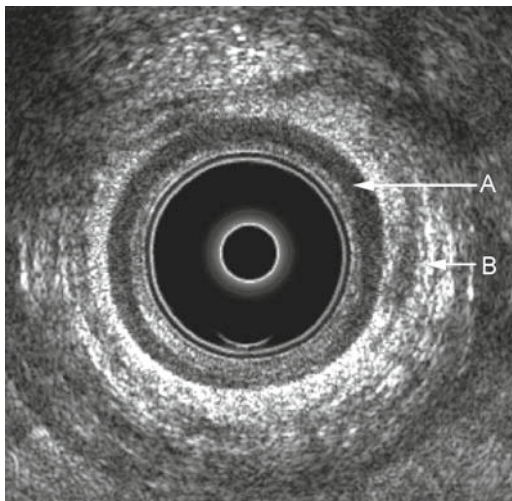


Fig. 7.11. This image depicts the characteristic appearance of the mid anal canal. The circular hypoechoic structure represents the internal anal sphincter (A), surrounded by the thicker hyperechoic circumferential external anal sphincter (B).

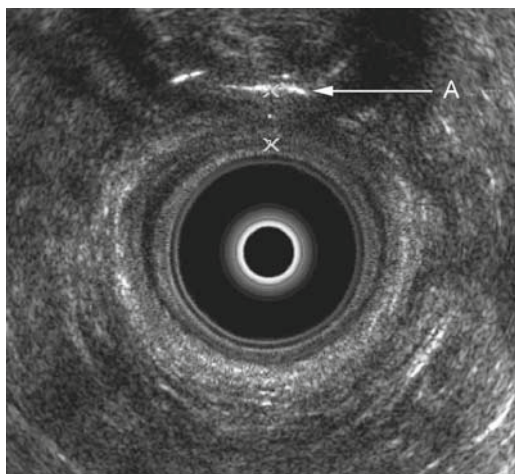


Fig. 7.12. This image depicts the technique used to measure the anterior perineal body in a female patient. The examiner's finger is placed in the vagina, and the hyperechoic curvilinear structure (A) seen anteriorly delineates the examiner's finger. The two crosshatches between the examiner's finger and the transducer measure the thickness of the perineal body in this intact sphincter at the mid anal canal level.

Evaluation of Fecal Incontinence

- EAUS has an important role in the evaluation of fecal incontinence, accurately delineating anal sphincter anatomy. Causes of anal sphincter defects include obstetric injuries, anorectal surgeries, traumatic injuries, and congenital abnormalities.
- Fecal incontinence is eight times more frequent in women, the most common cause being obstetric trauma leading to injury of the anal sphincter muscles or traction neuropathy involving the pudendal nerve.
- Although anal sphincter injury identified during delivery does not lead to significant deterioration in sphincter function immediately, it is suspected to lead to fecal incontinence in approximately 40% of women in long-term follow-up despite primary sphincter repair.
- Patients may also develop delayed symptoms of incontinence several years after an unrecognized sphincter injury.

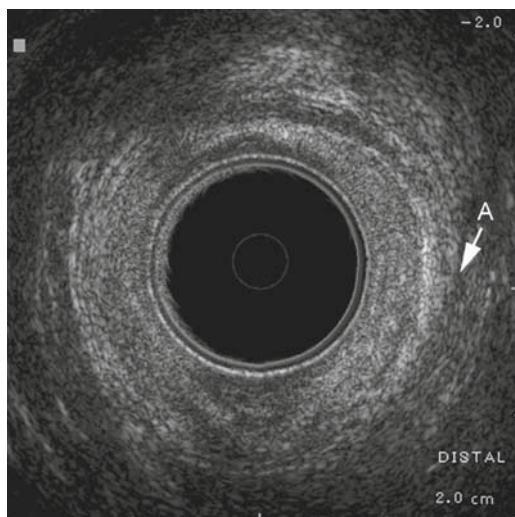


Fig. 7.13. This image represents the distal anal canal below the inferior level of the internal sphincter, where only the hyperechoic circumferential fibers of the superficial external anal sphincter (A) are imaged.

- The introduction of EAUS has led to the recognition of unsuspected sphincter defects in asymptomatic, continent women thought to have normal perineums.
- Traumatic sphincter disruption can frequently be associated with a subsequent rectovaginal fistula. These patients may be anally continent but have symptoms of fecal incontinence associated with the fistula. Because these patients may have an unrecognized anal sphincter defect, all patients with rectovaginal fistula should undergo preoperative evaluation for occult sphincter defects by EAUS.
- Local tissues are inadequate for endorectal advancement flap repairs in patients with anal sphincter defects and these patients should be treated by sphincteroplasty with levatoroplasty.
- EAUS has become the best modality to accurately demonstrate the anatomy of the anal canal as well as anal sphincter defects that contribute to fecal incontinence.
- Defects in the external anal sphincter usually appear hypoechoic, although some may appear hyperechoic or demonstrate mixed echogenicity.

- Defects of the internal anal sphincter are represented by the lack of segment of the hypoechoic band of internal sphincter muscle. There is usually associated contralateral thickening of the hypoechoic internal anal sphincter.
- With complete sphincter disruption, EAUS demonstrates the ends of the internal and external anal sphincter widely separated and bridged with intervening scar tissue of variable echogenicity (Fig. 7.14).
- An examining digit used to measure the perineal body distance in the mid anal canal can accentuate an anterior sphincter defect, helping to identify a sphincter injury (Fig.7.15).
- EAUS provides an objective means to evaluate the anal sphincter mechanism in patients with postoperative fecal incontinence after anorectal surgery such as hemorrhoidectomy, fistulotomy, lateral internal sphincterotomy, or sphincteroplasty.
- The identification of localized sphincter defects is important in the evaluation of the incontinent patient, because these defects may be amenable to surgical repair.

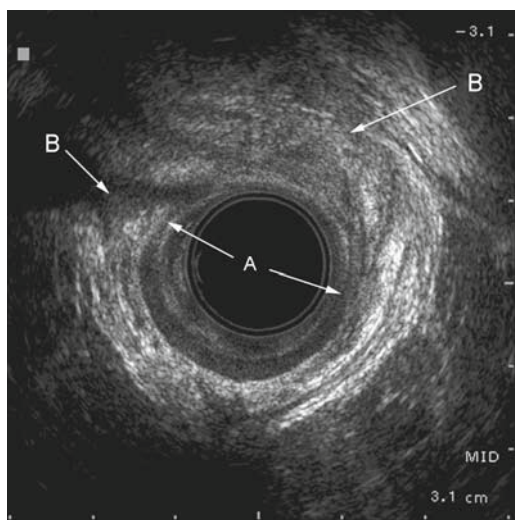


Fig. 7.14. This image depicts a complete anterior sphincter disruption in a female patient. The hypoechoic internal anal sphincter can be seen completely disrupted in its anterior location (A arrows). Similarly, the hyperechoic external anal sphincter is completely disrupted anteriorly (B arrows).

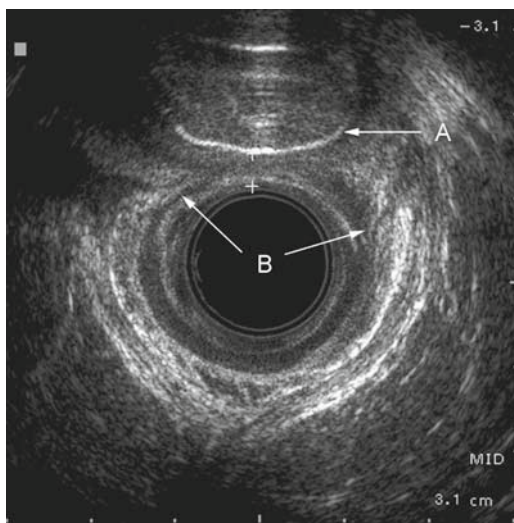


Fig. 7.15. This image demonstrates the measurement of the anterior perineal body in this patient with an anterior sphincter disruption. The curvilinear hyper-echoic structure (A) is the examiner's finger in the vagina. This technique can often accentuate the defect (B) seen in the internal anal sphincter and the external anal sphincter, and documents the decreased thickness of the anterior sphincter and perineal body.

- Anorectal manometry and pudendal nerve terminal motor latency testing are complementary but do not definitively correlate with a surgically correctable defect.
- EAUS remains the definitive test that can identify a surgically correctable defect in a symptomatic patient with fecal incontinence.

Evaluation of Perianal Sepsis and Fistula-in-Ano

- Occasionally, an abscess is strongly suspected on clinical grounds but is not readily identified on physical examination. In these situations, an EAUS may be useful in the evaluation of perianal or perirectal abscesses. EAUS can be helpful to localize an obscure abscess to plan the appropriate surgical intervention.
- Often, clinical examination of perianal or perirectal abscesses is quite painful and examination under anesthesia is required. Because the ultrasound equipment is portable, the EAUS

examination can be performed in the operating room while the patient is anesthetized.

- Abscesses appear as hypoechoic areas often surrounded by a hyperechoic border.
- In patients with perianal Crohn's disease, EAUS may be useful in distinguishing discrete abscesses that require surgical drainage from inflammation that requires medical treatment.
- The use of EAUS has also been evaluated in patients with ileoanal pouch anastomosis and can be helpful in demonstrating pouch pathology including inflammation, abscesses, and fistulas.
- Use of EAUS can be helpful in identification of fistulous communications in patients with complex and recurrent fistula-in-ano. Fistula tracts are generally hypoechoic defects that can be followed to identify direction and extent. The anatomic details of the fistula tract can be delineated in relation to the anal sphincter. The EAUS examination should include the anal canal and distal rectum to search for the presence of high blind tracts. Hydrogen peroxide has been used to enhance the imaging of complex fistula. Hydrogen peroxide causes a release of oxygen, accentuating the fistula and appears as a brightly hyperechoic image on the ultrasound image. The technique increases the identification of the internal opening to greater than 90%. An example of a fistula-in-ano with hydrogen peroxide enhancement is demonstrated in Fig. 7.16.

Anal Canal Neoplasms

- Endoanal ultrasonography images the normal anal canal and associated pathologies quite well. EAUS can have an important role in the evaluation of benign and malignant anal canal neoplasms.
- Benign neoplasms such as lipomas and leiomyomas can be demonstrated along with their relationship to adjacent anal canal structures. Lesions within the anal canal appear as hypoechoic areas. Tissue diagnosis may be obtained with ultrasound-directed needle biopsies when desired.
- Anal canal malignancies evaluated by EAUS include leiomyosarcomas, malignant melanomas, anal canal adenocarcinomas, and squamous cell carcinomas.
- Squamous cell or epidermoid carcinoma of the anal canal are the most common anal canal malignancy. EAUS can be used in

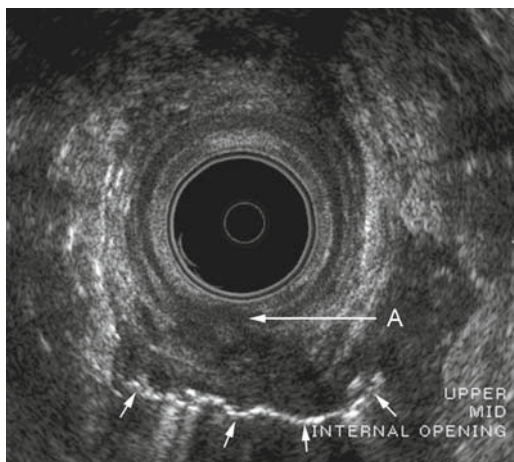


Fig. 7.16. This image depicts a fistula-in-ano that has been enhanced by the introduction of hydrogen peroxide. The hyperechoic features posteriorly represent the hydrogen peroxide within the fistula tract (*short arrows*). There is an obvious hypoechoic defect in the internal anal sphincter in the midline posteriorly (A), representing the internal fistula opening. The hypoechoic horseshoe tract can be seen extending toward the patient's left.

the initial evaluation to stage the lesion as well as in follow-up for patients with squamous cell carcinoma of the anal canal.

- Because squamous cell carcinomas of the anus are primarily treated nonoperatively with combined chemoradiation therapy, it is desirable to have an accurate method of staging to assess response to multimodality therapy.
- Although clinical (digital) examination is important in the assessment of squamous cell carcinoma of the anus, EAUS is more precise in accurately measuring the actual size and circumferential involvement of the lesion. EAUS staging (uTNM) of anal cancers corresponds to the TNM [UICC (International Union Against Cancer)] staging (Table 7.3).
- The extent of sphincter involvement can be determined and other staging systems stage these lesions based on depth of invasion. One such staging system is depicted in Table 7.4).

Three-Dimensional Ultrasound

- Three-dimensional ultrasound allows for multiplanar imaging of both the rectum and the anal canal.

Table 7.3. Ultrasound staging classification (uTNM) for anal canal cancer.

<i>Primary tumor (T)</i>	
Tx	Primary tumor cannot be assessed
T0	No evidence of primary tumor
Tis	Carcinoma in situ
T1	Tumor 2 cm or less in greatest dimension
T2	Tumor more than 2 cm but no more than 5 cm in greatest dimension
T3	Tumor more than 5 cm in greatest dimension
T4	Tumor of any size that invades an adjacent organ(s), e.g., vagina, urethra, bladder (involvement of the sphincter muscle(s) alone is not classified as T4)
<i>Regional lymph nodes (N)</i>	
Nx	Regional lymph nodes cannot be assessed
N0	No regional lymph node metastasis
N1	Metastasis in perirectal lymph node(s)
N2	Metastasis in unilateral internal iliac and/or inguinal lymph node(s)
N3	Metastasis in perirectal and inguinal lymph nodes and/or bilateral internal iliac and/or inguinal lymph nodes
<i>Distant metastasis</i>	
Mx	Distant metastasis cannot be assessed
M0	No distant metastasis
M1	Distant metastasis

Table 7.4. Ultrasound staging classification by depth of invasion (uTNM) for anal canal cancer.

uT1	Tumor confined to the submucosa
uT2a	Tumor invades only the internal anal sphincter
uT2b	Tumor penetrates into the external anal sphincter
uT3	Tumor invades through the sphincter complex and into the perianal tissues
uT4	Tumor invades adjacent structures

- Three-dimensional ultrasound can be used to assess anal fistulous tracts, to evaluate anal sphincter injury, as well as to stage both rectal and anal tumors.
- Comparison of standard two-dimensional ultrasound with 3D-ERUS and endorectal MRI and reported an accuracy for depth of wall invasion by rectal cancer of 84, 88, and 91, respectively.

- The accuracy of 3D-ERUS for predicting lymph node status was 84.8% compared with 66.7% for conventional ERUS.
- Three-dimensional EAUS has also been applied to benign anal disorders such as anal sphincter injury and anal fistula assessment.

8. Preoperative Management: Risk Assessment, Medical Evaluation, and Bowel Preparation

A. Perioperative Risk Assessment Scoring Systems

- Risks related to surgery are a function of many factors. Patient-related factors include the underlying disease processes and the patient's physical ability to tolerate the physiologic stress related to the surgical procedure. Increasing amounts of data now show that risk is also affected by the volume of a procedure performed at the medical institution, but perhaps most importantly by the experience, training, and volume of surgery performed by the individual surgeon.
- Scoring systems assess the patients' risk for morbidity and mortality as a result of anesthesia and surgery. These systems generally use data acquired during pre-hospital and in-hospital care, and some supplement this with components measuring operative severity.
- Some classification systems are designed to allow comparison of results between institutions and surgeons, whereas others are designed to distinguish patients who subsequently will have postoperative adverse events from those who will not.
- A primary aim of a scoring system is the evaluation of therapeutic benefit, i.e., the ratio of the relative harm and the relative benefit that are likely to follow a specific operation for a specific illness, whether in a specific patient, institution, or health system. Parameters that are useful in this evaluation include the natural history of the disease process, and the urgency of a specific procedure.

Table 8.1. Perioperative scoring systems (references in text).

Physiologic scores	Preoperative scores
APACHE (I and II)	ASA grading
E-PASS	Goldman cardiac risk index
ISS/TRISS	Hospital prognostic index
POSSUM	Prognostic nutritional index
P-POSSUM	Pulmonary complication risk
SAPS	
Sepsis score	
Sickness score	
Therapeutic intervention score	

- Age may have an influence on operative risk, as many elderly patients require concurrent management of multiple organ degenerative diseases. Elderly patients often tolerate operations well but tolerate complications poorly, hence prediction of the potential morbidity of an operation is particularly important in this group of patients.
- Scoring systems also provide a useful means of comparing outcomes from different institutions and patient groups by correcting for different comorbidities.
- Various scoring systems have been developed in an effort to quantify the risk of a patient from disease or intervention, and systems can be classified as preoperative or physiologic (Table 8.1).

Risk Assessment for Complications from Specific Organ Systems

Cardiac Risk

Goldman Cardiac Risk

- The Goldman risk model is probably the best-accepted model for pure determination of cardiac risk for surgery. Point scores are assigned to each of nine clinical factors and patients are divided into four risk classes based on the total point score (Table 8.2).
- This is an important score because it reminds clinicians of the major cardiac risk factors in noncardiac surgery. Although the system is easy to use and utilizes relative weighting of risk factors, it was designed in the 1970s, and has not been updated for modern practice in anesthesia, medicine, or surgery.

Table 8.2. Goldman cardiac risk index.

Cardiac risk event		Points	
Myocardial infarction within 6 months		10	
Age >70 years		5	
S3 gallop or jugular venous distension		11	
Important aortic valve stenosis		3	
Rhythm other than sinus, or sinus rhythm and atrial premature contractions on last preoperative electrocardiogram		7	
More than five premature ventricular contractions per minute anytime before surgery		7	
Poor general medical status		3	
Intraperitoneal, intrathoracic, or aortic operation		3	
Emergency operation		4	
Class	Points	Life-threatening complication risk (%)	Cardiac death risk (%)
I	0–5	0.7	0.2
II	6–12	5	2
III	13–25	11	2
IV	26	22	56

Respiratory Risk

Pulmonary Complication Risk

- Findings on respiratory examination, chest X-ray, Goldman's cardiac risk index, and the Charlson comorbidity index have been used for predicting respiratory complications.

Risk Assessment for Postoperative Morbidity and Mortality

American Society of Anesthesiologists Classification

- The American Society of Anesthesiologists (ASA) classification system (Table 8.3) was initially developed to alert anesthesiologists to preexisting diseases. Because of the ease of use,

Table 8.3. ASA classification scheme.

I	Normal healthy patient
II	Mild systemic disease
III	Severe, noncapacitating systemic disease
IV	Incapacitating systemic disease, threatening life
V	Moribund, not expected to survive 24 h
E	Emergency

and the fact that no tests are required, it has also been used to estimate operative risk.

- ASA class directly correlates with perioperative mortality and morbidity and also correlates significantly with perioperative variables such as intraoperative blood loss, duration of postoperative ventilation, and duration of intensive care unit (ICU) stay.
- Disadvantages to using the ASA score are that the score awarded depends on the subjective clinical judgment of the attending anesthesiologist, and that the small numbers of groups available means there can be little meaningful comparison between different surgeons or institutions.

Prognostic Nutritional Index

- The prognostic nutritional index (PNI) was devised to predict complication risk based on mortality, and correlates with postoperative sepsis and death.
- The PNI uses four factors, namely, serum albumin level, serum transferrin level, triceps skinfold thickness, and cutaneous delayed-type hypersensitivity.
- Serum albumin level, serum transferrin level, and delayed hypersensitivity were the only accurate predictors of postoperative morbidity and mortality.
- In addition to predicting postoperative morbidity and mortality, PNI can be used for predicting patients who might need nutritional support in the perioperative period.

APACHE (Acute Physiology and Chronic Health Evaluation) Scoring Systems

- This score was initially designed primarily for patients in the ICU but has been used for the assessment of patients with severe

trauma, abdominal sepsis, postoperative enterocutaneous fistulas, acute pancreatitis, and to predict postoperative outcome.

- The main disadvantage is that it is not independent of the effects of treatment, thus scoring for emergency patients being admitted to the ICU is best performed before surgical intervention. Other disadvantages are that it is relatively complex and does not take into consideration the nutritional status of the patient or cardiology findings that add to operative risk.
- APACHE scores also do not take into account the extent of surgery. The APACHE III has been proposed more recently, but it is also very complex for routine use.

Possum

- The POSSUM (Physiological and Operative Severity Score for enUmeration of Mortality and morbidity) was developed by multivariate discriminant analysis of retrospective and prospective data, primarily to permit surgical audit for assessment of quality of care.
- It has been suggested that it works independent of geographical factors, and several publications have now come from the United States suggesting that it may also have a role in this health care system.
- POSSUM calculates expected death and expected morbidity rates based on 12 physiologic variables and six operative variables each of which are scored 1, 2, 4, or 8 (Table 8.4).

Table 8.4. Parameters for calculation of the POSSUM score.

Physiologic parameters	Operative parameters
Age (years)	Operative severity
Cardiac signs/chest X-ray	Multiple procedures
Respiratory signs/chest X-ray	Total blood loss (mL)
Pulse rate	Peritoneal soiling
Systolic blood pressure (mm Hg)	Presence of malignancy
Glasgow coma score	Mode of surgery
Hemoglobin (g/dL)	
White cell count ($\times 10^{12}/L$)	
Urea concentration (mmol/L)	
Na ⁺ and K ⁺ levels (mmol/L)	
Electrocardiogram	

- The major advantage is that it predicts both morbidity and mortality and has successfully been used for a comparative audit of performance among surgical units, hospitals, and countries.
- Disadvantages include that it does not take into account differences among surgeons, anesthesiologists, and operating time, all of which may influence outcome.
- Comparison of APACHE II with POSSUM showed that POSSUM is superior in predicting mortality in patients admitted to a high-dependency unit after general surgery.

Portsmouth Modification of POSSUM (P-POSSUM)

- One concern with POSSUM has been that it may overpredict mortality and morbidity rates by up to six times with a minimum mortality of 1.1%. P-POSSUM was therefore developed using a different mathematical formula to counter these disadvantages, with the minimum mortality score in P-POSSUM reduced to 0.2%.

Other Scoring Systems

- Various other scoring systems have also been developed primarily for assessment of critically ill patients in the ICU and for trauma and sepsis, and these are listed in Table 8.1.

Risk Assessment for Colorectal Disease

- Preoperative pulmonary and nutritional problems have been significant contributing factors in patients who died from sepsis after colon resection in the elderly. Others have suggested that age, congestive heart failure, hepatic, renal or pulmonary impairment, and extent of involvement by malignancy and postoperative complications were associated with greater mortality after colon surgery.
- Recently, POSSUM was found to allow a realistic comparison of performance of different units performing colorectal resection and also permit comparison of outcome after colorectal resection among different surgeons. POSSUM has also been reported in patients undergoing laparoscopic colectomy but even the P-POSSUM overpredicted mortality and morbidity.

B. Preoperative Medical Evaluation

- Young patients having minor surgery will require no assessment.
- Young patients having more significant surgery may require minor evaluation, whereas older patients having minor surgery may require a similar level of evaluation. Older patients, and those with more extensive comorbidities will require assessment and possible treatment before surgery.
- In a large prospective clinical-epidemiologic study, Arvidsson and colleagues found that a standardized assessment before surgery, by a combination of questionnaires, interview, physical examination, and laboratory screening identified a high proportion of patients who were likely to have an adverse event in the postoperative period.

Preadesthesia Interview

- Of the techniques available that are used in preoperative evaluation of patients, history taking is the most efficient and profitable.
- A preoperative questionnaire is suitable for patients undergoing daycare surgery, because most of these patients are at low risk.
- History taking should include information on the condition for which the procedure is being performed, history of surgical procedures (local procedures that may complicate surgery such as reoperative pelvic surgery, as well as general procedures that may complicate recovery such as prior splenectomy), and prior outcomes with intubation and anesthesia.
- Special consideration should be given to cardiopulmonary function, allergy, renal and hepatic function, bleeding tendency, and medication use.
- History of chronic medical conditions of the cardiorespiratory system and medications including dosage is important.
- Aspirin and other nonsteroidal anti-inflammatory drugs are best discontinued 1 week before surgery.
- Cessation of smoking 8 or more weeks before surgery helps optimize the mucociliary apparatus of the patient before surgery.
- Review of functional status of the patient, activities of daily living (ADL), and social support are also important, although

this primarily relates to longer term recovery, hospital stay, and likely discharge status from hospital, rather than direct perioperative morbidity and mortality.

- History taking for cardiac assessment has been reasonably well standardized. The primary factors to be considered are whether the patient has recent myocardial infarction, decompensated heart failure, unstable angina, symptomatic arrhythmias, or symptomatic valvular heart disease. In general, noninvasive testing is most effective in intermediate-risk patients, whereas invasive evaluation should be considered in those with multiple risk factors and ischemia on preoperative testing, because perioperative beta-blockade may be inadequate.
- Patients having extensive major surgery should meet the anesthesia service before surgery, for assessment as well as instruction about what will happen around the time of surgery.
- While this evaluation may be performed by nurse practitioners, patients with complex anesthetic histories or with major perioperative risk factors may require formal anesthetic assessment by a staff anesthesiologist.

Physical Examination

- General indicators of fitness of a patient for surgery include activities of daily living competence (ADL) and general mobility.

Preoperative Tests

- Preoperative tests serve to complement the history and physical examination in assessing the suitability of the patient for surgery. They have been used to assess levels of known disease, detect unsuspected but modifiable conditions that may be treated to reduce risk before surgery, or detect unsuspected conditions that may not be possible to treat, and therefore simply be baseline results before surgery.
- Many patients undergoing minor surgery need minimal investigation, even if they have chronic medical conditions. Review of current evidence indicates that routine laboratory tests are rarely helpful except in the monitoring of known disease states.
- Because reference intervals of most tests take the normal distribution and standard deviation of the population into consideration, cut-off points for normality are set such that patients

whose test results exceed the upper 2.5% of healthy individuals or are below the lower 2.5% of healthy individuals are said to have abnormal results. Thus, 5% of patients whose values are outside the reference range do not necessarily have disease and may be normal.

- Age, history of chronic heart disease, renal disease, emergency surgery, and type of operation are predictors of the risk of mortality.
- Guidelines for preoperative testing based on best available evidence are important for efficient resource utilization and prevention of undue surgical risk to the patient.
- Review of previous tests helps avoid duplication of tests and also helps identify potential problems.

Assessment of Specific Organ Systems

Cardiac Evaluation

- The detection of a rhythm other than sinus and the presence of premature atrial contractions and frequent premature ventricular contractions increase the risk of perioperative cardiac events.
- The American College of Cardiology (ACC) and American Heart Association (AHA) recommendations for preoperative cardiac evaluation consider the magnitude of the particular procedure being performed and patient factors that influence perioperative cardiac risk. History of coronary artery disease, cardiovascular procedures, and symptoms of angina or congestive heart failure are important.
- Patients without symptoms and with a normal cardiac stress test within 2 years or coronary artery bypass graft in the last 5 years, those who are clinically stable and underwent angioplasty 6 months to 5 years previously do not need any further assessment.
- Patients who had an angioplasty within 6 months and those having emergency surgery may need cardiac evaluation and angiography.
- Patients with intermediate risk and poor functional capacity may need stress testing.
- Assessment of left ventricular function by radionuclide scan or echocardiography is also indicated for patients in whom an impaired left ventricular function is suspected on clinical examination or radiology although the best test remains unclear.

- Cardiac interventions are generally only recommended for patients who would otherwise have benefited regardless of any unplanned noncardiac surgery. These recommendations have been reviewed and summarized by the ACC (www.acc.org/clinical/guidelines/perio/update/fig1.htm) and others.

Transfusion and Hematologic Evaluation

- Most patients with anemia tolerate operations well unless they have associated disease, and therefore anemia rarely changes management unless operative blood losses are expected to be great.
- Risk of thromboembolism and bleeding disorders can be assessed by a detailed history and by tests that measure coagulation factors (prothrombin and partial thromboplastin time) and that assess platelet count and function (bleeding time). Measures to reduce the risk of thromboembolism have been well documented and are part of the practice parameters available from the American Society of Colon and Rectal Surgeons (see Appendix 1).
- Blood grouping and cross-matching is obviously critical when planning major surgery in which significant blood losses may occur.
- An important consideration is to have a routine sample for blood type on file for patients undergoing major surgery, even if transfusion is not expected, and cross-matching would not usually take place. This allows a double level of security when urgent samples are sent if bleeding occurs during surgery.
- Anemic patients who are scheduled for elective surgery may be treated preoperatively by allogenic transfusion but consideration is also given to autologous donation, erythropoietin, intraoperative hemodilution with autotransfusion, or consideration of cell salvage techniques, which are still being evaluated in colorectal surgery.
- Preoperative autologous donation (PAD) has been criticized recently because of cost-ineffectiveness, large wastage of PAD units, and the potential for leaving patients more anemic after surgery than without PAD.

Renal Function Evaluation

- Age, hypertension, and diabetes may be indications for preoperative selective renal function testing.

- When indicated, measurement of serum electrolytes in the preoperative period helps in preventing perioperative problems. This is particularly true for serum potassium, because both hypokalemia and hyperkalemia may lead to cardiac conduction disturbances.
- Normal renal function is necessary for the excretion of the nondepolarizing muscle relaxants used for anesthesia and surgery.
- Renal function is also a consideration when choosing postoperative analgesic regimens including nonsteroidal medications such as Ketoralac.

Respiratory Tract Evaluation

- Patients with a history of chronic lung disease require careful assessment to minimize problems with anesthesia.
- Common pulmonary complications after surgery are atelectasis, pneumonia, and bronchitis and predisposing risk factors include cough, dyspnea, smoking, history of lung disease, obesity, and abdominal or thoracic surgery.
- Cessation of smoking 8 weeks before surgery is beneficial to the patient by allowing recovery of the mucociliary apparatus.
- Bronchodilators are helpful in patients with asthma and bronchitis
- Active pulmonary infection should be treated before surgery when possible.
- A Global Initiative for Chronic Obstructive Lung Disease (COLD) now recommends optimal treatment for COLD patients, and these treatments may need to be optimized before surgery.
- The incidence of abnormalities detected on a routine preoperative chest film is higher in elderly patients but most occur in patients with recognizable risk factors.
- Preoperative chest X-rays may be of value in ruling out metastases but do not otherwise have a major influence on the decision to operate or on the type of anesthesia, and abandonment of routine ordering of preoperative chest X-rays does not produce adverse patient effects.
- The Royal College of Radiologists recommended preoperative chest X-rays only for patients with acute respiratory symptoms, possible metastases, those with suspected or established cardiorespiratory disease without a chest X-ray in the preceding 12 months, and recent migrants from endemic countries.

- There are no well-established guidelines as to who requires pulmonary function testing. Such candidates may include patients with chronic pulmonary disease, wheezing or dyspnea on exertion, chest wall and spinal deformities, morbid obesity, heavy smokers with persistent cough, thoracic surgery, elderly patients (>70 years of age), and patients who are to undergo upper abdominal surgery.

Neurologic System

- The prevalence of occult cerebrovascular disease in elderly patients, who constitute a large proportion of patients requiring surgical attention, is a special concern.
- An asymptomatic carotid bruit indicates the presence of peripheral vascular disease and is an indication for further evaluation by duplex scanning. However, prophylactic endarterectomy is not indicated usually, because the increased risk of a perioperative stroke compared with the unselected population is small.
- Symptomatic disease that is untreated or undiagnosed before preoperative assessment should be assessed and treated before all but emergency surgery.
- Patients at high risk may be kept on aspirin products during the time of surgery to minimize their risk of stroke. Some may require endarterectomy before their scheduled surgery, although this is quite rare.

Metabolic and Endocrine System

- Assessment for diabetes, thyroid disorders, and other endocrine problems is an integral part of preoperative evaluation.
- Obesity is now so prevalent that fasting blood glucose in obese patients may identify cases of unexpected diabetes.
- Pregnancy may dictate reassessment of the indication for surgery, type of procedure being performed, and issues related to anesthesia.
- Patients on steroids may need extra dosage (stress coverage) in the perioperative period.
- Patients with known diabetes will need careful management of their blood sugar in the perioperative period, with standard recommendations for insulin and oral hypoglycemics.

Nutritional Assessment and Hepatic Function

- Nutritional measurements help in assessing the physiologic status and optimizing function of the patient with regard to immunology, fluid balance, and metabolic response to trauma and surgery.
- Patients at particular concern for malnutrition are those who have lost more than 10% of their body weight in the previous 6 months, and those with an albumin less than 3 g/dL.
- Malnourished patients have increased complications after surgery, although nutrition must be supplemented for at least 2 weeks before clinical outcome parameters are improved.
- Abnormal liver function may affect hemostatic mechanisms and drug metabolism, but is an unusual clinical problem.
- Hepatitis may pose increased risk to the medical personnel taking care of the patient.

Preoperative Assessment Specific for Colorectal Procedures

- For patients undergoing surgery for colorectal disorders, a previous major laparotomy may preclude laparoscopic surgery or indicate an increased risk of conversion to open surgery.
- Body habitus of the patient, mental status, visual acuity, and the presence of other disorders such as arthritis may determine the decision on whether a stoma is formed and its placement.
- Assessment of patients' attitudes toward surgery, addressing their concerns, and counseling them regarding what to expect during hospitalization forms an integral part of the preoperative evaluation.

Current Recommendations

- Tests that need to be performed include hemoglobin for evidence of anemia and as a baseline level for postoperative management.
- Renal and liver function tests are indicated only in patients with medical conditions or taking medication that would indicate these tests.
- Preoperative blood glucose determination is obtained in patients 45 years of age or older because current recommendations suggest that all patients older than 45 years ought to be screened for diabetes mellitus which increases perioperative risks.

- A urine pregnancy test ought to be considered for all women of childbearing age who are at risk for pregnancy.
- Coagulation tests are only indicated in patients on anticoagulation, with a family or personal history of bleeding disorder, or those with liver disease.
- Patients undergoing major surgery with a potential for blood loss should have a type and screen taken for filing in the laboratory, even if transfusion is not expected. This may help minimize the risk of later transfusion reaction.
- Electrocardiogram is indicated in male patients older than 40 years of age, females older than 50 years, and those with a history suggestive of cardiac disorders.
- Chest X-rays are performed on the basis of findings from the medical history or physical examination.
- As part of preoperative risk assessment, patients found to have medical conditions requiring further specific therapy before surgery should also be considered for more intensive medical supervision. This is important while in the hospital for their surgery, and also as part of their post-discharge follow-up.

C. Bowel Preparation

Method of Bowel Preparation

- Sodium phosphate
 - Lower-volume sodium phosphate preparations are now used routinely by many surgeons, but should be avoided in those with significant history of cardiac or renal dysfunction.
 - Another variation is sodium phosphate pills. These are taken as a series of 28–32 pills in split doses. This preparation also has concerns about hydration and electrolyte changes.
 - Any sodium phosphate preparation may cause hypocalcemia, hyperphosphatemia, and hypokalemia, leading to increased caution for their use in the elderly and those with renal dysfunction or taking certain blood pressure medication.

- Lavage Solutions
 - Solutions containing electrolytes and osmotic agents such as polyethelene glycol (PEG) or vitamin C are available. They are available in 4 L solutions or when combined with stilulant laxatives (bisacodyl) function well with 2 L of solution. Flavoring is available.
 - The solutions provide excellent cleansing and do not have many of the limitations of sodium phosphate. Compliance can be an issue in some patients and must be used with caution in the face of partial obstruction.

Whether to Use an MBP

- Over the last decade, several studies have suggested that a mechanical preparation may not be necessary.
- These studies, along with a series of randomized, controlled trials evaluating the use or avoidance of MBP, culminated in the recent publication of a Cochrane review on the subject (Table 8.5). Of the five randomized trials over the last decade, two showed higher anastomotic leak rates with bowel preparation. The remaining trials showed no difference.
- A Cochrane review was performed to analyze all randomized, controlled data and specifically to determine the effect of MBP on morbidity and mortality rates after elective colorectal surgery. Of patients with anastomoses, there were 576 MBP patients and 583 without MBP. There was no difference in anastomotic leak rates for low anterior resection (12.5 vs. 12%), or colonic surgery (1.2 vs. 6%) in patients with or without MBP. Overall anastomotic leak rates were significantly lower without MBP (5.5 vs. 2.9%; $P = 0.02$). Mortality, peritonitis, reoperation, wound infection, and extraabdominal complications were similar between groups. The results failed to support the hypothesis that MBP reduces complication rates, but because there was no a priori hypothesis that MBP might increase complication rates, this could not be stated.
- Avoidance of bowel preparation may not be possible for laparoscopic approaches for technical reasons, however, it may be considered for open surgery.

Table 8.5. Randomized, controlled trials and Cochrane report relating to preoperative mechanical bowel preparation (all results as MBP versus no MBP, %).

Author	Year	n	Anastomotic leak	Wound infection	Mortality
Brownson et al.	1992	179	11.9 VS. 1.5 ^A	5.8 VS. 7.5	0.0 VS. 0.0
Burke et al.	1994	169	3.8 VS. 4.6	4.9 VS. 3.4	2.4 VS. 0.0
Santos et al.	1994	149	10.0 VS. 5.0 ^A	24.0 VS. 10.0	0.0 VS. 0.0
Miettinen et al.	2000	267	4.0 VS. 2.0	4.0 VS. 2.0	0.0 VS. 0.0
Zmora et al.	2003	249	4.2 VS. 2.3	6.6 VS. 10.0	1.7 VS. 0.8
Guenga et al.	2003	1,159	5.5 VS. 2.9	7.4 VS. 5.7	0.6 VS. 0.0
Slim et al.	2004	1454	5.6 VS. 3.2 ^A	7.4 VS. 5.7	1.4 VS. 0.8

^aSignificant result

Bowel Preparation in Special Situations

- Obviously, patients with acute intestinal or colonic obstruction cannot be given a high-volume or cathartic bowel preparation. Other patients such as those with obstructive symptoms or a partial obstruction, may be suitable for milder preparative agents. Options include prescribing small volumes of magnesium citrate, sodium phosphate, or PEG or using dietary restriction over a longer period of time than overnight.

D. Prophylactic Antibiotic Usage (See Appendix 2)

- There was an evolution from using antibiotics for 5 days, down to the current situation in which they are generally given to cover the time of surgery itself, or used for 24 h maximum, unless a therapeutic course is indicated for clinical reasons.
- In the 17 trials comparing single-dose to multiple-dose (two or more doses) regimens, using the same antibiotic or combinations of antibiotics, no trial found a difference in wound infection rates, and a pooled analysis also showed no statistically significant difference. This single-dose policy also reduces risk of toxicity, costs, and possibility of developing resistance to the antibiotic used.
- Prophylactic antibiotics are ideally given within 1 h of the skin incision or at the time of anesthetic induction. If necessary they are repeated after 4–6 h to keep adequate circulating levels, particularly if there has been significant blood loss.
- Antibiotics need to cover Gram positive, negative, and anaerobic bacteria. Current choices usually include a second-generation cephalosporin with or without metronidazole, or an agent such as amoxicillin/clavulanic acid.
- In patients with penicillin allergy, ciprofloxacin or gentamicin, clindamycin, and metronidazole may be used.
- The use of oral neomycin and metronidazole with parenteral amikacin and metronidazole has been compared to intravenous antibiotics alone. The combination of oral and intravenous antibiotics reduced wound infection rates, and this was supported by a metaanalysis of prior literature.

E. Prophylaxis for Endocarditis and Prosthesis

- Patients undergoing invasive colorectal procedures are at varying risk for endocarditis and infection of prosthesis. The American Society of Colon and Rectal surgeons has published Practice Parameters (Appendix 2) to guide surgeons on selecting appropriate measures for at risk patients. For Additional discussion, see Chap. 9.

F. Communication with the Patient and Laying the Groundwork for Postoperative Recovery

- No preoperative visit is complete without providing information on expected postoperative outcomes.
- Patients should be advised of the surgery they will undergo, their expected milestones in recovery, and possible complications, including issues such as readmission, which may occur in 10% or more of these patients undergoing major abdominal surgery.

G. Conclusion

- Assessment of the patient undergoing surgery is of extreme importance in providing patients with a safe recovery from their operation. This permits stratification of patients into groups that require intensive, moderate, or minimal investigation or treatment before anesthesia.
- Tests to investigate patients should be used selectively based on increasingly accepted guidelines. Patients who need such evaluation and treatment before surgery should also be seen by the relevant medical specialty when in the hospital, and receive any necessary instructions for appropriate medical follow-up after their surgery.
- MBP continues to be used by the majority of colorectal surgeons, based on traditional practice patterns. Several randomized, controlled trials now suggest that this practice may be unnecessary.

- Patients undergoing bowel resection should be given antibiotic prophylaxis using one dose of parenteral broad-spectrum agents at the time of induction of anesthesia.

Appendix 1: Practice Parameters for the Prevention of Venous Thromboembolism

Risk Classification

Low-Risk Patients

The typical low-risk patient is one undergoing minor surgery who has one or no risk factors. No specific measures are recommended for patients at low risk other than early ambulation. Unprotected, these patients have a 2% chance of calf vein thrombosis and a negligible risk of pulmonary embolus.

Moderate-Risk Patients

The typical moderate-risk patient is older than 40 years of age, undergoing major abdominal surgery, with no other major risk factors. Moderate-risk patients can be treated with either intermittent pneumatic compression (IPC) alone or low-dose unfractionated heparin (LDUH). Moderate-risk patients have two risk factors. Unprotected, these patients have a 10–20% risk of calf vein thrombosis, and a 1–2% chance of a pulmonary embolism.

High-Risk Patients

High-risk patients have three or four risk factors. The typical high-risk patient is older than 40 years of age, is having major abdominal surgery, and harbors additional risk factors. High-risk patients can be treated with LDUH (bid or tid) or low-molecular-weight heparin (LMWH), although standard unfractionated heparin seems to be more cost effective. If heparin cannot or should not be used, IPC should be substituted. When heparin has not been started preoperatively, the patient should be reevaluated for postoperative heparin. Unprotected, these patients have a 20–40% risk of calf vein thrombosis and a 2–4% risk of pulmonary embolism.

Very High-Risk Patients

A high-risk patient is upgraded to a highest-risk category when certain additional risk factors are present. These include a history of thromboembolic events, hypercoagulable states, and possibly malignancy. Assuming no contraindication, highest-risk patients ideally should receive pharmacologic treatment such as LDUH (bid or tid) or LMWH. Untreated, these patients have a 40–80% risk of calf vein thrombosis and a 4–10% risk of pulmonary embolism (see Table 8.6).

Intuitively, there may be some advantage to a strategy of dual methods, i.e., combining intermittent pneumatic compression with heparin. Several investigators have suggested this. This has been shown to be efficacious for patients undergoing cardiac and hip replacement surgery, but thus far there are no published data for colon and rectal surgery patients.

Appendix 2: Practice Parameters for Antibiotic Prophylaxis to Prevent Infective Endocarditis or Infective Prosthesis During Colon and Rectal Endoscopy

These parameters are based in part on the recently updated recommendations made by the AHA and the previously published parameters developed by The American Society of Colon and Rectal Surgeons. According to the AHA, the risk for endocarditis is determined by the patient's pre-existing cardiac condition and the surgical procedure in question. The major changes in the new AHA guidelines are the following: (1) it was emphasized that invasive procedures are not the cause of most cases of endocarditis; (2) cardiac conditions are stratified by the potential outcome if endocarditis develops; (3) procedures causing bacteremia are more clearly specified; (4) an algorithm for antibiotic prophylaxis for patients with mitral valve prolapse was developed; (5) prophylactic regimens for oral or dental procedures were modified; and (6) prophylactic regimens for genitourinary and gastrointestinal procedures were simplified. The AHA considers lower gastrointestinal endoscopy to be a low-risk procedure for initiating problematic bacteremia, and The Standards Task Force concurs. The Task Force considered other direct and indirect support for the use of antibiotic prophylaxis in patients with cardiac or other prostheses. It is the consensus of The Standards Task Force

Table 8.6. Recommendations for VTE prophylaxis by risk classification.

Thromboprophylaxis by risk classification ^a				
	Low	Moderate	High	Highest
Example	Ambulatory surgery, no risk factors	Major abdominal sx, age >40 years, no other risk factors	Major abdominal sx, age >60 years, additional risk factors	Major abdominal sx, prior VTE, malignancy, or hypercoagulable state
Calf vein thrombosis (without prophylaxis)	2	10–20	20–40	40–80
Clinical PE	0.2	1–2	2–4	4–10
Primary prophylaxis	None	IPC	LDUH (q 8–12 h) or LMWH	LDUH (q 8–12 h) or LMWH
Alternate prophylaxis	None	LDUH (q 12 h) or LMWH	IPC ^b	Heparin and IPC ^c

Figures are percentages

sx symptoms; VTE venous thromboembolism; PE pulmonary embolism; q 8–12 h, every 8–12 h

^aModified with permission from Clagett GP, Anderson FA Jr, Geerts W, et al. Prevention of venous thromboembolism. Chest 1998;114:531S–560S

^bIntermittent pneumatic compression boots offer prophylaxis where the risk of bleeding is high. Heparin may be started postoperatively after the risk of bleeding has passed

^cSome data suggest that IPC combined with heparin may offer increased protection. Where the risk of bleeding is high, IPC may be used intraoperatively and heparin may be added postoperatively after the risk of bleeding has passed

Table 8.7. Conditions associated with endocarditis (high risk).

Prosthetic cardiac valves

History of endocarditis

Surgically constructed systemic pulmonary shunts

Complex cyanotic congenital heart disease

Vascular grafts (first 6 months after implantation)

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that prophylaxis be considered only for the high-risk groups listed in Table 8.7. The complex nature of individualized patient care does not allow standards to be spelled out for every clinical category.

9. Postoperative Management: Pain and Anesthetic, Fluids and Diet

A. Pain Control

- Adequate pain control is necessary to maximize cardiac and respiratory function and decrease the risk of complications.
- The Joint Commission on Accreditation of Healthcare Organizations (JCAHO) now requires specific assessment and documentation of treatment of pain.

Physiology

- Acute pain is “the initiation phase of an extensive, persistent nociceptive and behavioral cascade triggered by tissue injury.”
- The cascade begins with tissue injury that causes nociceptive neurons to begin firing and the local release of inflammatory mediators in the periphery. Once nociceptors become sensitized, the threshold necessary for further activation is lowered and their discharge rate increases.
- Put simply, less painful stimuli ultimately result in more pain perception. This effect is amplified by the environment of inflammation and its mediators.

Techniques

- In the inpatient setting of abdominopelvic surgery, the major modalities of postoperative pain control are patient-controlled anesthesia (PCA with opioids, intermittent administration of opiates or nonsteroidal antiinflammatory drugs (NSAIDs), and epidural anesthesia (with opiates or anesthetics).

- Preemptive analgesia is another tactic and includes preincisional infiltration of local anesthetics and administration of NSAIDs and intraoperative epidural anesthesia.

Opioids

- Opioids are the most frequently used medication in perioperative pain management.
- Their mechanism is via specific opioid receptors as well as nonspecific antiinflammatory actions. They block transmission of nociceptive afferent signals in the spinal dorsal horn and involve efferent messaging by activating inhibitory pathways supraspinally. Additionally, they act locally in the areas of tissue injury to inhibit inflammation.
- Opioid side effects include respiratory depression, pruritus, nausea, vomiting, and constipation.
- Titration of drugs administered for pain is extremely important in avoiding respiratory depression as the respiratory center receives nociceptive input that counterbalances the depression.
- When pain is reduced by other means such as adjunct medications and nerve blocks, the amount of narcotic must be reduced.
- The most frequently used opioid is morphine. It is the standard against which all other choices are compared.
- Other opioids include meperidine (Demeral) and hydromorphone (Dilaudid).
 - Meperidine has an anticholinergic effect and the potential for less smooth muscle spasm in areas such as the colon, biliary tract, and renal.
 - The analgesic effects of meperidine are inferior to those of morphine. Its duration of effectiveness is significantly less than 4 h. When administered by the intramuscular (IM) route its absorption is highly variable with variable blood levels resulting in poor pain control.
 - Meperidine causes central nervous system excitation, seizures, increased respiratory depression, has a propensity for addiction, and produces metabolites with little analgesic but significant neurotoxic potential when administered in repeated doses.
 - Meperidine, given its short duration of action and significant risk of serious side effects with repeated use, should have an extremely limited role in pain management of postoperative

patients. These factors have led the JCAHO to discourage the use of meperidine in its pain guidelines.

- The route of administration of opioids is more important than the specific opioid used in terms of onset of action.
- For the intravenous (IV) route and the oral route, there is little difference among various opioids.
- The IV route is effective within minutes, whereas the oral route varies between 1 h for standard release and 2–4 h for sustained relief.
- The greatest variability occurs with IM administration based on the lipophilic nature of the drug. The more lipophilic, the quicker the onset of pain relief.
- For IV delivery, PCA has been used successfully for more than 30 years and is one of the recommended modes of pain control by the American Society of Anesthesiologists in their practice guidelines. Improved pain control, patients' satisfaction, and decreased pulmonary complications have been found in two large reviews comparing PCA with conventional opioid analgesia in postoperative patients.
 - Although slightly more expensive, PCA opioid use is a safe and effective mode of delivery.
 - Making the transition from IV pain control to oral pain control should be made with knowledge of the pain requirements based on the most current IV dosages. Table 9.1 lists equianalgesic doses of the IV and oral forms of several frequently used medications.

Nonopioid

Nonsteroidal Antiinflammatory Drugs

- Nonsteroidal medications inhibit cyclooxygenase (COX) in the periphery and spinal cord and this may be the mechanism by which they are effective in diminishing hyperalgesia. Their action is mediated by their effect on COX-2 receptors and result in analgesic and antiinflammatory effects.
- The side effects are largely a result of inhibition of COX-1 receptors which occur most frequently in the gastrointestinal (GI) tract, renal tissue, and platelets.
- Overall, the use of these agents in postoperative surgical patients has been found to be safe, but there are risks of GI bleeding, renal injury, and surgical bleeding.

Table 9.1. Equianalgesic dosages of frequently prescribed IV and oral medications.

	Approximate equianalgesic		Starting dosage, adults >50 kg	
	IV/SC/IM	Po	IV/SC/IM	Po
Morphine	10 mg q 3–4 h	30 mg q 3–4 h	10 mg q 3–4 h	30 mg q 3–4 h
Codeine	75 mg q 3–4 h	130 mg q 3–4 h	60 mg q 2 h	60 mg q 3–4 h
Hydromorphone	1.5 mg q 3–4 h	7.5 mg q 3–4 h	1.5 mg q 3–4 h	6 mg q 3–4 h
Hydrocodone		30 mg q 3–4 h		10 mg q 3–4 h
Meperidine	100 mg q 3 h	300 mg q 2–3 h	100 mg q 3–4 h	
Oxycodone		30 mg q 3–4 h		10 mg q 3–4 h

Source: Tarascon Pocket Pharmacopeia, 2002 classic shirt pocket edition. Loma Linda, CA: Tarascon Publishing. PO, per os

Antihistamines

- Histamine is known to activate nociceptive fibers and may participate in mediating pain. For this reason, antihistamines have been proposed as adjuncts to pain management.
- The mechanism of antihistamines in analgesia is unclear but may involve opioid receptors or presynaptic inhibition of histamine receptors.
- The confounding factors of sedation and poor methodology do not allow for recommendations for their use as single agents.

Epidural Anesthesia

- Epidural anesthesia functions at the dorsal horn preventing afferent conduction of nociceptive stimuli.
- For patients undergoing laparotomy and lower abdominal and pelvic surgery, epidural anesthesia may have better pain control, patient satisfaction, and potentially return of bowel function with fewer side effects.
- In a randomized study of colorectal patients undergoing thoracic epidural placement for colorectal resections, resolution of ileus and control of postoperative pain was significantly improved compared with those receiving a PCA. These findings were supported in a series of patients undergoing proctocolectomy.
- In a series of patients undergoing laparoscopic colon resection randomized to epidural versus PCA, the differences were not significant.
- The type of medication infused may also have a significant influence on the outcomes postoperatively as discussed in a Cochrane review in which those patients receiving local epidural anesthetics had reduced GI paralysis with comparable pain control.
- The additional time and cost involved with an epidural has been the primary reason it has not been adopted in a more widespread manner.

Preemptive Analgesia

- The debate over the effectiveness of preemptive analgesia continues.

- The concept is that by preventing the initial stimulation of central pain pathways, there will be decreased sensitization to noxious stimuli. When increased sensitization occurs, it is referred to as hyperalgesia and suggests that the same stimuli will produce different degrees of effects based on the state of the target.
- Hyperalgesia may result from upregulation of afferent pathways and the inflammatory mediators involved in the perception of pain. This led to the evaluation of preemptive analgesia in human studies.
- A review of the 80 randomized controlled trials regarding the comparison of preemptive and postoperative pain relief attempted to reach a consensus regarding preemptive analgesia trials in humans. The findings were that “timing of analgesia did not influence the quality of postoperative pain control, whatever the type of preemptive analgesia.”
- It has been suggested that the focus should shift from comparing preoperative and postoperative analgesia, to developing more comprehensive, multimodality paradigms of surgical pain control.

“Nontraditional” Adjuncts

- Acupuncture and acupressure have been used for thousands of years and are now being increasingly used in Western medicine. There are many reports of their use in control of surgical pain, but few of these are randomized.
- The methods include needles, pressure, and electrical stimulation and the number and location of sites is variable. The purported benefits are decreased need for opioids, decreased nausea, and lower plasma cortisol and epinephrine release.
- Modalities that address the psychological perception of pain, rather than only the physiologic, are being examined. It has been suggested that techniques such as massage may better address the psychological aspect. In the one randomized study of this in patients with acute surgical pain, there was no difference in the consumption of opioids in 202 patients. For similar reasons, relaxation techniques and the use of music have been suggested.
- Overall, the data are very limited for these therapies.
- Their role in the management of acute postoperative pain remains to be seen in larger, randomized trials.

B. Perioperative Fluid Management

- Basic fluid requirements under normal circumstances are approximately 2,500 cc/day in a 70-kg adult. This allows for the 1,500 cc of urine necessary to excrete waste products including urea, potassium, and sodium.
- A very simple formula for calculating basic fluid needs is 1,500 cc for the first 20 kg with 20 cc/kg for the remaining weight.
- As a result of surgical stress, there is an increase in renin, aldosterone, and antidiuretic hormone release and activation of the sympathetic system resulting in sequestration of fluid (third spacing) and increased volume requirements.
- Additional losses may occur from blood loss, diarrhea, nasogastric tubes, and abdominal drains and these should be accounted for.
- Table 9.2 lists the composition of the frequently administered fluids and should serve as a guide for replacement based on calculated fluid losses.
- The amount of IV fluids that should be administered has been questioned. In two randomized controlled trials of colorectal patients, a restricted perioperative fluid administration schedule was evaluated. The groups randomized to the restricted fluid had fewer complications in terms of cardiopulmonary events and tissue healing complications as well as quicker resolution of intestinal ileus.

C. Ulcer Prophylaxis

- In many institutions, ulcer prophylaxis is a routine part of the postoperative orders. In patients without risk factors, or personal history, this is unnecessary.
- The incidence of clinically significant GI bleeding in hospitalized critically ill patients is less than 0.2%. Mechanical ventilation, coagulopathy, prolonged hypotension, and organ failure have been the most consistently identified risk factors for the development of stress ulcer bleeding.
- Table 9.3 lists the most common agents used for ulcer prophylaxis along with their mechanisms.

Table 9.2. Composition of extracellular fluid and common crystalloid solutions.

Type	Na+	Cl-	K+	Ca ⁺⁺	Mg ⁺⁺	HCO ₃ ⁻	Lactate
Extracellular fluid	142	103	4	5	3	27	
NaCl 0.9% (normal saline)	154	154					
Lactated Ringers	131	111	5	2			29
D5/0.45% saline	77	77					
Plasmalyte 148 glucose (plasmalyte)	148	97	5		1	40	
Sodium bicarbonate 8.4%	1,000					1,000	

Table 9.3. Mechanism of frequently used ulcer prophylaxis medications.

	Mechanism
Antacids	Neutralizes acid
Sucralfate	Mucosal production Stimulates mucous, HCO_3^- , prostaglandin secretion (inhibits acid secretion) Coat ulcer base
H2 Antagonists	Blocks stimulation of histamine receptor and production of H^+
Proton pump	Blocks H^+/K^+ ATPase pump (final step of acid inhibitors production)

- In reviewing studies comparing therapies for stress ulcer prophylaxis, Hiramoto et al. concluded that H2 antagonists, sucralfate, and proton pump inhibitors are effective in decreasing the risk of clinically significant bleeding. Proton pump inhibitors, are the most potent gastric acid suppressant and, theoretically, may be more effective.

D. DVT Prophylaxis

- Although the occurrence of a fatal pulmonary embolism (PE) is rare, venous thromboembolism (VTE), both symptomatic and asymptomatic, is relatively common in the surgical patient. In one study, 0.8% of patients admitted after surgical procedures developed symptomatic VTE. Of note, 66% of these occurred within 3 months of discharge.
- PE is the most common preventable cause of death in hospitalized patients in the United States (reported in 0.45% of deaths).
- Many prophylactic therapies are available with variable costs and potential risks (Table 9.4).
- Stratification of patients based on their risk for occurrence of VTE/PE should guide the choice of prophylaxis (Table 9.5).

Elastic Stockings

- Graduated compression stockings function by compressing the lower extremity in a gradual manner, with the greatest pressure at the ankle, encouraging venous return.

Table 9.4. Common causes of hypercoagulability.

Risk factor
Age
Type of Surgery
Orthopedic lower extremity
Major surgery
Previous VTE
Malignancy
Pregnancy
Estrogen use
Obesity
Heart failure
Thrombophilic disorders
Factor V Leiden
Essential thrombocytosis
Prothrombin G 20210 A mutation
Immobilization
Hospitalization

Table 9.5. DVT prophylaxis guidelines.

	Age (Years)	Surgery	Risk fac- tors	DVT	PE	Recommen- dation
Low	<40	Minor	None	0.4%	<0.5%	Early ambula- tion or Elas- tic stockings or IPC
Moderate				2–4%	1–2%	Early ambula- tion and Elastic stock- ings or IPC or LDUH or LMWH
A	Any	Minor	Present	4%		
B	<40	Major	None			
C	40–60	Minor	None			
High				4–8%	2–4%	Early ambula- tion and Elastic stock- ings and IPC or LDUH or LMWH
	>60	Minor	±Other			
	>40	Major	None			
	<40	Major	Present			

- If not fitted properly, they may actually be constrictive and increase the venous pressure below the knees, decreasing venous return.
- In a Cochrane review, they reduced the risk of VTE in moderate-risk patients.
- As a solo prophylaxis, they should be reserved for the low-risk patient. Otherwise, they should be used in conjunction with other measures.

Sequential Compression Devices

- These devices offer a very effective, low-risk prophylaxis for DVT.
- The mechanism is direct and systemic. Locally, they compress the deep venous system decreasing stasis and encouraging venous return. On a systemic level, they increase the fibrinolytic activity by reducing plasminogen activator.
- An additional consideration is compliance. For maximal benefit, they should be placed before the induction of anesthesia and function throughout an operation.
- Postoperatively, their effectiveness can be compromised because of patient, physician, and nursing compliance.
- When used properly, SCDs are a safe and effective prophylactic measure in the low- and moderate-risk patient.

Low-Dose Unfractionated Heparin

- Unfractionated heparin has been evaluated since the 1970s as a form of prophylaxis and has been shown to be safe in the majority of surgical patients.
- It consists of molecules that range in size from 3,000 to 33,000 Da and binds to antithrombin (ATIII) and accelerates the inhibition of thrombin and other coagulation factors, particularly factor X.
- In a large randomized trial from 1970, low-dose unfractionated heparin (LDUH) decreased the risk of fatal PEs in the postoperative population from 0.7% to 0.1% in 4,000 patients. This was supported in a large metaanalysis of 70 randomized trials. The risk of DVT, PE, and fatal PE was decreased by more than 50%.
- Although effective, one concern has been the risk of bleeding. There has been a small increase in postoperative bleeding in most studies, but the majority of these events are wound hematomas.

- A more frequent side effect of heparin is heparin-induced thrombocytopenia (HIT). It is less common with prophylactic than therapeutic heparin, but may occur in 5–15% of patients.
 - HIT may cause a paradoxical hypercoagulable state with arterial and venous thrombosis.
 - The platelet count should be followed in patients receiving routine heparin and discontinued immediately if diminishing.
- It is recommended that subcutaneous (SC) heparin be started within 2 h of an operation and continued until the patient is fully ambulatory.
- The dosage is generally 5,000 U every (q) 12 h. This may be increased in those patients in the high-risk category to 7,500 U q 12 h or 5,000 U q 8 h.

Low-Molecular-Weight Heparin

- LMWH consists of heparin molecules in a smaller range and size than LDUH (3,500–6,000 Da).
- The mechanism is the same as LDUH regarding the acceleration of ATIII inactivation of Xa, but it does not inactivate thrombin. It also does not bind as strongly to plasma moieties so has greater bioavailability, longer half-life, and more predictable plasma levels.
- The incidence of HIT is also lower than LDUH (2.7 vs. 0%).
- LMWH is at least as effective as LDUH in preventing DVT in postoperative general surgery and colorectal surgery patients without an increase in bleeding complications.
- LMWH is not the standard prophylaxis for surgical patients due to cost-effectiveness issues. LMWH is twice as expensive as LDUH therapy.
- Although heparin and enoxaparin are equally effective, low-dose heparin is a more economically attractive choice for thromboembolism prophylaxis after colorectal surgery.

E. Duration

- The risk of DVT and PE does not end with the discharge of the patient from the hospital. This is especially true given the

decreasing lengths of stay and, therefore, the decreasing time available for prophylaxis while patients are hospitalized.

- In a randomized prospective trial of 332 patients deemed high risk having undergone curative pelvic or abdominal cancer resection, those patients who received 21 additional days of enoxaparin had a 4.8% rate of DVT versus 12.0% in the group receiving only in hospital prophylaxis. Given these findings, consideration for extended prophylaxis in patients who are at moderate and high risk for thrombotic events must be given.
- The American Society of Colon and Rectal Surgeons Practice Parameters for prevention of venous thromboembolism are presented in Appendix 1, Chap. 8.

F. Anticoagulation

- Clearly, postoperative bleeding risks are influenced by the surgical procedure performed.
- Overall, the risk of thrombotic and embolic events may be increased in the surgical patient and those in whom warfarin therapy has been abruptly stopped.
- In surgical patients not anticoagulated, changes in levels of fibrin D-dimer and other hemostatic markers associated with thrombosis have been found to be increased.
- In those patients taking oral anticoagulation, there is biochemical evidence that there may be a rebound hypercoagulable state after the withdrawal of oral anticoagulation, perhaps increasing the risk even more. Most studies have not borne this out in clinical practice.
- An estimation of risk will help in guiding the need and timing for beginning anticoagulation postoperatively. A summary of the risk categories based on diagnosis and the general recommendation for anticoagulation is shown in Table 9.6.

G. Diet

- The resumption of a diet is critical to the recovery of the patient undergoing intestinal surgery. Before discharge, it is accepted

mechanism, this has prompted most surgeons to abandon their routine use.

- The advent of laparoscopic colon resection has facilitated a more aggressive approach to postoperative feeding regimens. Several trials demonstrated that the majority of patients tolerated oral intake in the immediate postoperative period, regardless of the presence or absence of traditional markers of return of GI function. This approach has been used in the open colectomy patients as well.
- In addition to having been shown to be safe and well tolerated, there are several theoretical advantages to early feeding. The potential benefits are related to maintenance of intestinal integrity from a biochemical and immunologic perspective. It has been clearly shown that malnutrition in the surgical patient is associated with increased morbidity and mortality.
- Early feeding after elective abdominal surgery and specifically colon surgery, has been shown to be safe and generally well tolerated. This may improve patients' comfort, and there is a growing body of evidence that early nutrition may improve outcome and reduce complications. These data are most convincing for the malnourished patient, and for the use of enteral nutrition.

H. Steroids

- It is not infrequent that patients undergoing colorectal surgical procedures are taking exogenous steroids. Usually this is in the inflammatory bowel disease population.
- Important considerations include identifying those patients at risk for adrenal insufficiency, equivalent oral and parenteral dosages, the effect of surgical stress on dosage requirements, and the timing of tapering to presurgical dosages or cessation of treatment.
- Glucocorticoids are essential for protein, carbohydrate, and fat metabolism. Their overall effect is to increase gluconeogenesis by allowing for the production of amino acids by proteolysis and lipolysis. They also stimulate metabolism by their inotropic effects and enhancement of norepinephrine and epinephrine.

- It has been clearly demonstrated that adrenal atrophy and suppression occurs with exogenous steroid administration. This is a result of the negative feedback effect on adrenocorticotrophic hormone by exogenous cortisol and the lack of stimulation of the adrenal cortex. This can take up to 1 year to recover and patients are frequently asymptomatic during this time if not exposed to stress. During this period, the potential for acute adrenal insufficiency exists.
- In actuality, the occurrence of adrenal insufficiency in the surgical population is quite rare.
- The risk of suppression can be predicted and this is shown in Table 9.7.
- As to the question of testing of the adrenal axis, it has not been clearly demonstrated that identified suppression leads to clinical insufficiency.
- The duration of the taper postoperatively is most impacted by the surgical procedure. For most outpatient procedures, the degree of postoperative stress is considered minor and patients can be returned to their preoperative dose immediately. For major surgery, stress dosages should be continued until signs of surgical stress have resolved. This varies from patient to patient as postoperative ileus, cardiac and pulmonary complications and infections pose additional stress. For patients with an uncomplicated postoperative course, this generally begins on the third day. Once the taper begins, it can be carried out rapidly over a period of a few days to the preoperative

Table 9.7. Risk of adrenal suppression from exogenous steroids and recommendations for replacement.

	Dose	Duration	Recommendation
High risk ^a	>20 mg/day	>3 weeks	100 mg at induction 100 mg q 8 h throughout period of "stress"
Intermediate	>5 mg/day	>3 weeks	Prophylaxis or testing of the axis
	<20 mg/day		
Low	Any dose	>3 weeks	No prophylaxis
	<5 mg/day	Any time	

^aPatients with Cushing's syndrome are considered high risk regardless of dosage or duration of steroid administration

Table 9.8. Equivalent steroid dosages.

Glucocorticoid	Equivalent dose (mg)	Half-life (h)
Prednisone	5	18–36
Dexamethasone	0.5	36–54
Hydrocortisone	20	8–12
Methylprednisolone	4	18–36

dosage. Table 9.8 shows the equivalent steroid dosages for the parenteral and enteral steroids.

- It is important to recognize the signs of adrenal insufficiency because they may occur both in the immediate postoperative period and beyond in the event of a complication (bowel obstruction, anastomotic leak, surgical and nonsurgical infections). Symptoms of adrenal insufficiency may include hypoglycemia, cardiovascular collapse, fatigue, abdominal pain, nausea, and vomiting. In the postoperative patient presenting with a change in intestinal function, steroid withdrawal should be considered in the at-risk population.

I. Clinical Pathways

- An aspect of practicing evidence-based medicine is the development of standardized postoperative protocols. Potential benefits of standardized care include decreased length of stay with more efficient utilization of hospital beds and personnel, and potentially fewer mistakes.
- Preoperatively, patients should be educated regarding the expectations of the pathways in terms of their activity and diet. Additionally, an attempt to explain realistic expectations of what patients may expect in terms of pain and discomfort will help in compliance with the protocol. The caregivers, both family and hospital staff, must also be involved and aware of the pathway. Preoperative printed instructions and wall charts may help in achieving this understanding.

10. Postoperative Complications

A. Unrecognized Enterotomies and Enterocutaneous Fistulae

- Patients undergoing extensive adhesiolysis are at highest risk for enterotomies. An enterotomy in and of itself is not a complication, rather it is the failure to recognize and adequately repair an enterotomy that leads to trouble.
- In cases in which any significant degree of adhesiolysis is performed, the entire bowel should be carefully inspected at the end of the procedure.
- Although the natural history of serosal tears is unknown, they should be repaired when recognized with imbricating seromuscular sutures.
- Full-thickness enterotomies can be repaired using a number of different and equally effective techniques.
- In cases in which multiple enterotomies have occurred within a short segment of bowel, resection of the involved segment with primary anastomosis is performed. If the mesentery has also been injured during the course of adhesiolysis, the viability of the bowel ends should be confirmed before anastomosis.
- Failure to recognize an enterotomy at the time of surgery will lead to one of several postoperative complications:
 - The patient may develop peritonitis within the first 24–48 h after surgery. This may be difficult to detect in the background of narcotic analgesia and the surgeon and patient's expectation of postoperative incisional pain.
 - The diagnosis is purely based on patient appearance and examination. The usual markers of bowel perforation (leukocytosis, fever, and pneumoperitoneum) are not

reliable, because they are normal findings in the early postoperative patient.

- A high index of suspicion should be maintained with a low threshold for reexploration. Reoperation within the first several days is usually not difficult because significant adhesions have not yet formed. Most enterotomies found in this situation can be repaired primarily, provided that the bowel edges are viable. Should the repair fail, if the repair can be placed directly under the midline fascial closure, this may result in the development of a direct enterocutaneous fistula rather than recurrent peritonitis.
- If conditions are not favorable for primary repair, a stoma should be created.
- An unrecognized enterotomy may also present as an enterocutaneous fistula, with enteric drainage emanating from the incision or wound later in the postoperative course.
 - If there are no signs of sepsis, a nonoperative approach may be considered, especially if the patient is more than 1 week removed from surgery. The patient is placed on bowel rest, broad-spectrum antibiotic coverage is initiated, and a computed tomography (CT) scan is obtained to assess for an associated abscess or fluid collection. If a fluid collection greater than 4 cm in diameter is present, percutaneous, radiologically guided drainage should be considered.
 - If available, an enterostomal therapist should be involved to assist with pouching the fistula in order to protect the skin from irritating enteric contents.
 - In most cases, parenteral nutrition will be started to meet the patient's caloric and protein requirements in anticipation of a prolonged period of fasting.
 - H₂ antagonists may be added to decrease gastric secretions.
 - Somatostatin analogs may also be used to decrease the volume of fistula output, although they do not seem to increase the rate of spontaneous fistula closure.
 - The rate of spontaneous small bowel fistula closure varies but is typically less than 50%. Chances of spontaneous closure are thought to be reduced by high output because of proximal location, distal obstruction, local sepsis, radiation exposure, a short or epithelialized tract, malignancy, a foreign body in the tract (e.g., mesh, sutures), Crohn's disease, and malnutrition.

- Most enterocutaneous fistulae that close spontaneously will do so within the first month.
- Surgical intervention should be delayed until all sepsis has resolved, adequate nutrition has been restored, and intraabdominal adhesions have softened to the point of allowing safe reoperation. Most authors recommend a delay of at least 6 weeks since the last laparotomy, but 3–6 months may be more appropriate. The ultimate healing rate after definitive surgical repair is approximately 80%.

B. Anastomotic Complications

- Anastomotic complications can lead to emergent reoperation and/or a prolonged, complicated, and costly postoperative hospitalization. If the patient recovers from the acute event, chronic sequelae may develop because of stricture or pelvic fibrosis leading to poor bowel function and the possibility of further revisionary surgery or permanent fecal diversion.
- Anastomotic complications are usually related to technical factors (ischemia, tension, poor technique, stapler malfunction) or preexisting conditions in the patient such as local sepsis, poor nutrition, immunosuppression, morbid obesity, and radiation exposure. The contribution of the former may be minimized by a careful, methodical approach to construction of the anastomosis (Table 10.1).
- Nutritional status, degree of immunosuppression, and general medical condition should be considered when deciding whether

Table 10.1. Steps to minimize risk of leak from colorectal or coloanal anastomoses.

1. Ensure good blood supply (pulsatile bleeding from marginal artery at level of anastomosis)
2. Ensure tension-free anastomosis by complete mobilization of splenic flexure (includes high ligation of IMA and ligation of inferior mesenteric vein at lower border of pancreas)
3. Avoid use of sigmoid colon in creation of anastomoses
4. Inspection of anastomotic donuts for completeness after circular stapled anastomoses
5. Air or fluid insufflation test to rule out anastomotic leak immediately after construction in the operating room

or not to perform a primary anastomosis. If severe malnutrition (albumin <2.0 or weight loss $>15\%$) or significant immunosuppression (chemotherapy, high-dose steroids) are present, a proximal stoma (eg. an end colostomy and Hartmann stump) will minimize the risk of complications. Colostomy takedown can then be performed if and when these factors have been corrected.

- When operating in the radiated pelvis, one end of the bowel used to construct the anastomosis should come from outside the field of radiation.

Bleeding

- Anastomotic bleeding is common and varies greatly in severity. In most cases, bleeding is minor and is manifested by the passage of dark blood with the patient's first bowel movements after surgery. In rare instances, bleeding can be massive and require transfusion and active intervention.
- Bleeding can occur after either stapled or hand-sewn anastomoses, but is probably more common with the former. This complication can be reduced by careful inspection of the staple line, particularly in the case of side-to-side/functional end-to-end anastomoses.
- Bleeding from circular stapled anastomoses or from the staple lines of ileal or colonic J pouches is usually not diagnosed until after the patient has left the operating room. After performing proctoscopy to evacuate clot from the rectum or neorectum, a rectal tube or catheter is inserted and a 1:100,000 solution of saline and epinephrine is instilled.
- If bleeding is severe, angiography may be required to localize the site and allow selective infusion of vasopressin. Alternatively, colonoscopy may be used. If the anastomosis can be visualized, the bleeding site can be treated with either cautery, clips, or injection of epinephrine. In rare cases, reoperation with resection of the bleeding anastomosis is required.

Leaks

- The lowest leak rates are seen after small bowel or ileocolic anastomosis (1–3%) whereas the highest occur after coloanal anastomosis (10–20%).
- Vignali et al. reported on 1,014 colorectal anastomoses. The overall clinical leak rate was 2.9%. The incidence of leak was

strongly associated with the distance of the anastomosis from the anal verge.

- Another high-risk anastomosis is the ileal pouch-anal anastomosis. Leak rates of 5–10% have been reported. Data from series of ileal pouch-anal anastomosis in patients with ulcerative colitis identify prednisone dosage >40 mg/day as a significant risk factor.

Role of Fecal Diversion

- The creation of a proximal diverting stoma minimizes the severe consequences of an anastomotic leak but it does not reduce the incidence of leak itself.
- A diverting stoma should be considered for any high-risk anastomosis [coloanal, low colorectal (<6 cm from anal verge)]. In addition, patient factors such as severe malnutrition, significant immunosuppression, and purulent peritonitis or pelvic sepsis should be considered as indications for diversion. Consideration should also be given to the patient's comorbidities and general condition; in cases in which the "physiologic reserve" necessary to tolerate an anastomotic leak does not exist, the use of a proximal stoma should be strongly entertained.
- In fact, recent data from a large randomized trial assessing the efficacy of short-course neoadjuvant radiation therapy in rectal cancer found that a protecting stoma reduces the need for surgical intervention should an anastomotic leak occur.

Role of Pelvic Drains

- The use of pelvic drains is controversial.
- The use of drains has not been shown to be of benefit or harm in a recent, large randomized study and in a metaanalysis.
- In the absence of data suggesting harm, the authors routinely drain low colorectal or coloanal anastomoses, especially after neoadjuvant therapy.

Management of Anastomotic Leak

- Anastomotic leaks can be divided into "free" and "contained" varieties.
- Free leaks are those in which fecal contents leak from the anastomosis and spread throughout the abdominal cavity. Patients

usually present with fever, tachycardia, leukocytosis, and diffuse peritonitis. Feculent fluid may present itself through the surgical incision or via the pelvic drains. Hypotension and other signs of systemic sepsis may ensue. If the patient is stable, radiologic investigation is helpful to localize the leak and to determine its size and severity.

- Patients with “free” leaks should be taken to the operating room after fluid resuscitation and administration of broad-spectrum intravenous antibiotics.
- Surgical treatment will be dictated by the findings at operation. Most leaking colorectal anastomoses will require abdominal washout and takedown of the anastomosis with creation of an end-colostomy and Hartmann stump.
- Leaking ileocolic or small bowel to small bowel anastomoses can occasionally be repaired primarily in carefully selected circumstances, i.e., small defect with viable edges. However, resection of the anastomosis with either reconstruction or creation of a stoma is the wisest and most conservative option.
- If the viability of the bowel ends is questionable, takedown of the anastomosis and creation of a stoma is mandatory.
- “Contained” leaks are those in which the extravasation of contrast material is limited to the pelvis and usually result in the development of a pelvic abscess (Fig. 10.1).
 - If the abscess cavity is small and contrast flows freely back into the bowel, the patient may be treated with intravenous antibiotics, bowel rest, and observation.
 - If the abscess is larger or somewhat removed from the site of the anastomosis, then percutaneous abscess drainage using CT or ultrasound guidance may avoid laparotomy. Such leaks rarely require subsequent fecal diversion.

Fistulae

- Anastomotic leaks may also result in fistulae to the skin, vagina, male genitourinary system, or chronic presacral abscess (presacral sinus).
- Colocutaneous fistulae will frequently close with conservative management consisting of either bowel rest with total parenteral nutrition or a low residue diet and pouching of the fistula to

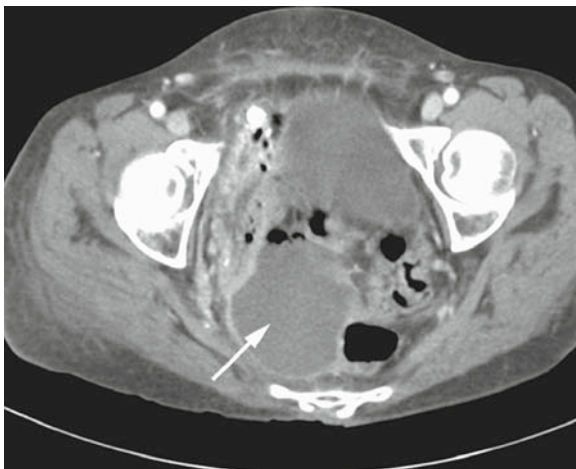


Fig. 10.1. Pelvic abscess resulting from ileocolic anastomotic leak (*white arrow*). Extravasated enteric contrast can be seen in the right pelvis tracking down toward the abscess.

protect the surrounding skin. If drainage persists, reoperation for fistula takedown and reconstruction of the anastomosis can be performed after a delay of 3–6 months.

- Colovaginal fistulae are usually the consequence of either an anastomotic leak necessitating through the vaginal cuff in a patient who has undergone a prior hysterectomy or the inclusion of the vagina during creation of a stapled anastomosis. In either case, spontaneous closure is rare.
 - If the vaginal drainage is copious and intolerable to the patient, proximal fecal diversion may be necessary.
 - After a waiting period of 6–12 weeks, reoperation may be performed. Options include attempts at local repair using mucosal flaps (colonic or vaginal)/sleeve advancements or laparotomy with redo coloanal anastomosis, either primary or delayed (“Turnbull-Cutait pullthrough”).
- Chronic presacral abscess or sinus may result from a posterior leak in a coloanal or ileal pouch-anal anastomosis.
 - Patients may have an occult presentation consisting of vague pelvic pain, fevers, frequency of stool, urgency, and bleeding.

- A pelvic CT scan will usually show presacral inflammatory changes and a contrast enema will confirm the presence of a sinus tract originating from the posterior midline of the anastomosis and extending cephalad into the presacral space.
- Examination under anesthesia can then be performed with careful inspection of the anastomosis. A probe or clamp is placed through the anastomotic defect and the chronic presacral cavity is simply laid open using cautery and gently curetted of granulation tissue. This will allow free drainage of the presacral abscess and healing by secondary intention. This may result in a chronic posterior sinus or “pseudo-diverticulum.”

Stricture

- Anastomotic stricture may be the end result of anastomotic leak or ischemia.
- It typically presents 2–12 months after surgery with increasing constipation and difficulty evacuating.
- If the initial resection was done for malignancy, recurrence as a cause of the stricture must be excluded with a combination of CT scan and fluorodeoxyglucose-positron emission tomography (PET) scan.
- Biopsy is mandated if a mass or abnormality is identified.
- Low colorectal, coloanal, or ileal pouch-anal anastomotic strictures may be successfully treated with repeated dilatations using an examining finger or rubber dilators. Dilation is more successful if initiated within the first few weeks after surgery.
- Almost all coloanal or ileoanal anastomoses will stricture to some degree during the early postoperative period, especially if a diverting stoma is present. All such anastomoses should undergo digital examination at 4–6 weeks after surgery and just before stoma closure (usually at 2–3 months).
- Higher colorectal, colocolic, or ileocolic strictures may be approached using endoscopic balloon dilatation.
- If these measures fail, or if the stricture is extremely tight or long, revisionary surgery may be required. These are difficult operations, however, because of the pelvic fibrosis that develops after anastomotic leak and complications are common. In some cases, permanent fecal diversion is the only option.

C. Genitourinary Complications

Ureteral Injuries

- Injury to the ureters typically occurs at one of four specific points in the procedure.
- The first is during high ligation of the IMA where the junction between the upper and middle thirds of the left ureter lies in close proximity to the vessels. Failure to mobilize the ureter laterally before ligation of the IMA may result in its inclusion with the vascular pedicle when clamped and subsequent division. It is good practice to always confirm the position of the left ureter before and after applying clamps to the IMA and before division of the vessel. Injury at this level is usually limited to transection and can be repaired primarily using an end-to-end, spatulated anastomosis performed over a stent.
- The second point of danger is during mobilization of the upper mesorectum near the level of the sacral promontory. It is at this point that the ureters cross over the bifurcation of the iliac artery and course medially as they enter the pelvis.
- The left ureter may be closely associated with the sigmoid colon and can even be adherent secondary to prior inflammatory processes. The injury may be tangential and not readily recognized in the setting of a phlegmon or abscess.
- Injury at this level is usually managed by either primary repair or ligation of the distal stump and creation of a ureteroneocystostomy with a Boari flap or psoas hitch repair.
- The third point of risk is during the deepest portion of the abdominal phase of the operation. Anterolateral dissection in the plane between the lower rectum, pelvic sidewall, and bladder base can result in ureter injury at the ureterovesical junction. The ureter may also be injured at this level during division of the lateral stalks.
- The final area of risk is during the most cephalad portion of the perineal phase of the operation. If exposure is limited (obese patient, android pelvis), the ureter may be unknowingly divided near the ureterovesical junction. In either of these circumstances, the injury can be managed by creating a ureteroneocystostomy.
- Should ureteral injury occur, the key to minimizing its consequence is immediate (intraoperative) recognition and repair of the injury.

- In cases in which a difficult pelvic dissection is anticipated, because of prior pelvic surgery, inflammation, or a locally advanced tumor, the preoperative placement of ureteral stents can be invaluable. Although the literature does not demonstrate that stents prevent ureteral injuries, palpation of the stents can aid in localization of the ureters and can also facilitate identification and repair should injury occur.
- In cases in which the surgeon is suspicious of occult injury, indigo carmine can be administered intravenously. After several minutes, the urine will turn blue-green and the operative field can then be inspected for staining.
- Unfortunately, the literature suggests that less than 50% of ureteral injuries are identified intraoperatively, usually because the injury is not suspected. Ureteral stents should be used selectively, however, because their use can lead to complications such as obstruction secondary to hematoma, perforation, or acute renal failure.

Urethral Injuries

- Iatrogenic injury to the urethra may be the result of abdominoperineal resection (APR). The injury typically occurs during the perineal portion of the procedure and usually involves the membranous or prostatic portion.
- Intraoperatively, urethral injury may be recognized by visualization of the Foley catheter through the defect.
- These injuries may be difficult to avoid in the presence of a large, deeply penetrating anterior tumor in which involvement of the prostate gland can occur. Desmoplastic reaction to the tumor or edema from neoadjuvant radiation therapy may also obscure anatomic planes.
- Small injuries can be repaired at the time of surgery using 5-0 chromic sutures with the Foley catheter left in place to stent the repair for 2–4 weeks.
- Larger injuries or those not presenting until the postoperative period (urine draining from the perineal wound) require proximal urinary diversion via suprapubic catheter and delayed repair. This should be performed by a skilled urologist with experience in urethral reconstruction and typically utilizes a gracilis muscle flap.

Bladder Injury

- Bladder injuries are relatively frequent and are, in most cases, related to resection of an adherent rectosigmoid tumor or diverticular phlegmon.
- When created purposefully or recognized immediately, defects in the bladder dome are easily repaired in two layers with a Foley catheter then left in place for 7–10 days postoperatively.
- Before removal, a cystogram may be obtained to confirm healing.
- Injuries not recognized at the time of surgery will present in the postoperative period with urine in the abdominal cavity, pneumaturia, or fecaluria. Initially, fecal and urinary diversion may be necessary to temporize the situation until reoperation can be safely performed.

Urinary Dysfunction

- Urinary dysfunction is one of the most common urinary complications of APR. Some degree of voiding difficulty occurs in up to 70% of patients after APR, but it is usually confined to the early postoperative period.
- In most instances, urinary retention is the result of denervation of the detrusor muscle causing partial paralysis. Bladder contractility is under parasympathetic control via pelvic nerve branches originating from the inferior hypogastric plexus. These nerves can be injured if the endopelvic fascia is breached, especially during blunt dissection of the rectum. Temporary dysfunction of these nerves is nearly universal after APR, even when a meticulous sharp dissection is used.
- Most patients, however, will only require maintenance of a Foley catheter for 5–7 days postoperatively.

Sexual Dysfunction

- Recent series report an incidence of sexual dysfunction of 15–50% in male patients undergoing APR for rectal cancer. This wide range is likely attributable to several factors such as patient age, preoperative libido, use of adjuvant radiation therapy, varying definitions of dysfunction, time point of follow-up, and social barriers preventing a frank discussion of the problem.

- The type of dysfunction is dependent on the pattern of nerve injury. Damage to the superior hypogastric (sympathetic) plexus during high ligation of the IMA or to the hypogastric nerves at the sacral promontory during mobilization of the upper mesorectum, results in ejaculatory problems such as retrograde ejaculation. This is the most common type of sexual dysfunction seen in male patients after APR and is also the type most likely to resolve with time (6–12 months).
- Damage to the pelvic plexus during the lateral dissection or to the nervi erigentes or cavernous nerves while dissecting the anterior plane (abdominal or perineal phase) may result in erectile dysfunction.
- The cavernous nerves arise from branches of the pelvic plexus and course anterior to Denonvillier's fascia at the lateral border of the seminal vesicles. Parasympathetic innervation from these routes controls the inflow to and retention of blood within the corpora cavernosa. The important anatomic relations of the pelvic nerves are illustrated in Fig. 10.2.
- Risk of injury to these nerves may be reduced by tailoring the anterior dissection based on the location of the tumor.
- The highest risk of parasympathetic nerve injury occurs when dissection is performed in the plane anterior to Denonvillier's fascia and flush with the posterior aspect of the seminal vesicles and prostate.
- For posterior tumors, Denonvillier's fascia is preserved by dissecting between it and the fascia propria of the rectum in order to protect the small cavernous nerves.
- Using a "nerve sparing" approach to total mesorectal excision, several authors have reported an incidence of erectile dysfunction of 5–15% after proctectomy for rectal cancer. Factors shown to increase risk are older age, poor preoperative libido, and low rectal tumor requiring APR (two- to threefold increase compared with low anterior resection).
- Although harder to quantify, sexual dysfunction also occurs in women after proctectomy. It is characterized by dyspareunia and inability to produce vaginal lubricant and achieve orgasm. The incidence is lower than that seen in males and varies between 10 and 20%.

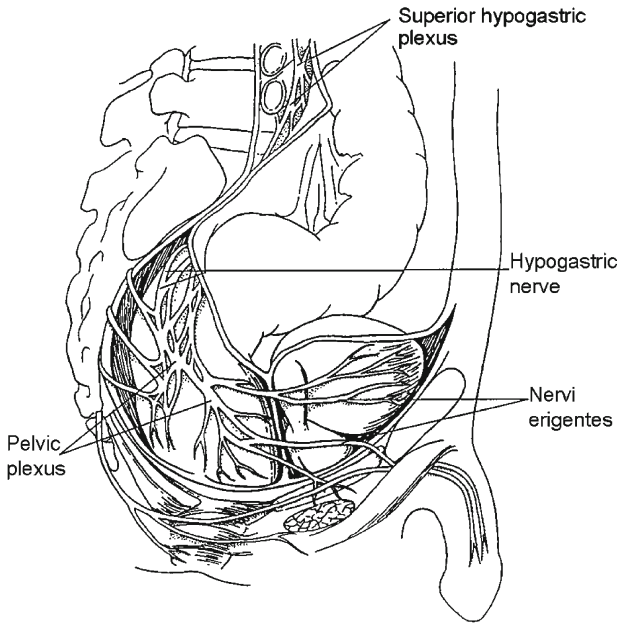


Fig. 10.2. Anatomic relations of the pelvic nerves. Damage to the superior hypogastric plexus during high ligation of the IMA or to the hypogastric nerves at the sacral promontory during mobilization of the upper mesorectum results in retrograde ejaculation. Damage to the pelvic plexus during the lateral dissection or to the nervi erigentes or cavernous nerves while dissecting the anterior plane may result in erectile dysfunction.

Female Infertility

- Several recent studies have documented decreased fertility in women who have undergone restorative proctocolectomy for ulcerative colitis or familial adenomatous polyposis.
- The postoperative infertility rate exceeds 50% in this group when defined as “one year of unprotected intercourse without conception.” This has important implications in both preoperative patient counseling and in the modification of operative technique to minimize the effect of pelvic adhesions on fertility.
- Women of childbearing age should be informed of this potential complication before elective restorative proctocolectomy because it may influence the timing of surgery.

- Because pelvic adhesions are thought to interfere with egg transit from the ovary to the fallopian tube, measures to minimize their occurrence may be of benefit. Tacking the ovaries to the anterior abdominal wall outside of the pelvis and wrapping the adnexa with an anti-adhesion barrier sheet are frequently used techniques but there are no data to support their efficacy.

Trapped Ovary Syndrome

- Trapped ovary syndrome is a fairly common complication after restorative proctocolectomy in young women. The adhesions that form after ileal pouch-anal anastomosis trap the ovaries in the pelvis and cover the fallopian tubes.
- With each ovulatory cycle, there is release of fluid into the pelvic cavity defined by these adhesions. As fluid accumulates and the cavity expands, patients will complain of pelvic or lower abdominal pain relevant to the side of the trapped ovary.
- A CT scan or ultrasound will reveal a cystic lesion in the pelvis containing no air and with no surrounding inflammatory reaction. Operative findings are a cyst containing clear or tan fluid, surrounded by adhesions and with the ovary attached.
- Treatment consists of unroofing and evacuation of the cyst, pelvic adhesiolysis, and suspension of the ovary to the pelvic brim or iliac fossa with sutures.
- Trapped ovary syndrome may be prevented by suspending the ovaries at the time of restorative proctocolectomy and by placement of an adhesion barrier film in the pelvis.

Small Bowel Obstruction

- Perhaps the most critical components in the management of patients with bowel obstruction are the recognition and prevention of the disastrous effects of bowel ischemia.
- It is also important to distinguish between early (<30 days) and late postoperative small bowel obstruction.

Presentation and Diagnosis

- Nausea and vomiting, colicky pain, abdominal bloating, and obstipation are the hallmark signs of small bowel obstruction. The degree to which each of these contributes to the clinical

picture will depend on the location, degree, and duration of the obstruction.

- The commonly regarded hallmarks of strangulated bowel are fever, tachycardia, leukocytosis, sepsis, peritoneal signs, and the presence of continuous as opposed to intermittent pain. If any of these are found, the suspicion of ischemia should be high. These signs may also be found in patients without strangulation and are, therefore, nonpathognomonic.
- In many cases, however, this determination is not made until laparotomy, and timely surgical intervention in symptomatic patients may be the best means of avoiding the progression to bowel ischemia.

Radiographic Studies

Plain Radiographs

- An acute abdominal series is the initial imaging study performed in most patients suspected of having small bowel obstruction and consists of both upright and supine abdominal films and an upright chest X-ray.
- Typical findings include dilated, air-filled loops of small bowel, air-fluid levels, and an absence or paucity of colonic air. These findings may be absent, however, when the obstruction is proximal or the dilated bowel loops are mostly fluid filled.
- The sensitivity of plain radiographs in detecting small bowel obstruction is approximately 60%.
- The findings of pneumatosis intestinalis or portal vein gas is worrisome for advanced bowel ischemia.

CT Scan

- Abdominopelvic CT scanning is increasingly used as a primary imaging modality in patients suspected of having small bowel obstruction.
- In addition to establishing the diagnosis, CT may also be able to precisely define a transition point and reveal secondary causes of obstruction such as tumor, hernia, intussusception, volvulus, or inflammatory conditions such as Crohn's disease and radiation enteritis.
- CT may also reveal closed loop obstructions or signs of progressing ischemia such as bowel wall thickening, pneumatosis, or portal vein gas.

- Several studies have shown that the sensitivity of CT in diagnosing small bowel obstruction approaches 90–100%.

Contrast Studies

- In patients with distal small bowel obstruction, a contrast enema is an efficient means by which colonic obstruction can be excluded.
- Antegrade studies of the small bowel can help to differentiate partial from complete obstruction, and may therefore predict the need for surgical intervention.
- In fact, some authors have used small bowel contrast studies as a “screening test” for patients presenting with adhesive obstructions. Failure of contrast material to reach the colon by 24 h is used as an indication for prompt surgical exploration.
- Several studies have also shown that the antegrade administration of contrast agents may speed the resolution of partial small bowel obstruction, presumably through an osmotic effect. However, conflicting data also exist and the therapeutic effects of the small bowel contrast study remain to be defined.

Initial Therapy and Nonoperative Management

- Once the diagnosis of small bowel obstruction is made, the patient is admitted to the hospital. Those with peritonitis, perforation, or signs of ischemic bowel are immediately prepared for laparotomy with expeditious correction of fluid and electrolyte deficits.
- A urinary catheter is inserted to guide resuscitation with the end points being resolution of tachycardia and hypotension and/or achieving a urine output of at least 0.5 cc/kg/h.
- Broad-spectrum antibiotic coverage is initiated.
- A nasogastric tube is inserted preoperatively to decompress the stomach, because these patients are at risk for aspiration on induction of general anesthesia.
- If signs of perforation or ischemia are not present, a trial of expectant management may be undertaken. Patients with partial small bowel obstructions secondary to adhesions will resolve with a nonoperative approach in 80% of cases. The success rate for patients initially presenting with complete obstruction is significantly lower.

- The nonoperative management of small bowel obstruction consists of fluid and electrolyte replacement, bowel rest, and tube decompression.
- The debate between standard nasogastric tube versus long nasoenteric tube decompression has mostly settled in favor of the nasogastric tube. Long tubes are more difficult to place, requiring special expertise, serial radiographic studies, or endoscopy to guide insertion.
- Narcotic analgesics may be administered to comfort the patient, but not to the point of diminishing mental status. The practice of withholding pain medication to avoid masking the signs of perforation or ischemia is probably unnecessary.
- Serial abdominal examinations (ideally just before the next dose of analgesics) should be performed to assess for increasing tenderness or the presence of peritoneal signs. Any change in the patient's condition that suggests developing bowel ischemia mandates exploratory laparotomy.
- In general, a nonoperative course may be followed for 24–48 h. If the obstruction has not resolved within that time period, it is unlikely to do so and laparotomy is advised.

Decision to Operate

- Patients with fever, peritonitis, pneumoperitoneum, or overt sepsis should undergo emergent laparotomy because these are hard signs of transmural bowel necrosis.
- It is not uncommon for patients with small bowel obstruction to present with tachycardia, relative hypotension, mild acidosis, and leukocytosis, all of which may be secondary to dehydration. These patients should be aggressively rehydrated with isotonic intravenous fluids and the above parameters should be reassessed. Persistence of any of these signs after fluid resuscitation should prompt immediate laparotomy.
- Distinguishing between partial and complete obstruction is also a key element in deciding which patients should be taken for early operation. As stated above, the likelihood of resolution of a complete obstruction with expectant management is low (20%).
- The passage of stool or flatus cannot be relied on as an accurate predictor because patients with complete obstruction may continue to pass stool and flatus until the bowel distal to the site of

obstruction is evacuated. However, if this continues for more than 12 h after the onset of obstructive symptoms, the likelihood of complete obstruction is diminished.

- The passage of large volumes of nonbloody, watery stool along with vomiting and distension is pathognomonic for partial small bowel obstruction.
- The onset of flatus, however, usually signals the beginning of resolution of the obstruction because flatus is produced from swallowed air.

Surgical Technique

- After the adequacy of resuscitation is confirmed and broad-spectrum antibiotics active against enteric pathogens are administered, the peritoneal cavity is entered through a midline incision. This is a point in the operation where the risk of inadvertent enterotomy is very high because bowel loops are distended and often adherent to the undersurface of the abdominal wall.
- In the most favorable scenario, a single constricting band will be encountered that can be sharply divided to relieve the obstruction. In the worst cases, the peritoneal cavity will be totally obliterated by scar tissue. An orderly and systematic approach to adhesiolysis is advised in these instances.
- Assessment of bowel viability is usually possible by using the triad of color, peristalsis, and mesenteric pulsations. In cases in which these signs are questionable, the ischemic segment should be wrapped in warm, wet packs and viability reassessed after 15 min. If viability is still in doubt, use of the Doppler probe or systemic injection of fluorescein dye followed by inspection of the bowel under a Wood's lamp may aid in decision making.
- If the area in question is a short segment, it may be best to proceed with resection. If an extensive segment of questionable viability is present, then a second-look operation 24 h later should be planned before committing the patient to a massive small bowel resection.

Special Situations

Early Postoperative Bowel Obstruction

- Early postoperative bowel obstruction is generally defined as mechanical obstruction occurring within 1 month of abdominal

or pelvic surgery. This condition is special in that attempts at relaparotomy in the early postoperative period frequently result in disastrous complications.

- An intense inflammatory response usually begins within the abdomen at 7–10 days postoperatively and persists for at least 6 weeks. If forced to operate during this period of time, the surgeon is likely to encounter dense hypervascular adhesions that may obliterate the peritoneal cavity. The risk of enterotomy and subsequent fistulization is extremely high. In addition, vascular or extensive serosal injury of the bowel may lead to massive resections.
- Therefore, immediate reoperation for early postoperative bowel obstruction is not advised, especially considering the fact that the development of strangulation in this setting is extremely rare. These patients should be managed conservatively with nasogastric or long tube suction and intravenous fluids. If resolution does not occur within the first 5–7 days, a percutaneous gastrostomy tube may be placed for longer-term decompression, and the patient is started on hyperalimentation. Patients may be discharged from the hospital on this regimen and laparotomy performed in 6 weeks if the obstruction has not resolved.
- However, if peritonitis or signs of sepsis are present initially or develop during the course of nonoperative therapy, a CT scan should be performed immediately. Any abscess or fluid collection caused by an enteric leak can be percutaneously drained and a controlled enterocutaneous fistula established. Exploration is usually only required in cases of ischemic or necrotic bowel.
- There is a place for very early exploration within the first 10 days postoperatively if obstruction is recognized promptly. The adhesions encountered during this time period have not usually become severe and can be dealt with safely.

Anastomotic “Overhealing”

- Anastomotic overhealing is a rare cause of postoperative small bowel obstruction. It is most often attributable to early adhesion and healing of the staple lines of the linear cutter between the limbs of a functional end-to-end/side-to-side anastomosis. This is best prevented by maximally distracting the two staple lines as the transverse staple line is placed to close the enterotomy made to introduce the side-to-side stapler.

- When this occurs in the early postoperative period, it will be easily diagnosed with a water-soluble contrast study, especially if administered via a long tube near the point of obstruction.
- The treatment should be conservative initially and may include long tube decompression.

Prevention of Adhesions

- More than 90% of patients undergoing abdominal surgery will develop some degree of intraabdominal adhesions. Adhesion formation can occur wherever the visceral or parietal peritoneum has been disturbed.
- Once an area of injury is established, fibrin is deposited and then organizes to form a matrix for collagen deposition. Bowel motility and endogenous lubricants attempt to counteract this process, but in most cases, adhesions will eventually result as the deposited collagen matures.
- The progression from early to mature adhesions usually takes approximately 6 weeks.
- Several strategies have been developed to minimize, prevent, or influence adhesion formation. Gentle handling of tissues, avoiding the deposition of talc by wearing powder-free gloves, and copious lavage of the peritoneal cavity at the conclusion of the operative procedure are simple means that should be used in all cases.
- Recently, agents have been developed to reduce or eliminate adhesions through a barrier mechanism. The best studied of these is a bioresorbable membrane of modified sodium hyaluronate and carboxymethylcellulose. A large multicenter study by Becker et al. has shown that this material substantially reduces the extent, incidence, and severity of adhesion formation. Its efficacy in reducing the incidence of adhesive bowel obstruction has recently been reported. However, the decrease in incidence of bowel obstruction from 3.4% in the control group to 1.8% in the treatment group is of uncertain clinical significance.
- The use of adhesion barriers in patients at high risk for subsequent reoperation because of disease or previous adhesions may be justified by the likely improvement in the ease and safety of the subsequent abdominal reentry and explorations. One of the problems with the barrier material is that it only prevents adhesions between the surfaces where it is applied.

D. Pelvic Bleeding

- Serious pelvic bleeding may be encountered during proctectomy and is usually caused by injury to the presacral venous plexus or the internal iliac vessels or their branches.
- Presacral venous hemorrhage is especially challenging because the anatomy and fragility of the presacral venous plexus make control of bleeding difficult.
- Direct finger pressure should be used to gain temporary control of bleeding while allowing the anesthesia team to “catch up” with the resuscitation (adequate IV lines, blood availability, invasive monitors, etc.).
- Once the patient is stabilized, several methods exist for establishing hemostasis. The most common of these is the use of sterile thumb-tacks or specially designed “occluder pins” that are driven into the sacrum at right angles and directly over the site of bleeding. His method works best with midline hemorrhage over healthy bone.
- Pelvic bleeding may also be controlled by packing several laparotomy sponges tightly into the pelvis with the ends being brought out through the lower portion of the abdominal wound. The abdomen is then closed and the patient is taken to the intensive care unit for blood transfusion, fluid resuscitation, correction of coagulopathy, and general support. After 24–48 h, the patient is returned to the operating room for removal of the packs.

Wound Infection and Intraabdominal Abscess

Wound Infection

- Because of the large bacterial content of the colon (10^{10} anaerobes and 10^8 aerobes/gram of stool), wound infection rates are high after colorectal surgical procedures.
- Risk factors for wound infection have been identified and include malnutrition, diabetes mellitus, immunosuppression, age >60 years, American Society of Anesthesia score >2, fecal contamination, length of hospitalization before surgery, and extensive surgery.
- Recently, there is a growing body of literature that shows that mechanical bowel preparation does not decrease the incidence of wound infection.
- Wound infections typically present on or around the fifth postoperative day and are characterized by erythema, warmth, tenderness, fever, and purulent drainage.

- Initial treatment consists of opening a portion of the skin incision over the area of maximal change to allow drainage. Antibiotics are not prescribed unless there is cellulitis present.
- If a significant amount of necrotic tissue is present, it should be débrided. Once the wound is adequately drained, a packing regimen is begun and the wound is allowed to heal by secondary intention.
- Large wounds may be treated with application of a vacuum-assisted wound closure device. After the wound has been débrided by several days of wet to dry dressing changes, the vacuum-assisted closure device is applied (V.A.C.; KCI Therapeutic Services, San Antonio, TX). The advantages of this system are simplification of wound care and quicker closure. The dressing only needs to be changed every 3–5 days and wounds typically close within several weeks.
- Several situations require more aggressive treatment. Deep infection involving the rectus muscle and fascia may occur and result in dehiscence. These patients are usually taken back to the operating room for debridement of the necrotic fascial edges and repair of the dehiscence.
- Invasive wound infections with either clostridium perfringens or beta-hemolytic streptococcus is a potentially life-threatening complication. These infections may have an atypical presentation in that they can occur within the first 1–2 days after surgery and may be associated with minimal skin changes. The combination of fever and unusually severe wound pain early in the postoperative course should prompt opening of the skin incision.
- A necrotizing infection is suggested by the drainage of thin gray fluid. The key to timely diagnosis and treatment of these severe infections is a high level of suspicion. The patient should be taken to the operating room for a thorough wound exploration. All devitalized tissue should be removed and the fascia excised back to healthy, bleeding edges. Broad-spectrum antibiotic coverage should include high-dose penicillin.

Intraabdominal Abscess

- Intraabdominal abscesses can result from anastomotic leaks, enterotomies, or spillage of bowel contents at the time of surgery.
- Patients will usually present with fever, leukocytosis, and abdominal or pelvic pain 5–7 days after surgery.

- The diagnostic modality of choice is a CT scan of the abdomen and pelvis performed with intravenous and oral contrast (and rectal contrast in the patient with a colorectal anastomosis). The finding of a fluid collection with a thickened, enhancing rim and surrounding inflammatory stranding is diagnostic. Air bubbles may also be present in the collection. Proximity to a staple line and the presence of contrast material in the abscess suggest an anastomotic leak as its cause.
- Most intraabdominal or pelvic abscesses can be successfully treated with percutaneous catheter drainage performed under ultrasound or CT guidance. Intravenous antibiotics should also be administered.
- A CT scan or contrast study through the catheter may be performed 48 h after drainage to assess its efficacy.
- Once the abscess cavity has collapsed and no fistula to the bowel is identified, the catheter can be safely removed.
- Some abscesses cannot be drained percutaneously because of their location and lack of a safe “radiographic window” for drainage.
- Reported success rates for percutaneous drainage of intraabdominal abscesses range from 65 to 90% and depend on size, complexity, etiology, and microbial flora.

Perineal Wound Infection

- Perineal wound infection and delayed healing are major causes of morbidity after APR with the incidence ranging from 11 to 50%.
- The rigidity of the lower pelvis combined with wide resection of the perineal soft tissues and levator muscles results in dead space cephalad to the skin closure which is easily infected.
- Technical modifications that may reduce the incidence of perineal wound problems include reapproximation of the subcutaneous tissues, suction drainage of the pelvis (with or without irrigation) to prevent hematoma formation and resultant fibrosis, and filling of the dead space with an omental pedicle graft.
- The area of raw surface deep in the pelvis also frequently fills with small bowel and may lead to small bowel obstruction. The bowel can be excluded from the pelvis by closing the pelvic peritoneum when possible, pulling the uterus posteriorly to close the defect, or by rotating the cecum into the pelvis.

- Several risk factors for perineal wound complications have been identified. Foremost among these is the use of neoadjuvant radiation therapy. In one study, the incidence of perineal wound infection increased from 13 to 34% with the addition of preoperative radiation whereas the rate of nonhealing at 30 days increased from 19 to 51%.
- Other factors are long operative time (>300 min), intraoperative hypothermia, and fecal contamination during the perineal dissection. Patients with anorectal Crohn's disease are also at increased risk when undergoing APR for rectal cancer. However, an intersphincteric dissection in patients with inflammatory bowel disease allows closure of the external sphincter and may improve wound healing (Fig. 10.3).

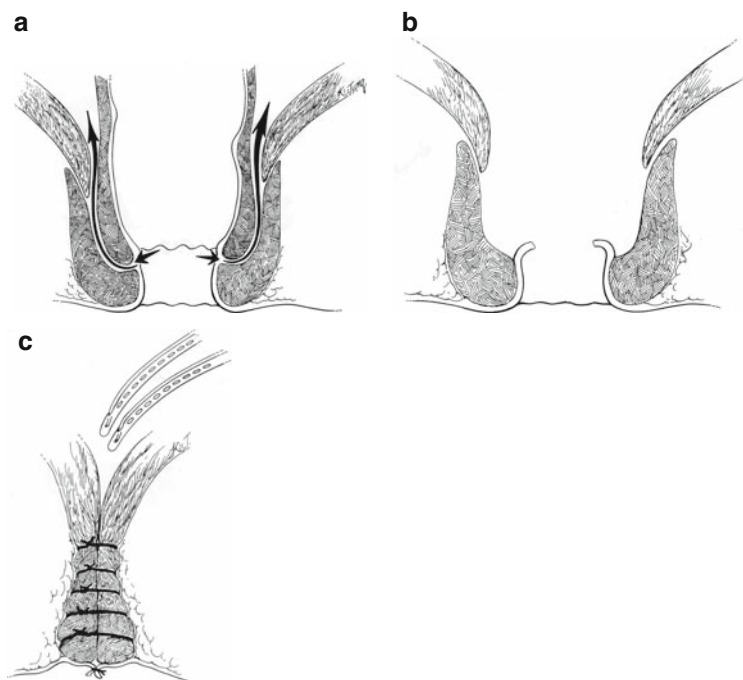


Fig. 10.3. Technique of intersphincteric proctectomy. (a) The mucosa overlying the intersphincteric groove is incised near the dentate line and the dissection is carried cephalad between the internal and external sphincters. (b) This results in retention of the external sphincters and levators which are then able to be closed in the midline (c).

- If infection does occur, the skin should be opened to allow drainage and a program of wet to dry packing begun. A vacuum-assisted closure device can then be placed, as described above. In cases in which a chronic perineal sinus develops, closure of the defect will require wound debridement or myocutaneous flap reconstruction with gracilis, inferior gluteus, or rectus abdominus muscle.

11. Benign Anorectal: Hemorrhoids

A. Anatomy

- Hemorrhoids are cushions of specialized, highly vascular tissue found within the anal canal in the submucosal space.
- The term “hemorrhoidal disease” should be reserved for those vascular cushions that are abnormal and cause symptoms.
- These cushions of thickened submucosa contain vascular spaces (sinusoids), elastic tissue, connective tissue, and smooth muscle (see Fig. 11.1).
- Some of the vascular structures within the cushion when examined microscopically lack a muscular wall. The lack of a muscular wall characterizes these vascular structures as sinusoids and not veins.
- Studies have shown that hemorrhoidal bleeding is arterial and not venous. Hemorrhage occurs from damaged presinusoidal arterioles that communicate with the sinusoids in this region. The hemorrhage is bright red in appearance and has an arterial pH.
- The venous plexus and sinusoids below the dentate line, constitute the external hemorrhoidal plexus which drain primarily via the inferior rectal veins into the pudendal veins and then to branches of the internal iliac veins. Venous drainage also occurs to a lesser extent via the middle rectal veins to the internal iliac veins. The overlying tissue is somatically innervated and is therefore sensitive to touch, pain, stretch, and temperature.
- The subepithelial vessels and sinuses above the dentate line constitute the internal hemorrhoid plexus and drain by way of the middle rectal veins to the internal iliacs.
- The vascular cushions within the anal canal contribute to anal continence and function as a compressible lining that protects

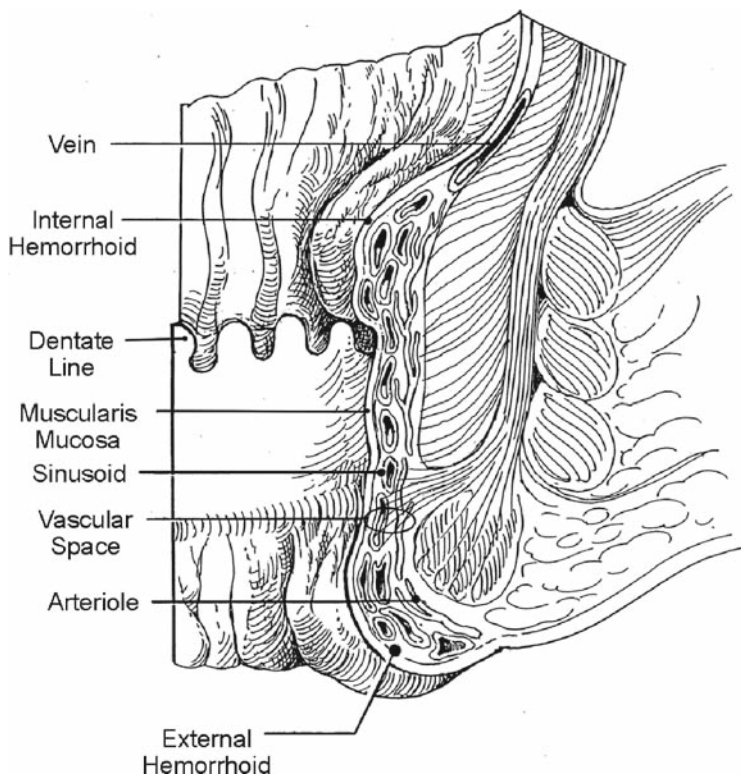


Fig. 11.1. Anal cushion showing Treitz's muscle derived from the conjoined longitudinal muscle of the anal canal.

the underlying anal sphincters. Additionally, the cushions are critical in providing complete closure of the anus, further aiding in continence. As an individual coughs, strains, or sneezes, these fibrovascular cushions engorge and maintain closure of the anal canal to prevent leakage of stool in the presence of increased intrarectal pressure.

- Additionally, this tissue likely supplies important sensory information that enables individuals to discriminate between liquid, solid, and gas, further aiding in continence.
- It is essential to consider that while undertaking any treatment for hemorrhoidal disease the fibrovascular cushions are a part of normal anorectal anatomy and are important in the continence mechanism. Therefore, surgical removal may result in varying

degrees of incontinence particularly in individuals with marginal preoperative control.

- There are three main vascular cushions located in the left lateral, right anterior, and right posterior positions of the anus.
- Most individuals have additional smaller accessory cushions present in between the main cushions.
- The position of hemorrhoids within the anal canal, however, remains remarkably consistent. The configuration of these cushions is quite constant and borne out by the fact that the same configuration can be found in children, the fetus, and even in the embryo.
- The topographic location of pathology around the anus should be described in anatomic terms (anterior, posterior, right lateral, left lateral, etc.) and not by the numbers on the face of a clock. In this way, regardless of whether the patient is in a prone, supine, or lateral position, the pathology can always be accurately located.

B. Etiology

- Etiologic factors thought to be contributory to the pathologic changes in the vascular cushions include constipation, prolonged straining, irregular bowel habits, diarrhea, pregnancy, heredity, erect posture, absence of valves within the hemorrhoidal sinusoids, increased intraabdominal pressure with obstruction of venous return, aging (deterioration of anal supporting tissues), and internal sphincter abnormalities.
- One of the most important etiologic theories is the “sliding anal cushion theory.” Thompson concluded that a sliding downward of the anal lining is responsible for the development of hemorrhoids.
- Repeated stretching of the anal supporting tissues (submucosal Treitz’s muscle and elastic connective tissue framework) which normally functions to anchor and suspend the anal canal lining causes fragmentation of the supporting tissues and subsequent prolapse of the vascular cushions.
- Straining and irregular bowel habits may be associated with engorgement of the vascular cushions making their displacement more likely.

C. Epidemiology

- The reported prevalence of hemorrhoids in the United States is 4.4%, peaking between the ages of 45 and 65.
- Increased prevalence rates are seen in Caucasians and in individuals with higher socioeconomic status. Whether this is secondary to differences in health-seeking behavior rather than true prevalence remains to be proven.

D. Classification

- Hemorrhoids are divided into two types, external and internal. External hemorrhoids are located in the distal one-third of the anal canal, distal to the dentate line, and are covered by anoderm (modified squamous epithelium lacking any skin appendages) or by skin. Internal hemorrhoids are located proximal to the dentate line and are covered by columnar or transitional epithelium. Because this overlying tissue is viscerally innervated, it is not sensitive to touch, pain, or temperature, making it easily amenable to office procedures. Internal hemorrhoids are further subclassified into degrees based on size and clinical symptoms as initially reported by Banov et al. (see Table 11.1). Mixed or combined hemorrhoids are defined as the presence of both internal and external hemorrhoids.

E. Symptoms

- Many patients seen in the office complaining of “hemorrhoids” are frequently found to have other anal problems such as pruritus ani, anal fissures, fistulas, and skin tags.
- A careful history and physical examination including anoscopy will frequently lead to the correct diagnosis. Patients with hemorrhoid disease may complain of bleeding, mucosal protrusion, pain, mucus, discharge, difficulties with perianal hygiene, a sensation of incomplete evacuation, and cosmetic deformity. The presence, quantity, frequency, and timing of bleeding and prolapse should be noted.

Table 11.1. Classification of internal hemorrhoids.

	First degree	Second degree	Third degree	Fourth degree
Finding	Bulge into the lumen of the anal canal $\pm$ painless bleeding	Protrude at the time of a bowel movement and reduce spontaneously	Protrude spontaneously or with bowel movement, require manual replacement	Permanently prolapsed and irreducible
Symptoms	Painless bleeding	Painless bleeding Anal mass with defecation Anal burning or pruritus	Painless bleeding Anal mass with defecation Feeling of incomplete evacuation Mucous leakage Fecal leakage Perianal burning or pruritus	Painless or painful bleeding Irreducible anal mass Feeling of incomplete evacuation Perianal burning or pruritus
Signs	Bright red bleeding Bleeding at end of defecation Blood drips or squirts into toilet	Bright red bleeding Prolapse with defecation	Difficulty with perianal hygiene Bright red bleeding Blood drips or squirts into toilet Prolapsed hemorrhoids reduce manually Perianal stool or mucous Anemia extremely rare	Difficulty with perianal hygiene Bright red bleeding Blood drips or squirts into toilet Prolapsed hemorrhoids always out Perianal stool or mucous

- A thorough dietary and medication history should also be done because certain medications, diets, and or dietary indiscretions cause or exacerbate constipation or diarrhea.
- Symptoms from external hemorrhoids are usually secondary to thrombosis and physical examination shows a tender, bluish-colored lump at the anus distal to the dentate line associated with acute pain.
- Thrombosed external hemorrhoids can bleed secondary to pressure necrosis and subsequent ulceration of the overlying skin.
- External skin tags are folds of skin that arise from the anal verge. These tags may be the end result of prior episodes of thrombosed external hemorrhoids. Enlarged skin tags or external hemorrhoids may interfere with anal hygiene leading to perianal burning or pruritus.
- Internal hemorrhoids are painless unless thrombosis, strangulation, gangrene, or prolapse with edema occurs. Despite what is written, patients will frequently come to the office complaining of “painful hemorrhoids” even when none of these conditions exist.
- Once other sources of pain are ruled out, careful inquiry regarding the description of their pain further elucidates that patients frequently describe their anal pain as “burning” in nature. This may be secondary to perianal irritation from mucous or fecal leakage leading to secondary pruritus ani.
- Bleeding from internal hemorrhoids is bright red and associated with bowel movements. The bleeding usually occurs at the end of defecation. The patient may complain of blood dripping or squirting into the toilet or blood on the toilet tissue.
- Prolapse of the hemorrhoid cushions may manifest itself as an anal mass, mucous discharge, or a sensation of incomplete evacuation. The examiner should ascertain whether the hemorrhoids reduce spontaneously or require manual reduction.

F. Differential Diagnosis

- Because most patients that come into the office or emergency room with anal symptomatology complain of “hemorrhoids,” it is important to rule out other causes (see Table 11.2).

Table 11.2. Differential diagnoses.

	Acute pain	Chronic pain	Bleeding	Pruritus or discharge	Lump or mass
Possible diagnoses	Fissure	Fissure	Fissure	Fistula	Abscess
	Abscess	Abscess	Polyps	Anal warts	Skin tags
	Fistula	Fistula	Colorectal cancer	Anal incontinence	Anal tumor
	Thrombosed hemorrhoid	Anal stenosis	Inflammatory bowel disease	Rectal prolapse	Rectal tumor
		Anal Crohn's	Proctitis	Pruritus ani	Rectal polyps
		Thrombosed hemorrhoid	Internal hemorrhoids	Hypertrophied anal papilla	Rectal prolapse
			Ruptured thrombosed external hemorrhoid	Prolapsed hemorrhoid	Anal Crohn's
					Prolapsed anal papilla
					Thrombosed or prolapsed hemorrhoid

- If the patient's main complaint is anal pain, then other diagnoses should routinely be sought unless thrombosis or prolapse of hemorrhoids is obvious. The causes of pain are almost invariably found in pathology distal to the dentate line, i.e., fissure, abscess, fistula, external hemorrhoid thrombosis, or prolapsed thrombosed internal hemorrhoids.

G. Examination

- After a general patient assessment, the patient is ideally examined in the prone jackknife position on a proctologic table.
- Patients with a history suggestive of hemorrhoid disease with an unremarkable examination in the prone jackknife position should be examined in a sitting position on the commode while asking the patient to strain.
- Oftentimes, pathology is uncovered when gravity assists in the examination. In patients who are unable to tolerate the jackknife position (morbidly obese, pregnant, elderly, patient with knee or hip joint pathology, pulmonary disease) or when a proctologic table is not available, examination should be performed in the modified left lateral (Sims) position.
- Calmly reassure your patients at the start of the examination and routinely discuss what you are about to do before actually carrying out anal inspection, palpation, digital rectal examination, anoscopy, and proctoscopy, which should be performed on all patients if feasible.
- Gentle spreading of the buttocks allows careful inspection of the squamous portion of the anal canal as well as the perianal, genital, perineal, and sacrococcygeal regions. Skin tags, external hemorrhoids, fissures, fistulas, infection, hemorrhoid prolapse, mucosal prolapse, rectal prolapse, tumors, skin lesions, thrombosis, and rashes all can be diagnosed on careful visual inspection if present.
- Palpation of the perianal region can localize pain, tenderness, induration, or masses.
- Digital examination gently performed localizes pain, masses, abscesses, and assesses sphincter tone.
- Anoscopy permits visualization of the anoderm and internal hemorrhoidal cushions. Anoscopy is best performed with a side-viewing anoscope especially when hemorrhoid ligation is being considered.

- Although the degree of prolapse may be ascertained if the patient is asked to strain, a more accurate assessment of prolapse can be made if inspection takes place while the patient is sitting and straining on a commode.
- Proctoscopy or flexible sigmoidoscopy is performed when possible to assess the rectum and lower colon for neoplasms and inflammatory bowel disease.
- At a minimum, patients with anorectal complaints should undergo anoscopy, rigid proctosigmoidoscopy, and/or flexible sigmoidoscopy and further work-up depends on findings at physical examination, patient age, and history.
- Although patients may be too uncomfortable to undergo these procedures at the initial visit, it is important that they are performed before discharging the patient from your care.
- Total colon examination via colonoscopy or air-contrast barium enema is indicated when no source is evident on anorectal examination, the bleeding is atypical for hemorrhoids, anemia or Hemoccult-positive stool is present, or significant risk factors for colonic neoplasia exist (age, family history, or personal history of polyps).
- Because hemorrhoids are rarely the cause of anemia (0.5 patients/100,000 population), total colon examination is indicated even in the very young patient.
- Patients less than 40 years of age with hemorrhoid disease compatible with their symptomatology probably require no further work-up.
- Patients older than 40 years of age with minimal hemorrhoid disease, additional symptoms, or positive family history for colorectal cancer should undergo a total colon examination with either a colonoscopy or double contrast barium enema to identify other etiologies for bleeding that are not obvious on initial examination.

H. Treatment

- Treatments are classified into three categories (1) dietary and lifestyle modification; (2) nonoperative/office procedures; and (3) operative hemorrhoidectomy.
- In general, less symptomatic hemorrhoids, such as those that cause only minor bleeding, can be treated with simple measures such as dietary modification, change in defecatory habits, or office procedures.

- More symptomatic hemorrhoids such as third or fourth degree are more likely to require operative intervention.

Dietary and Lifestyle Modification

- Because prolonged attempts at defecation, either secondary to constipation or diarrhea, have been implicated in the development of hemorrhoids, the main goal of this treatment is to minimize straining at stool. This is usually achieved by increasing fluid and fiber in the diet, recommending exercise, and adding supplemental fiber agents (psyllium) to the diet in patients unable to consume sufficient amounts of fiber in their diets.
- Reduced hemorrhoidal bleeding has been shown with the use of psyllium in a double-blind, placebo controlled trial; however, other studies are less favorable. Psyllium works in conjunction with water to add moisture to the stool and subsequently decrease constipation. Psyllium may also be therapeutic in treating diarrhea. It may add bulk to liquid stools therefore increasing the consistency and decreasing the volume.
- Dietary modification with fiber supplementation (psyllium, methylcellulose, calcium polycarbophil) is one of the mainstays of therapy for patients with hemorrhoidal disease. In the majority of cases, symptoms of bleeding and pain improve over a 6-week period.
- A diet high in fiber (20–35 g/day) including the consumption of plenty of fruits and vegetables is recommended especially if the patient has a history of constipation or straining.
- A common problem with fiber supplementation is noncompliance because of either poor palatability or symptoms of bloating, increased flatus, and abdominal cramps. Compliance is improved by starting at lower doses and slowly increasing the quantity of fiber ingested until the desired stool consistency is achieved.
- Some common fiber products currently available are listed in Table 11.3.
- If dietary modification fails to relieve symptoms, then further therapy is indicated (see Table 11.4).
- Oftentimes, simply asking an individual to curtail reading on the commode resolves the hemorrhoidal symptoms.

Table 11.3. Fiber supplements.

Type of fiber	Trade name	Available fiber
Psyllium	Metamucil™	3.4 g/teaspoon
	Metamucil capsules™	0.52 g/capsule
	Konsyl™	6.0 g/teaspoon
Methylcellulose	Citrucel™	2.0 g/dose
Calcium polycarbophil	FiberCon™	0.5 g/capsule
	Konsyl fiber tablets™	0.5 g/tablet

Table 11.4. Management of internal hemorrhoids by classification.

Treatments	First degree	Second degree	Third degree	Fourth degree	Acute pro-lapse with thrombosis
Dietary	X	X	X	X	X
Banding	X	X	X		
Sclerotherapy	X	X	X		
Infrared coagulation	X	X	X		
Excisional hemorrhoidectomy			X	X	Emergent
Stapled hemorrhoidopexy		X	X	X (?)	
Multiple thrombectomies and multiple bandings					X

- Lifestyle and dietary modifications along with ruling out proximal sources of bleeding are all that is required for the majority of patients complaining of hemorrhoidal disease.

Medical Therapy

- Rigorous levels of evidence do not exist to support the use of topical therapies, whether physical or pharmacologic (sitz baths, anesthetics, phlebotonics, corticosteroids, or ice).
- Most studies have used poor methods with lack of controls, multiple associated components, and heterogeneous preparations. Therefore, firm recommendations cannot be made at the

Table 11.5. Registered Cochrane review titles on hemorrhoid management.

Cochrane review title	Author	Primary aim
Laxatives and topical treatments for hemorrhoids	Alonso-Coello and Lopez-Yarto	To determine the efficacy of laxatives and topical treatments in improving the symptoms derived from symptomatic hemorrhoids
Nonoperative treatment for hemorrhoidal disease	Thaha, Campbell, and Steele	To determine the long-term therapeutic efficacy of various non-operative treatment methods in controlling hemorrhoidal symptoms
Phlebotonics for hemorrhoids	Alonso, Johanson, Lopez-Yarto, and Martinez	To determine the efficacy of phlebotonics in improving the symptoms derived from symptomatic hemorrhoids
Circular stapled anopexy vs. excisional hemorrhoidectomy for treatment of hemorrhoidal disease	Thaha, Campbell, Staines, Nyström, Steele	To assess stapled anopexy with excisional methods

time of the writing of this chapter. Cochrane reviews on related registered Cochrane titles are listed in Table 11.5.

- Despite the lack of any rigorous evidence, probably the most effective topical treatment for the relief of symptoms comes in the way of warm (40°C) sitz baths. Soaking time should be limited (15 min) to prevent edema of the perianal and perineal skin.
- The application of ice packs to the anal region also may relieve symptoms and is acceptable provided that contact time is not prolonged.
- Pharmaceutical preparations such as creams, ointments, foams, and suppositories have little pharmacologic rationale in the management of hemorrhoidal disease. Suppositories never remain within the anal canal and usually end up in the lower rectum where they may provide an emollient effect or lubrication to the stool.
- Popular topical soothing agents are frequently combined with corticosteroids and or anesthetics. Although individuals may report empirical symptomatic benefit with their use, patients must be advised against prolonged use because of possible local allergic effects or sensitization of the skin. Symptom

improvement with the use of these agents may be due to the interminant nature of hemorrhoid symptoms.

- Calcium dobesilate (calcium 2,5-dihydroxybenzenesulfonate) is a drug with previously demonstrated efficacy in the treatment of diabetic retinopathy and chronic venous insufficiency. These beneficial effects of the drug are related to its ability to decrease capillary permeability, platelet aggregation, and blood viscosity and to increase lymphatic transport. A randomized, double-blind, controlled study was conducted to investigate the efficacy of oral calcium dobesilate therapy in treating acute attacks of internal hemorrhoids. Together with recommendations about diet and bowel discipline, oral calcium dobesilate treatment provided efficient, fast, and safe symptomatic relief from acute symptoms of hemorrhoidal disease.

Office Treatments

Rubber Band Ligation

- Rubber band ligation is a method of tissue destruction and fixation. It is one of the most widely used techniques in the United States to treat first-, second-, and third-degree internal hemorrhoids.
- The rubber band is placed on the redundant mucosa a minimum of 2 cm above the dentate line causes strangulation of the blood supply to the banded tissue, which sloughs off in 5–7 days leaving a small ulcer that heals and fixes the tissue to the underlying sphincter.
- Rubber band ligation is recommended for individuals with first- or second-degree hemorrhoids and, in some circumstances, third-degree hemorrhoids.
- Several commercially available types of hemorrhoid ligators are available. A suction ligator (McGown™, Pembroke Pines, FL) (see Fig. 11.2a) draws the hemorrhoid tissue into the ligating barrel via suction, and closing the handle inserts a band around the hemorrhoid.
- The advantage of this ligator is that only one hand is required for placement of the band, making an assistant unnecessary for the procedure. The disadvantage of the suction ligator is that the ligating barrel is usually smaller than other ligators, hence less tissue is banded.

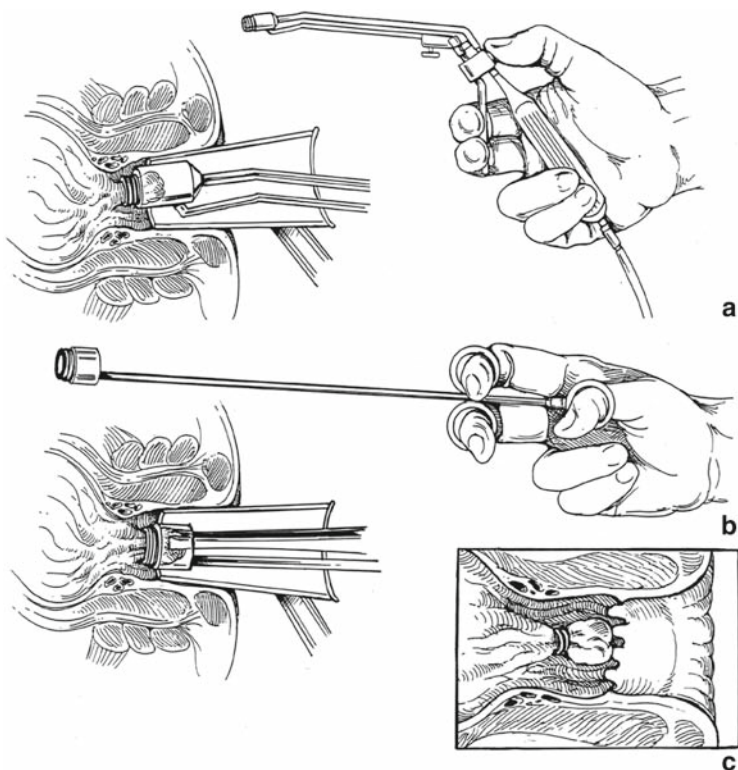


Fig. 11.2. Banding an internal hemorrhoid. (a) The internal hemorrhoid is teased into the barrel of the ligating gun with a McGown suction ligator, or (b) a McGivney type ligator. (c) The apex of the banded hemorrhoid is well above the dentate line in order to minimize pain. (Reprinted from Beck D, Wexner S. *Fundamentals of Anorectal Surgery*. 2nd ed. Copyright 1998, with permission from Elsevier.)

- With the conventional ligators, an atraumatic clamp is used to draw hemorrhoid tissue into the barrel of the ligator and a small rubber band is placed (see Fig. 11.2b, c). Disadvantage compared with the suction ligator is that two hands are required for placement of a band necessitating an additional assistant for the procedure and the grasped tissue may be torn by excessive traction. An advantage is that a greater amount of excess hemorrhoid tissue can be eliminated with these ligators.

- An alternative device developed for hemorrhoid banding consists of a disposable syringe-like hemorrhoid ligator, invented to simplify the banding procedure for both patient and surgeon (see Fig. 11.3).
- It is imperative to avoid banding too close to the dentate line or incorporating internal sphincter into the ligator because this can lead to severe pain or pelvic sepsis. It has been shown that multiple hemorrhoid groups can be banded at a single session with no significant increase in morbidity when compared with single ligation. Some surgeons prefer banding one group initially to monitor patient response and then perform multiple bandings at a subsequent session if the initial banding was well tolerated.

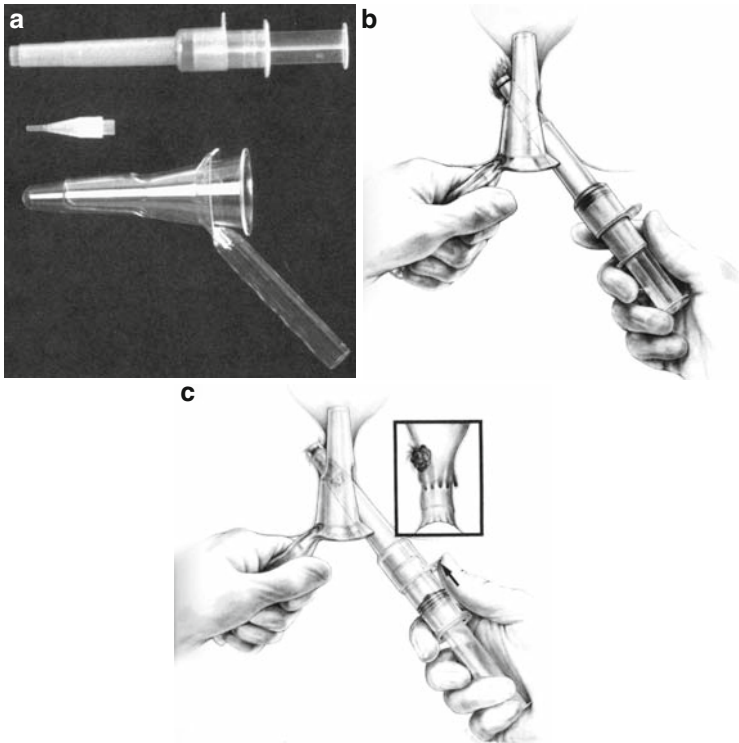


Fig. 11.3. (a) O'Regan disposable banding system (Medsurge Medical Products Corp., Vancouver, Canada). (b, c) Technique of internal hemorrhoid ligation using the O'Regan ligating system.

- Banding patients on sodium warfarin or heparin therapy must be done cautiously because subsequent sloughing of tissue may lead to massive hemorrhage.
- Complications of hemorrhoid banding include pain, thrombosis, bleeding, and life-threatening perineal or pelvic sepsis. The most common complication of rubber band ligation is pain, which is reported in 5–60% of patients.
- Constipation should be avoided during treatment because it has been shown to worsen the outcome of rubber band ligation.
- There have been reported cases of life-threatening perineal and/or pelvic sepsis after hemorrhoid banding. Frequent symptoms are anal pain, fever, and difficult urination. This necrotizing perineal or pelvic sepsis is rare but mandates emergent attention (intravenous fluids, antibiotics, and perineal examination and debridement).
- The risk of necrotizing infection seems to be increased in individuals with immune compromised states, including patients with uncontrolled acquired immunodeficiency syndrome, neutropenia, and severe diabetes mellitus.
- Approximately two-thirds to three-quarters of all individuals with first- and second-degree hemorrhoids respond to banding although this may need to be repeated at a later date.
- The majority of patients experience relief of symptoms with banding, but more than one banding session may be required.

Infrared Photocoagulation, Bipolar Diathermy, and Direct-Current Electrotherapy

- These techniques rely on coagulation, obliteration, and scarring which eventually produce fixation of the hemorrhoid tissue.
- The infrared coagulator works best with small, distal, bleeding, first- and second-degree hemorrhoids. It has been described to be slightly less painful than rubber banding. In three randomized trials, hemorrhoid bleeding was successfully controlled in the majority of patients with first- and second-degree hemorrhoids.
- Bipolar diathermy or coagulation (BICAP; Circon ACMI, Stamford, CT) is essentially electrocautery in which the heat does not penetrate as deeply as in monopolar coagulation.
 - First-, second-, and third-degree hemorrhoids have been treated with success rates varying from 88 to 100% whereas

up to 20% of patients may need excisional hemorrhoidectomy for prolapsing tissue.

- Direct-current electrotherapy is applied through a probe placed via an anoscope onto the mucosa at the apex of the hemorrhoid.
 - This technique, however, has not been widely accepted primarily because of the lengthy treatment times and limited effect in higher-degree hemorrhoids.

Sclerotherapy

- This office method relies on the injection of chemical agents into hemorrhoids that create fibrosis, scarring, shrinkage, and fixation of the hemorrhoid by obliterating the vascularity with a sclerosant solution.
- Frequently used agents include 5% phenol in oil, 5% quinine and urea, or hypertonic salt solution.
- Sclerotherapy should not be performed in the face of anorectal infection or with prolapsed thrombosed hemorrhoids.
- Sclerotherapy can be used in patients on long- or short-term anticoagulation.
- Repetitive sclerotherapy should be used with caution because of the potential of scarring and stricture formation.
- Sclerotherapy works best for first- and second-degree hemorrhoids.

Anal Dilatation or Stretch

- Although it has had its proponents, primarily in European countries, subsequent reports have shown endosonographic evidence of sphincter injury as well as high rates of associated incontinence especially with long-term follow-up.

Cryotherapy

- Cryotherapy is based on the concept that freezing the internal hemorrhoid at low temperatures can lead to tissue destruction.
- The procedure is time consuming and associated with a foul-smelling profuse discharge, irritation, and pain.

- The procedure should no longer be recommended for the treatment of internal hemorrhoids.

External Hemorrhoids

Acute Thrombosis

- Patients with a thrombosed external hemorrhoid typically present with complaints of a painful mass in the perianal region.
- The pain is frequently described as burning in nature. The pain associated with the abrupt onset of an anal mass usually peaks at around 48 h and subsides significantly after the fourth day (see Fig. 11.4). The skin overlying the thrombosed hemorrhoid may necrose and ulcerate, resulting in bleeding, discharge, or infection.
- Treatment should be aimed at relief of pain. The management will depend, therefore, on the patient's symptoms at the time seen. If the pain is intense, then excision of the thrombosed external hemorrhoid should be offered. If the pain is subsiding, then conservative nonoperative management is warranted.
- Nonoperative treatment consists of warm sitz baths, nonconstipating analgesics, and bulk-producing fiber supplements. Anoscopy and proctoscopy to rule out associated anorectal disease are postponed to a later date when the patient is not in acute pain.

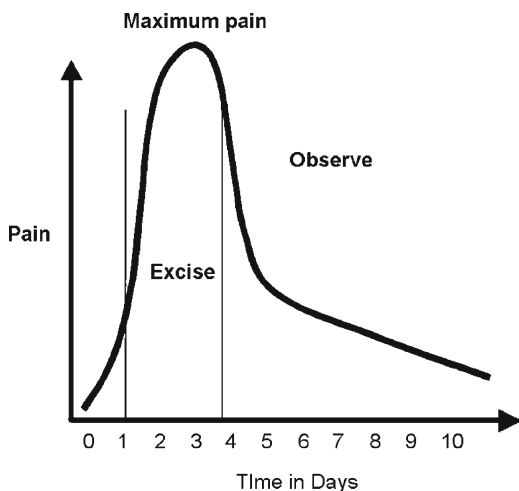


Fig. 11.4. Timing of excision of a thrombosed external hemorrhoid.

- The operative treatment of a thrombosed external hemorrhoid demands excision of the entire thrombus. This can be done in the clinic, office, or emergency room under local anesthesia (0.5% lidocaine mixed with equal amounts of 0.25% bupivacaine containing 1:200,000 epinephrine).

Operative Hemorrhoidectomy

- Hemorrhoidectomy is indicated for patients with symptomatic combined internal and external hemorrhoids who have failed or are not candidates for nonoperative treatments. This would include patients with extensive disease, patients with concomitant conditions such as fissure or fistula, and patients with a preference for operative therapy.
- Only about 5–10% of patients need surgical hemorrhoidectomy.
- Recurrence with operative hemorrhoidectomy is uncommon and hemorrhoidectomy is the most effective treatment for hemorrhoids, especially those that are third degree.
- Hemorrhoidectomy can be performed using a variety of techniques or instruments; however, most are variants of either a closed or open technique.
 - The Milligan–Morgan technique (open) is widely used in the United Kingdom (Fig. 11.5). It involves excision of the external and internal hemorrhoid components leaving the skin defects open to heal by secondary intention over a 4- to 8-week period.
 - The Ferguson hemorrhoidectomy (closed) involves excision of the external and internal hemorrhoid components with closure of the skin defects primarily (Fig. 11.6).
- Table 11.6 lists four randomized prospective studies comparing open vs. closed hemorrhoidectomy. The majority of trials showed no difference in pain, analgesic use, hospital stay, and complications, whereas complete wound healing shows mixed results.
- One of the most significant obstacles to patients seeking surgical management of their hemorrhoids is postoperative pain. Narcotics are often required to control pain and patients are frequently not back to their usual activities including work for 2–4 weeks.
- The majority of randomized trials have shown no difference between diathermy or scissor excision hemorrhoidectomy (see Table 11.7).

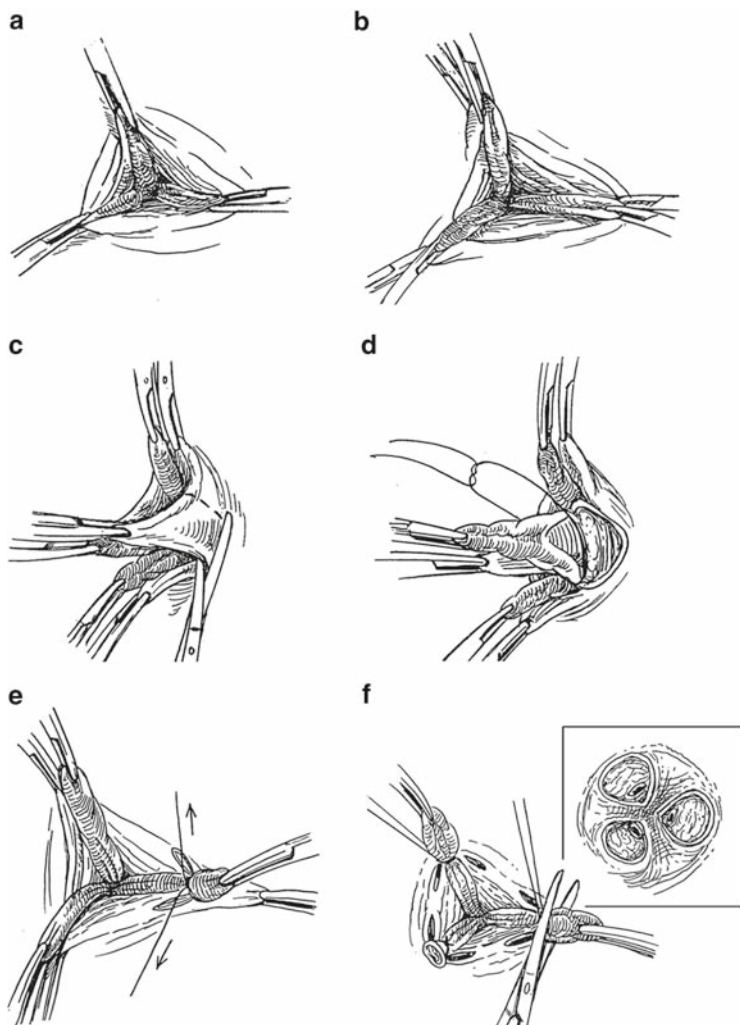


Fig. 11.5. Open (Milligan-Morgan) hemorrhoidectomy. (a) External hemorrhoids grasped with forceps and retracted outward. (b) Internal hemorrhoids grasped with forceps and retracted outward with external hemorrhoids. (c) External skin and hemorrhoid excised with scissors. (d) Suture placed through proximal internal hemorrhoid and vascular bundle. (e) Ligature tied. (f) Tissue distal to ligature is excised. Insert depicts completed three bundle hemorrhoidectomy.

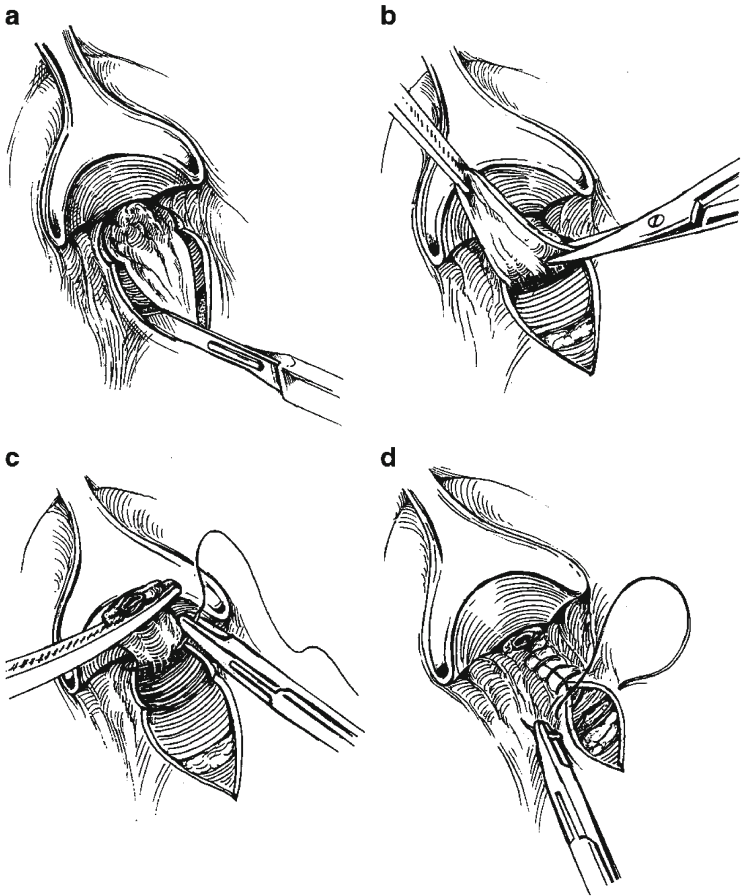


Fig. 11.6. Modified Fergusson excisional hemorrhoidectomy. (a) Double elliptical incision made in mucosa and anoderm around hemorrhoidal bundle with a scalpel. (b) The hemorrhoid dissection is carefully continued cephalad by dissecting the sphincter away from the hemorrhoid. (c) After dissection of the hemorrhoid to its pedicle, it is either clamped, secured, or excised. The pedicle is suture ligated. (d) The wound is closed with a running stitch. Excessive traction on the suture is avoided to prevent forming dog ears or displacing the anoderm caudally.

Table 11.6. Randomized, prospective studies of open vs. closed hemorrhoidectomy.

Author	N	Pain	Complete wound healing	Analgesics	Hospital stay	Complications
Ho	67	n.s.	O > C	n.s.	n.s.	n.s.
Carapeti	36	n.s.	n.s.	n.s.	n.s.	n.s.
Arbman	77	n.s.	C > O	n.s.	n.s.	n.s.
Gencosmanoglu	80	C > O	C > O	C > O	n.s.	C > O

C close; O open; n.s. not significant

Table 11.7. Randomized, prospective studies of LigaSure™ vs. diathermy hemorrhoidectomy.

Author	N	Operative time	Blood loss	Hospital Stay	Postoperative pain	Complications
Jayne	40	L < D	L < D	L < D	n.s.	n.s.
Palazzo	34	L < D	?	n.s.	n.s.	n.s.
Franklin	34	L < D	?	n.s.	L < D	?

L LigaSure™; D diathermy; n.s. not significant; ? not reported; N number

- Complications associated with hemorrhoidectomy include urinary retention (2–36%), bleeding (0.03–6%), anal stenosis (0–6%), infection (0.5–5.5%), and incontinence (2–12%).
- Over the past 6–7 years, stapled “hemorrhoidopexy” has been developed as an alternative to standard Ferguson or Milligan–Morgan hemorrhoidectomy mainly because of the pain associated with traditional hemorrhoid surgery (see Fig. 11.7).
- The procedure involves the use of a specially designed circular stapler (Ethicon Endo-Surgery), which performs a circumferential resection of mucosa and submucosa above the hemorrhoids and then staples closed the defect (see Fig. 11.8). This procedure is more of a hemorrhoidopexy than a hemorrhoidectomy.
- This procedure can be used for patients with all degrees of hemorrhoids, however is best reserved for patients with second- and third-degree hemorrhoids that do not respond to

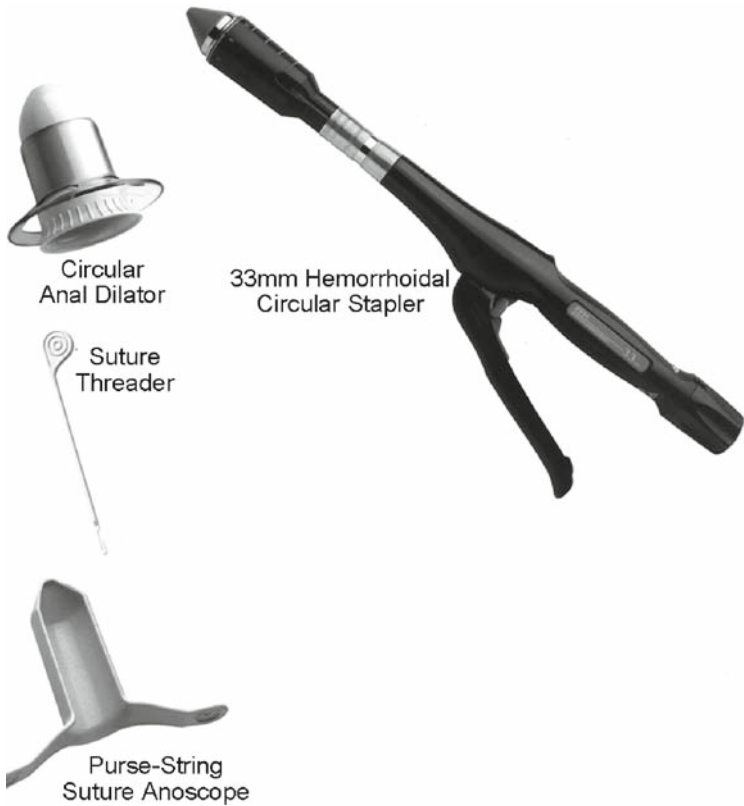


Fig. 11.7. Second generation PPH-03 hemorrhoid stapler. Shown are 33-mm hemorrhoidal circular stapler, suture threader, circular anal dilator, and pursestring suture anoscope. (Reprinted with permission from Ethicon Endo-Surgery.)

banding and fourth-degree hemorrhoids that are reducible under anesthesia.

- A number of randomized, controlled trials comparing stapled hemorrhoidopexy with conventional hemorrhoidectomy have been published as well as reviewed and are listed in Table 11.8.
- The majority of studies show that stapled hemorrhoidopexy is less painful, and allows earlier return to work compared with conventional hemorrhoidectomy.

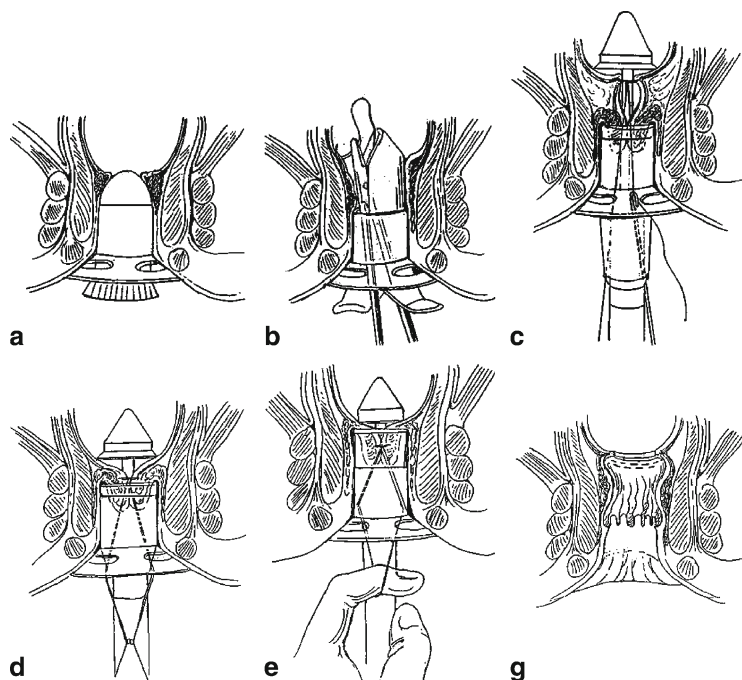


Fig. 11.8. Stapled anoplasty (procedure for prolapse and hemorrhoids). **(a)** Retracting anoscope and dilator inserted. **(b)** Monofilament pursestring suture (eight bites) placed using operating anoscope approximately 3–4 cm above anal verge. **(c)** Stapler inserted through pursestring. Pursestring suture tied and ends of suture manipulated through stapler. **(d)** Retracting on suture pulls anorectal mucosa into stapler. **(e)** Stapler closed and fired. **(f)** Completed procedure.

- Despite these early encouraging results and safety profile, several serious complications have been reported including rectal perforation, retroperitoneal sepsis, pelvic sepsis, and death.
- One other disadvantage of the stapling procedure is that it does not address fibrotic external hemorrhoids or additional anorectal pathology such as fissures or skin tags.

Table 11.8. Prospective, randomized trials comparing stapled hemorrhoidopexy with excisional hemorrhoidectomy.

with excisional hemorrhoidectomy.						
Author	Year	Location	No.	No. PPH patients (excisional patients)	Follow-up	Conclusions regarding stapled hemorrhoidopexy
Ho	2000	Singapore	57	62 MM	3 mo	Similar LOS, less pain at bowel movement, less analgesics, earlier return to work, similar complications, similar manometry and U/S data
Mehigan	2000	United Kingdom	20	20 MM	4 mo	Less pain, same LOS, similar complications, earlier return to activity
Rowsell	2000	United Kingdom	11	11 MM	6 wk	Shorter LOS, less pain, earlier return to activity
Boccasanta	2001	Italy	40	40 MM	20 mo	Less OR time, less pain, similar complications, earlier return to work, same recurrence
Brown	2001	Singapore	15	15 MM	6 wk	For thrombosed internal hemorrhoids: less pain, more complications, earlier return to work
Shalaby	2001	Egypt	100	100 MM	1 y	Less OR time and LOS, less pain, earlier return to work, less anal discharge, fewer complications
Correa-Rovelo	2002	Mexico	42	42 Ferg	6 mo	Less OR time, less pain, fewer complications, shorter time to BM, earlier return to activity

(continued)

Table 11.8. (continued)

Author	Year	Location	No.	No. PPH patients (excisional patients)	Follow-up	Conclusions regarding stapled hemorrhoidopexy
Hetzer	2002	Switzerland	20	20 Ferg	1 y	Less OR time, less pain, similar complications, earlier return to work, same recurrence
Ortiz	2002	Spain	27	28 MM	1 y	Less OR time, less pain, similar return to work, similar complications, more recurrent prolapse
Pavlidis	2002	Greece	40	40 MM	1 y	Less OR time, shorter LOS, less pain, less analgesics, greater satisfaction, similar symptom control
Wilson	2002	United Kingdom	32	30 MM	8 wk	Less OR time, shorter LOS, shorter postoperative time with anal pad, more postoperative bleeding, reduced anal discharge, shorter time to work
Cheetham	2003	United Kingdom	15	16 MM	18 mo	Less pain, earlier time to work, two PPH patients with persistent pain/fecal urgency, same satisfaction, similar symptom control
Kairaluoma	2003	Finland	30	30 MM	1 y	Less pain, earlier return to work, similar complications, more treatment failures
Maw	2003	Singapore	101	98 MM	Perioperative	No difference in rate of bacteremia

(continued)

Table 11.8. (continued)

Author	Year	Loca- tion	No. PPH patients (exci- sional patients)		Folow- up	Conclusions regard- ing stapled hemor- rhoidopexy
			No.			
Palimento	2003	Italy	37	37 MM	6 mo	Less OR time, less pain, less pain with BM, similar return to activity, similar symptom control
Senagore	2003	United States	77	79 Ferg	1 y	Less pain, less pain at BM, less analgesics, fewer re-treatments, similar symptom control

Los length of stay; *OR* operating room; *PPH* procedure for prolapse and hemorrhoids; *uls* ultrasound; *BM* bowel movement; *wk* week; *MM* Milligam–Morgan, *Ferg* Ferguson, *mo* month; *y* years

Stapling Technique

- It is important to remember that this technique does not completely excise the hemorrhoids; rather, it returns the tissues to their physiologic location.

I. Strangulated Hemorrhoids

- Strangulated hemorrhoids arise from prolapsed third- or fourth-degree hemorrhoids that become incarcerated and irreducible because of prolonged swelling.
- Patients usually have a long-standing history of prolapse and may present with complaints of severe pain and urinary retention.
- Examination shows a rosette of thrombosed external hemorrhoids and prolapsed incarcerated internal hemorrhoids with marked edema. This can progress to subsequent ulceration and necrosis if left untreated.
- Treatment usually consists of urgent or emergent hemorrhoidectomy in an operating room. An open or closed technique can

be performed unless tissues are necrotic in which case the open technique should be performed.

- An alternative treatment that can be performed in the office or emergency department setting consists of locally anesthetizing the area, collapsing the tissues via massage, reducing the internal hemorrhoids and performing multiple external thrombectomies, and multiple rubber band ligations. This can provide immediate relief and future hemorrhoidectomy is seldom needed.
- A randomized trial comparing open hemorrhoidectomy vs. incision and ligation for acute hemorrhoidal disease showed both techniques to be safe and with a trend toward earlier recovery from the incision ligation technique.

J. Hemorrhoids, Varices, and Portal Hypertension

- Anorectal varices essentially provide a collateral pathway to decompress the portal system into the systemic circulation. Despite this communication between the portal and systemic systems, the incidence of hemorrhoidal disease in patients with portal hypertension is no greater than in the general population.
- Anorectal varices are actually quite common in patients with portal hypertension. However, unlike esophageal varices, anorectal varices rarely bleed and are implicated in less than 1% of massive bleeding episodes in patients with portal hypertension.

K. Hemorrhoids in Pregnancy

- Although hemorrhoidal symptoms often occur and are exacerbated during pregnancy, the majority that intensify during delivery usually resolve.
- Hemorrhoidectomy during pregnancy should only be offered for acutely thrombosed and prolapsed hemorrhoidal disease.

- If required, the procedure should be performed under local anesthesia with the patient in the left anterolateral position to rotate the uterus off the inferior vena cava.

L. Hemorrhoids and Crohn's Disease

- Crohn's disease of the intestine in and of itself is not an absolute contraindication to hemorrhoidectomy. However, extreme caution and careful patient selection are warranted.
- In a study published from St. Mark's hospital, the rate of severe complications was high. Approximately 30% of their Crohn's patients treated for hemorrhoids required a proctectomy for complications possibly related to the treatment.
- Hemorrhoidectomy in patients with anorectal Crohn's disease or Crohn's proctitis should be avoided because of a substantially increased risk of local complications and subsequent need for proctectomy.

M. Hemorrhoids and the Immunocompromised

- Management of hemorrhoidal disease in the immunocompromised patient is challenging and fraught with difficulties secondary to poor wound healing and infectious complications.
- Although infection with the human immunodeficiency virus is not a contraindication to hemorrhoidectomy, it cannot be recommended for patients with the acquired immunodeficiency syndrome because of increased complications.

N. Posthemorrhoidectomy Hemorrhage

- Severe hemorrhage after hemorrhoidectomy is a rare complication occurring in approximately 2% (0.6–5.4%) of patients.
- The majority of patients will respond to packing or tamponade with a Foley catheter balloon. Approximately 15–20% of patients may need suture ligation to control the postoperative bleed.

Appendix: Practice Parameters for Ambulatory Anorectal Surgery

Prepared by The Standards Task Force, The American Society of Colon and Rectal Surgeons

Drs. Ronald Place and Neal Hyman, Project Coordinators; Clifford Simmang, Committee Chairman; Peter Cataldo; James Church; Jeff Cohen; Frederick Denstman; John Kilkenny; Juan Noguera; Charles Orsay; Daniel Otchy; Jan Rakinic; Joe Tjandra

Ambulatory Facilities

Anorectal Surgery May Be Safely and Cost-Effectively Performed in an Ambulatory Surgery Center.

Level of Evidence – Class III (Appendix A, see Table 11.9). It has been estimated that 90% of anorectal cases may be suitable for ambulatory surgery. A wide variety of anorectal conditions including condylomata, fissures, abscesses, fistulas, tumors, hemorrhoids, pilonidal disease, and various miscellaneous conditions have been shown to be amenable to surgery on an outpatient basis. An admission rate of 2% has been reported. A reduction in hospital charges of 25–50% has also been noted.

Patients with American Society of Anesthesiology (ASA) Classifications I and II Are Generally Considered Suitable Candidates for Outpatient Anorectal Surgery (Appendix B, see Table 11.10). Selected ASA Category III Patients May Also Be Appropriate Candidates.

Level of Evidence – Class III. Multiple factors must be considered in determining the appropriateness of performing anorectal surgery in the ambulatory setting. The ASA physical status classification is useful to determine the risk of anesthesia. The magnitude of the proposed surgery, type of anesthesia, availability of appropriate instrumentation, ability of the patient to follow instructions, distance of the patient's home from the surgical center, and home support structure all need to be considered.

Table 11.9. Levels of evidence.

Level I: Evidence from properly conducted randomized, controlled trials

Level II: Evidence from controlled trials without randomization, or cohort or

case-control studies, or multiple times series, dramatic uncontrolled experiments

Level III: Descriptive case series or opinions of expert panels

Table 11.10. ASA physical status classification.

Class I: Patient has no systemic disturbance (e.g., healthy, no medical problems)
Class II: Patient has mild to moderate systemic disturbance (e.g., hypertension, diabetes)
Class III: Patient has severe systemic disturbance (e.g., heart disease that limits activity)
Class IV: Patient has severe systemic disturbance that is life-threatening (e.g., unstable angina, active congestive heart failure)
Class V: Patient is moribund and has little chance of survival (e.g., ruptured abdominal aortic aneurysm)

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Preoperative Evaluation

Preoperative Investigations (e.g., Laboratory Studies and Electrocardiograms) Should Be Dictated by History and Physical Examination.

Level of Evidence – Class III. Multiple studies have documented that patient history and physical examination are the key elements of an appropriate preoperative evaluation. Routine preoperative investigations that are not warranted on the basis of history and physical seem to provide little further information. There is clear evidence that nonselective preoperative screening yields few abnormal results.

One study of 1,200 patients undergoing ambulatory surgery revealed that the vast majority of abnormalities could have been predicted by history and physical examination. These abnormalities did not predict perioperative complications or the need for hospital admission. A separate study of 1,109 patients undergoing elective surgery revealed that 47% of laboratory investigations duplicated tests performed within the previous year. Meaningful changes in the repeat laboratory values were very rare. Such abnormalities were predictable by the patient's history. A further study of 5,003 preoperative screening tests revealed 225 abnormal results. Only 104 were of potential importance and the abnormality caused action in only 17 cases. It was believed that only four patients could have had a conceivable benefit from their preoperative screening test.

Similar studies have been performed to investigate the value of specific tests. A study of 12,338 patients undergoing invasive procedures was performed to examine the value of determining activated partial thromboplastin time as a routine. Ninety-two percent of the patients were

believed to be at low risk (there were no clinical factors to suggest the bleeding tendency). In these patients, it was shown that no information was gained from activated partial thromboplastin time, and therefore, clotting studies had no role as a screening test in asymptomatic patients. Similarly, routine cardiac workup seems unjustified. The risk of a perioperative myocardial infarction in patients without clinical evidence of heart disease is 0.15%. This risk increases significantly in patients who had a previous myocardial infarction. History and physical examination are the cornerstones of appropriate preoperative evaluation.

Intraoperative Considerations

Most Anorectal Surgery May Be Safely and Cost-Effectively Performed Under Local Anesthesia; Regional or General Anesthesia May Be Used Depending on Patient or Physician Preference.

Level of Evidence – III. The use of local anesthetics such as monitored anesthetic care for anorectal surgery is safer and has fewer complications than other anesthetic techniques. Perianal infiltration of local anesthetics is a simple procedure that is easily learned. Injection of the local anesthetics can be accomplished in less than 5 min and the operation begun immediately. However, the anesthetic technique used for any procedure should be the one that provides for maximal safety and efficacy.

Postoperative Considerations

Anorectal Surgery Patients May Safely Be Discharged from the Postanesthesia Care Unit.

Level of Evidence – II. The time course for recovery from anesthesia includes early recovery, intermediate recovery, and late recovery. Early recovery is the time interval for anesthesia emergence and recovery of protective reflexes and motor activity. The Aldrete score has been used for 30 years to determine release from phase 1 (early) recovery to a hospital bed or phase 2 (intermediate) recovery. Intermediate recovery is the period during which coordination and physiology normalize to an extent that the patient can be discharged from phase 2 recovery in a state of “home readiness” and be able to return home in the care of a responsible

adult. The Post-Anesthetic Discharge Scoring System has been shown to be efficacious for discharge.

Multiple Modalities May Be Used to Achieve Adequate Postoperative Pain Control.

Level of Evidence – II. If local anesthetics are not used as the primary anesthetic technique, their use will provide prolonged postoperative analgesia. Oral narcotics may be used as primary postoperative analgesia. The use of nonsteroidal antiinflammatory drugs, particularly intramuscular or intravenous Toradol® (Roche Pharmaceuticals, Nutley, NJ) or sulindac suppositories has also shown improved analgesia, lower narcotic usage, and lower rates of urinary retention. Although the effect is unknown, oral metronidazole shows improved postoperative pain control.

Postoperative Urinary Retention Can Be Reduced by Limiting Perioperative Fluid Intake.

Level of Evidence – III. Multiple studies have shown that limiting perioperative fluid lowers the incidence of postoperative urinary retention. These same studies show conflicting evidence over the relationship between gender, age, and the quantity of narcotic medication and urinary retention. Hemorrhoidectomy and the performance of multiple anorectal procedures have higher rates of urinary retention.

Postoperative Education Should Include Recommendations for Sitz Baths, Fluid Intake, and Activity Limitations.

Level of Evidence – III. Textbooks of anorectal surgery advocate consistent instructions before discharge from ambulatory surgery. Although derived from common sense, scientific justification does not exist. With appropriate communication, ambulatory anorectal surgery may be performed with a high degree of patient satisfaction.

12. Benign Anorectal: Anal Fissure

A. Epidemiology

- An anal fissure, or fissure-in-ano, is an oval, ulcer-like, longitudinal tear in the anal canal, distal to the dentate line.
- Fissures can occur at any age, but are usually seen in younger and middle-aged adults.
- In almost 90% of cases, fissures are identified in the posterior midline, but can be seen in the anterior midline in up to 25% of affected women and 8% of affected men.
- Fissures occurring in lateral positions should raise suspicions for other disease processes, such as Crohn's disease, tuberculosis, syphilis, human immunodeficiency virus (HIV)/acquired immunodeficiency syndrome (AIDS), or anal carcinoma (Fig. 12.1).
- Early, or acute, fissures have the appearance of a simple tear in the anoderm, whereas chronic fissures, defined by symptoms lasting more than 8–12 weeks, are further characterized by edema and fibrosis.
- Typical inflammatory manifestations of chronic fissures include a sentinel pile, or skin tag, at the distal fissure margin and a hypertrophied anal papilla proximal to the fissure in the anal canal. In addition, fibers of the internal anal sphincter (IAS) are often visible at the fissure base.

B. Etiology

- Trauma to the anal canal secondary to the passage of a hard stool is believed to be a common initiating factor. A history of

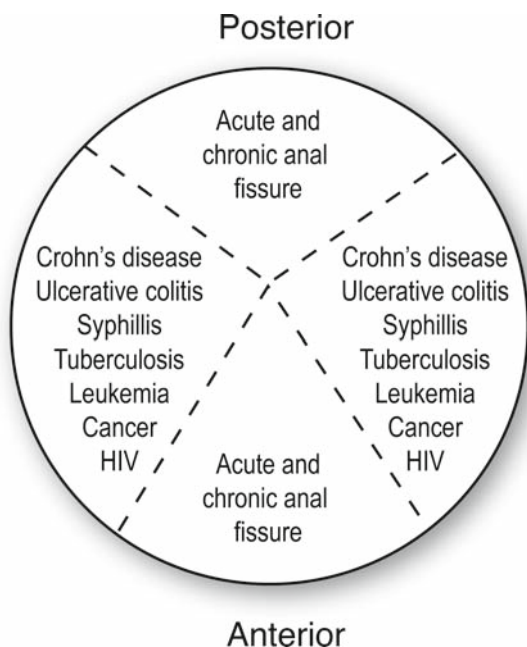


Fig. 12.1. The location of anal fissure suggests their cause.

constipation is not universally obtained, however, and some patients report an episode of diarrhea before the onset of symptoms.

- Physiologic studies using ambulatory manometry have confirmed the presence of sustained resting hypertonia in fissure patients.
- Further observations have delineated an inverse relationship between anal canal pressure and perfusion of the anoderm.
- Schouten et al. measured anodermal blood flow in healthy individuals using Doppler laser flowmetry, and found that the posterior midline had the lowest perfusion when compared with the other three quadrants. In addition, there was a significant inverse correlation between posterior midline anodermal blood flow and maximum resting anal pressure in a large cohort of patients that included normal controls and fissure patients. Those with fissures demonstrated the highest resting anal pressures and the lowest posterior blood flow of any group.
- These same authors were able to demonstrate normalization of sphincter hypertonia and anodermal blood flow after lateral internal sphincterotomy (LIS) in anal fissure patients.

C. Symptoms

- The clinical hallmark of an anal fissure is pain during, and particularly after, defecation.
- In acute fissures, pain may be short-lived, or it can last several hours or even all day in the presence of a chronic fissure.
- The pain is frequently described as passing razor blades or glass shards. Understandably, patients with anal fissures may often fear bowel movements.
- Rectal bleeding, although not uncommon, is usually limited to minimal bright red blood seen on the toilet tissue.

D. Diagnosis

- Diagnosis is suggested by patient history and confirmed by physical examination. Most fissures are readily visible by simply spreading the buttocks with opposing traction of the thumbs (Fig. 12.2).

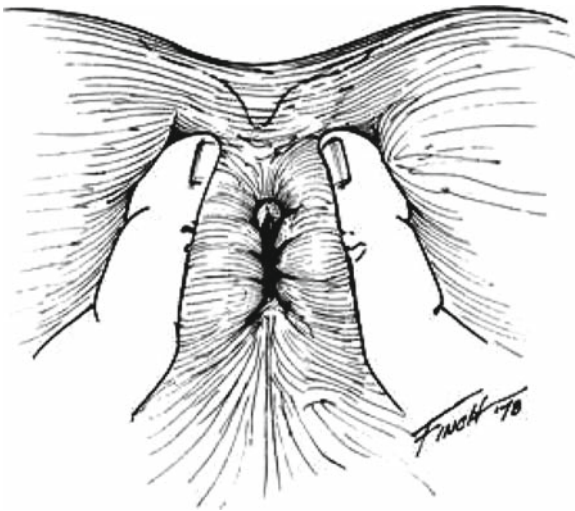


Fig. 12.2. Examination revealing an anal fissure.

- Once the presence of a fissure is verified, further attempt to examine the anal canal with insertion of a finger or endoscopic instrumentation (anoscopy or proctoscopy) is not appropriate. Most patients are far too tender to justify such invasive evaluation, which should be delayed or deferred until symptoms have resolved.
- The differential diagnosis includes perianal abscess, anal fistula, inflammatory bowel disease, sexually transmitted disease, tuberculosis, leukemia, and anal carcinoma.
- Atypical fissures, such as those occurring off the midline, multiple, painless, and nonhealing fissures, warrant further evaluation, via examination under anesthesia and possible biopsy and cultures.

E. Management

Conservative

- Almost half of all patients diagnosed with an acute fissure will heal with conservative measures, i.e., sitz baths and psyllium fiber supplementation, with or without the addition of topical anesthetics or anti-inflammatory ointments.
- In a double-blind, placebo-controlled trial, fissure recurrence was measured after 1 year in three groups. Significantly fewer recurrences (16%) were seen in patients receiving 15 g of unprocessed bran daily, when compared with 60% of patients receiving 7.5 g daily or 68% of patients on placebo.

Operative Treatment

- Operative procedures, such as manual anal dilatation or internal sphincterotomy, have been advocated as initial modes of treatment because they produce permanent reductions in maximum resting anal pressures.

Anal Dilatation

- Inconsistencies with regard to technique, specifically extent and duration of sphincter stretch, have cast some doubt about true success rates of this procedure.

- Additional widespread criticism of the technique stems from reported complications of incontinence, secondary to diffuse sphincter damage.

Lateral Internal Sphincterotomy

- Exceptional healing and low recurrence rates have invariably been reported, and LIS has emerged as the “gold standard” for the treatment of anal fissure (Table 12.1).
- Persistent incontinence to gas and stool has emerged as a major concern after sphincterotomy.
- Littlejohn and Newstead reported a retrospective review of 287 patients who underwent tailored sphincterotomy, i.e., division of the IAS for the length of the fissure, rather than to the dentate line. There were no reports of incontinence to liquid or solid stool. The incidence of urgency was 0.7%; gas incontinence, 1.4%; and minor staining, 35%.
- Other technical variations that have influenced patient outcomes after LIS have been described (Figs. 12.3, and 12.4). With regard

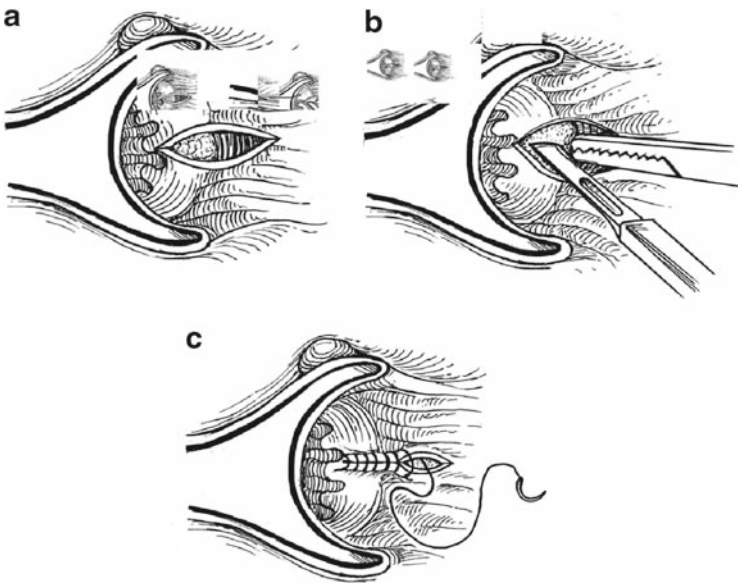


Fig. 12.3. Open lateral internal anal sphincterotomy. (a) Radial skin incision distal to the dentate line exposing the intersphincteric groove. (b) Elevation and division of the internal sphincter. (c) Primary wound closure.

Table 12.1. Results of LIS.

Year	Author	n	Success (%)	Recurrence (%)	Incontinence (%) ^a	Follow-up (type)	Follow-up (mo)
1980	Abcarian	150	100	1.3	0	C	NS
1981	Keighley et al.	71	100	25	2	I, E	12
1982	Ravikumar et al.	60	97	0	5	C	24
1984	Hsu and MacKeigan	89	100	5.6	0	C	NS
1984	Jensen et al.	30	100	3	0	Q, E	18
1985	Walker et al.	306	100	0	15	I	52
1987	Gingold	86	100	3.5	0	C	24
1987	Weaver et al.	39	93	5.1	2.5	I, E	17
1988	Lewis et al.	350	94	6	6	I	37
1988	Zinkin	151	94.7	NS	NS	None	0
1989	Khubchandani and Reed	717	97.7	NS	35.1	Q	52.9
1992	Kortbeek et al.	112	95.5	NS	NS	I	1.5
1994	Pernikoff et al.	500	99	2	16	Q	78
1994	Romano et al.	44	100	0	9	E	8
1995	Leong and Seow-Choen	20	100	NS	0	I, E	6.5
1995	Prohm and Bonner	177	96	3.3	1.6	E	1.5
1995	Usatoff and Polglase	98	90	20	18	Q	41
1996	Garcia-Aguilar et al.	864	96	11	37.8	Q	63.5
1997	Hananel and Gordon	312	98.6	1.4 ^b	–	C	NS
1997	Littlejohn and Newstead	352	99.7	1.4	1.4	C	9
1999	Nyam and Pemberton	585	96	8	15	Q	72
2004	Wiley et al.	76	96	NS	6.8	Q	12
2004	Parellada	27	100	NS	15	E	2.5

C chart review; E examination; I interview; Q questionnaire; NS not stated

^aIncludes seepage and incontinence to flatus and stool

^bRecurrence and persistence combined

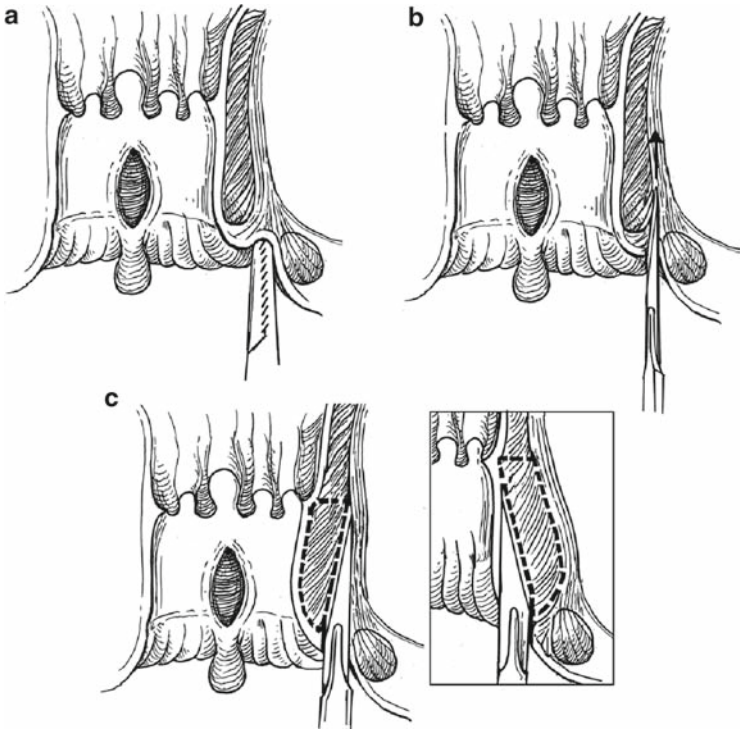


Fig. 12.4. Closed lateral internal anal sphincterotomy. (a) Location of the intersphincteric groove. (b) Insertion of knife blade in the intersphincteric plane in performing a “blind” lateral subcutaneous internal anal sphincterotomy. (c) Lateral to medial division of the IAS (insert: medial to lateral division of the muscle).

to open or closed sphincterotomy, several retrospective analyses and at least one randomized trial report similar rates of initial healing and fissure recurrence.

- In a randomized trial, patient satisfaction was rated as excellent or good after removal of these structures in 84% of patients, compared with 58% of patients whose polyps and papillae were left intact.

Advancement Flaps

- One prospective trial of the use of advancement flaps for chronic anal fissures has been conducted to date. When patients were randomized to receive LIS or advancement flap, there was

no significant difference between healing rates (100% in the sphincterotomy group vs. 85% in the flap group, $P = .12$).

Medical Management

Sphincter Relaxants

- Increasing concerns with long-term complications associated with the operative management of anal fissures has led to the development of “chemical sphincterotomy,” aimed at reducing mean maximum resting anal pressures, without permanent sphincter injury. Preparations have included (1) various nitrate formulations, including nitroglycerin (NTG) ointment, glyceryl trinitrate (GTN), and isosorbide dinitrate (ISDN); (2) oral and topical calcium channel blockers, including nifedipine and diltiazem (DTZ); (3) adrenergic antagonists; (4) topical muscarinic agonists, i.e., bethanechol; (5) phosphodiesterase inhibitors; and (6) botulinum toxin (BT).
- However, there is increasing controversy in this area. Whereas one recent review concluded “first-line use of medical therapy cures most chronic fissures cheaply and conveniently,” a systematic review of the literature published at the same time concluded “medical therapy for chronic anal fissure...may be applied with a chance of cure that is only marginally better than placebo...[and] far less effective than surgery.”

Topical Nitrates

- The IAS is a smooth muscle whose tone is affected by both intrinsic myogenic properties and extrinsic neural influences.
- Nitric oxide is the predominant nonadrenergic, noncholinergic neurotransmitter in the IAS. Release of nitric oxide results in IAS relaxation. Exogenous nitrates release nitric oxide in vivo and have been used as nitric oxide donors.
- Studies by Loder et al. and Guillemot et al. demonstrated decreased resting anal pressure with 0.2% GTN. This led to a series of retrospective and prospective reports, as well as randomized trials, supporting the use of various nitrate preparations in the treatment of anal fissures (Table 12.2).
- Additional randomized, placebo-controlled trials have demonstrated comparable healing rates of 46–70% in patients with

Table 12.2. Randomized trials of NTG therapy.

Year	Author	n	Treatment	Follow-up	Success (%)
1997	Lund et al.	80	0.2% GTN bid placebo	8 weeks	68 39
1997	Oettle	24	0.2% GTN tid LIS	4 weeks	83.3 100
1997	Bacher et al.	35	0.2% GTN 2% lidocaine	4 weeks	80 40
1999	Kennedy et al.	43	0.2% GTN placebo	4 weeks	46 16
1999	Carapeti et al.	70	0.2% GTN tid 0.2% GTN tid (titrated to 0.6%) placebo	8 weeks	67 32
2000	Altomare et al.	132	0.2% GTN bid placebo	4 weeks	49.2 51.7
2000	Zuberi et al.	42	0.2% GTN 10 mg NTG patch LIS	8 weeks	66.7 63.2 91.7
2000	Richard et al.	82	0.2% GTN LIS	6 months	27.2 92.1
2001	Evans et al.	65	0.2% GTN tid LIS	8 weeks	60.6 97
2001	Chaudhuri et al.	19	0.2% GTN bid placebo	6 weeks	70 22.2
2002	Libertiny et al.	70	0.2% GTN LIS	2 years	45.7 97.1
2002	Bailey et al.	304	0.1%, 0.2%, and 0.4% GTN bid/tid placebo	8 weeks	50% across board
2003	Scholefield et al.	200	0.1%, 0.2%, and 0.4% GTN bid/tid placebo	8 weeks	46.9, 40.4, 54.1, 37.5

GTN glyceryl trinitrate; NTG nitroglycerin; LIS lateral internal sphincterotomy; *bid* twice daily; *tid* three times daily

chronic anal fissures after application of 0.2% GTN ointment 2–3 times daily for 4–8 weeks.

- Chemical sphincterotomy with GTN may be tried as the initial treatment in patients with chronic anal fissure.
- Carapeti et al. reported headaches in 72% of patients receiving GTN vs. 27% of controls receiving placebo.

Calcium Channel Blockers

- Carapeti et al. investigated the use of topical DTZ in the treatment of anal fissure, after a prior randomized trial demonstrated that the majority of fissure patients treated with GTN developed headaches. After application of 2% DTZ gel three times daily in ten patients, 67% obtained healed fissures after 8 weeks of treatment. No headaches or side effects were reported.
- Randomized, controlled trials comparing topical nifedipine gel with a combination of topical lidocaine and hydrocortisone gels have also demonstrated superiority of nifedipine in the treatment of anal fissures.
- Jonas et al. performed a randomized, controlled trial to ascertain whether different routes of administration had similar healing rates. The authors randomized 50 patients to receive 60 mg of oral DTZ or 2% topical DTZ gel twice daily. Complete healing occurred in 38% of patients taking oral treatment vs. 65% of patients using topical therapy. Side effects were reported in 33% of patients treated orally.
- In a prospective, double-blind trial by Ezri and Susmallian, 52 patients were randomized to receive topical GTN or nifedipine. The healing rate was higher ($P < .04$) with nifedipine (89%) as compared with GTN (58%). Side effects occurred more frequently ($P < .01$) with GTN (40%) than nifedipine (5%), a finding that was similar to the other trials. Recurrences within a 6-month period were common in both groups: 31% for GTN and 42% for nifedipine.
- Based on these study results, topical calcium channel blockers appear to be as effective as topical nitrates, with fewer side effects. Initial data suggest that long-term recurrences may be similar between both treatment groups, but further studies are warranted. Currently, topical calcium channel blocker preparations are not commercially available in the United States.

Adrenergic Antagonists

- The effect of alpha-1 adrenergic blockade on anal sphincter pressure has been studied in two prospective trials.
 - In the first study, reduction in anal pressure was observed in both groups.
 - In the second study, the trial was not completed because of lack of efficacy.

Cholinergic Agonists

- Carapeti et al. documented reduced anal sphincter pressure using bethanechol in a dose-finding study.

Phosphodiesterase Inhibitors

- Early work by Jones et al. has demonstrated an in vitro effect of increasing concentrations of various phosphodiesterase inhibitors on internal sphincter tone. This may spark future clinical trials in the treatment of anal fissure.

Botulinum Toxin

- Botulinum Toxin (BT) is an exotoxin produced by the bacterium *Clostridium botulinum*. When injected locally, BT binds to the presynaptic nerve terminal at the neuromuscular junction, thereby preventing release of acetylcholine and resulting in temporary paralysis of skeletal muscle.
- Findings suggest that the predominant effect of BT on the IAS is sympathetic blockade.
- BT injections can be given easily, on an outpatient basis, and are well tolerated.
- The commercial availability of BT has prompted several prospective trials examining its efficacy in the treatment of anal fissure (Table 12.3).
- The dose of BT injected is critical to successful healing in anal fissures. Siproudhis et al. reported that a single 20-U injection of BT was not superior to that of placebo in a randomized, double-blind trial of 44 patients with chronic anal fissure.
- Lindsey et al. concluded that BT should be considered as a second-line, and perhaps a first-line, agent in the treatment of chronic anal fissures before pursuing surgical options.
- In a prospective, randomized trial, Brisinda et al. directly compared BT injection and topical NTG as first-line agents in the treatment of chronic anal fissures. BT injections (20 U) were given on each side of the IAS and 0.2% NTG ointment was applied twice daily for 6 weeks.
 - Regarding nonsurgical treatment of chronic anal fissure, the authors concluded that BT was more effective than NTG therapy.

Table 12.3. Prospective BT trials.

Year	Author	n	Treatment	Follow-up	Success (%)	Side effects
1998	Maria et al.	30	BT 20 U (2 doses) Saline	2 months	73.3 13.3 ($P = .003$)	
1999	Brisinda et al.	50	BT 20 U (2 doses) 0.2% NTG	2 months	96 60 ($P = .005$)	20% headaches
2002	Colak et al.	62	BT Lidocaine	2 mo	70.6 21.4 ($P = .006$)	
2002	Brisinda et al.	150	BT 20 U, 30 U BT 30 U, 50 U	2 months	89 96	
2003	Siproudhis et al.	44	BT 20 U (1 dose) Saline	4 weeks	22.7 22.7	
2003	Mentes et al.	101	BT 0.3 U/kg LIS	12 months	75.4 94 ($P = .008$)	16% incontinence

BT botulinum toxin; *U* units; *LIS* lateral internal sphincterotomy

- There has been only one prospective, randomized trial to date comparing BT to LIS in the treatment of chronic anal fissures.
 - After 1 month, fissures were completely healed in 62.3% of patients in the BT group vs. 82% of patients in the LIS group ($P = .023$). By 2 months, healing rates were 73.8% in the BT group and 98% in the LIS group ($P < .0001$).
 - Although initial success and fewer complications were found with BT therapy, long-term results were not as encouraging when compared with LIS.

- Late recurrence rates 42 months after BT treatment of chronic anal fissures have been reported in a prospective trial by Minguez et al. Only patients with complete healing 6 months after BT injections were included for reassessment in 6-month intervals. Fissure recurrence was demonstrated in 41.5% of patients. Stratification by various clinical parameters revealed that higher risks of recurrence were associated with anterior location, chronicity of disease (longer than 12 months), multiple injections, and dosage greater than 21 U.

F. Special Situations

Low Pressure Fissures

- Unlike the classic anal fissures described previously, low pressure fissures are not appropriate candidates for operative sphincterotomy.
- Patients within this category include those with impaired continence and fissure recurrence after sphincterotomy. Anal fissures sustained after childbirth are also associated with reduced anal canal pressures.
- Optimal treatment of low-pressure fissures is unclear. Nyam et al. reported the results of an island flap in 21 patients with preoperative median resting anal pressures and squeeze pressures significantly lower than controls or patients with high-pressure fissures.
 - The authors concluded that the island advancement flap “provides a useful alternative” for recurrent anal fissures, or low-pressure anal fissures, in which sphincterotomy “might jeopardize continence.”

Crohn's

- Sweeney et al. reviewed the natural history of Crohn's fissures in 61 patients, in whom anal fissure was the only anal pathology. Fissure healing occurred in 42 of 69 patients (60.8%) during medical treatment for Crohn's disease.
- Traditionally, anorectal surgery in patients with Crohn's disease has been approached with caution. Complications resulting in

proctectomy and fears regarding postoperative incontinence, exacerbated by preexisting diarrhea, have precluded perianal operations in these patients (although impairment of continence after such operations has not been studied in this population). As a result, most authorities argue that initial treatment of Crohn's fissures should be focused on controlling diarrhea.

- If fissure persists despite conservative measures, examination under anesthesia and limited sphincterotomy should be performed.
- Currently, there are no data to support the use of topical sphincter relaxants or BT in the treatment of fissures in Crohn's disease.

Human Immunodeficiency Virus

- Distinction between HIV-associated fissures and HIV-associated ulcers is necessary for optimization of fissure management in this patient population. Fissures in HIV-positive patients have a typical appearance, whereas HIV ulcers are deep and broad based and can occur anywhere within the anal canal.
- There is a paucity of current information on HIV-associated fissures, and no available data about risk of postoperative incontinence or use of topical sphincter relaxants or BT as treatment options.

13. Benign Anorectal: Abscess and Fistula

A. Introduction

- Anorectal abscesses and fistula-in-ano represent different stages along the continuum of a common pathogenic spectrum. The abscess represents the acute inflammatory event whereas the fistula is representative of the chronic process.

B. Abscess

Anatomy

- Successful eradication of anorectal suppuration and fistula-in-ano requires an in-depth understanding of anorectal anatomy. Essential is an understanding of the existence of potential anorectal spaces (Fig. 13.1a).
- The perianal space is located in the area of the anal verge. It becomes continuous with the ischioanal fat laterally while it extends into the lower portion of the anal canal medially. It is continuous with the intersphincteric space.
- The ischioanal space extends from the levator ani to the perineum.
- The intersphincteric space lies between the internal and external sphincters and is continuous inferiorly with the perianal space and superiorly with the rectal wall.
- The supralelevator space is bounded superiorly by peritoneum, laterally by the pelvic wall, medially by the rectal wall, and inferiorly by the levator ani muscle.

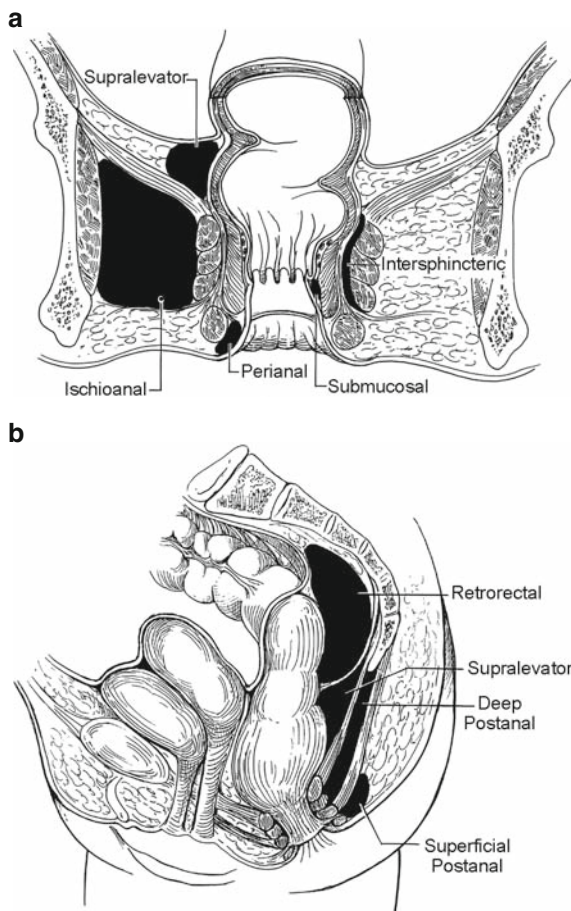


Fig. 13.1. Anorectal spaces. (a) Coronal section. (b) Sagittal section. (From Vasilevsky CA. Anorectal abscess and fistula-in-ano. In: Beck D, ed. Handbook of Colorectal Surgery. 2nd ed. Copyright 2003 by Taylor & Francis Group LLC (B). Reproduced with permission of Taylor & Francis Group LLC (B) in the format Textbook via Copyright Clearance Center.)

- The deep postanal space is located between the tip of the coccyx posteriorly and lies below the levator ani and above the anococcygeal ligament (Fig. 13.1b).
- At the level of the dentate line, the ducts of the anal glands empty into the anal crypts.

Table 13.1. Etiology of anorectal abscess.

Nonspecific
Cryptoglandular
Specific
Inflammatory bowel disease
Crohn's disease
Ulcerative colitis
Infection
Tuberculosis
Actinomycosis
Lymphogranuloma venereum
Trauma
Impalement
Foreign body
Surgery
Episiotomy
Hemorrhoidectomy
Prostatectomy
Malignancy
Carcinoma
Leukemia
Lymphoma
Radiation

Pathophysiology

Etiology

- Ninety percent of all anorectal abscesses result from nonspecific cryptoglandular infection whereas the remainder result from the causes as listed in Table 13.1.
- Obstruction of a duct may result in stasis, infection, and formation of an abscess. Persistence of anal gland epithelium in part of the tract between the crypt and the blocked part of the duct results in the formation of a fistula.
- Predisposing factors include diarrhea and trauma in the form of a hard stool.
- Associated factors may be anal fissures, infection of a hematoma, or Crohn's disease.

Classification

- Abscesses are classified according to their location in the aforementioned potential anorectal spaces: perianal, ischioanal,

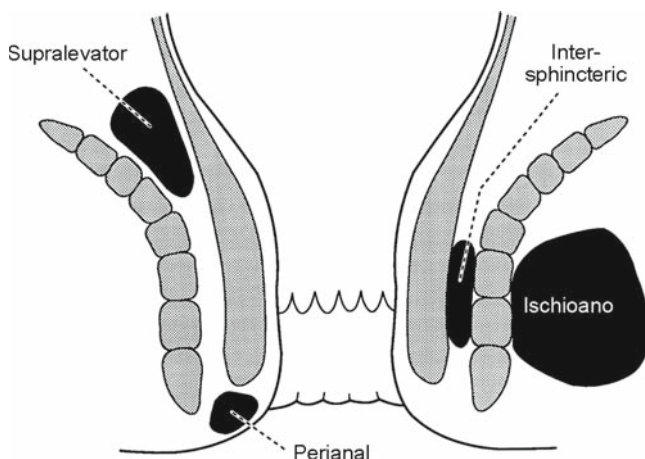


Fig. 13.2. Classification of anorectal abscess. (Reprinted from Vasilevsky CA. *Fistula-in-ano and abscess*. In: Beck DE, Wexner SD, eds. *Fundamentals of Anorectal Surgery*. London: WB Saunders, copyright 1998, with permission from Elsevier.)

intersphincteric, and supralelevator (Fig. 13.2). Perianal abscesses are the most common type whereas supralelevator abscesses are the rarest.

- Pus can also spread circumferentially through the intersphincteric, supralelevator, or ischioanal spaces, the latter via the deep postanal space, resulting in a horseshoe abscess.

Evaluation and Treatment

Symptoms

- Pain, swelling, and fever are the hallmarks associated with an abscess.
- Severe rectal pain accompanied by urinary symptoms such as dysuria, retention, or inability to void may be suggestive of an intersphincteric or supralelevator abscess.

Physical Examination

- Inspection will reveal erythema, swelling, and possible fluctuation.
- It is crucial to recognize that no visible external manifestations will be present with the intersphincteric or supralelevator abscesses despite the patient's complaint of excruciating pain.

- Although digital examination may not be possible because of extreme tenderness, palpation, if possible, will demonstrate tenderness and a mass.
- With a supralevator abscess, a tender mass may be palpated on rectal or vaginal examination.
- Anoscopy and sigmoidoscopy are inappropriate in the acute setting.

Treatment

General Principles

- Essentially, the treatment of an anorectal abscess involves incision and drainage.
- Watchful waiting under the cover of antibiotics is ineffective and may allow the suppurative process to progress resulting in the creation of a more complicated abscess and thus possible injury to the sphincter mechanism.
- Rarely, delay in diagnosis and management of anorectal abscesses may result in life-threatening necrotizing infection and death.

Operative Management

Incision and Drainage

- Perianal abscesses can be effectively drained under local anesthesia. After the most tender point has been determined, the area is infiltrated with 0.5% lidocaine with 1:200,000 epinephrine. A cruciate or elliptical incision is made and the edges are trimmed to prevent coaptation which may result in poor drainage or recurrence (Fig. 13.3). No packing is required.
- Most ischioanal abscesses can be incised and drained in a similar manner with the site of incision shifted close to the anal side of the abscess, minimizing the complexity of a subsequent fistula.
- Large ischioanal or horseshoe abscesses often require drainage with the patient under a regional or general anesthetic and in the prone jackknife or left lateral (Sim's) position. The location of infection is often in the deep postanal space.
 - Counter-incisions are made over each ischioanal fossa to allow drainage of the anterior extensions of the abscess (Hanley procedure) (Fig. 13.4).
- Because the diagnosis of an intersphincteric abscess is entertained when the patient presents with pain out of proportion

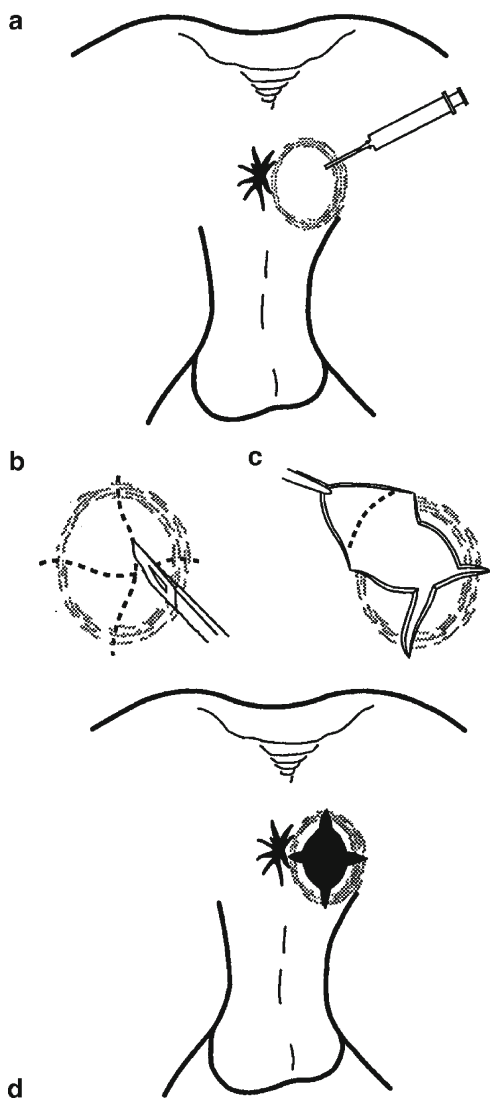


Fig. 13.3. Drainage of abscess. (a) Injection of local anesthesia. (b) Cruciate incision. (c) Excision of skin. (d) Drainage cavity.

to the physical findings, an examination under anesthesia is mandatory to completely assess the cause of the pain. Once the diagnosis is established, either by palpation of a protrusion

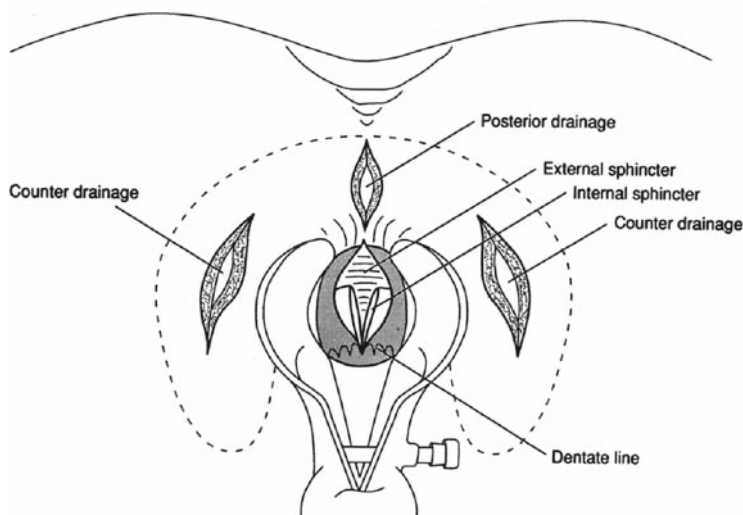


Fig. 13.4. Drainage of horseshoe abscess.

into the anal canal or by needle aspiration in the intersphincteric plane, treatment consists of dividing the internal sphincter along the length of the abscess cavity. The wound is then marsupialized to allow adequate drainage and quicker healing.

- Before the treatment of a supralelevator abscess, it is essential to determine its origin because it may arise from an upward extension of an intersphincteric or an ischioanal abscess, or downward extension of a pelvic abscess (Fig. 13.5).

Catheter Drainage

An alternative method of treatment is catheter drainage.

- Using local anesthetic, a stab incision is made over the abscess cavity near the anus.
- A 10–16 French soft latex mushroom catheter is inserted over a probe into the abscess cavity.
- The shape of the catheter holds it in place and the external end is trimmed 2–4 cm outside the skin.
- The patient is instructed on wound care and is seen in follow up in 7–10 days. The catheter is removed if drainage has stopped and the cavity has closed down around the catheter.

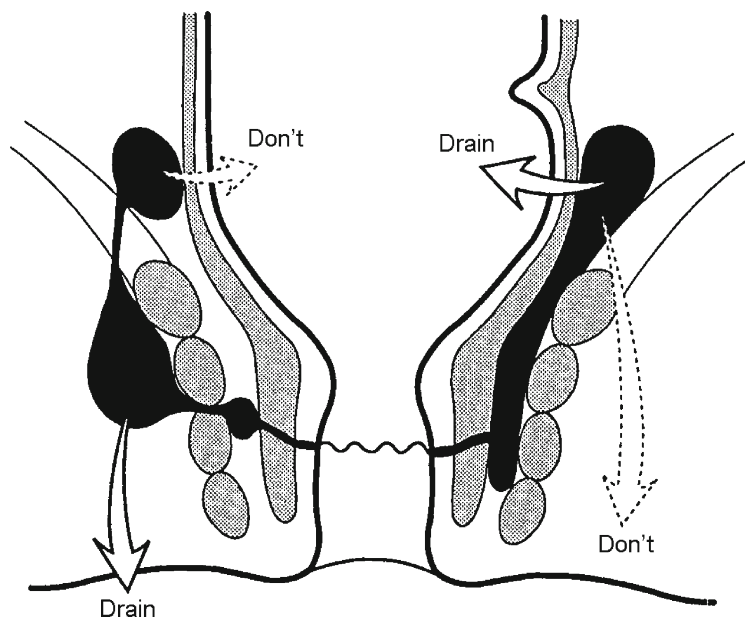


Fig. 13.5. Drainage of a supralelevator abscess.

Primary Fistulotomy

- A point of controversy is whether primary fistulotomy should be performed at the time of initial abscess drainage. A recent meta-analysis which compared incision and drainage alone to primary fistulotomy demonstrated that primary fistulotomy resulted in an 83% reduction in recurrence but higher risk of incontinence to flatus. On the other hand, 72% of patients who underwent incision & drainage alone did not develop a recurrence.
- Primary fistulotomy eliminates the source of infection and decreases the rate of recurrence, obviating the need for subsequent surgery with the potential to decrease disability and morbidity.
- Opponents are reluctant to perform primary fistulotomy in the presence of acute inflammation because the search for an internal opening may lead to creation of false passages resulting in neglect of the main source of infection.
- Failure to identify an internal opening has been reported to occur in as high as 66% of patients. In addition, 34–50% of patients who present with an abscess for the first time will not

develop a fistula. Thus, primary fistulotomy in these patients would be unnecessary and may result in needless disturbances of continence.

- Of those patients whose abscesses are drained, 11% may develop a fistula whereas 37% may develop a recurrent abscess. This is most often observed in conjunction with ischioanal abscesses.
- A prospective, randomized trial of drainage alone vs. drainage and fistulotomy for acute perianal abscesses with proven internal openings revealed that incision and drainage alone demonstrated no statistical significance in recurrence compared with concurrent fistulotomy although there was a tendency to recurrence in the former group.
- If the internal opening of a low transsphincteric fistula is readily apparent at the time of abscess drainage, primary fistulotomy is feasible with the following exceptions (1) patients with Crohn's disease, (2) patients with acquired immunodeficiency syndrome (AIDS), (3) elderly patients, (4) patients with high transsphincteric fistulas, and (5) women with anterior fistulas and episiotomy scars.
- The decision to perform a primary fistulotomy should be individualized but should only be attempted by a surgeon with a sound knowledge of the regional anatomy. Insistence upon finding a fistula may encourage creation of a false passage and unnecessary division of sphincter muscle.
- Many of the former proponents of primary fistulotomy have abandoned this approach and have instead elected to await the appearance of a fistula after drainage only to treat it with fibrin glue anal plug so as to avoid cutting any sphincter muscle.

Antibiotics

- There is little if any role for antibiotics in the primary management of anorectal abscesses except as an adjunct in patients with valvular heart disease or prosthetic valves, extensive soft tissue cellulitis, prosthetic devices, diabetes, immunosuppression, or systemic sepsis.

Postoperative Care

- Patients are instructed to continue with a regular diet and to take a bulk-forming agent, non-codeine-containing analgesic, and sitz baths.

- Patients are generally seen in follow-up in 2–4 weeks or for intersphincteric or supralelevator abscesses, 2 weeks postoperatively.

Complications

Recurrence

- After incision and drainage, ischioanal and intersphincteric abscesses are associated with the development of recurrent abscesses or fistulas in as many as 89% of patients.
- Reasons for recurrence of anorectal infections include missed infection in adjacent anatomic spaces, the presence of an undiagnosed fistula or abscess at initial abscess drainage, and failure to completely drain the abscess.

Extra-Anal Causes

- Extra-anal disease should be considered once the usual causes of recurrence have been ruled out. Hidradenitis suppurativa and downward extension of a pilonidal abscess should be considered. A prospective review of recurrent anorectal abscesses by Chrabot et al. reported hidradenitis in one-third of patients with recurrent abscesses. In addition, the possibility of Crohn's disease should be suspected.

Incontinence

- Incontinence may result after incision and drainage of an abscess either from iatrogenic damage to the sphincter or inappropriate wound care. Continence may be compromised if the superficial external sphincter is inadvertently divided during drainage of a perianal or deep postanal abscess in a patient with preoperative borderline continence.
- Prolonged packing of a drained abscess may impair continence by preventing the development of granulation tissue and promoting the formation of excess scar tissue.
- Although advocated to decrease recurrence rates, primary fistulotomy may result in unnecessary division of sphincter muscle in acutely inflamed tissue.

Special Considerations

Necrotizing Anorectal Infection

- Rarely, anorectal abscesses may result in necrotizing infection and death. Factors thought to be responsible include delay in

diagnosis and management, virulence of the organism involved, bacteremia and metastatic infections, or underlying disorders such as diabetes, blood dyscrasias, heart disease, chronic renal failure, hemorrhoids, and previous abscess or fistula.

Symptoms and Signs

- Spreading soft tissue infection of the perineum can be classified into two groups.
 - The first group includes anorectal sepsis in which the infection extends superficially around the perineum resulting in necrosis of skin, subcutaneous tissue, fascia, or muscle. Perianal crepitation, erythematous, indurated skin, blistering, or gangrene may be present (Fig. 13.6).
 - The second group includes sepsis in which the preperitoneal or retroperitoneal spaces have become involved. Subtle signs may be present which include abdominal wall induration, tenderness, or a vague mass. It is important to realize that systemic symptoms such as fever, tachycardia, and vascular volume depletion may precede the appearance of overt signs of infection.

Treatment

- Treatment consists of vigorous intravenous fluid hydration, restoration of electrolyte balance, and insertion of a Foley catheter.
- Accompanying coagulopathy, respiratory insufficiency, and renal failure must be aggressively treated.
- Invasive monitoring and ventilatory support may be necessary.
- Pus or necrotic tissue from the infected region must be cultured for aerobes and anaerobes. A Gram stain can be used to distinguish between the presence of clostridial and nonclostridial organisms.
- Empiric broad-spectrum antibiotic therapy should be instituted regardless of Gram stain and culture results. The chosen antibiotic regimen should be effective against *Staphylococci* and *Streptococci*, Gram-negative *coliforms*, *Pseudomonas*, *Bacteroides*, and *Clostridium*. For Gram-positive rods seen on Gram stain, antibiotics administered should include sodium penicillin G in doses of 24–30 million units per day and an aminoglycoside. Tetanus toxoid should also be administered.



Fig. 13.6. Necrotizing anorectal infection.

- Surgical treatment consists of wide radical debridement until healthy tissue is encountered. The goals of surgical debridement are to remove all nonviable tissue, halt the progression of infection, and alleviate the systemic toxicity.
- It is crucial to realize that the preoperative skin changes may be minimal compared with the operative findings which may include edema, liquefactive necrosis of subcutaneous tissues, watery pus formation, and extensive necrosis of underlying fascia. Reexamination under anesthesia is usually necessary because this is the only manner by which adequate wound examination can be conducted.
- The need for colostomy is a debatable issue and has been recommended if the sphincter muscle is grossly infected, if there is colonic or rectal perforation, if the rectal wound is large, if the patient is immunocompromised, or if incontinence is present.
- Although antibiotics and adequate surgical drainage are thought to be sufficient, the use of hyperbaric oxygen (HBO) has been advocated as an adjunct to treatment, particularly in patients with diffuse spreading infections who do not have chronic obstructive pulmonary disease. It is postulated that HBO has a direct antibacterial effect on anaerobic bacteria by diminishing the effect of endotoxins and optimizing leukocyte phagocytic function. HBO may also promote wound healing by facilitating fibroblast proliferation.

- Despite aggressive surgical and multidisciplinary management of anorectal sepsis, mortality rates ranging from 8 to 67% have been reported. This high mortality rate is attributable in part to the aggressive nature of the infection and to the underlying comorbid diseases that are present in these patients. Mortality rates are 2–3 times higher in diabetics, in elderly patients, and in patients in whom treatment is delayed.

Anal Infection and Hematologic Diseases

- Acute anorectal suppuration poses an interesting and often life-threatening problem in patients with acute hematologic diseases. In patients with acute leukemia, mortality rates of 45–78% have been reported.
- There is a definite relationship between the number of circulating granulocytes and the incidence of perianal infection in patients with hematologic diseases. In one study, patients with neutrophil counts below 500 per cubic millimeter had an incidence of anorectal infections of 11% whereas those with counts greater than 500 per cubic millimeter had an incidence of 0.4%.
- The most important prognostic indicator was the number of days of neutropenia during the infectious episode.
- The most common presenting symptoms include fever which precedes pain, and urinary retention. Point tenderness and poorly demarcated induration constitute the earliest signs, whereas external swelling and fluctuation often appear late in the course of infection.
- Controversy surrounds the treatment of acute anorectal infections in patients with hematologic malignancies. Surgery has generally been avoided because what may seem to be simple incision and drainage may produce scant or no pus and may instead cause hemorrhage, poor wound healing, or expanding soft tissue infection.
- Any patient with perianal pain is assumed to have a perianal complication and is started on precautionary measures which consist of no digital rectal examinations, suppositories, or enemas. Sitz baths, stool softeners, bulk agents, and analgesia are advised.
- On aspiration of most abscesses in this group, the most common organisms have been found to be *Escherichia coli* and group

D streptococcus. Consequently, infections are successfully controlled with a third-generation cephalosporin combined with anaerobic coverage or an extended spectrum penicillin in combination with an aminoglycoside and an anti-anaerobic antibiotic. This combination has been associated with an 88% success rate.

- Because appropriate antibiotic coverage has been found to control infection successfully, surgery has generally been recommended only if there is obvious fluctuation, progression of soft tissue infection, or persistent sepsis after a trial of antibiotic therapy.

Anorectal Sepsis in the Patient Positive for the Human Immunodeficiency Virus

- Patients who are human immunodeficiency virus (HIV) positive and present with abscesses require drainage either by incision and drainage or use of catheter drainage.
- Because these patients are immunosuppressed, adjunctive antibiotics should be used.
- Efforts should be directed at keeping wounds small because these patients are at risk of poor wound healing. An increased incidence of perianal sepsis may be observed in HIV-positive patients.

C. Fistula-in-Ano

Pathophysiology

Etiology

- A fistula is defined as an abnormal communication between any two epithelium-lined surfaces. A fistula-in-ano is an abnormal tract or cavity communicating with the rectum or anal canal by an identifiable internal opening. Most fistulas are thought to arise as a result of cryptoglandular infection.

Classification

- The most helpful yet complicated classification of fistula-in-ano is that described by Parks et al. (Table 13.2). It has been

Table 13.2. Classification of fistula-in-ano.

Intersphincteric
Simple low tract
High blind tract
High tract with rectal opening
Rectal opening without perineal opening
Extrarectal extension
Secondary to pelvic disease
Transsphincteric
Uncomplicated
High blind tract
Suprasphincteric
Uncomplicated
High blind tract
Extrasphincteric
Secondary to anal fistula
Secondary to trauma
Secondary to anorectal disease
Secondary to pelvic inflammation

suggested that its use is particularly applicable to the treatment of recurrent fistulas.

Intersphincteric Fistula-in-Ano

- This fistula is the result of a perianal abscess. The tract passes within the intersphincteric space (Fig. 13.7a). This is the most common type of fistula and accounts for approximately 70% of fistulas.

Transsphincteric Fistula-in-Ano

- In its usual variety, this fistula results from an ischioanal abscess and constitutes approximately 23% of fistulas seen. The tract passes from the internal opening through the internal and external sphincters to the ischioanal fossa (Fig. 13.7b).
- One form of transsphincteric fistula is the rectovaginal fistula. This is discussed further in Chap. 14.

Suprasphincteric Fistula-in-Ano

- This fistula results from a supralelevator abscess and accounts for approximately 5% of fistulas in some series (Fig. 13.7c).

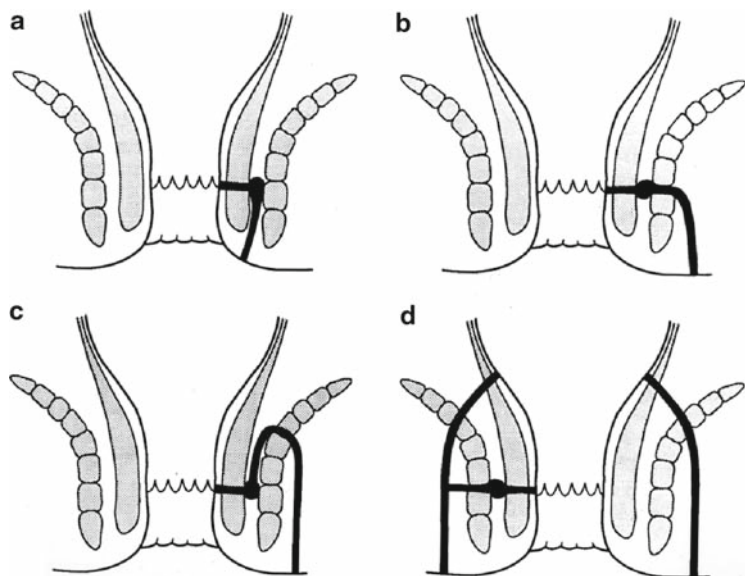


Fig. 13.7. Classification of fistula-in-ano. (a) Intersphincteric. (b) Transsphincteric. (c) Suprasphincteric. (d) Extrasphincteric.

Extrasphincteric Fistula-in-Ano

- This constitutes the rarest type of fistula and accounts for 2% of fistulas (Fig. 13.7d).

Evaluation and Treatment

Symptoms

- A patient with a fistula-in-ano will often recount a history of an abscess that has been drained either surgically or spontaneously. Patients may complain of drainage, pain with defecation, bleeding caused by the presence of granulation tissue at the internal opening, swelling, or decrease in pain with drainage.
- Additional bowel symptoms may be present when the fistula is secondary to proctocolitis, Crohn's disease, actinomycosis, or anorectal carcinoma. Systemic diseases such as HIV, carcinoma, and lymphoma should be entertained.

Physical Examination

- The external or secondary opening may be seen as an elevation of granulation tissue discharging pus. This may be elicited on digital rectal examination.
- In most cases, the internal or primary opening is not apparent.
- The number of external openings and their location may be helpful in identifying the primary opening. According to Goodsall's rule (Fig. 13.8), an opening seen posterior to a line drawn transversely across the perineum will originate from an internal opening in the posterior midline. An anterior external opening will originate in the nearest crypt. Generally, the greater the distance from the anal margin, the greater the probability of a complicated upward extension.
- Cirocco and Reilly found that Goodsall's rule was accurate in describing the course of anal fistulas with a posterior external opening. It was inaccurate in patients with anterior external openings because 71% of these fistulas tracked to a midline anterior primary opening. This was especially true in women in whom fistulas with anterior external openings tracked in a radial manner in only 31%.

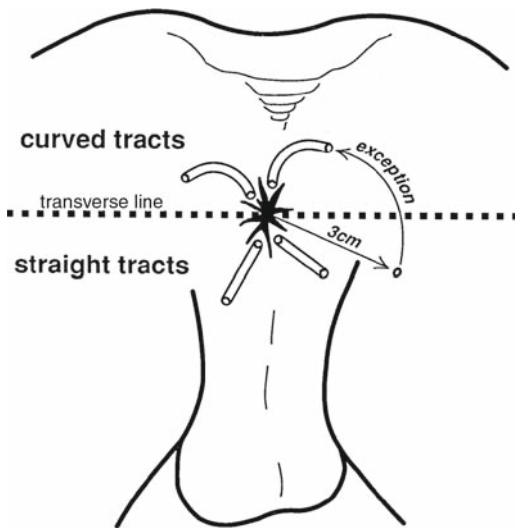


Fig. 13.8. Goodsall's rule.

- Digital rectal examination may reveal an indurated cord-like structure beneath the skin in the direction of the internal opening with asymmetry between right and left sides. Internal openings may be felt as indurated nodules or pits leading to an indurated tract.
- Posterior or lateral induration may be palpable indicating fistulas deep in the postanal space or horseshoe fistulas.

Investigations

- Anoscopy should be done before operation in an attempt to identify the primary opening.
- Sigmoidoscopy should be performed to locate a proximal internal opening and to exclude underlying pathology such as proctitis or neoplasia.
- Colonoscopy or barium enema and a small bowel series are indicated in patients who have symptoms suggestive of inflammatory bowel disease and in patients with multiple or recurrent fistulas.
- Although anal manometry is not generally required, it may be useful as an adjunct to planning the operative approach in women with previous obstetric trauma, in an elderly patient, a patient with Crohn's disease or AIDS, or in a patient with a recurrent fistula.
- The role of preoperative imaging is to demonstrate clinically undetected sepsis, to serve as a guide at the time of the initial surgery, to determine the relationship of the fistula tract to the sphincter mechanism, and to reveal the site of sepsis in a recurrent fistula, all serving to decrease recurrence rates associated with fistula surgery. Imaging may take the form of fistulography, computed tomography (CT) scan, endoanal ultrasound, and magnetic resonance imaging (MRI).

Fistulography

- Fistulography, which involves cannulation of the external opening with a small feeding tube and injection of water-soluble contrast may be useful in the evaluation of recurrent fistulas or in Crohn's disease where previous surgical forays or disease may have altered anorectal anatomy.

- Fistulography is invasive and potentially may result in the dissemination of sepsis.

CT Scan

- CT scanning performed with intravenous and rectal contrast is a noninvasive method used to assess the perirectal spaces. Its use may be to distinguish an abscess requiring drainage from perirectal cellulitis. It does not permit visualization of tracts in relation to the levators.

Endoanal Ultrasound

- The role of endoanal ultrasound is to establish the relation of the primary tract to the anal sphincters, to determine if the fistula is simple or complex with extensions, and to determine the location of the primary opening. It may aid in the identification of complex fistulas and may serve as an adjunct in the evaluation of complex suppuration to assess the adequacy of drainage (Fig. 13.9a).
- Although this investigative modality is rapid and well tolerated, it is operator dependent and scars or defects caused by previous sepsis, surgery, or trauma will confuse ultrasonographic interpretation and make delineation of fistula tracts difficult. The concomitant use of hydrogen peroxide (Fig. 13.9b) or Levo-vist™ at the time of ultrasound examination has been found to improve its accuracy.

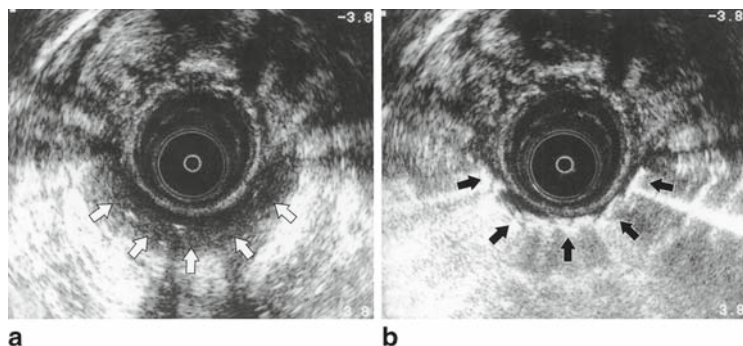


Fig. 13.9. (a) Anal endosonogram; arrows indicate fistula tract; (b) with hydrogen peroxide; arrows indicate better delineation of fistula tract. (Courtesy Dr. Julio Faria.)

Magnetic Resonance Imaging

- MRI in the form of endoanal coil, body coil, and phase array coil (Fig. 13.10) may be of value in the assessment of patients with complex fistulas and in those with anatomic distortion resulting from previous surgery.
- MRI has been found to accurately delineate the presence and course of a primary fistulous tract but also demonstrates the site and presence of any secondary extensions. It also provides the most accurate imaging technique of localizing the site of the internal opening because its location can be inferred from the proximity of the tract in the intersphincteric space.
- The use of the endoanal coil has been found to be superior to external MRI for the identification of complex sphincter anatomy especially in the demonstration of the morphology of the internal and external sphincters; however, definition may fall off outside the sphincter and may fail to show the tracts that lie beyond its range. It is also painful.

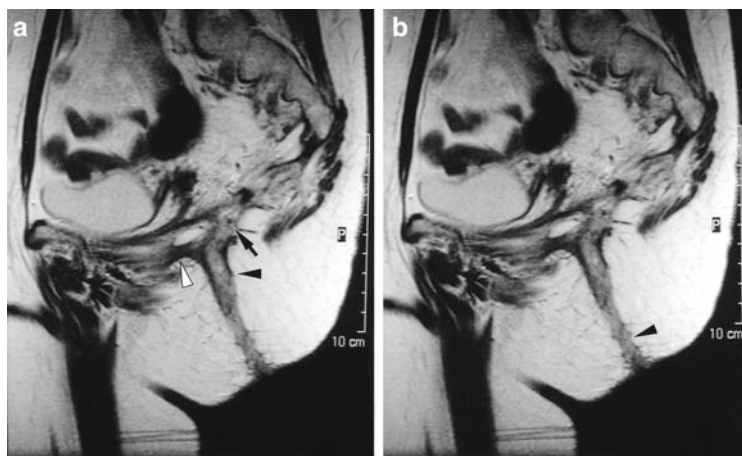


Fig. 13.10. Phase array MRI. (a) White arrowhead indicates levators; black arrowhead indicates fistula tract to rectum; black arrow shows tract crossing levator. (b) Arrowhead indicates tract going to skin.

Treatment

General Principles

1. The principles of fistula surgery are to eliminate the fistula, prevent recurrence, and preserve sphincter function. Success is usually determined by identification of the primary opening and dividing the least amount of muscle possible.
2. Several methods have been proposed to identify the primary opening in the operating room:
 - Passage of a probe or probes from the external opening to the internal opening or vice versa.
 - Injection of a dye such as dilute solution of methylene blue, milk, or hydrogen peroxide, and noting their appearance at the dentate line. Although methylene blue may stain surrounding tissues, diluting it with saline or hydrogen peroxide will obviate this problem.
 - Following the granulation tissue present in the fistula tract.
 - Noting puckering of an anal crypt when traction is placed on the tract. This may be useful with simple fistulas but is less successful in the more complicated varieties.

Operative Management

Lay-Open Technique

- A probe is inserted from the external opening along the tract to the internal opening at the dentate line. The tissue overlying the probe is incised and the granulation tissue curetted and sent for pathologic evaluation.
- If desired, the wound may be marsupialized on either edge by sewing the edges of the incision to the tract with a running locked absorbable suture. There is no need to insert packing if an adequate unroofing has been accomplished (Fig. 13.11a–c).

Seton

- The problem of preserving anal continence and treating the fistula is more complicated when managing high transsphincteric fistulas.

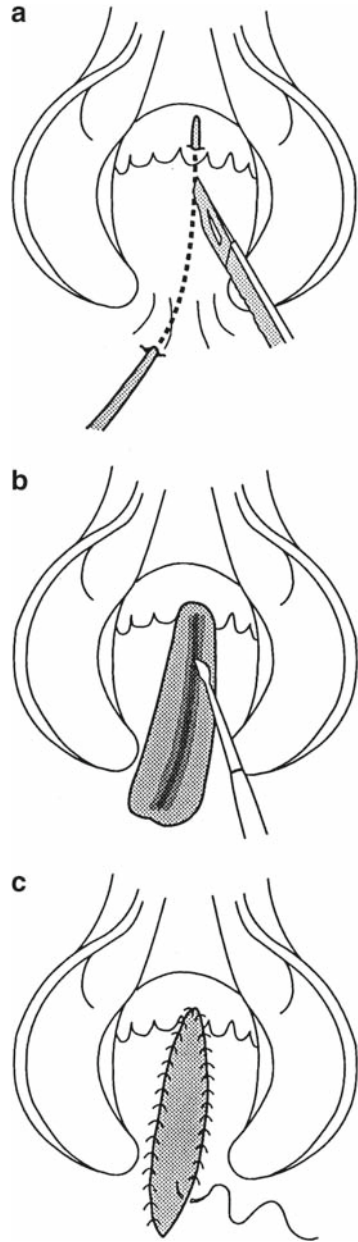


Fig. 13.11. Technique of laying open. (a) Insertion of probe and incision of tissue overlying probe. (b) Curettage of granulation tissue. (c) Marsupialization of wound edges.

- If the tract is seen to cross the sphincter muscle at a high level, the use of the lay-open technique in combination with insertion of a seton is safer.
- A seton may be any foreign substance that can be inserted into the fistula tract to encircle the sphincter muscles. Materials frequently used include silk or other nonabsorbable suture material, Penrose drains, rubber bands, vessel loops, and silastic catheters.
- The lower portion of the internal sphincter is divided along with the skin to reach the external opening and a nonabsorbable suture or elastic suture is inserted into the fistulous tract. The ends of the suture or elastic are tied with multiple knots to create a handle for manipulation (Fig. 13.12). This form of seton, known as a cutting seton, is tightened at regular intervals to slowly cut through the sphincter. This allows the tract to become more superficial, converting a high fistula into a low one. The proximal fistulotomy subsequently heals by stimulating fibrosis behind it reestablishing continuity of the anorectal ring to prevent separation of the sphincter muscle at a second-stage repair 8 weeks later when the remaining external sphincter is divided.

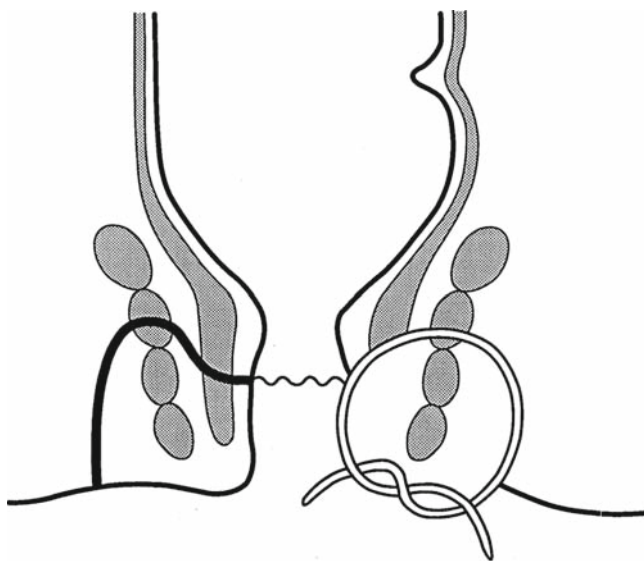


Fig. 13.12. Seton.

- A seton may also be used as a drain which is left loosely in place to facilitate prolonged drainage.
- Specific indications for seton use include the following:
 - To identify and promote fibrosis around a complex anal fistula that encircles most or all of the sphincter mechanism.
 - To mark the site of a transsphincteric fistula in cases of massive anorectal sepsis where the normal anatomic landmarks have been distorted.
 - Anterior, high transsphincteric fistulas in women. Because the puborectalis is absent in this area and the external sphincter is quite tenuous, primary fistulotomy may result in incontinence.
 - The presence of a high transsphincteric fistula in a patient with AIDS in whom healing is known to be poor.
 - To avoid premature skin closure and formation of recurrent abscesses and promote long-term drainage in patients with Crohn's disease. In these patients, a silastic catheter can be left in place for a prolonged period of time to promote epithelialization of the fistula tract or tracts.
 - When there is suspicion that primary fistulotomy will result in incontinence such as in those patients with multiple simultaneous fistulas, patients who have undergone multiple prior sphincter operations such as fistulotomy or internal sphincterotomy, and in elderly patients with weakened sphincter muscles.
- Another option available to treat transsphincteric fistulas without division of muscle involves the use of a dermal island flap.
- The horseshoe variety of the suprasphincteric fistula also presents the problem of complete sphincter involvement combined with the presence of multiple external openings a great distance from the cryptoglandular source. Treatment consists of identification of the internal opening and proper drainage of the postanal space as was previously described. The horseshoe extensions are enlarged for counter-drainage and the granulation tissue is curetted.

Anorectal Advancement Flap

- When the traditional laying-open technique may be inappropriate, for example, in anterior fistulas in women, in patients with inflammatory bowel disease, in patients with high transsphincteric and suprasphincteric fistulas, as well as in those with previous multiple

sphincter operations, multiple and complex fistulas, the use of an anorectal advancement flap has been advocated (Fig. 13.13 a–d).

- Advantages of this technique include a reduction in the duration of healing, reduced associated discomfort, lack of deformity to the anal canal, as well as little potential additional damage to the sphincter muscles because no muscle is divided.
- The base of the flap should be twice the width of the apex to maintain good blood supply. Successful results have reported in more than 90% of patients.
- Factors associated with poor outcomes include Crohn's disease and steroids. Cigarette smoking was found to be another significant variable in another study.

Fistulectomy

- Although excision of the fistula or fistulectomy was thought to be a satisfactory method of treatment of fistula-in-ano, its

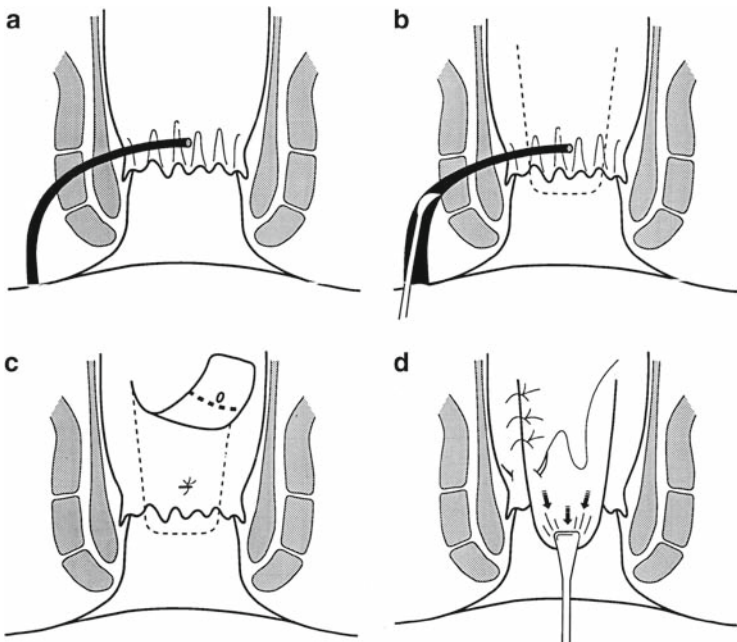


Fig. 13.13. Anorectal advancement flap. (a) Transsphincteric fistula-in-ano. (b) Enlargement of external opening and curettage of granulation tissue. (c) Mobilization of flap and closure of internal opening. (d) Suturing of flap in place covering internal opening.

use is no longer recommended. Larger wounds are created significantly prolonging wound healing time. A greater separation of muscle ends occurs and there is greater risk of injuring or excising underlying muscle thereby increasing the risk of incontinence.

Fibrin Glue

- This treatment modality is appealing because it is a noninvasive approach that avoids the risk of incontinence associated with fistulotomy. In the case of failure, it may be repeated several times without jeopardizing continence.
- Enthusiasm generated because of short-term success rates of 70–74% has been tempered because of delayed fistula recurrence despite initial apparent healing. Closure rates as low as 15% have been reported.
- Suggested reasons for failure include inadequate curettage of the tract, presence of a short tract and presence of a cavity on endoanal ultrasound.

Bioprosthetic Fistula Plug

- Recently, the use of a bioprosthetic plug made from lyophilized porcine intestinal submucosal has been described for complex anal fistulas.
- The technique involves preoperative enema prior to the procedure. Patients are given intravenous metronidazole just prior to the start of the procedure. Fistula tracts are irrigated with hydrogen peroxide prior to insertion of the tract. The plug is rehydrated in sterile saline and a 2-0 vicryl is secured to the tapered end of the plug. The ends of the suture are attached to a fistula probe at the primary opening. The suture is then pulled from the primary opening to exit at the secondary opening. Excess plug at the internal opening is trimmed flush with the mucosa and the plug is sutured deep to the internal sphincter with a figure of eight 2-0 absorbable suture. A small mucosal advancement flap may be placed over the top of the plug to ensure that it is buried in the tract. Any excess plug is excised at the secondary opening which is left open to allow drainage.
- Patients are advised to avoid vigorous physical activity for two weeks after plug placement to minimize the chance of plug dislodgement.

- The technique seems to work best with long tracts without active sepsis. It is not suitable for short rectovaginal fistulas. An additional limitation has been the relatively high cost of the plug.
- A recent prospective study demonstrated 84% early healing., Longer follow-up was associated with progressively increasing failure rates of 27.2% at 8 weeks, 38.6% at 12 weeks and 45.4% at 13 months High failure rate was associated with complex fistulas and patients with Crohn's Disease.
- Another recent prospective study found that the use of the fistula plug was associated with a low rate of healing and a high rate of perianal sepsis. There was a suggestion of increased healing without complication in patients who underwent a concomitant advancement flap.

Postoperative Care

- After the lay-open technique, patients are placed on regular diets, bulk agents, and non-codeine-containing analgesia. Patients are instructed to take frequent sitz baths to ensure perianal hygiene. Patients are evaluated at 2-week intervals to ensure that healing has occurred from the depths of the tract. Granulation tissue can be cauterized using silver nitrate sticks and cotton-tipped swabs are often used to probe the depths of the incision to ensure that adequate healing is occurring.
- After the advancement flap technique, the Foley catheter is removed on the following day. The authors prefer to maintain patients on intravenous therapy with no oral nutrition for 5 days to allow adequate healing of the flap. Several of the editors do not limit oral intake in the postoperative period, which significantly shortens the hospital stay.

Complications

Incontinence

- Minor disorders of continence after fistulotomy have been reported to range from 18 to 52% whereas soiling and insufficiency have been reported in as many as 35–45% (Table 13.3). The occurrence of continence disorders has been found to be related to the complexity of the fistula and to the level and location of the internal opening.

Table 13.3. Results of fistula surgery.

Author	Year	No. of patients	Recurrence (%)	Incontinence (%)
Marks and Ritchie	1977	793	—	3, 17, 25 ^a
Vasilevsky and Gordon	1985	160	6.3	0.7, 2.0, 3.3 ^b
Fucini	1991	99	3.0	0, 0.2, 0.5 ^c
Van Tets	1994	19	—	33.0
Sangwan	1994	461	6.5	2.8
Garcia-Aguilar et al.	1996	293	7.0	42.0
Mylonakis et al.	2001	100	3.0	0, 6.0, 3.0 ^d
Malouf et al.	2002	98	4.0	10
Westerterp et al.	2003	60	0	50

^a3% solid stool, 17% liquid stool, 25% flatus

^b0.7% solid stool, 2.0% liquid stool, 3.3% flatus

^c0% solid stool, 0.2% liquid stool, 0.5% flatus

^d0% solid stool, 6.0% soiling, 3.0% gas

- Patients with complicated fistulas, high openings, posterior openings, and fistula extensions have been found to be at higher risk.
- In the treatment of complicated fistulas and those with high openings, more muscle is divided, thus decreasing anal pressures whereas posterior fistula wounds have been associated with higher rates of incontinence because of their more circuitous routes.
- If the edges of the fistulotomy wound do not approximate precisely, the anus may be unable to properly close, resulting in intermittent leakage of gas and stool. In addition to these factors, impaired continence was associated with increasing age and female gender. The latter is probably the result of partial anal sphincter disruption and/or traction injury to the pudendal nerves sustained during vaginal delivery.
- Although excellent results using a seton have been reported, its use does not protect against the development of impaired continence.
- Major fecal incontinence was reported in 6.7% after a review of several series (Table 13.4). The degree of incontinence is thought to be influenced by the patient's preoperative state of control as well as to how the anal wound heals.
- Excellent results with respect to continence have been reported with the use of the advancement flap although recent reports have observed disturbances in continence in 9–35%.

Table 13.4. Results of staged fistulotomy using a seton.

Author	Year	Recurrence (%)	Incontinence (%)
Ramanujam et al.	1983	1/45 (2)	1/45 (2)
Fasth et al.	1990	0/7 (0)	0/7 (0)
Williams et al.	1991	2/28 (8)	1/24 (4)
Pearl et al.	1993	3/116 (3)	5/116 (5)
Van Tets	1994	–	15/29 (54)
Graf et al.	1995	2/25 (8)	11/25 (44)
Garcia-Aguilar et al.	1996	6/63 (9)	39/61 (64)
Hasegawa et al.	2000	8/32 (25)	15/32 (4.8)

Recurrence

- Recurrence rates after fistulotomy range from 0 to 18%.
- Causes include failure to identify a primary opening or recognize lateral or upward extensions of a fistula.
- Premature closure of the fistulotomy wound can be obviated by producing an external wound twice the size of the anal wound resulting in proper healing of the internal wound before the external wound.
- Although recurrence rates after anorectal advancement flaps were initially reported to be low, with long-term follow-up, recurrence rates of 40% have been reported.
- Early postoperative complications that have been reported after fistula surgery include urinary retention, hemorrhage, fecal impaction, and thrombosed external hemorrhoids, which were found to occur in less than 6% of cases.
- With attention to both operative detail and postoperative follow-up, these complications can be reduced to a minimum.

Special Considerations

Crohn's Disease

- Anal fistulas are the most difficult and challenging complication of Crohn's disease to manage.
- They constitute the most common perianal manifestations, occurring in 6–34% of patients.
- Patients with colonic Crohn's have a higher incidence with the rate approaching 100% in those with rectal Crohn's.
- Delineation of the fistulous tract is especially important in Crohn's disease because many fistulas may be complex in nature.

- MRI has been found to detect abscesses that were clinically unsuspected on clinical examination and has been helpful in determining the relationship of the fistulous tract to the sphincter muscles.
- Therapeutic goals in managing anorectal fistulas in Crohn's disease remain the alleviation of symptoms and preservation of continence. Surgical treatment of fistulas is associated with poor and delayed wound healing and with the risk of sphincter injury.
- "Incontinence is likely to be the result of aggressive surgeons, not of aggressive disease." A conservative approach has therefore been advocated, especially because 38% of such fistulas have been reported to heal spontaneously without any surgical intervention.
- Medications used in the treatment of fistulas include antibiotics such as metronidazole and ciprofloxacin and immunomodulators such as corticosteroids, 6MP, azathioprine, and infliximab.
- Although several studies have reported spontaneous closure of fistulas in 34–50% of patients treated with metronidazole, improvement is usually seen after 6–8 weeks of treatment with relapses common once the medication is discontinued.
- A recent study that looked at the long-term effects of 6MP and azathioprine found that these medications were efficacious in only one-third of patients with fistulizing perianal disease.
- The use of infliximab has been associated with a 62% reduction in draining fistulas. The combination of infliximab and 6MP may prolong the effect of initial infliximab treatment on fistula closure.
- Although fistulas may occur in as many as 73% of patients after previous abscess drainage, it is imperative that primary fistulotomy not be performed because of the high risk of creating false passages and injuring the sphincter mechanism.
- Low fistulas with simple tracts can be managed with the standard lay-open method in the absence of active proctitis.
- Fistulotomy has been associated with prolonged healing. Factors associated with delayed healing are rectal involvement, anorectal complications (especially strictures), and the presence or absence of an internal opening.
- Incontinence has been reported in patients with proctitis who have not undergone anal surgery. A patient with severe rectal involvement and even a simple low fistula is not a candidate for fistulotomy. Division of any sphincter muscle in this situation may result in frank incontinence because the noncompliant rectum acts as a conduit rather than as a reservoir.

- The results with the use of fibrin glue have been disappointing with high recurrence rates reported.
- Results with the fistula plug have been equally disappointing. This is, however, an attractive alternative which avoids sphincter muscle division and probably should be tried initially since failure does not preclude performance of other procedures in the future.
- It is thought that diarrhea from either associated intestinal involvement or multiple previous small bowel resections is important in control disorders in these patients. Appropriate medical therapy should be used to control the diarrhea.
- The importance of quiescent intestinal disease for successful outcome of local fistula surgery has been suggested but not generally accepted and practical.
- A covering stoma may be beneficial in the patient who has undergone multiple unsuccessful repairs.

Fistula-in-Ano in the HIV-Positive Patient

- Anal fistulas are prevalent in the anoreceptive HIV-positive individual.
- Although anal fistulas in HIV-positive patients arise from the dentate line similar to those in HIV-negative patients, they are more likely to have incomplete anal fistulas leading to blind sinus tracts.
- Concern for wound healing has tempered enthusiasm for operative intervention. However, selective operative management will result in a high rate of complete or partial wound healing with symptomatic relief without excessive morbidity or mortality.
- Severity of illness must be assessed before operative intervention because patients with more advanced disease are less likely to heal their wounds. Data are conflicting as to whether preoperative CD4+ lymphocyte counts can be related to poor wound healing; however, Consten et al. found that low CD4+ lymphocyte counts in patients with perianal sepsis were a risk factor for disturbed wound healing.
- Use of Highly Active Antiviral therapy (HAART) may reduce the incidence of opportunistic infections and anorectal disease and aid healing.
- Care should be exercised to avoid creation of large wounds and to preserve as much sphincter muscle as possible because these patients may be prone to diarrhea which may overwhelm a partially divided sphincter.

- In patients who are good operative risks, fistulotomy is appropriate in patients with intersphincteric or low transsphincteric fistulas.

D. Rectourethral Fistulas

Pathophysiology

- Rectourethral fistulas are rare but devastating complications that may occur after radical prostatectomy, radiation treatment for prostate cancer, trauma, recurrent perineal abscess, or after treatment with radiofrequency hyperthermia for benign prostatic hypertrophy. It may occur after trauma, as a result of Crohn's disease.
- The prostatic urethra is the most common site for fistulization to occur because this portion of the urethra is adjacent to the rectal wall.

Evaluation and Treatment

Symptoms

- The most common symptoms include leakage of urine through the rectum during voiding, pneumaturia, and fecaluria. These symptoms will tend to occur during the early postoperative period after prostatectomy.

Investigations

- Prostate-specific antigen determination should be done to rule out recurrence of carcinoma.
- Digital rectal examination should always be performed to determine if there is any anorectal pathology that could be the cause.
- Sigmoidoscopy will show the fistula opening which is located on the anterior rectal wall and in addition rule out rectal pathology as a source.
- Cystoscopy and retrograde urethral cystography should be performed to determine the presence of a urethral stricture. Assessment of urinary continence should be done before any attempt at surgical repair.

Operative Treatment

- Operative repair of rectourethral fistulas is challenging because of technical difficulties that are often encountered as a result of difficult exposure. Multiple repairs have been developed but there is no consensus as to which is best. Traditionally, it has been suggested that the first attempt at repair is the best and that subsequent repairs become more difficult.
- Treatment consisting of fecal diversion with either colostomy or ileostomy and urinary diversion with suprapubic catheterization under cover of antibiotics has been described in the management of rectourethral fistulas secondary to radiation when the urethral defect has been found to be too large to repair. This has been associated with bouts of recurrent sepsis and persistent symptoms.

Transabdominal Approach

- The transabdominal approach combines the use of abdomino-anal pullthrough in combination with omental interposition.

Perineal Approach

- Perineal approaches using the gracilis muscle, dartos, or Martius flap have been described.

Anterior Trans-Anorectal Approach

- In this approach, a midline perineal incision is deepened by incising all structures superficial to the prostatic capsule which include the superficial perineal fascia, the central tendon of the perineum, and the internal and external sphincters. This approach allows better access in the repair of complicated membranoprostatic fistulas with preservation of continence and erectile function.

Per-Anal Approach

- This approach has the theoretical advantages of minimal scarring and fewer wound infections although it suffers from limited exposure.
- It involves the use of a full-thickness advancement of anterior rectal wall protected by diverting colostomy.

Kraske Laterosacral Approach

- This approach provides excellent exposure without division of the sphincter mechanism. The need to excise two to three sacral segments as well as the nerves, muscles, and ligaments around them pose a disadvantage.

York Mason (Trans-Sphincteric) Approach

- This approach affords a rapid, bloodless exposure through fresh territory and allows for complete separation of the urinary and fecal streams.

Transanal Endoscopic Microsurgery

- This highly specialized technique allows for a meticulous two-layer closure of the rectal wall and may be combined with transurethral fulguration of the opposite urethral opening of the fistula.

Cystectomy and Ileal Conduit

- Cystectomy and ileal conduit may be considered for those patients with a low probability of success in resolving the fistula or in maintenance of urinary continence.

Appendix: Practice Parameters for Treatment of Fistula-in-Ano

Prepared by the Standards Task Force, American Society of Colon and Rectal Surgeons

Acute Suppuration (Abscess)

Presentation and Management

An abscess should be drained in a timely manner; lack of fluctuance is not a reason for delay in treatment. If the abscess is superficial, it may be drained in the office setting using a local anesthetic. If the patient

is too tender to permit examination and drainage, then these measures should be undertaken in the operating room. Antibiotics may have a role as adjunctive therapy in special circumstances, including valvular heart disease, immunosuppression, extensive cellulitis, or diabetes. Location of the abscess should be documented. If possible, anoscopy should be performed to reveal the primary site of infection. Patients should notify the physician if pain recurs after abscess drainage.

Chronic Suppuration (Fistula)

Physical Examination

Inspection and palpation form the basis of the initial evaluation. Specifically, external (secondary) openings are sought, because their relationship to the anal canal provides a clue to the origin of the abscess-fistula. Anoscopy may be useful to identify an internal opening. If clinically indicated, proctosigmoidoscopy or colonoscopy may be suggested to exclude more proximally located inflammatory disorders with which fistulas can be associated.

Radiographic Evaluation

Ultrasound, fistulography, computed tomography, and magnetic resonance imaging are not routinely indicated in the initial evaluation of fistulas but may be helpful in identifying an occult cause of recurrent fistula.

Treatment

Simple Fistulas May Be Treated by Fistulotomy. Fistulotomy is preferred to fistulectomy, because the former technique does not involve excision of the sphincter. Primary fistulotomy is appropriate in cases of intersphincteric and low transsphincteric fistulas. Exceptions may include an anteriorly based transsphincteric fistula in a female, a diabetic patient, or a patient with a weakened sphincter. Patients with irritable bowel syndrome or increased stool frequency may require staged fistulotomy with a seton.

Recurrent Abscess-Fistula/Incontinence. Repeat fistulotomy can be used in treatment of recurrent fistula. If the patient with a recurrent

fistula has symptomatic incontinence, then a physiologic investigation may be warranted.

Selective Complex Fistulas May Require Treatment Other Than Fistulotomy. These indications include (1) high transsphincteric fistula, (2) extrasphincteric fistula, (3) anterior fistulas in females, (4) patients with coexisting inflammatory disease, (5) patients with immunosuppressive disease such as human immunodeficiency virus, (6) elderly patients with poor sphincter function, (7) uncertainty by the surgeon of level of fistula in relation to sphincter, (8) multiple simultaneous fistulas, and (9) patients with multiple prior sphincter surgeries or injuries. Either seton placement or advancement flap closure should be considered. The seton may be used in either a cutting or draining manner, depending on the clinical situation and the patient's underlying condition.

Special Considerations

Rectovaginal Fistulas

For a traumatic (postobstetric) fistula, a 3- to 6-month waiting period after injury is generally useful to promote fibrosis of the injured muscle. A fistulotomy is not generally used if it results in undue amounts of sphincter division. Treatment alternatives include transanal or transvaginal advancement flap closure, closure of the rectovaginal septum, conversion to a complete perineal laceration with layered closure, sphincteroplasty, and muscle interposition.

Radiation-Associated Fistulas

Interposition flap or transabdominal approaches have the highest success rates, depending on the level of the fistula.

High Fistulas

For some surgeons, the transabdominal approach is more familiar and involves division of the fistula with layered closure and interposition of omentum. Alternatively, an anterior resection or coloanal anastomosis may be considered.

Suprasphincteric Fistulas

Treatment requires an appreciation that the tract involves the entire external sphincter complex and the puborectalis muscle. Useful treatment options include division of the internal sphincter with concomitant seton placement, excision and drainage of the tract with closure of the internal opening, and advancement flap closure.

Horseshoe Fistula

The internal opening and postanal (or deep anterior anal) space should be drained with or without a seton. The horseshoe portion of the fistula should be curetted and counterdrained rather than unroofed.

Human Immunodeficiency Virus Infection

Large open wounds and sphincter division should be avoided. In general, minimally immunocompromised patients can undergo standard fistulotomy, whereas patients with higher degrees of immunosuppression should undergo placement of a noncutting (draining) seton.

Crohn's Disease

Initial management should be directed at resolving rectal inflammation. Such medical management may include antidiarrheals, topical enemas, antibiotics, suppositories, or systemic steroids and/or immunosuppressive agents. Fistulotomy is a reasonable alternative in most cases of intersphincteric or low transsphincteric fistulas. More complex fistulas can be treated with drainage, seton placement, or flap closure based on the patient's level of continence or extent of concomitant intestinal disease. Ultimately, a temporary or permanent stoma may be indicated.

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14. Benign Anorectal: Rectovaginal Fistulas

A. Etiology

- Obstetric injury is the most frequent cause of acquired rectovaginal fistulas but infection and other forms of trauma may also result in these fistulas. After an obstetric injury, the fistula may be manifest immediately but more frequently appears 7–10 days after delivery. Fistulas occur most often after a third- or fourth-degree laceration. Inadequate repair, breakdown of the repair, or infection may result in fistula formation.
- In developed nations, rectovaginal fistulas occur after 0.06–0.1% of vaginal deliveries.
- Disease processes may also cause rectovaginal fistulas. Cryptoglandular infection may result in an abscess spontaneously draining into the vagina resulting in a fistula.
- Rectal and gynecologic malignancies may result in fistulas as a result of local extension of the tumor or secondary to treatment with radiotherapy.
- Women with inflammatory bowel disease, Crohn's disease more frequently than ulcerative colitis, may develop rectovaginal fistulas.
- Operative trauma may also result in a rectovaginal fistula. Complications of rectal or vaginal surgery usually result in fistulas opening low in the rectum. High fistulas are most frequently complications of low stapled colorectal or ileoanal anastomoses.
- Pouch vaginal fistulas are reported in 3–12% of patients. The mechanism is usually that a portion of the posterior vaginal wall is included in the anastomosis or that an abscess secondary to an anastomotic leak drains into the vagina.

- Fistulas have also been reported after vaginal dilatation of a radiated vaginal cuff, fecal impaction, viral and bacterial infection in human immunodeficiency virus patients and sexual assault.

B. Evaluation

- There are two primary goals in the evaluation of women with possible rectovaginal fistulas: identification of the fistula site and assessment of the surrounding tissue. The type of investigation required varies with the underlying etiology of the fistula.

Identification of Fistula Site

- In most women with complaints consistent with a rectovaginal fistula, the site can be readily identified on examination. Visual examination may show the dark red rectal mucosa contrasting with the pale mucosa of the vagina. A dimple may be palpable in the anterior midline on rectal examination.
- The rectal opening is frequently visible on anoscopy.
- A methylene blue test may confirm the presence of a communication and aid in locating the site. During this test, a vaginal tampon is inserted and then the patient is given an enema colored with methylene blue. If the patient retains the enema, staining on the tampon is highly suggestive of a rectovaginal fistula.
- Alternatively, saline can be instilled in the vagina with the patient in the lithotomy position. The rectum is then insufflated with air and the vagina observed for bubbles.
- Radiographic tests may help identify an elusive fistula. One option is vaginography. The examination is performed by instilling contrast into the vagina.
 - The technique has a sensitivity of 79–100% for the detection of the fistula tract.
 - Vaginography is most helpful for colovaginal and enterovaginal fistulas; it is less useful for low rectovaginal fistulas.
- Computed tomography scans may identify the fistula tract and characterize the surrounding tissue.
- Both magnetic resonance imaging (MRI) and ultrasound are used to identify fistulas with reasonable specificity and low sensitivity.

Assessment of Local Tissue

- The second goal of evaluation is to determine the etiology and to assess the surrounding tissue. The necessary tests are determined by the suspected etiology of the fistula.
- If the mechanism of injury is childbirth, the patient with a fistula is at significant risk of a sphincter defect.
- Ultrasound or MRI should be done to assess the anal sphincter.
- One study found that 100% of women presenting with a rectovaginal fistula after a delivery had a sphincter defect.
- Multiple perianal fistulas suggest Crohn's disease as the etiology. Evaluation of the intestinal tract by colonoscopy and contrast studies is indicated in patients with known or suspected inflammatory bowel disease. One must be careful to consider the patient's obstetric history even if she carries the diagnosis of Crohn's disease.
- Biopsy of a detectable mass should be done for suspected malignancy.
- It is critical that recurrent carcinoma be distinguished from irradiation injury. In patients with a history of malignancy treated by radiation, examination under anesthesia with biopsies is often necessary. Two series report an approximately 50% incidence of recurrent cancer on biopsies of these fistulas.

C. Classification

- A variety of classification systems exist for rectovaginal fistulas. Most systems classify by size, location, and etiology.
- Daniels classified fistulas by their location along the rectovaginal septum as low, middle, or high.
 - The rectal opening is at the dentate line and the vaginal opening just inside the vaginal fourchette in low fistulas.
 - The vaginal opening is at or near the cervix in high fistulas. Middle fistulas are located between high and low fistulas.
 - This system is useful in that high fistulas are more likely to require laparotomy; perineal approaches are appropriate for most low and middle fistulas.
- Saclarides argues that a classification system based on etiology is the most useful for the treating physician. A system determined by etiology would take into consideration the state of

the surrounding tissue both anatomically and functionally as well as the health of the patient.

- None of these systems have been tested to see whether they are predictive of outcome but a strong case can be made that etiology is the best guide to patient management.

D. Conservative Management

- For women with small fistulas and minimal symptoms, medical management is appropriate. Optimizing the patient's bowel function, particularly controlling diarrhea, is beneficial. Unfortunately, for the majority of women with rectovaginal fistulas, the symptoms are intolerable.

E. Surgical Techniques

Local Repairs

General Considerations

- A local repair is appropriate for the first or second repair in women with rectovaginal fistulas and intact sphincter muscles.

Fibrin Sealant

- Most studies that include rectovaginal fistulas report discouraging results of 0–33% success in very small numbers of patients.

Advancement Flaps

- Advancement flaps may be approached transrectally, vaginally, or through the perineum. An advantage of the transanal approach is direct access to the rectal side of the fistula which is the high pressure side (Fig. 14.1).
- The literature contains many case series of endorectal advancement flaps (Table 14.1).
- Lowry and colleagues reported a success rate of more than 80% in first and second repairs but only 55% in patients with two prior repairs.

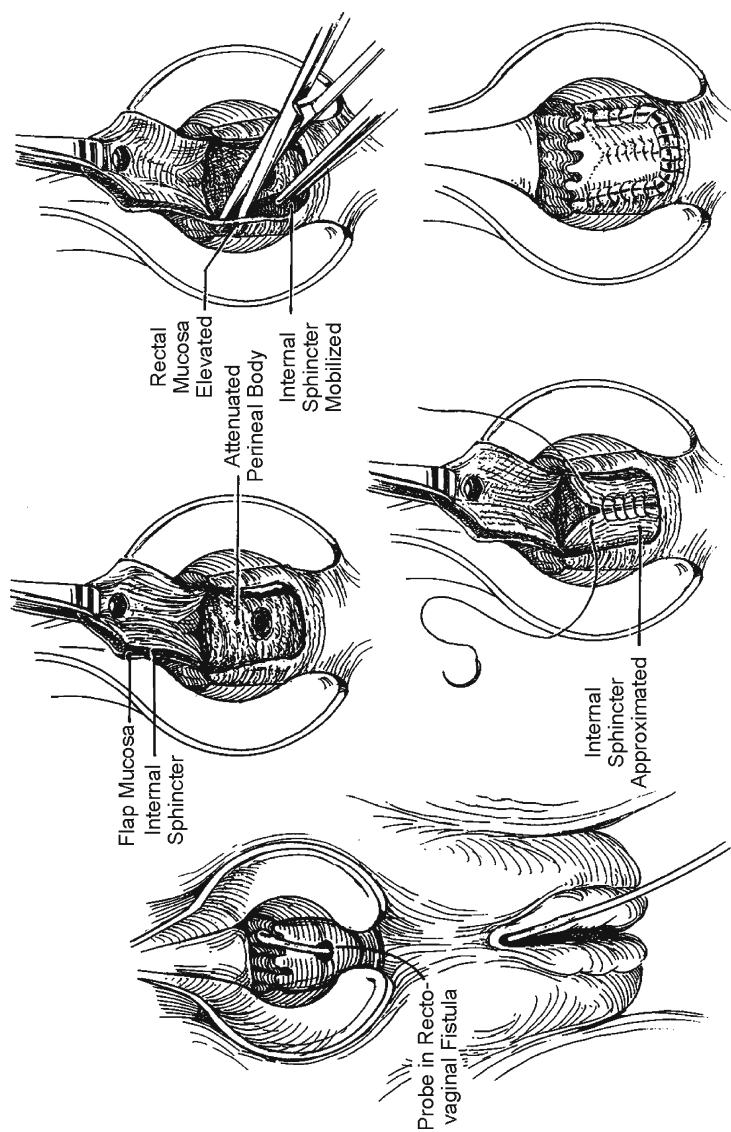


Fig. 14.1. Endorectal advancement flap.

Table 14.1. Results of endorectal advancement flaps.

Author	Year	No. of patients	Success (%)	Comments
Greenwald and Hoexter	1978	20	100	Tract excised, layered closure under flap
Hoexter et al.	1985	15	100	Repair as above
Wise et al.	1991	40	85	15 concomitant sphincteroplasty
Lowry	1991	85	78	25 concomitant sphincteroplasty
Kodner et al.	1993	71	93	Unknown no. sphincteroplasty
Khanduja et al.	1994	16	100	Patients without incontinence
MacRae et al.	1995	28	29	50% obstetric, previous failed repairs
Mazier et al.	1995	19	95	67% simple
Watson and Phillips	1995	12	58	Ultimate success 83%, 25% stomas
Tsang et al.	1998	27	41	All obstetric
Hyman	1999	12	91	Etiology not reported
Joo et al.	1998	20	75	Ultimate success, all Crohn's
Baig et al.	2000	19	74	7 concomitant sphincteroplasty
Mizrahi et al.	2002	32	56	Mixture of etiologies
Sonoda et al.	2002	37	43	Mixture of etiologies
Zimmerman et al.	2002	21	48	6 concomitant sphincteroplasty 12 labial flap transposition

- Sonoda and colleagues also found that a diagnosis of Crohn's disease was associated with a higher failure rate in their study of 105 endorectal advancement flaps.
- Success rates of 84–100% are reported with vaginal flaps.
- Anocutaneous flaps are an option for distal rectovaginal or anovaginal fistulas.

Rectal Sleeve Advancement

- An alternative transrectal approach is a rectal sleeve advancement involving mobilization of the distal rectum and advancement to cover the fistula.

- The rectum is pulled through the anal canal, the diseased portion excised, and healthy tissue sutured to anoderm below the dentate line. This technique is reported in patients with a rectovaginal fistula and inflamed anal canal and distal rectum from Crohn's disease.
- This technique is useful for someone with a rectovaginal fistula and a stricture because both problems will be corrected with the procedure.

Excision of Fistula with Layered Closure

- Another option is excision of the fistula tract and layered closure.
- Layered closure may actually be performed through the rectum, vagina, or perineum.
- The fistula tract is excised. Vaginal mucosa, rectovaginal septum, rectal muscle, and rectal mucosa are closed in succession.
- Using layered closure, successful repair is reported in 88–100% of patients in the small series published.

Perineo-proctotomy

- Perineo-proctotomy is conversion to a fourth-degree laceration (Fig. 14.2).
- This approach begins with the identification of the fistula and division of the bridge of skin, subcutaneous tissue, sphincter muscle, rectal and vaginal walls overlying the fistula. The tract is excised and both the rectal and vaginal walls are dissected away from the muscle. After repair of both the rectal and vaginal defects, the external sphincter muscle is reapproximated.
- Success rates for fistula closure range from 87 to 100% in small series.

Inversion of Fistula

- The vaginal mucosa is mobilized circumferentially around the fistula. The tract is excised and a pursestring suture used to invert the fistula into the rectum.
- One small series reports success in 8 of 11 patients; a more recent series reports a 100% success rate in 47 women.

Complex Repairs

- The complex repairs involve the interposition of well-vascularized tissue between the rectum and the vagina; that tissue may be muscle, omentum, or healthy bowel.

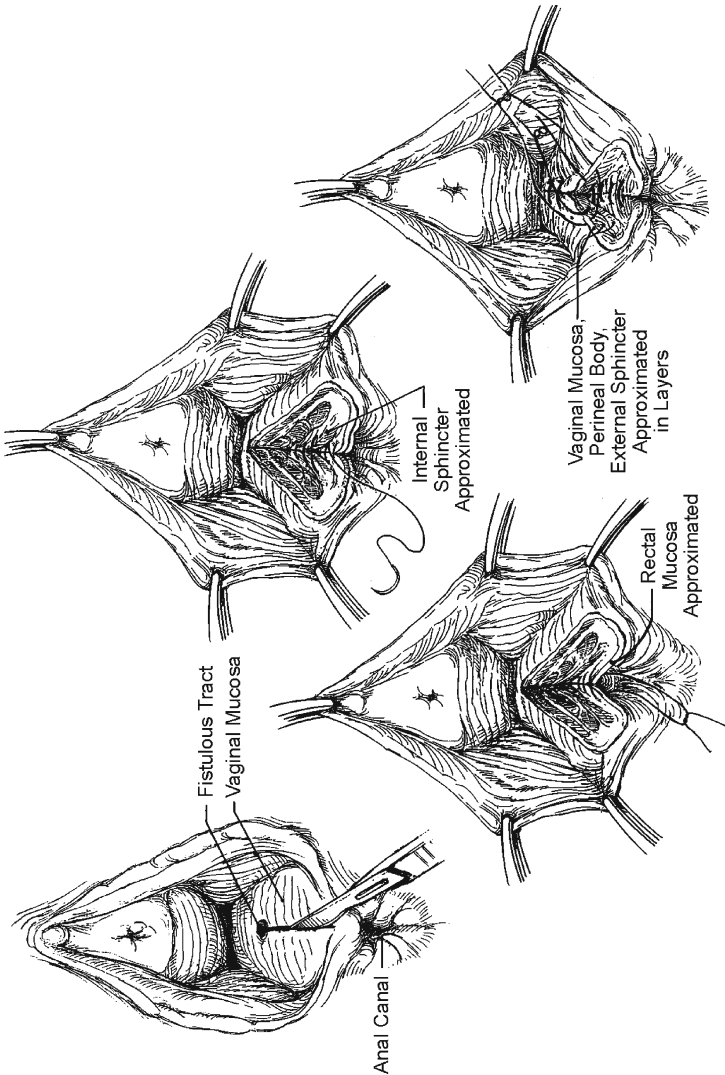


Fig. 14.2. Perineo-proctotomy.

Table 14.2. Results of sphincteroplasty for rectovaginal fistula.

Author	Year	No. of patients	Success (%)
Russell and Gallagher	1977	9	96
Lowry	1991	29	93
Wise et al.	1991	15	100
Khanduja et al.	1994	11	100
MacRae et al.	1995	7	86
Tsang et al.	1998	35	80
Yee et al.	1999	22	91
Halverson et al.	2001	14	65

Tissue Interposition: Muscle

- The most common tissue interposition technique is a sphincteroplasty utilized when a defect in the external sphincter is present with the rectovaginal fistula. In that situation, an overlapping sphincteroplasty will correct the fistula and the incontinence.
- Successful closure of rectovaginal fistulas with this operation is reported in 65–100% of patients (Table 14.2).
- When the sphincter muscle is intact or the fistula is above the sphincter muscles, rectus, bulbocavernous, gracilis, gluteus, and sartorius muscles have been used to repair rectovaginal fistulas.

Tissue Interposition: Bowel

- Healthy bowel may be interposed in one of two ways. An extended low anterior resection may be done with excision of the rectum containing the fistula and an anastomosis below. The vaginal defect is closed and if possible separated from the new anastomosis with omentum.
- Parks and associates described a sleeve coloanal technique when the fistula is very low.

Choice of Treatment

- For any patient with a rectovaginal fistula, conservative management is an option if the symptoms are tolerable.

Rectovaginal Fistulas Secondary to Obstetric Injury

- Rectovaginal fistulas may close spontaneously in the early postpartum period; all others require surgery to close.
- It is important that the surrounding tissue be free of infection and induration before proceeding with surgery. For most patients, treatment of infection and time will allow the surrounding tissue to soften.
- An important part of the evaluation of women with rectovaginal fistulas caused by obstetric injury is assessment of anal sphincter anatomy and function. In multiple studies, the incidence of associated sphincter defect is close to 100% in this subset of patients. Therefore, both closure of the fistula and continence should be considered important outcome measures.
- For women with intact sphincters and a rectovaginal fistula after childbirth, a simple local repair is recommended.
 - In most practices, these women represent only a small portion of the patients with rectovaginal fistulas because the majority will have a concomitant sphincter defect.
- For women with sphincter defects, sphincteroplasty closes the fistula and repairs the sphincter defect. A perineo-proctotomy is also appropriate. The advantage of this technique is the excellent exposure it provides; the disadvantage is the risk of incontinence if intact sphincter muscle is divided.

Rectovaginal Fistulas Secondary to Cryptoglandular Disease

- When rectovaginal fistulas secondary to cryptoglandular disease are reported, they represent only a small portion of most series.
- Evaluation must include a search and treatment of associated local sepsis with the possible use of a seton.
- Endoanal ultrasound should be performed to exclude an occult sphincter defect. If none is found, an endorectal advancement flap is the most frequently used procedure.

Rectovaginal Fistulas Secondary to Crohn's Disease

- Given the nature of Crohn's disease, control of symptoms becomes the primary goal as opposed to elimination of the fistula

in this subset of patients. In addition, the treatment is in more flux than any other subset of patients.

- Medical management with antibiotics and immunosuppressive medication is able to control symptoms but rarely closes fistulas.
- Surgical therapy often required proctectomy because of associated proctitis and was not uniformly successful even in the absence of inflammation.
- A randomized, controlled trial found that infliximab was significantly better than placebo in healing fistulas in Crohn's disease. Subsequent studies have confirmed a 24–55% healing rate by assessment of clinical symptoms.
 - Although this therapy is promising for perianal fistulas, it is not clear that rectovaginal fistulas respond as well.
- Surgical therapy often requires proctectomy because of associated proctitis. If there is no active proctitis, various advancement flap techniques have been reported; while successful repairs are possible they are not uniformly successful even in the absence of inflammation.
- At the present time, the following treatment program seems reasonable:
 - Each patient should be assessed to determine the presence of associated proctitis and undrained local sepsis.
 - Patients with associated proctitis require appropriate medical or surgical management for that condition. In either case, any local sepsis should be drained, all tracts identified, and setons placed if appropriate.
 - Until more definitive data are available, a trial of infliximab should be considered.
 - Setons should be removed before the last infusion. If symptoms resolve or are minimal, then conservative therapy is appropriate.
 - No clear recommendation regarding maintenance infliximab or immunosuppressive medication is possible at this time.
- If a persistent fistula results in significant symptoms and any associated proctitis resolves, then surgical intervention is appropriate.
- The necessity of diversion is controversial but it is often performed in this subset of patients.
- Whether the use of infliximab or other new medications will result in improved outcomes remains to be seen.

Rectovaginal Fistulas Secondary to Malignancy

- The treatment of these fistulas is dictated by the type of underlying malignancy.
- For rectal cancer invading the vagina, resection with or without reconstruction is required. If preoperative adjuvant therapy is given, diversion before initiation of treatment may be necessary for the patient's comfort.
- For squamous cell carcinoma of the anus, a preexisting fistula or one that develops during chemoradiation often requires diversion for symptom control.
- If the treatment eliminates the tumor, muscle interposition may be considered after resolution of acute radiation effects.
- If tumor persists after chemoradiation, an abdominal perineal resection is necessary.

Rectovaginal Fistulas Secondary to Radiation Therapy

- The evaluation of patients with fistulas secondary to radiation must be more intensive than most other patients with rectovaginal fistulas. Because of their usual age, they are more likely to have significant medical conditions. In addition, it is paramount that the fistula site be biopsied to exclude recurrent cancer.
- Diversion for a minimum of 6 months is recommended to allow inflammation in the surrounding tissue to resolve.
- Decisions about surgical intervention center on the patient's overall medical condition, the degree of symptoms caused by the fistula and any associated abnormalities, and the risk of a proposed corrective procedure. Not uncommonly, the combination of those factors makes a colostomy alone the most reasonable choice. This is particularly appropriate if the patient is experiencing significant fecal incontinence.

Iatrogenic Rectovaginal Fistulas

- The choice of treatment for an iatrogenic fistula is based on the causative operation.
- Once a fistula occurs, temporary diversion is often necessary to control pelvic sepsis.

- Some fistulas will close spontaneously although this is less likely if the patient has received pelvic radiation.
- Repair is determined by the level of the fistula. High fistulas usually require repeat resection with anastomosis or interposition of omentum or muscle. Low fistulas may be amenable to rectal or vaginal advancement flaps. Large fistulas or one failing initial attempts at repair will require tissue interposition.

Persistent Rectovaginal Fistulas

- Repeat repairs after one attempt seem to have a reasonable success rate. However, several studies report a higher failure rate after two or more procedures so subsequent options should be chosen carefully.
- From the data available, it seems that a reasonable approach to recurrent rectovaginal fistulas would begin with a planned waiting period of a minimum of 3 months. In the interval, the status of the sphincter muscle and surrounding tissue should be evaluated. Any areas of sepsis must be drained.
- For low fistulas, the treatment choice depends on the status of the sphincter and the number of prior repairs.
- If there is a defect in the sphincter muscle, sphincteroplasty is the appropriate choice.
- The role of diversion is not established but seems to be primarily control of symptoms except perhaps in patients with Crohn's disease.
- Recurrent fistulas involving the middle of the vagina almost always require tissue interposition.
- High fistulas require resection or tissue interposition through an abdominal approach.

15. Pilonidal Disease and Hidradenitis Suppurativa*

A. Pilonidal Disease

Background and Incidence

- “Pilonidal disease” refers to a subcutaneous infection occurring in the upper half of the gluteal cleft. It may present as an acute “pilonidal abscess,” or as an indolent wound, resistant to spontaneous healing, and causing drainage and discomfort.
- It typically presents in the second decade of life, but also occurs in teenagers and in patients in their thirties.
- It afflicts men more often than women at a ratio of three or four to one, and is more common in individuals with more body hair.
- Patients typically present initially with pain, redness, and swelling in the midline gluteal cleft region overlying the sacrum and coccyx.
- Many patients will spontaneously drain their abscesses, which will temporarily relieve the symptoms. This may set up a chronic cycle of drainage and recrudescence of the abscess before the patient eventually seeks medical attention. Thus, some patients may already have a chronic condition at the time of their initial presentation.
- Patients may also present with a history of having had many different surgical procedures performed in the past for their disease. They may have a persistent wound from a midline

*The opinions or assertions contained herein are the private views of the authors and are not to be construed as official or as reflecting the views of the Department of the Army or the Department of Defense.

excision or a failed flap procedure. Those patients with long-standing disease typically have multiple sinuses that usually extend cephalad from where the midline pits lie.

- The term “pilonidal,” means “hair nest.”
- The term pilonidal “cyst” is a misnomer, because no epithelialized wall exists in the cavities this disease creates.
- Pilonidal “sinus” or “disease” are the more accurate terms.

Pathogenesis

- Empiric data currently support the theory that pilonidal disease is an acquired condition. Pilonidal disease has been observed in the hands of barbers and sheep shearers, implying that shed hairs may initiate the condition.
- In addition, pilonidal lesions appear to have the pathologic characteristics of a foreign body reaction, presumably from burrowed hair and debris.
- Pilonidal disease likely results from problems that attack epidermis in the gluteal cleft, rather than from a problem in the deep tissues, or problems with midline skin itself.
- John Bascom believes that the skin in the natal cleft is perfectly normal, but that conditions that exist there may predispose a patient to pilonidal disease.
 - Bascom theorizes that vacuum forces and negative suction in the natal cleft draws hair and debris into the midline pits, which are stretched and ruptured hair follicles, resulting in obstruction. These stretched follicles, he believes, stretch and eventually rupture into the subcutaneous tissue, causing the classic pilonidal abscess. The midline “pits” communicate with chronic abscesses containing trapped hair and debris via sinus tracts.
 - Presently, the ideas of Bascom and others about the pathogenesis of pilonidal disease are based on empiric evidence.
- No published experiments exist that directly prove or refute the current theories about how pilonidal disease occurs.

Initial Presentations: Pilonidal Abscess

- The presenting symptoms for many patients include pain, swelling, and erythema near the top of the natal cleft, with or without spontaneous drainage.

- An *acute pilonidal abscess* is no different from an acute abscess in any other location on the body. It requires incision and drainage before considering any other definitive therapy.
- A *chronic abscess* is really an established pilonidal sinus cavity, which chronically drains and fails to heal because of retained hair and foreign material.
- A *recurrent abscess* is an acute abscess, which occurs after apparent complete healing of pilonidal disease in the past.
- Excision in a patient in the presence of acute inflammation and swelling is ill advised. Many times the midline pits will not be visible until after the inflammation subsides. Abscesses should be drained with an incision parallel to the midline and at least 1 cm lateral to it (if possible) to facilitate healing of the wound (Fig. 15.1).
- Packing of such wounds serves no good purpose, is painful, and potentially interferes with drainage and healing.
- Antibiotics are only necessary in the patient with significant cellulitis.

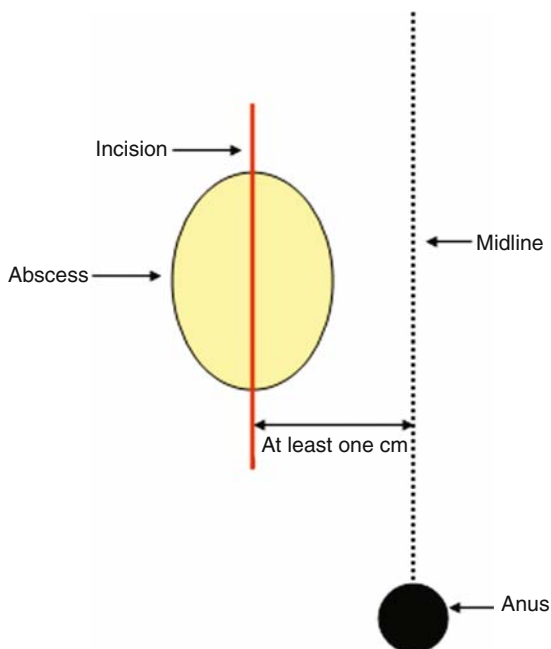


Fig. 15.1. Incision placement for acute pilonidal abscess.

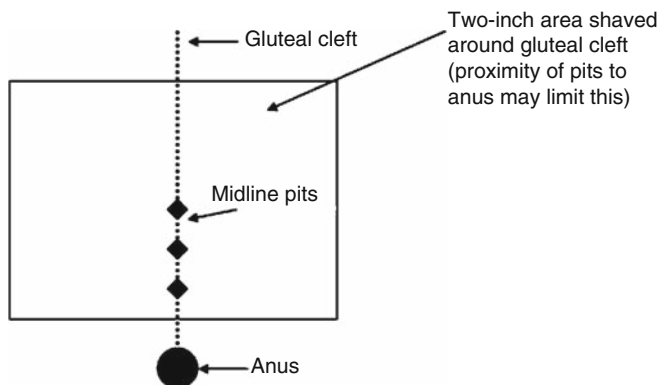


Fig. 15.2. Shaving technique.

- Simply cover the wound with a dressing and have the patient do sitz baths or use a hand-held shower 2–3 times a day.
- The patient should return to the office every week or two until the wound heals. Any hair that has grown back within 2 in. of the entire gluteal cleft is shaved at each visit (Fig. 15.2).

Initial Presentation: Draining Pilonidal Chronic Abscess

- Pilonidal disease has been treated in many different ways, but no treatment has proved completely satisfactory.

Nonsurgical Approach

Shaving

- For the initial treatment of chronic disease (which can be a chronic sinus that has never been treated or any persistent disease that has failed to heal despite treatment), shaving alone has been advocated as the sole alternative treatment for pilonidal disease.
- Physicians should consider shaving as the initial therapy in all patients without an acute or chronic abscess and localized disease. However, no one knows how long one should continue shaving in order to prevent recurrence. Currently, we recommend shaving until complete healing has occurred.

Surgical Approaches

Midline Excision

- The most frequently performed operation for pilonidal disease is midline excision, with or without primary closure of the wound, because most chronic or recurrent disease presents while localized to the midline. In this procedure, only the clearly abnormal tissue in the midline is excised. It is not necessary to always excise down to presacral fascia.
- No clear benefit exists for the use of primary closure after midline excision. Proponents of primary closure cite the accelerated healing rate in patients in whom this approach is successful. However, this comes with the price of a significantly increased chance of more wound infections.

Unroofing and Secondary Healing

- Midline excision without primary closure leaves a large wound, which is associated with long healing times. If wound closure is not indicated (i.e., with an associated abscess), a smaller wound with much shorter healing times can be achieved with unroofing or laying open of the pilonidal sinus (Fig. 15.3a). Open wounds require dressing changes and wound care, but unroofing is associated with half the healing time of wide and deep excision. The recurrence rate is less than 13% with this technique.

Bascom's Chronic Abscess Curettage and Midline Pit Excision (Bascom I)

- Bascom bases this procedure on the premise that efforts to help patients with pilonidal disease should be directed at changing the gluteal cleft conditions rather than excising a large amount of normal tissue associated with the diseased areas. In patients who present initially with a chronic abscess, this procedure has given excellent results (Fig. 15.3b).
 - He does this by making a generous, vertically oriented incision through the site of the abscess cavity more than 1 cm off the midline (in some cases more than one chronic abscess is present) and then curetting it out, without excising the fibrous abscess wall.
 - The connecting tracts to the midline pits are also identified and the overlying skin undermined so that they drain to the site of the incision.

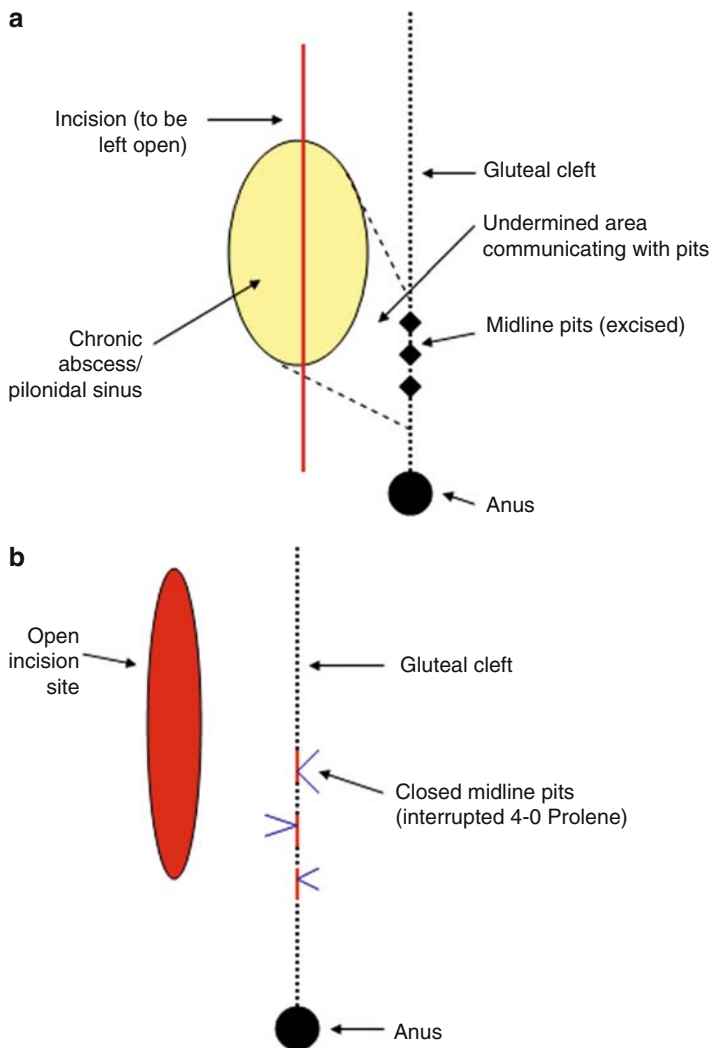


Fig. 15.3. (a) Bascom procedure. Lateral incision and debridement of cavity. (b) Bascom procedure. Removal of a midline pits with small incisions after lateral debridement, and closure of midline wounds without closure of the lateral incision.

- The midline pits are then excised using a small diamond-shaped incision to circumferentially remove each of them. According to Bascom, the excised pit should be about the size of a grain of rice.

- The undermined flap of skin, between the incision and drainage site and the excised midline pits, is then tacked down, and the pit excision sites are closed with either subcuticular or vertical mattress, nonabsorbable suture (4-0 or 3-0)
- Once this has been accomplished, meticulous shaving of the gluteal cleft should continue at least once a week until the wound has healed. Shaving can be done in the physician's office, or at home by a family member or friend who has been given the proper instruction.
- To date, no trials compare Bascom's procedure with another approach to chronic abscess.

Treatment: Recurrent Disease and Severe Disease

- Controversy exists over how to treat and follow patients who heal, but continue to present with multiple recurrent disease despite attempts at limited surgery and the other conservative measures discussed above.
- In addition to midline excision, the surgical options often used today, after initial shaving and hygiene methods have failed, include rhomboid flaps, Z-plasty, the Karydakís procedure, Bascom's cleft lift procedure, V-Y plasty, gluteus maximus myocutaneous flaps, and skin grafting (Table 15.1).
- The major disadvantages with flaps are longer operative times, greater blood loss, potential flap loss, and infection. However, these flaps do offer a quicker time to healing than midline excision, with no increase in infection rate.

Table 15.1. Complex pilonidal procedure results.

Procedure	% Healing (mean)	% Complications (mean)	% Recurrence (mean)
Rhomboid flap	100	13.5	4.9
Karydakís	–	8.5	1
Bascom cleft lift	100	–	0
V-Y plasty	100	8	0
Z-plasty	100	–	0
Myocutaneous flap	100	100	0
Skin graft	96.6	–	1.7

Rhomboid Flap

- The rhomboid, or Limberg flap, is a cutaneous rotational flap used to fill soft tissue defects and is ideally suited for this purpose with regard to pilonidal disease (Fig. 15.4a–d).
- Despite the overall good results with use of the rhomboid flap for recalcitrant pilonidal disease, this technique necessitates excision of a large amount of normal tissue and subsequently

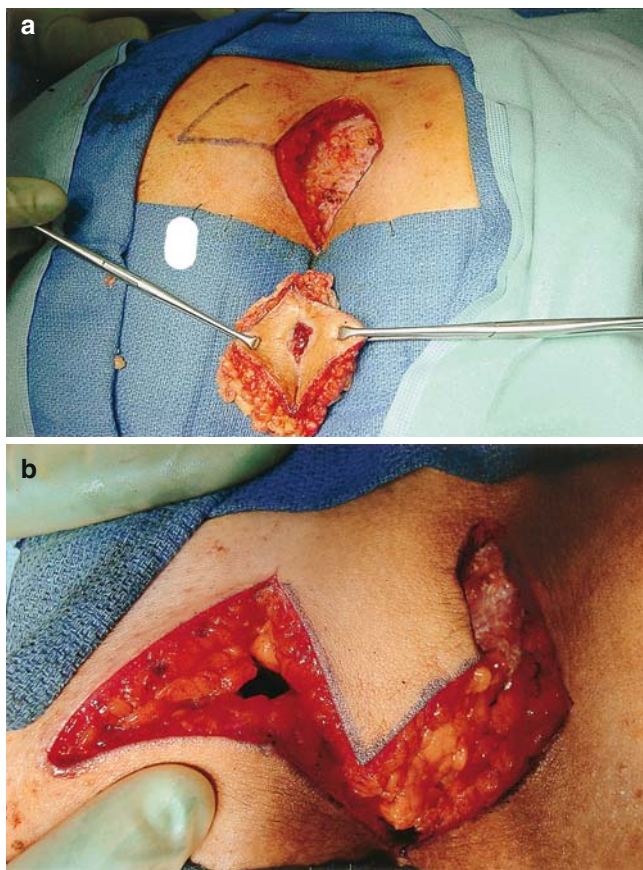


Fig. 15.4. Rhomboid flap technique for recurrent pilonidal disease. (a) Initial excision of the sinus cavity. Counter incisions are created as shown. (b) Flaps are raised and maneuvered as shown to close defect. (c) Final surgical result. (d) Result at 1 month postoperatively.

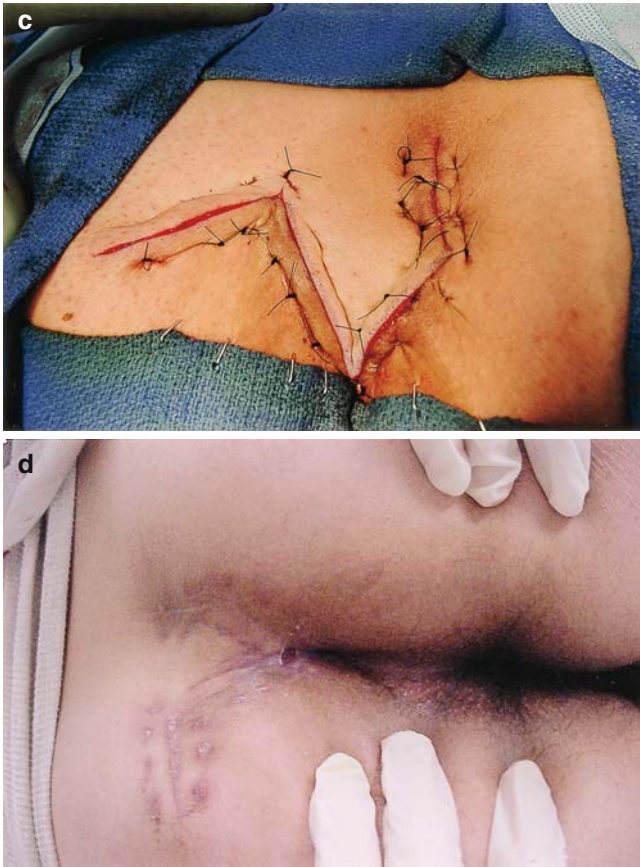


Fig. 15.4. (continued)

creates a large scar at the flap site (Figure 15.4d). Also, many patients with chronic abscesses have their abscesses located so lateral and cephalad to the midline area containing the pits, that it makes the use of this technique more morbid because of the size of the flap required to cover the excised area.

- With disease localized more or less to the midline, however, any abscess cavities and all the pits are easily excised. In addition, this technique works particularly well for flap coverage of chronic wounds (as a result of midline excisions) in the gluteal cleft that have failed to heal over a prolonged period of time.

Karydakis Flap

- The two goals of this procedure are (1) to eccentrically excise “vulnerable” tissue in the midline, or laterally displace it; and (2) to laterally displace the surgical wound out of the midline gluteal cleft.
- The large numbers of patients that have received this operation along with the good reported results make this an attractive option to consider. However, no one else has ever studied this or reported their results, nor are there any comparative trials.

Bascom Cleft Lift (Bascom II)

- The key difference between the cleft lift procedure and other flap-based procedures is that the cleft lift procedure excises no normal subcutaneous tissue.

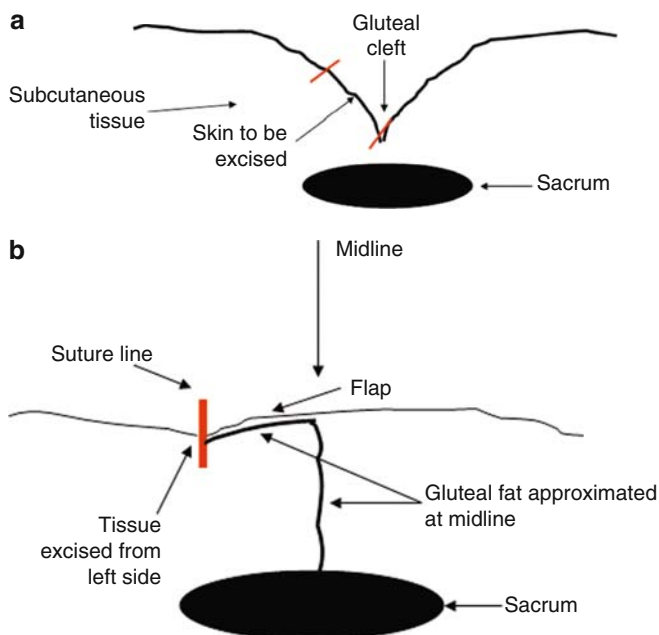


Fig. 15.5. (a) Cleft-lift technique as described by Bascom for nonhealing midline wounds. (b) Final result after flaps are raised and underlying gluteal fat is approximated.

- The goal of the cleft lift procedure is to undermine and completely obliterate the gluteal cleft in the diseased area.
- This procedure detaches the skin of the gluteal cleft from the underlying subcutaneous tissue as a flap. A portion of this flap containing the diseased skin is then excised from the side of the buttocks to which the flap will be sutured (Fig. 15.5a, b).
- The median follow-up was 20 months (range, 1 month to 15 years) and all patients remained healed. This procedure has enjoyed spectacular results in Dr. Bascom's hands, but it awaits duplication elsewhere.

V-Y Plasty

- It may have applicability in some situations in which other flaps have failed, such as the rhomboid flap.

Z-plasty

- Surgeons experienced with this technique recommend that an asymmetric closure, such as the Karydakis, be considered initially before using the rotational flap procedures, because these may be unnecessarily complex.

Myocutaneous Flaps

- Larger areas of disease with large, deep wounds may require myocutaneous flaps.
- Most surgeons reserve this technique for the most severe cases, usually after failure of simpler techniques.

Skin Grafting

- No study looking at skin grafting for pilonidal disease has been published since 1983 when Guyuron et al. published their retrospective study of 58 patients so treated.
- The authors recommended use of this method for recurrent or extensive pilonidal disease.

Summary

- The algorithm in Fig. 15.6 delineates an approach to pilonidal disease based on the evidence presented in this section.
- Conservative treatment ought to form the cornerstone of therapy – specifically, wide, meticulous shaving and hygiene.

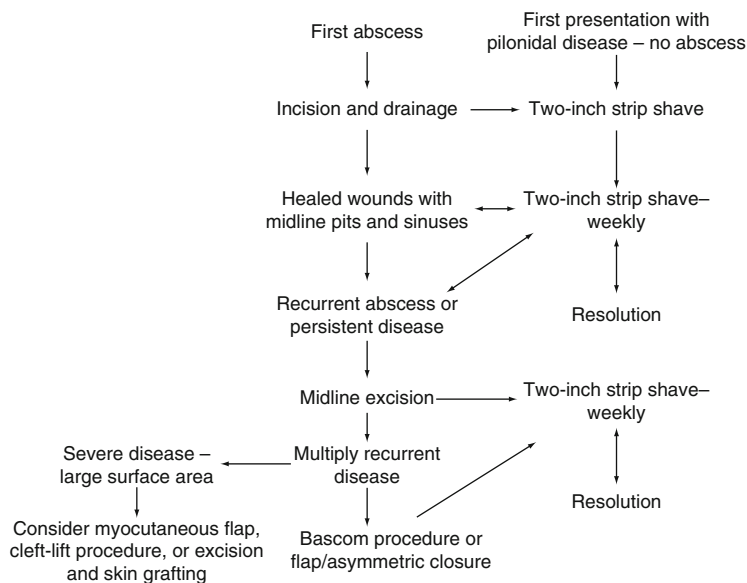


Fig. 15.6. Pilonidal disease algorithm.

The best evidence available suggests that shaving should be done until healing is complete, either in patients treated primarily this way, or those treated with surgery. When patients present initially with simple midline pits, sinuses, and various symptoms, such as pain and occasional drainage, but no acute abscess, shaving can again be offered as the initial treatment.

- A patient who presents with an acute pilonidal abscess should have incision and drainage, ideally making the incision lateral to the midline whenever possible. At the same time, one should do a 2-in. strip shave circumferentially around the affected area.
- The majority of patients do not recur after conservative treatment consisting of incision and drainage and shaving. For these reasons, we do not recommend continued shaving once healing is complete.
- Patients who present with multiply recurrent pilonidal disease, meaning disease occurring sometime after healing of prior episodes (i.e., abscesses, new pits) are more challenging.
 - In this case, we prefer to move on to the Bascom chronic abscess curettage and midline pit excision, or a cutaneous

flap procedure. For the initial management of the chronic abscess, virtually all cases can be done as an outpatient in the operating room under local anesthesia with conscious sedation.

- Neither antibiotics nor drains have been shown to be helpful on a routine basis. However, when taking on complex flap procedures or skin grafts, antibiotics may be used perioperatively based on evidence from other arenas of surgery proving their benefit.
- The evidence presented here also shows that more complications and recurrences occur with midline excision and primary closure than with open excision alone. However, time to healing is greater with open excision.
- Despite the good results reported with the flaps and asymmetric closures for pilonidal disease, midline excision or unroofing does seem to work most of the time, and has the advantage of simplicity.
- Cutaneous rotational flaps and asymmetric closures may best be reserved for the patient with a laterally located chronic abscess, multiply recurrent disease, a large area of involvement, or a nonhealing wound.
- If the patient presents with a draining sinus, alternately known as a chronic abscess, the surgeon first needs to note the location of the sinus relative to the midline. In the case in which all the disease, sinuses, and pits are located near and in the midline, then a conservative midline excision is a reasonable first-line treatment. A Bascom procedure for a chronic abscess/sinus is also reasonable.
- Many times, however, multiple draining sinuses exist and can be located far enough away from the midline that a simple midline excision becomes impractical because of the larger wound created. In this case, we typically make a choice between a Bascom I and a rhomboid flap.
- As always, shaving should continue with the proper vigilance until healing is complete.
- For a small, chronic nonhealing wound from a prior operation for pilonidal disease, a rotational flap is ideal. We prefer the rhomboid flap for this purpose. For extensive recurrence in the midline with abscesses and multiple nonhealing wounds, the Bascom II procedure has shown great promise.

B. Hidradenitis Suppurativa

Background

- Hidradenitis suppurativa is a cutaneous condition that involves skin containing apocrine sweat glands.
- Areas of the body where this often occurs include the perineum, the axilla, and the groin. It presents initially as an abscess, but typically is recurrent in the affected area and ultimately can lead to severe scarring and disability for the patient.

Incidence and Etiology

- One in every 300 individuals may be affected in some way.
- African-Americans seem to be affected more often than Caucasians, and perianal disease seems to be more common in males.
- Almost all patients present after puberty and before the age of 40, implicating hormones and the development of secondary sexual characteristics as causative.
- Other endocrine associations include diabetes mellitus, hypercholesterolemia, and Cushing's disease.
- Obesity has been implicated as a predisposing factor presumably from shearing forces in the affected areas.
- Perianal hidradenitis affects males twice as often as females, but hidradenitis in all locations may be more common in females and African-American persons.
- Fortunately for sufferers of perianal hidradenitis, it seems to recur less often after surgical treatment (<0.5%) than does inguinal-perineal disease (37–74%).

Bacteriology

- Wound cultures from hidradenitis patients have grown *Staphylococcus epidermidis*, *Escherichia coli*, *Klebsiella*, *Proteus*, alpha *Streptococcus*, anaerobic bacteria, and diptheroids, although negative cultures are common.

Pathogenesis

- Most authors agree that hidradenitis suppurativa originates from obstruction of apocrine sweat glands by keratin. However,

it is unknown why this occurs in some people and not in others (females, African-Americans, etc).

- These glands secrete a milky, odorless fluid that only becomes malodorous after it interacts with bacteria on the skin. The apocrine glands secrete into the hair follicle as opposed to directly onto the skin like eccrine sweat glands.
- The function of apocrine secretion is unknown. Nevertheless, obstruction leads to secondary bacterial infection and rupture of the gland into the dermis and subcutaneous tissue, thus causing cellulitis, abscess, and draining sinuses.
- This process then leads to the characteristic “pit-like” scars from chronic fibrosis of the destroyed glandular unit.

Differential Diagnosis

- Cutaneous infections such as furuncles, carbuncles, lymphogranuloma venereum, erysipelas, epidermoid or dermoid cysts, and tuberculosis can be particularly troublesome.
- In particular, it must be distinguished from other fistulizing or sinus-forming processes of the perineum. Crohn’s disease typically affects the anus and rectum with fistulas arising from the dentate line or higher in the rectum.
- Hidradenitis does not affect the rectum, because apocrine glands only exist in the lower two-thirds of the anal canal and do not penetrate into the sphincter complex. Thus, patients will not have sinus or fistula tracks to or from the rectum.
- Fistulas from hidradenitis should only connect areas of involved skin, and not penetrate the anal sphincters
- Several cases of squamous cell carcinoma in chronic hidradenitis wounds have also been published.
 - The association seems to be rare with affected patients, who usually have had untreated disease for longer than 20 years.

Treatment: Initial

- Hidradenitis suppurativa typically presents with pain, erythema, and swelling in the affected area. Patients with cellulitis and no definable clinical abscess may be successfully treated with antibiotics that cover skin flora, such as *Staphylococcus* species, over 1–2 weeks.

- The safest course of action with any patient who presents with an obvious abscess is incision and drainage.
- Eighty-three percent of patients will have recurrent localized sepsis of some sort after initial incision and drainage or limited excision.

Treatment: Chronic

- Chronic disease is simply any hidradenitis disease persisting or recurring after initial treatment. This could present as recurrent abscesses, nodules, sinuses, fistulas, cellulitis, or any combination of these problems.
- Unless the surgeon excises all this skin, the patient will technically be at risk for recurrence, although not every patient eventually goes on to radical excision.
- Excision with healing by secondary intention is probably the most widely used surgical treatment.
- Only the grossly involved apocrine bearing skin (but all of it) in the perianal area should be excised full thickness into the uninvolved gluteal fat.
 - This method is simple and almost never requires fecal diversion. It also allows completion of the procedure as an outpatient. Perioperative antibiotics are unnecessary.
 - Patients with large areas of involvement may undergo staged excision. The extent of excision should remain outside the anal verge as long as there is no obvious involvement or history of involvement in the anal canal.
- Patients with chronic disease, extensive scarring, and sinus tracts rarely respond to conservative measures. The gold standard of care remains wide excision of all skin bearing involved apocrine glands. Reconstruction then can follow a number of paths – unroofing of sinus tracts with or without marsupialization, cutaneous flap closure, myocutaneous flap closure, or excision and simple healing by secondary intent.
- Patients who might benefit from diversion are those who cannot take care of their wounds long term and those who have both hidradenitis and Crohn's disease, although this is rarely needed.

Summary

- The algorithm in Fig. 15.7 depicts our suggested approach to treating patients with perianal hidradenitis suppurativa. Patients

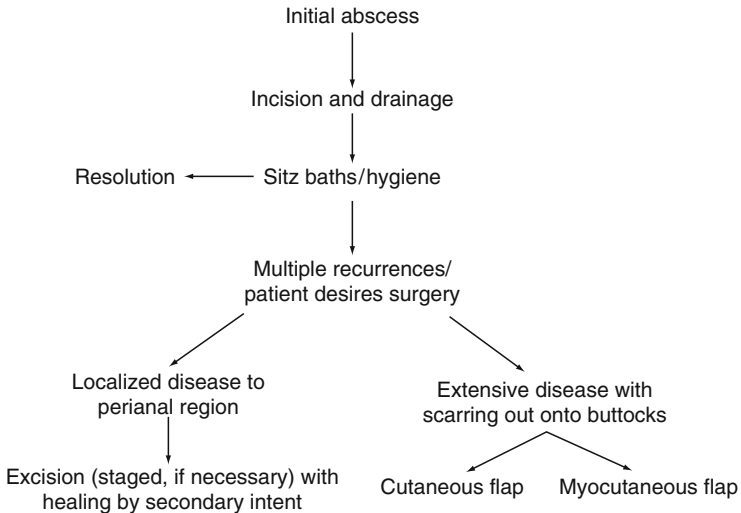


Fig. 15.7. Perianal hidradenitis suppurativa algorithm.

who present initially with an acute abscess, and a history and examination consistent with hidradenitis, should have incision and drainage, ideally in an office setting.

- Physicians should reserve antibiotics for those patients with a component of cellulitis as discussed above, or those who are immunocompromised.
- It is important to rule out other causes of perianal sepsis in the early stages of the disease, such as Crohn's disease or perirectal abscesses from a cryptoglandular source.
- For those patients with chronic and/or recurring disease, we proceed to definitive excision, as long as the diagnosis is not in doubt and we have exhausted the simpler alternatives.
- Flap procedures are reserved for patients with extensive scarring and tissue damage out onto skin distant from the anus, such as the buttocks.
- Even relatively large open wounds around the anus heal remarkably well in the absence of Crohn's disease and other inflammatory, malignant, or infectious processes, compared with how similar wounds typically heal in other areas of the body. Because of this, it is usually not necessary to use flaps after skin excisions for hidradenitis around the anus, especially when using a staged approach.

- If circumferential disease is present and requires excision, we excise half of the involved perianal skin down to subcutaneous fat and allow the wound to heal by secondary intent, which may take up to 3 months. We excise the other half after complete healing of the first wound.
- If circumferential excision of perianal skin is considered in a single procedure, we take care not to excise the skin at or inside the anal verge. This diminishes the risk of anal stricture. For patients whose disease does not extend out more than 5 or 6 cm from the anal verge, this approach works very well.
- We consider a flap-based procedure for those patients with much wider involvement extending out onto the buttocks.

16. Perianal Dermatology and Pruritus Ani

A. Introduction

- Perianal skin is subject to virtually all of the diseases that affect skin in other areas of the body. The differential diagnosis of perianal skin is presented in Table 16.1. This list includes a variety of diagnoses, which almost never present as isolated perianal disease, but there are common diseases such as psoriasis that may present in isolation without obvious ties to other areas of the body unless a careful search is made.
- Successful treatment of perianal disease requires accurate diagnosis to eliminate diseases that have specific cause and treatment (e.g., psoriasis, candida, Bowen's disease).
- Recognition of important treatable causes requires a disciplined, organized approach to diagnosis with frequent use of biopsy.
- The importance of complete, accurate evaluation is emphasized by a St. Louis University series in which a study of 209 patients with the presenting symptom of pruritus over a 2-year period revealed that 75% of patients had coexisting anal or colorectal pathology. The diagnoses included 11% with rectal cancer, 6% with anal canal cancer, and 2% with colon cancer, although the majority of patients had hemorrhoids or fissure.

B. Definitions

- Pruritus ani is a term of Latin derivation, which means itchy anus.

Table 16.1. Differential diagnosis of anal dermatoses.

Inflammatory disease	Nonsexual infectious disease
Pruritus ani	Pilonidal disease
Psoriasis	Hidradenitis suppurativa
Lichen planus	Fistula-in-ano
Lichen sclerosis et atrophicus	Crohn's disease
Atrophoderma	Tuberculosis
Contact (allergic) dermatitis	Actinomycosis
Seborrheic dermatitis	Herpes zoster
Atopic dermatitis	Vaccinia
Radiation dermatitis	Fournier's gangrene
Behçet's syndrome	Tinea cruris
Lupus erythematosus	Candidiasis
Dermatomyositis	"Deep" mycoses
Scleroderma	Amebiasis cutis
Erythema multiforme	Trichomoniasis
Familial chronic pemphigus (Hailey-Hailey)	Schistosomiasis cutis
Pemphigus vulgaris	Bilharziasis
Cicatricial pemphigoid	Oxyuris (pinworm)
	Creeping eruption (larva migrans)
	Larva currens
	Cimicosis (bed bugs)
	Pediculosis (lice)
	Scabies
Sexually transmitted disease	Premalignant and malignant disease
Gonorrhea	Acanthosis nigricans
Syphilis	Leukoplakia
Chancroid	Mycosis fungoides
Granuloma inguinale	Leukemia cutis
Lymphogranuloma venereum	Basal cell carcinoma
Molluscum contagiosum	Squamous cell carcinoma
Herpes simplex	Melanoma
Condyloma acuminata	Bowen's disease (AIN)
	Extramammary Paget's disease

Source: Modified from Corman.

- Pruritus ani has been classified into primary and secondary. The primary form is the classic syndrome of idiopathic pruritus ani, whereas the secondary form implies an identifiable cause or a specific diagnosis.
- Accurate description of the morphology of skin lesions can aid in the diagnosis and follow-up of patients with pruritic complaints.

- Macules are flat spots.
- Papules are elevated circumscribed solid lesions, raised spots.
- Vesicles are separations of the epidermis and dermis filled with serum.
- Bulla are larger vesicles or blisters.
- Pustules contain pus.
- Ulcers are surface lesions with loss of continuity of the skin and may result from rupture of vesicular lesions, infection, or trauma.
- Intertrigo is inflammation seen between two opposing skin surfaces, often the result of mixed bacterial, fungal infection associated with moisture, obesity, and poor hygiene.

C. Physiologic Considerations

- Itch is a surface phenomenon mediated by pain fibers in the epidermis that may have a lower threshold for stimulation than pain.
- Itch receptors may be located more superficially than those dedicated to pain. Because receptors are superficial, innocuous, nondamaging stimuli such as wearing wool, or other minor mechanical stimuli may induce itching.
- In addition to histamine, kallikrein, bradykinin, papain, and trypsin experimentally produce itching, but these substances do not respond to blockade with histamine antagonists such as diphenhydramine, hence topical antihistamines are not always effective against itching.
- The phenomenon of hyperesthesia with chronic pain may have a parallel with itching, whereas minimal stimulation of the skin may induce itching; scratching with subsequent injury may produce an enlarging patch of itchy skin. Scratching produces inadequate feedback to inhibit itching; more scratching occurs with cutaneous injury, which provides an additional stimulus to scratch in a self-defeating loop.
- Itching attending the healing of surgical wounds and scars probably results from the combination of histamine release, release of other kinins and prostaglandins involved in the inflammatory phase of healing, and regeneration of nerves that may be thinly myelinated in immature scars.

- Antihistamines, topical anti-inflammatory agents (steroids), topical anesthetics, and aloe preparations (prostaglandin inhibitors) all have beneficial effects on the itching of healing wounds.

D. Etiology of Pruritus

- Because pruritus is a symptom that may have protean causes, it is useful to consider diagnoses that have been associated with pruritus ani. Table 16.2 is a list of diagnoses and conditions modified from Stamos and Hicks.

Localized Itch Syndromes

- Notalgia paresthetica is a defined syndrome with itching or pain of the upper mid back to either side of the scapular region.
- Dermographism has been reported as a cause of anogenital pruritus. It is not unreasonable to propose that the idiopathic form of pruritus ani may be a related disorder, and that the skin changes are the sole result of skin trauma. The effectiveness of the anal tattooing procedures, discussed later, lends some support to this hypothesis.

Fecal Contamination

- Good evidence supports fecal contamination as one cause of symptoms.
- Smith and colleagues in a rigorous study of 75 patients with pruritus found that half of their patients had poorly formed stools and 41% of their patients complained of soiling from daily to several times a week. Seepage of liquid and mucous was believed to be an important factor in the etiology of the symptoms. Coffee was demonstrated to lower anal resting pressure in 8 of 11 patients.

Viral Infection

- Condylomata acuminata are a common cause of itching, but the diagnosis is easily recognizable and should not be confused with idiopathic pruritus ani.

Table 16.2. Proposed etiologies of idiopathic pruritus ani.

Anatomic factors	Obesity, deep clefts, hirsutism, tight clothing
Anorectal disease	Fissure, fistula, tags, prolapsing papilla, hemorrhoids, mucosal prolapse, sphincter insufficiency, deforming scars
Antibiotics	
Contact dermatitis	Chemicals in topical preparations, toilet paper, wet wipes, alcohol, witch hazel, "caine" anesthetics, fecal soiling
Dermatoses	Psoriasis, seborrheic dermatitis, atopic dermatitis, lichen planus, lichen simplex, LS, dermatographism
Diet	Coffee (caffeinated and decaffeinated), chocolate, spicy foods, citrus fruits, tomatoes, beer, dairy products, vitamin A and D deficiencies, fat substitutes, consumption of large volumes of liquids
Diarrhea	Infectious diarrhea, irritable bowel syndrome, Crohn's disease, ulcerative colitis
Drugs	Quinidine, colchicine, intravenous steroids
Gynecologic conditions	Pruritus vulvae, vaginal discharge of infection
Idiopathic	
Infection	Viruses: herpes simplex, cytomegalovirus, papillomavirus; bacteria: <i>S. aureus</i> , beta hemolytic strep, mixed infections; fungi: dermatophytes, <i>Candida</i> species; parasites: pinworms, scabies, pediculosis; spirochetes: syphilis
Neoplasms	Bowen's disease (AIN), extramammary Paget's disease, squamous cell carcinoma variants, secreting villous tumors
Personal hygiene	Poor cleansing habits, over-meticulous cleansing producing mechanical trauma, use of soaps
Psychogenic/neurogenic	Anxiety, neurosis, psychosis, neurodermatitis, neuropathy, "itch syndromes"
Radiation	Radiation dermatitis, sphincter compromise or leakage caused by radiation proctitis
Systemic disease	Jaundice, diabetes mellitus, chronic renal failure, iron deficiency, thyroid disorders, lymphoma, polycythemia vera

Source: Modified from Stamos and Hicks, 1998.

- Herpes syndromes are usually accompanied by pain rather than itching and the clinical course is accompanied by a characteristic eruption consisting of red macules, which progress to vesicles that rupture, ulcerate, and may become secondarily infected. Culture or biopsy shows specific diagnostic findings.

- Molluscum contagiosum produces characteristic lesions, papular, 2- to 5-mm diameter, with central umbilication, usually clustered.
- Human immunodeficiency virus-associated lesions are rarely associated with chronic itching except for secondary fungal infections.
- No credible evidence exists for a viral etiology in idiopathic pruritus ani.

Fungal Infection

- Smith et al. found no instances of fungal infection in their investigation of pruritus in which each of 75 patients had scrapings and fungus cultures.
- Prolonged courses of steroids are said to enhance pathogenicity of *C. albicans* and to mask *Candida* infection.

Bacterial Infection

- Several non-sexually transmitted bacterial infections such as beta hemolytic *Streptococci* and *Staphylococcus aureus* are reported to cause longstanding pruritus.
- Erythrasma was reported to cause pruritus in 15 of 81 patients (18%) who had failed to respond to routine treatment. Wood's light fluorescence (coral pink) was the most reliable diagnostic maneuver, being positive in every case, but cultures of *Corynebacterium minutissimum* were positive in only four cases. Groin, thighs, and toes were also involved in every case and cure was achieved in all patients with erythromycin.

Table 16.3. Common sensitizing agents.

Ethylenediaminetetraacetic acid
Formalin
Lanolin (wood wax alcohol)
Mercury [Hg(NH ₂)Cl, thimerosal]
Neomycin
Nickel
Paraben mixtures
Paraphenylenediamine
Potassium dichromate
Rubber ingredients
Topical anesthetics (benzocaine, dibucaine)
Turpentine oil

Contact Dermatitis

- Contact dermatitis has been reported from a wide variety of preparations including topical anesthetics, topical antibiotics, topical antiseptics, topical antihistamines, and nickel. Common sensitizing agents identified in the dermatologic literature are listed in Table 16.3.
- The role of feces and seepage as a contact agent has been emphasized in almost every article devoted to pruritus ani.
- Contact dermatitis may have an irritant or allergic basis, but is recognized by being an eczematous inflammation characterized by erythema, scale, and vesicles.
- Avoidance of contact with the inciting agent is the obvious treatment, and topical steroids may be useful unless secondary infection is present.
- It is preferable to avoid soaps. Bath oils and emollient creams may be useful for cleansing.
- A large study of patch testing in 80 patients with pruritus ani in Sheffield, England, emphasized the importance of contact dermatitis as an aggravating factor. Fifty-five patients tested positive. Thirty-eight of the positives were to medicaments or their constituents including neomycin, fragrance mix, Peru balsam, and cinchocaine. After counseling, two-thirds of these 55 patients experienced improvement or resolution of their symptoms. These authors disputed the recommendation to use “wet wipes” for cleansing because of possible sensitization.
- Bruynzeel corroborates the potential sensitization from use of moist wipes containing methyldibromoglutaronitrile.
- Rohde believes that excessive exposure to water and the act of excessive cleansing itself may incite symptoms, and recommends the use of oils for cleaning.

Psoriasis

- Psoriasis has been an important underlying cause of pruritus in every series on this subject.
- Lochridge claimed the diagnosis of perianal psoriasis in 81 patients, all of whom responded to fluocinolone acetonide 0.025% (Synalar®) with normalization of the skin. He recommended a search for lesions elsewhere including elbows, knees, ankles, extensor surfaces of the forearm, base of the scalp, ear canals, eyelids, nipples, penis, vulva, or navel.

Lichen Sclerosis

- Lichen sclerosis (formerly lichen sclerosus et atrophicus) (LS) is a chronic disease of unknown cause, almost always occurring in women (female/male 10:1, usually seen on the penis in the male) which in females has a predilection for the vulva and perianal area.
- The skin has a characteristic appearance that is white, atrophic, and wrinkled.
- Involvement of the labia gives this condition a characteristic distribution that makes recognition easy once the diagnosis is considered.
- Treatment of LS with a potent topical steroid (clobetasol propionate 0.05%, Temovate®) for 6–8 weeks is highly successful, often resulting in normalization of the skin.
- Patients with LS in the vulva probably have a 4–5% incidence of squamous cell carcinoma arising in or adjacent to the LS.

Food Factors

- No controlled trials have been done to examine food stuffs or diet as a cause for itching, but strong opinions have garnered a revered place in the literature.
- Friend states that virtually all patients with idiopathic pruritus ani consume enormous quantities of liquids, are almost never constipated, and usually have loose stools.
- Friend states that there are six common foods that unequivocally cause idiopathic pruritus: coffee, tea, cola, beer, chocolate, and tomato (ketchup) and that total elimination will result in remission of itching in 2 weeks. After a 2-week elimination period, the food may be reintroduced to determine the threshold above which consumption causes symptoms. Thresholds are typically between 2–3 cups of coffee, 4 cups of tea, and less than 2 cans of beer.
- Smith et al. confirm the importance of poorly formed stool and coffee which may contribute to seepage and recommend a bulk agent taken at the same time of day to promote regular, complete emptying of stool.

Coexisting Anal Disease

- Coexisting surgical anal conditions (hemorrhoids, fissure, fistulas) may of themselves produce itching or aggravate any tendency to itch.
- Pirone et al. believe that correction of hemorrhoids, fissure, mucosal prolapse, and spasm can resolve fungal infection and the consequent pruritus.

Psychologic Factors

- Anxiety, stress, and fatigue added to personality, coping skills, and obsessive compulsive disorders probably have a role in the exacerbation of pruritus ani. Because of this, psychiatric drugs may have a role in its management in isolated cases.
- The preponderance of evidence suggests that idiopathic pruritus ani does not have a psychiatric basis except as a form of neurodermatitis. The fact that it responds to simple topical treatment with resolution of physical findings in most cases and is so common argues against an obscure etiology.

Steroid-Induced Itching

- Anogenital itching has been reported after bolus administration of intravenous dexamethasone. More often, itching occurs as a rebound phenomenon after withdrawal of steroids leading to their reinstitution and chronic use because symptoms always exacerbate after withdrawal.
- Steroids should always be viewed as potentially dangerous and should be used to achieve specific effects. Potency and dosing should be tapered in a planned manner with the goal of eliminating steroids altogether from a maintenance regimen. If elimination is not possible, alternate day therapy or intermittent therapy once or twice a week is to be preferred.

Skin Trauma

- Trauma can arise from physiologic processes such as diarrhea or frequent stools which may be associated with frequent wiping and maceration.

- Scratching either consciously or nocturnally while asleep may result in the classic lesion of lichen simplex chronicus.
- In most patients the problem is due either to inadequate cleansing of the anus or to over vigorous attempts to “polish it clean.”
- Most authors agree that contact dermatitis is a contributing cause of perianal irritation and that attempts to discontinue over-the-counter preparations (OTCs), perfumed, or scented products including toilet paper, should be made because of potential sensitizing agents (Table 16.3).
- Bland emollients, Acid Mantle®-based creams, and waterless cleansing agents are reasonable substitutes that may be used with tissue paper or cotton balls for cleansing and left on the skin.
- A dilute white vinegar (1 tablespoon in 8 ounces of water) and Burow’s solution (Domeboro®) are effective cleansing agents associated with little adverse reaction. Burow’s solution and acetic acid have been found to be an effective antibacterial in chronic otitis with little toxicity.

Neoplasms

- Perianal Paget’s disease is rare and large series do not exist, but more than half of patients in most series have itching, often for longer than 3 months.
- Perianal Bowen’s disease (intraepithelial squamous cell carcinoma in situ) is also rare, but in a series of 47 patients reviewed at the Cleveland Clinic, 28 (60%) had perianal itching as a presenting complaint.
- AIN is the sequel to human papillomavirus infection (associated with itching) and refers to premalignant change in the area of the dentate line and anal transitional zone.

E. Diagnosis of Perianal Disease

- It is often helpful in the differential diagnosis of anal and perianal disease processes to divide them into the general classifications of mass (inflammatory or neoplastic), rash, or fissure (primary or secondary).
- The morphology of a lesion is a starting point for diagnosis, but may not be specific, and the same disease may have several different appearances (Table 16.4).

Table 16.4. Morphology of perianal skin lesions.

Ulcers	Papules
Herpes genitalis	Venereal warts
Syphilis	Scabies
Trauma	Molluscum contagiosum
Chancroid	Candidiasis
Fixed drug eruption	Syphilis
Lymphogranuloma venereum	
Tularemia	
Behçet's syndrome	
Malignancy	
Donovanosis (granuloma inguinale)	
Candidiasis	
Histoplasmosis	
Mycobacterioses	
Amebiasis	
Gonorrhea	
Trichomoniasis	
Diffuse erythema	Crusts
Candidiasis	Herpes genitalis
Trauma	Scabies
Contact dermatitis	
Fixed drug eruption	
Miscellaneous findings	
Linear tracks: scabies	
Reddish flecks: crab louse excreta	
Maculae ceruleae (sky-blue spots): crab lice	
Nits: crab lice	
Hypertrophic: donovanosis	

History and Physical Examination

- History and physical examination, often overlooked in our technologic arrogance, is still the most basic maneuver for diagnosis of any disease (see Table 16.5).
- Inquiry about other skin diseases, allergic conditions such as asthma or urticaria, or sites of involvement may be the first clue to diagnosis of unrecognized psoriasis or atopic dermatitis. Patients may not relate the itch on their elbow to the itch around their anus.
- Erythrasma usually involves the groin and toes, usually is chronic, and is often associated with hyperpigmentation.

Table 16.5. Historical and physical factors aiding diagnosis of anal and perianal disease.

Historical

Other skin conditions, asthma, urticaria

Prior treatments/OTC topicals

Allergies

Chemicals/clothes/laundry

Antibiotic use

Systemic disease

Chronicity

Physical findings

Multiple sites (elbows, groins, intertriginous areas, labia, toe webs)

Mass or woody induration

Hyperpigmentation

Scale

Lichenification

Ulceration

Groin adenopathy

Defined edge or margin

- Patients frequently do not consider OTC or nonprescription preparations as medicines, but these may modify the appearance of a condition or even cause it.
- Knowledge of a patient's allergies is important not only for avoidance, but may aid in uncovering an unsuspected exposure to an occult ingredient.
- Patients sometimes have had patch testing and allergy consultation, and will not volunteer that information unless specifically asked. Patch testing, dermatologic consultation, and withdrawal of medication may be in order.
- Specific questions about infections, colds, or diarrheal illnesses treated with pills may be necessary to uncover antibiotic use.
- Patients sometimes will not list prednisone in their list of medications until asked a question pertinent to an illness such as arthritis or asthma or myalgias.
- A condition that has come and gone for years or that has seasonal exacerbation may be a clue to anal fissure, but could reflect dietary changes, type of clothes worn, or laundry practices.
- Physical examination should specifically look for other sites of involvement. The groin is a classic intertriginous area that is easily accessible in the prone jackknife or the lateral position and should be the first place one looks to confirm a suspected yeast or fungus diagnosis.

- Effective treatment of a patient with changes in the groin as well as the cleft requires attention to each area of involvement.
- A sharply defined border usually points to a definable diagnosis such as tinea, especially when accompanied by scale.
- Psoriasis usually has a sharply defined border, but in the cleft may lack the classic scale seen in skin that is exposed to air. In the confined, occluded area of the cleft, there usually is no scale.
- Neoplastic changes may appear sharply marginated, but margins may be microscopically involved, especially around the dentate line, even if grossly normal.
- Infiltrative processes may be less well defined as in Paget's disease of the anus with the same caveat about margins.
- Inflammatory changes of idiopathic nature often have borders that are indistinct and nondescript.
- Bright red erythema often is seen with perianal yeast. Erythema may be seen with chronic steroid use.
- Acute severe injury from prolonged diarrhea with frequent wiping produced the picture of lichen simplex chronicus, which was treated by specific treatment of the patient's diarrhea, cleansing with Burow's solution, and topical silver sulfadiazine to which cortisone was added.
- Chronic infected discharge may lead to hyperpigmentation in the cleft in this case caused by chronic pilonidal disease, but may also occur with fistulas, chronic yeast or fungus infection, or hidradenitis.
- Severe symptoms, especially paresthesias, coupled with scattered lesions may be a clue to herpes virus infection.
- LS characteristically involves the perineum and labia in the female and has a distinctive appearance with wrinkling of the skin. Biopsy is characteristic.
- Groin adenopathy, and whether or not the nodes are tender, can have specific relevance to diagnosis of perianal and anal disease (Table 16.6), especially sexually transmitted disease.

Laboratory Examination

- Ideally, infected material should be aspirated with a syringe and expelled into a sterile container. Next best is a swab of exudate collected from a deep portion of the lesion.
- Bacterial and fungal cultures should be placed into a bacterial transport medium and refrigerated if any delay in transport to the laboratory occurs.

Table 16.6. Differential diagnosis of groin adenopathy.

Benign reactive (shoeless walking)
Lymphoma
Carcinoma (penis, vulva, anal canal)
Sarcoidosis
Syphilis (nontender)
Leishmaniasis
Chancroid (tender)
Herpes genitalis (tender)
Lymphogranuloma venereum

- Anaerobic specimens require transport in a special anaerobic medium, and should not be refrigerated.
- The office should have arrangements with a laboratory, which will supply culture swabs with transport media appropriate for aerobic, anaerobic, fungal, and viral culture. These become outdated and can result in rejection of specimens for processing.
- Because staph and strep have been documented as causal agents, it is prudent to culture for pathogens in almost all cases in which treatment is not obvious.
- EMLA[®] cream, applied as a lubricant at the time of examination, may facilitate injection of local anesthetic, and biopsy may conveniently be done with either an 11 blade or skin punch blades that come in numerous sizes in separate sterile packages (Fig. 16.1). Bleeding from punch biopsy holes is readily controlled with silver nitrate sticks or GELFOAM[®] packing.

F. Treatment of Pruritus Ani

- A general strategy is presented in Table 16.7.
- Many investigators have alluded to the importance of controlling seepage and fecal contamination of the skin.
- Diet may directly contribute to itching and it is prudent to give patients a list of potential foods implicated in itching for an elimination trial.
- Patients with loose stools may benefit from the addition of fiber to absorb moisture and add bulk and improve emptying with defecation.

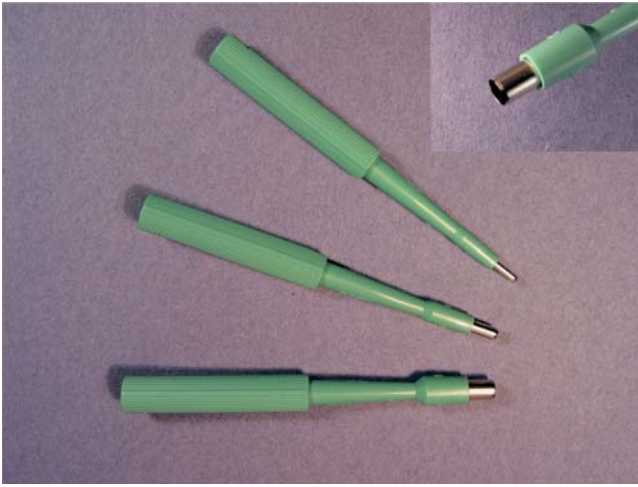


Fig. 16.1. Skin punch biopsy tools come in various sizes up to 1 cm in diameter (2, 3, and 5 mm pictured). They may be purchased as autoclavable sets which may be sterilized and reused, or for the occasional user, disposable punches are supplied in individually wrapped sterile packages. One advantage of the disposable instruments is that they are always sharp.

Table 16.7. Treatment of pruritus ani.

1. Specific directed treatment for a diagnosis
2. Eliminate offending agent [contact irritant (perfume, soap, toilet paper), organism]
3. Eliminate scratching (especially nocturnal)
4. Control symptoms
5. Hygienic measures (Dove® soap, detachable shower head, hair dryer to dry)
6. Withdraw inappropriate steroids
7. Treat infection (silver sulfadiazine cream, gentamicin or clindamycin topically, nystatin, clotrimazole)
8. Protect skin [barrier creams, powders (especially athlete's foot powder)]
9. Correct anal disease (fissure, hemorrhoids)
10. Judicious use of appropriate steroids
11. Emphasize control as a chronic condition
12. Reassess diagnosis if response to treatment is not appropriate
13. Anal tattooing in extreme cases

- Many patients who have tried fiber without benefit may benefit from judicious use of Imodium® or Lomotil® to lessen frequency and firm up stools. Questran®, in varied doses, has been helpful in my practice to firm loose stools.
- Environmental factors should be altered as much as possible with removal of irritants such as soaps, perfumes, dyes in clothes or wiping tissues, alcohol- or witch hazel-containing agents, and moisture.
- Dove® is free of conventional soap and is the preferred bathing agent.
- Bidets are not common in the United States, but detachable shower heads are common and inexpensive and when equipped with long tubing and handle may be a useful item for cleansing the perianal skin and anal canal and eliminating soap residues by flushing with water in the squatting position.
- Subsequent drying with a hair dryer can eliminate moisture, and application of an athlete's foot powder or barrier cream will lubricate and prevent maceration of the skin in the cleft and anal canal.
- Zeasorb® is an alternate lubricating, drying agent in powder form. Cornstarch is to be avoided because it is culture medium for yeast.
- Dilute white vinegar (1 tablespoon in an 8-ounce glass of water) on a cotton ball is a cheap effective nonsoapy cleanser that can be kept at the toilet when bathing is not handy.
- Burow's solution, 1:40 (Domeboro® tablet one in 12 ounces of water, or one in 6 ounces for 1:20) is another nonirritating cleanser that can be kept refrigerated in a plastic squeeze bottle and used in lieu of soap or plain water.
- Balneol® is a commercially available mineral oil-based preparation that can be kept in a pocket and squeezed onto toilet paper to make a soothing cleansing agent when using public facilities.
- Doxepin (Sinequan® orally) is available topically as an effective antihistamine (Zonalon®), but orally is 1,000 times more potent than diphenhydramine (Benadryl®) for elimination of itching and may be a useful adjunct at bedtime to avoid nocturnal scratching.
- Nocturnal scratching, of which the patient may be unaware, is probably a significant contributing factor in most cases of idiopathic pruritus ani. Patients who are awakened by the urge to scratch should be instructed to gently cleanse the area to eliminate any fecal seepage and reapply their steroid or barrier cream (whichever is in effect at the time) but not to scratch.

- No data exist on the influence of clothes or other fomites on pruritus, but from a practical standpoint, loose underwear that allows air circulation and promotes dryness makes sense.
- Fresh clothes should be used daily that have been laundered without perfume, perhaps with the addition of a small amount of chlorine bleach to secure lowered bacterial counts.
- Patients who come to the office with acute moderate to severe changes of the skin are treated by application of Berwick's dye (combination of gentian violet and brilliant green) which has alcohol content and stings, often relieving the itch.
 - The dye is dried with compressed air or a hair dryer. Benzoin tincture is applied over top of this as a barrier and dried similarly. This preparation will stay in place for several days if only water is used to cleanse and gives excellent temporary relief of symptoms and allows reepithelialization of broken skin.
 - Berwick's is suitable as an office applied remedy but is generally not for home application.
- Patients who have mild to moderate symptoms with minimal skin changes will often respond to topical 1% hydrocortisone cream which can be combined with menthol, 0.5–1.0%, and topical antibiotics (gentamicin, clindamycin, or bacitracin) or antifungals (clotrimazole, nystatin). This preparation is applied at night and in the morning after bathing, being used daily until symptoms subside.
- Patients with thickened skin and chronic moderate or severe changes should be approached with higher intensity therapy, with a medium or high potency steroid for a limited, defined period of time (Table 16.8; nonsteroidal topical therapies are listed in Table 16.9). It is important to prescribe brand names when dealing with topical steroids because of the vehicle in which it is delivered, and the particular salt matter as to potency (Table 16.8). For instance, betamethasone as Diprolene® is more than 1,000 times more potent than Valisone® cream, with Valisone® ointment somewhere in between.
- Emphasize to patients that a high-potency steroid should be used for a limited period of time, generally 4–8 weeks.
- When normalization of the skin has been achieved, switch them to a mild steroid such as hydrocortisone 1% or Locoid® 0.1% with tapering frequency of application down to once or twice a week or to total elimination.

Table 16.8. Relative potency of topical steroids (descending order).

<i>Group 1 (most potent)</i>	<i>Group 4</i>
Betamethasone dipropionate 0.05% (Diprolene [®])	Desoximetasone 0.05% (Topicort LP [®])
Clobetasol propionate 0.05% (Temovate [®])	Flurandrenolide 0.05% (Cordran [®])
<i>Group 2</i>	<i>Group 5</i>
Desoximetasone 0.25% (Topicort [®])	Betamethasone valerate cream 0.1% (Valisone [®])
Fluocinonide 0.05% (Lidex [®])	Hydrocortisone butyrate 0.1% (Locoid [®])
	Triamcinolone acetonide 0.1% (Kenalog [®])
<i>Group 3</i>	<i>Group 6 (least potent)</i>
Betamethasone valerate ointment 0.1% (Valisone [®])	Alclometasone dipropionate 0.05% (Aclovate [®])
Triamcinolone acetonide 0.5% (Aristocort [®])	Hydrocortisone 1%

Table 16.9. Nonsteroidal topical therapy for itching.

Berwick's dye (crystal violet 1% + brilliant green 1% + 95% ethanol 50% + distilled H ₂ O q.s.ad. 100%) with benzoin barrier
Burow's solution 1:40
Calmoseptine [®]
Camphor [®] (0.1–3%)
Capsaicin (Zostrix [®] 0.025%, Dolorac [®] 0.25%)
Cold compress (ice cube)
Doxepin 5% (Zonalon [®])
EMLA (eutectic mixture of local anesthetics)
Hot compress (120°F)
Macrolide topical agents (Tacrolimus and Pimecrolimus)
Menthol (0.125–1%)
Phenol (0.125–2%)
Pramoxine
Shake lotions (calamine + additives)
Topical "caines"

- Patients who have frankly eroded or denuded skin may benefit from topical antibiotics. Silver sulfadiazine cream to which hydrocortisone or triamcinolone and menthol have been added may be soothing and promote regrowth of epidermis over ulcerated areas while suppressing the inflammation that can cause fissuring in the skin.

Table 16.10. Adverse reactions to topical steroids.

Skin atrophy with telangiectasia, pseudoscars, purpura, striae, spontaneous bleeding
Tinea, impetigo, scabies incognito
Allergic contact dermatitis
Systemic absorption with adrenal suppression
Burning, itching, dryness from vehicle
Rebound worsening after withdrawal

- Skin atrophy is a serious problem with prolonged use of potent steroids, but each of the steroid preparations differs in its tendency to cause trouble.
 - Creams cause comparatively greater atrophy than ointment preparations containing identical ingredients.
 - Newer, double-ester, nonfluorinated steroids may prove to be less atrophogenic than the older preparations.
 - Macrolide topical immune modulators (tacrolimus and pimecrolimus) seem to be free of the problem of skin atrophy, a fact that enhances their appeal for use on the apposed skin of the cleft. These compounds may have some intrinsic antifungal activity as well.
 - Table 16.10 lists the potential complications of topical steroids, which are not to be taken lightly, and are all the more important because they are preventable complications of treatment excess.

Anal Tattooing

- Every practice has a small number of patients who respond poorly to treatment and whose symptoms are severe enough to alter life and happiness. These refractory patients may benefit from anal tattooing.
- A modified anal tattooing technique consists of the intradermal and subcutaneous injection of the following solution with the patient under intravenous sedation in the prone jackknife position: 10 mL 1% methylene blue + 5 mL normal saline + 7.5 mL 0.25% bupivacaine with epinephrine (1/200,000) + 7.5 mL 0.5% lidocaine.
- Certain individuals have found this sensation very disagreeable, so I am careful to warn them in detail before treatment.

17. Sexually Transmitted Diseases

A. Introduction

- Site and route of infection determine the symptoms caused by Sexually Transmitted Diseases (STDs).
- Infections of the distal anal canal, anoderm, and perianal skin are similar to lesions in other parts of the genitalia and perineum caused by the same organisms. These are typically the result of anal receptive intercourse but in some instances represent contiguous spread from genital infections.
- Proctitis from sexually transmitted organisms is almost always from anal intercourse.
- Current estimates are that less than 2% of adult males regularly practice anal receptive intercourse and between 2 and 10% participate in homosexual activity at any point in their life.
- Between 5 and 10% of females engage in anal receptive intercourse “with some degree of regularity” and females seem to be more likely than men to have unprotected anal intercourse.
- Difficulty in correct diagnosis and appropriate treatment of STDs of the anorectum is caused by several factors:
 - The signs and symptoms of infection are more organ related than organism related so that no symptom or symptom complex or physical finding is diagnostic for many STDs.
 - The presence of more than one organism is not uncommon, especially with anogenital ulcerations.
 - Determining true pathogen from colonizing organisms may be difficult.

- Lastly, there is a lack of rapid sensitive diagnostic tests for many STDs so that empiric treatment is frequently required.

B. Overview of Anorectal Immunology

- The mucosa shed from the rectum contains immunoglobulin A which traps foreign antigens and expels them with stool, preventing them from reaching the anorectal crypt cells.
- Cellular immunity is controlled by the Langerhans, or dendritic cells which communicate with the T cells through a complicated mechanism and essentially prime the T cells to identify foreign cells. This then allows the entire complement of cell-mediated immunity to destroy that which is alien.
- It is known that whereas human papilloma virus (HPV) increases Langerhans cells, human immunodeficiency virus (HIV) may damage their effectiveness. In addition, pathogens such as HPV and herpes simplex virus (HSV) invade into the host cell, combining with cellular elements or the genome, thus evading surveillance mechanisms.
- HIV is known to deplete cell-mediated immunity by depletion of T cells and destruction of Langerhans cells. This allows, through unknown mechanisms, propagation of oncogenic processes such as HPV to become dysplastic.
- Breakdown of the mucous complex protecting the rectum is seen in various diseases contracted through anal intercourse. The physical act of intercourse abrades the mucous lining and delivers pathogens directly to the crypt and columnar cells allowing for easy entry.
- In the case of recurrent viral attacks (HPV, HSV), it seems that the level of functioning T cells may have an impact on recurrence of warts or herpes outbreaks.
- The mechanics of anoreceptive intercourse, as compared with vaginal intercourse, almost always results in denuding of the protecting cellular and mucous layer of the anus and rectum.
- Latex allergies, with condom use, may also be seen causing severe invasive and erosive proctitis and should be in the differential of a caustic burn to the rectum after sexual anoreceptive intercourse.

C. Diagnosis and Management of Bacterial Pathogens

Gonorrhea

- *Neisseria gonorrhoeae*, the Gram-negative diplococcus responsible for gonorrhea, is probably the most common bacterial STD affecting the anorectum.
- Peak incidence for all forms of gonorrhea is in the late teens for females and early 20s for males. African-Americans have a 30-fold higher rate of infection than white Americans.
- Infection from *N. gonorrhoeae* occurs in columnar, cuboidal, or noncornified epithelial lined cells of the urethra, endocervix, rectum, and pharynx and is frequently asymptomatic.
- The incubation period ranges from 3 days to 2 weeks.
- Untreated infection may lead to disseminated gonococcal infection with transient bacteremia, arthritis, and dermatitis.
- Thirty-five to fifty percent of women with gonococcal cervicitis have concomitant rectal infection which is believed to be from contiguous spread from the genital infection.
- A large percentage of patients who culture positive for rectal gonorrhea are asymptomatic - up to 50% of males and 95% of females. Asymptomatic rectal infection constitutes the main reservoir of gonococcal disease in homosexual men.
- Symptomatic anorectal gonococcal infection results in pruritus, tenesmus, bloody discharge, mucopurulent discharge, and/or severe pain.
- External inspection of the anus is generally unremarkable; however, nonspecific erythema and superficial ulceration may occur.
- Anoscopy reveals a thick purulent discharge, which classically is expressed from the anal crypts as pressure is applied externally on the anus. Nonspecific proctitis may be present with erythema, edema, friability, and pus.
- Diagnosis is confirmed by culture on selective media (Thayer-Martin or Modified New York City) incubated in a CO₂-rich environment and Gram's stain of directly visualized discharge. The use of lubricants other than water may introduce antibacterial agents during anoscopy and decrease diagnostic yield.
- Nonculture detection of gonorrhea is being used more frequently especially in urethral and cervical infections. Nucleic acid amplification tests (NAATs) such as polymerase chain

Table 17.1. Treatment of anorectal gonococcal infection.¹⁴*One of the following as a single dose*

Ceftriaxone	125 mg intramuscularly
Ciprofloxacin	500 mg orally
Ofloxacin	400 mg orally
Levofloxacin	250 mg orally
Cefixime	400 mg orally

reaction (PCR) and ligase chain reaction (LCR) and nonamplified DNA probes provide sensitivities of greater than 95% but do not provide antibiotic susceptibility data.

- The most current recommended treatment regimens from the Centers for Disease Control (CDC) were published in 2002 and are listed in Table 17.1.
- Concurrent HIV infection does not alter treatment for anorectal gonorrhea. Because of the high rate of concomitant infection with chlamydia, patients treated for gonococcal infections should be given appropriate treatment for chlamydia at the same visit or measures to rule out chlamydial infection should be taken.
- Routine follow-up at 3 months is no longer necessary because current treatment provides near 100% efficacy. Patients with persistent symptoms after treatment should be followed and cultured as should those treated with nonstandard antibiotics.
- Sexual partners from the past 60 days should be treated and patient should abstain from intercourse until treatment is completed and symptoms resolved.

Chlamydia/Lymphogranuloma Venereum

- *Chlamydia trachomatis* is an obligate intracellular bacterium that is sexually transmitted and results in clinical infections that are similar to those caused by *N. gonorrhoeae*. Simultaneous infection with both organisms is common.
 - Chlamydia is the most frequently reported STD in the United States with an annual incidence of about 3 million cases per year.
 - Anorectal transmission of chlamydia is through anoreceptive intercourse although secondary involvement can occur as a late manifestation of genital infection.
 - The incubation period for chlamydia is 5 days to 2 weeks.

- Lymphogranuloma venereum (LGV) is caused by LGV serovars L1–L3
 - Serovars D through K [non-LGV serovars] are responsible for proctitis and common genital infections (chlamydia).
 - L1–L3 LGV serovars produce a much more aggressive infection with perianal, anal, and rectal ulceration.
 - Lymphadenopathy develops in draining nodal basins - iliac, perirectal, inguinal, and femoral - several weeks after initial infection. Large indurated matted nodes and overlying erythema may produce a clinical picture similar to syphilis.
- Diagnosis of chlamydia as the causative agent in proctitis can be difficult. Proper specimen collection increases diagnostic yield and consists of a cotton or Dacron swab with an inert shaft (plastic or metal).
 - Tissue culture for chlamydia is relatively insensitive and is not widely available because of cost and technical requirements.
- Antigen detection by direct fluorescent antibody (DFA) or enzyme immunoassay DFA is highly specific, widely available, and does not require rapid transportation or refrigeration.
- The two recommended treatment regimens for rectal chlamydia (non-LGV) are azithromycin, 1 g orally as a single dose or doxycycline, 100 mg orally, twice a day for 7 days.
- Treatment of LGV is with doxycycline or erythromycin for 21 days. In patients with HIV and LGV, prolonged therapy may be required.
- Abstinence from sexual intercourse should last until 7 days after treatment with azithromycin or completion of 7 days of doxycycline.

Syphilis

- Syphilis is an STD caused by the spirochete *Treponema pallidum* that can present in one of several progressive stages - primary (chancre or proctitis), secondary (condyloma lata), or tertiary.
- The primary stage of anorectal syphilis appears within 2–10 weeks of exposure via anal intercourse. The chancre begins as a small papule that eventually ulcerates.

- Anal ulcers are frequently painful (in contrast to genital ulcers) and without exudates. They may be single or multiple and located on the perianal skin, in the anal canal, or distal rectum. Differentiation from idiopathic anal fissures may be difficult.
- Painless but prominent lymphadenopathy is common.
- Untreated lesions in this stage will usually heal in several weeks.
- Hematogenous dissemination of untreated syphilis leads to a secondary stage that occurs 4–10 weeks after primary lesions appear. Nonspecific systemic symptoms from this infection include fever, malaise, arthralgias, weight loss, sore throat, and headache. A maculopapular rash is seen on the trunk and extremities.
- Condyloma lata, another secondary manifestation, are gray or whitish, wart-like lesions that appear adjacent to the primary chancre and are laden with spirochetes. Untreated, the symptoms of syphilis usually resolve after 3–12 weeks - of these patients, approximately one-fourth will have a relapse of symptoms in the first year. This is called early latent syphilis.
- Diagnosis in the primary or secondary stage is made by visualization of spirochetes on dark-field microscopic examination of scrapings from chancres.
- Positive nontreponemal tests should be confirmed by a treponemal test such as the fluorescent treponemal antibody absorption test (FTA-ABS), which remains positive for life.
- A single intramuscular injection of 2.4 million units of benzathine penicillin G is the treatment for primary and secondary syphilis. Penicillin-allergic patients are treated with doxycycline (100 mg orally, twice daily for 14 days) or tetracycline (500 mg orally, four times a day for 14 days).
- Partner notification, testing, and treatment depends on stage at diagnosis of the index case. At-risk partners include sexual contacts (a) within the prior 3 months plus duration of symptoms for patients with primary syphilis; (b) within the prior 6 months plus duration of symptoms for patients with secondary syphilis; and (c) within the prior year for those with early latent syphilis.

Chancroid

- Chancroid is an ulcerating STD caused by the Gram-negative, facultative anaerobic bacillus *Haemophilus ducreyi*.

- It is much more common in developing countries with a global incidence estimated at 6 million.
- Transmission of *H. ducreyi* is strictly via sexual contacts through breaks in the skin during intercourse and results in genital ulcers.
- Although chancroid ulcers are most frequently located on the genitalia, perianal abscesses and ulceration may occur.
- Diagnosis of chancroid is made by Gram stain and culture of *H. ducreyi* (on selective medium agar) from the base of ulcers.

Granuloma Inguinale (Donovanosis)

- Donovanosis is an ulcerating infection of the genitalia and anus caused by *Calymmatobacterium granulomatis* (also called *Donovania granulomatis*).
- Transmission is believed to occur from both sexual and non-sexual contact.
- It is rarely seen in the United States but is common in parts of Africa, South America, and Australia.
- Diagnosis can be made by tissue smear or biopsy that reveals Donovan bodies (small inclusions) within macrophages.
- Several antibiotic regimens have been recommended. The most recent CDC guidelines are doxycycline (100 mg orally, twice daily for 1 week) or trimethoprim-sulfamethoxazole (one 800 mg/160 mg tablet orally, twice a day for at least 3 weeks).

D. Diagnosis and Management of Viral Pathogens

Herpes Simplex Virus

- HSV is a DNA virus of the family *Herpesviridae* that includes varicella-zoster virus, Epstein-Barr virus, and Cytomegalovirus.
- Herpes is the most prevalent STD in the United States with the current seroprevalence rate for HSV-2 estimated to be 20% for the general population.
- Black females are the subgroup with the highest seroprevalence at 55%.
- Two serotypes of HSV are described. HSV-2 has been most associated with anogenital herpes infections. HSV-1 infection

most often presents as labial, oral, or ocular lesions but accounts for about 30% of genital infections.

- Asymptomatic infection with HSV is common.
- Transmission is via close contact with an individual who is shedding the virus and infection results from penetration of mucosal surfaces or breaks in the skin.
- Clinical infection presents first with systemic symptoms (fever, headache, myalgias), followed by local symptoms (pain, pruritus).
- Vesicles appear over the anogenital area, increase in number and size, and eventually ulcerate and coalesce. Vesicles and ulcerations heal over a mean time of 3 weeks.
- Anorectal involvement by HSV-2 is acquired by anorectal intercourse and is second only to gonorrhea as a cause of proctitis in homosexual men.
- Herpetic infection of the anorectum results in severe anal pain, tenesmus, hematochezia, and rectal discharge.
- The proctitis seen is typically limited to the distal 10 cm of the rectum with diffuse friability.
- Simultaneous with infection, HSV moves through peripheral sensory nerves to sensory or autonomic nerve root ganglia. Sacral radiculopathy of the lower sacral roots from this infection causes sacral paresthesias and neuralgias, urinary retention, constipation, and impotence.
- Tender inguinal adenopathy occurs in half of patients with HSV proctitis.
- Herpes has the ability to persist in their host because of latency - the viral genome maintained in a stable condition in host cell nuclei. For HSV, the site of latent infection is the sensory ganglia of nerves innervating the site of infection.
- Diagnosis is frequently made on clinical grounds alone. Cultures taken from ulcerations, rectal swabs, or biopsies confirm the diagnosis.
- In the past 5 years, the Food and Drug Administration (FDA) has approved several commercially available HSV serology tests. These tests have specificities and sensitivities of greater than 90% and are sure to become more frequently used in the diagnosis of HSV.
- Treatment of patients with anorectal herpes includes comfort measures such as warm soaks and oral analgesics.
- The only prospective, randomized trial of antiviral treatment for herpes proctitis demonstrated a shortened duration of

symptoms and period of viral shedding with oral acyclovir 400 mg, five times a day for 10 days. A three times per day dosing has been shown to be effective for genital herpes but has not been evaluated for herpes proctitis.

- Prompt initiation of treatment at onset of symptoms of HSV recurrence reduces duration of symptoms and healing times.
- As with all STDs, counseling of patients with HSV is an important part of treatment and prevention. Specific items that should be addressed are:
 - Infectivity is not isolated to symptomatic outbreaks; most sexual HSV transmission occurs during asymptomatic periods
 - Latent infection and the risk of recurrence; suppressive therapy does not eliminate latent infection or viral shedding
 - Abstinence is recommended while lesions are present
- Condoms are advised for all other times although they likely provide incomplete protection.
- Most recently, once-daily administration of valacyclovir has been shown to reduce the risk of HSV-2 transmission between HSV-2-seropositive patients and their seronegative sexual partners.

Human Papilloma Virus

- HPV is a DNA papovirus. Although HPV is not a reportable STD, it is probably the most common STD in the United States with an estimated incidence of more than 5 million cases per year (in contrast to chlamydia, being the most common of the reportable STDs).
- There are more than 80 subtypes of HPV, almost one-third of which cause anogenital warts.
- Subtypes 6 and 11 are the most common of the low-risk HPV subtypes, whereas subtypes 16 and 18 have the greatest associated risk of anal dysplasia and anal cancer.
- Transmission is via sexual contact with infected individuals with or without gross lesions, and asymptomatic infection is common. Perianal involvement can occur in the absence of receptive anal intercourse.
- Presenting complaints of perianal or anal condyloma acuminata include presence of a growth, pruritus, bleeding, chronic drainage, pain, and difficulty with hygiene.

- Physical examination is generally all that is required for diagnosis and shows the characteristic gray or pink fleshy, cauliflower-like growths of variable size in the perianal region.
- Anoscopy is an integral part of the evaluation. In the anal canal, the lesions tend to be small papules and involvement above the dentate line is rare.
- Examination should include the genitalia (including vaginal speculum examination and Pap smear), perineum, and groin folds.
- The goal of treatment of condyloma acuminata is destruction or removal of all gross disease while minimizing morbidity, although this does not ensure eradication of infection.
- Tangential excision, cryotherapy, or fulguration of small lesions can be performed as an office procedure with a local anesthetic with little discomfort or inconvenience to the patient. Larger lesions are treated by electrodesiccation.
- Pedunculated warts are simply transected at their base.
- Topical 5% lidocaine is helpful in decreasing postoperative pain.
- Oral analgesics and daily cleansing with mild soap and water are all that is required for postoperative care in most patients. Silver sulfadiazine or mupirocin are applied in cases in which postoperative bacterial infection is suspected.
- Overall condyloma clearance rates for surgical techniques range from 60 to 90% with recurrence rates of 20–30%.
- Imiquimod is an immune response modifier that increases local production of interferon. Complete response can be expected in 50% of patients treated with imiquimod with 11% of patients experiencing a recurrence. It is applied at bedtime three times a week, left in place for 6–8 h, and then removed by washing. Treatment may take up to 16 weeks.
 - Side effects of imiquimod include pain, burning, itching, and ulceration which may require cessation of therapy.
 - Imiquimod is used (1) as initial treatment with electrodesiccation reserved for those who have incomplete response, or (2) after destructive treatment and epithelial healing to treat remaining disease or decrease recurrence.
- Bushke and Loewenstein first described giant condyloma acuminata (GCA) in 1925. They are most associated with HPV types 6 and 11 but histologically demonstrate some differences from ordinary condyloma - marked papillomatosis, acanthosis, thickened rete ridges, and increased mitotic activity.

- The substantial percentage of cases with in situ or invasive squamous cell cancers have led to speculation that GCA represents part of a continuum from condyloma to invasive squamous cell cancer.
- Wide local excision with a 1-cm margin is the treatment of choice for these lesions. Local tissue flaps or grafted skin may be required to repair surgical defects.
- Chemoradiation is also an option in the treatment of GCA, especially in those patients who are poor surgical candidates or in whom clear surgical margin are not attainable. Complete regression of GCA with chemoradiation has been reported.

HPV, Anal Intraepithelial Dysplasia, and Anal Cancer

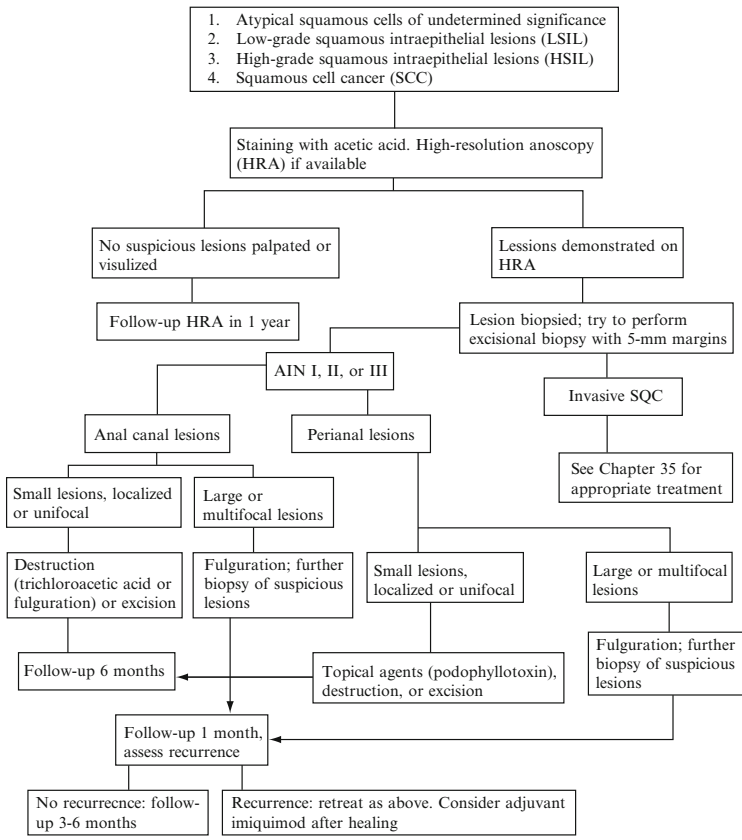
- Although it is clear that HPV has a significant role in the development of cervical cancer, its significance in the development of anal cancer and its presumed precursor (anal intraepithelial dysplasia or high-grade squamous intraepithelial lesions) are not as well defined.
- The risk of anal cancer developing in an HIV+ homosexual male is estimated to be 38 times that of the general population and twice the risk of an HIV-homosexual male.
- HPV infection has been reported in 93% of HIV+ homosexual males compared with 60% of HIV-homosexual males.
- Anal cytology has been suggested as a screening tool for detecting patients with anal dysplasia. Applying the current cervical cytology terminology, specimens are designated normal, atypical squamous cells of indeterminate significance (ASCUS), low-grade squamous intraepithelial lesions (LSIL), or high-grade squamous intraepithelial lesions (HSIL).
- One such evaluation and treatment algorithm recommends high-resolution (with acetowhitening and staining with Lugol's solutions) anoscopy with biopsy.
- Subsequent treatment is based on histologic findings which are typically reported as normal or AIN (anal epithelial neoplasia) I, II, or III. Options for treatment include local destruction (with topical agents, cryotherapy, or fulguration), excision, or observation.
- The incidence and predictability of the progression of AIN to invasive cancer is unclear.

- Data demonstrating efficacy (defined as long-term removal of AIN, prevention of anal cancer) of treatment is lacking. There is no evidence that destroying AIN III has any impact on survival.
- The absence of established benefit combined with the morbidity of treatment lead us and others to the recommendation that AIN (regardless of grade) be observed unless there are gross or ulcerated lesions present.
- It is the authors' belief that because the acquisition of anal cytology specimens require no particular expertise, this procedure should remain the domain of the patients' primary managing physicians who are most likely to have frequent contact with these patients (internist, general practitioner, infectious disease specialist).
- Patients with abnormal cytology should be referred to the colon and rectal surgeon who should evaluate patients with staining and magnification if possible to determine if biopsy or excision is required (Table 17.2).
- Two additional comments with regard to the association of HPV, HIV, and AIN should be made.
 - First, the use of highly active antiretroviral therapy (HAART, discussed in more detail later in the section on HIV) does not reduce the incidence of AIN. The clinical implications of this fact are: (a) anal cytology screening should not be stopped just because a patient is treated with HAART; and (b) with HIV patients living longer secondary to HAART, the incidence of anal cancers may increase.
 - Second, the prevalence of HPV and AIN is high in HIV-positive males with CD4+ counts less than 500×10^6 cells/L even in the absence of a history of anal intercourse. These patients should also be considered for cytologic screening.

Molluscum Contagiosum

- The molluscum contagiosum virus is a member of the poxvirus family and causes a benign papular condition of the skin.
- Transmission is by sexual and nonsexual contact.
- The incubation period is 1–6 months, followed by development of 2- to 6-mm flesh-colored, umbilicated papules.
- Diagnosis is usually made on clinical grounds but excisional biopsy demonstrates enlarged epithelial cell with intracytoplasmic molluscum bodies.

Table 17.2. Algorithm for management of patients with abnormal anal cytology.



- Treatment is generally through eradication with curettage, electrodesiccation, or cryotherapy. Podophyllotoxin (0.5%) and imiquimod (5%) have both been used as self-applied topical preparations with success. Neither is FDA approved for this use.

HIV and the Acquired Immunodeficiency Syndrome

- Whereas the incidence of HIV infection has apparently leveled, the numbers of new AIDS cases and deaths from AIDS have decreased. This is in large part attributable to HAART - combinations of potent anti-HIV drugs that are nucleoside analogs, non-nucleoside reverse transcriptase inhibitors, or

protease inhibitors. Table 17.3 shows the current classification system for patients who are HIV positive.

- Surgery for anorectal diseases is the most common indication for surgery in HIV-infected patients and in 5% of patients whose anorectal complaints are the presenting symptom of their HIV infection.
- Most of the indications for surgery are common to the population at large but some are unique to AIDS patients.
- Several studies demonstrate poor wound healing and increased morbidity in the surgical treatment of anorectal disease in AIDS patients.

Table 17.3. Revised classification system for HIV and AIDS⁷¹.

CD4 + T lymphocyte categories

Category 1: ≥ 500 cells/ μ L

Category 2: 200–499 cells/ μ L

Category 3: < 200 cells/ μ L

Clinical categories

Category A: HIV positive; asymptomatic; persistent generalized lymphadenopathy

Category B: Symptomatic conditions not listed in clinical category C; are conditions that are attributed to HIV infection; or conditions that have a clinical course or require management that is complicated by HIV infection. Examples include: bacillary angiomatosis, oropharyngeal or vulvovaginal candidiasis, cervical dysplasia, diarrhea (more than 1 month in duration), more than one episode of herpes zoster, pelvic inflammatory disease, peripheral neuropathy

Category C: Diagnoses included in the AIDS surveillance case definition - candidiasis (pulmonary or esophageal), invasive cervical cancer, Coccidiomycosis, extrapulmonary cryptococcosis, chronic intestinal cryptosporidiosis, Cytomegalovirus disease (other than liver, spleen, nodes) or retinitis, HIV-encephalopathy, HSV (chronic ulcers, pulmonary, or esophageal), histoplasmosis (disseminated or extrapulmonary), isosporiasis (chronic intestinal), Kaposi's sarcoma, Burkitt's lymphoma, immunoblastic lymphoma, primary brain lymphoma, *Mycobacterium avium* complex or any mycobacterium species other than *M. tuberculosis* (extrapulmonary or disseminated), *M. tuberculosis*, *Pneumocystis carinii* pneumonia, progressive focal leukoencephalopathy, recurrent *Salmonella septicemia*, toxoplasmosis of the brain, HIV wasting syndrome

Clinical categories

CD4 + categories	A1	B1	C1
	A2	B2	C2
	A3	B3	C3

Bolded groups are defined as AIDS

- Other factors to be considered in selecting appropriate treatment include any untreatable diarrheal conditions, degree of existing fecal incontinence, and the effect of the proposed surgical procedure on incontinence.
- Anal fissures that occur in HIV+ patients must be distinguished from idiopathic AIDS-related anal ulcers and ulcerating STDs such as HSV or syphilis. Anal fissures in this patient population are indistinguishable from those in the general population and their treatment is similar - initial conservative management with surgery for treatment failures.
- Treatment of fissures in HIV+ patients is modified by the factors described above and include controlling diarrhea when possible and encouraging abstinence from anoreceptive intercourse.
- Although data on the incidence of AIDS-related anal ulcers are lacking, it seems that they are less common with HAART because the lesions are most frequently associated with clinical AIDS and lower CD4+ counts.
- These ulcers can be distinguished from typical anal fissures because they are more proximal in the anal canal (frequently above the dentate line or anorectal ring), broader based, deeply ulcerating with destruction of sphincter planes, and may demonstrate mucosal bridging.
- Perianal suppurative diseases are common conditions in AIDS patients. Abscesses should be drained using small incisions, and placement of a mushroom catheter will lessen recurrent sepsis. Broad-spectrum antibiotics should be given in immune-compromised patients especially if cellulitis is present. Culture (to include mycobacterium) and histopathologic evaluation will help identify infection from atypical organisms and malignancy.
- The authors treat anal fistulas in AIDS patients with high viral loads and low CD4+ counts similar to Crohn's patients. Draining setons are placed liberally with selective use of fistulotomy for low uncomplicated fistulas. Fistulotomy in HIV+ patients with AIDS and normal CD4+ counts is based on criteria similar to HIV- patients.
- Thrombosed external hemorrhoids in patients with AIDS are treated the same as for HIV- patients. Acute thrombosis (24–48 h after onset of symptoms) is treated with excision. Subacute thrombosis (longer than 48 h from symptom onset) is treated conservatively with sitz baths and oral analgesics.
- Internal hemorrhoids present with symptoms of bleeding or prolapse. Initial treatment in patients with AIDS is with a

high fiber diet and bulking agents. Proximal colonic sources of bleeding should be excluded via colonoscopy. Patients who fail initial conservative measures are treated with rubber band ligation or infrared coagulation.

- It seems that asymptomatic HIV+ patients who do not meet the clinical or CD4+ count diagnostic criteria for AIDS (see Table 17.2) can be treated with hemorrhoidectomy with the expectation that they will have good symptomatic relief and normal wound healing. AIDS patients with more advanced disease (clinical category C) or low CD4+ counts (especially less than 100) are at increased risk for wound healing problems. The benefit of symptomatic relief may still warrant performing surgical treatment in this group.

18. Benign Colon: Diverticular Disease

A. Introduction

- The term “diverticular disease” of the colon represents a continuum of anatomic and pathophysiologic change within the colon related to the presence of diverticula.
- These changes most often occur in the sigmoid colon.
- It can refer to an asymptomatic state (diverticulosis) or any one of a number of diverse combinations of inflammatory symptoms, changes, and complications (diverticulitis).
- Symptoms may variably result from simple physiologic changes in colonic motility related to altered neuromuscular activity in the sigmoid colon, varying degrees of localized inflammatory response, or complex inflammatory interactions leading to diffuse peritonitis and septic shock.
- These more complex symptoms and resulting complications arise from breaches in the integrity of the wall of one or more diverticula.
- Diverticula may be true, containing all layers of the bowel wall (congenital), or false, lacking the muscular layer (acquired or pulsion diverticula).

B. Incidence

- Since the early twentieth century, an increasing prevalence of the disease has been recognized in industrialized countries.
- The incidence increases with age and the adoption of a diet high in red meat, refined sugars, and milled flour but low in whole grain breads, cereals, and fruits and vegetables.

- It is now estimated that the risk of developing diverticular disease in the United States approximates 5% by age 40 and may increase to more than 80% by age 80.
- It is now clear that not only diverticulosis but the incidence of related complications are increasing.
- An estimated 10–20% of people with diverticula develop symptoms of diverticulitis, and only 10–20% of these will require hospitalization.
- Of those that require hospitalization, 20–50% will require operative intervention.
- The percentage of hospitalized patients requiring operation has been increasing as outpatient management becomes more common and those admitted as inpatients are more seriously ill.
- Overall, less than 1% of patients with diverticula will ultimately require surgical management.
- The incidence of perforation is higher in males younger than age 50 but in females older than 50.

C. Pathophysiology

- Diverticulosis is associated with high intraluminal pressures.
- Pressures in patients with diverticular disease have been found as high as 90 mm Hg during peak contraction. This represents a value nearly nine times higher than seen in patients with normal colons.
- It is theorized that such pressures lead to segmentation. Segmentation refers to a process whereby the colon effectively functions as a series of separate compartments rather than a continuous tube.
- The high pressures that each compartment is capable of producing are directed toward the colonic wall rather than as propulsive waves. These pressures predispose to herniation of mucosa through the muscular defects that exist where blood vessels penetrate to reach the submucosa and mucosa (vasa recta brevia).
- Most of these penetrations occur between the mesenteric and anti-mesenteric tinea where, not coincidentally, most diverticula occur.
- As the mucosa herniates, it does so without dragging the muscular layer along, leaving the diverticula denuded of muscle and consistent with the definition of an acquired process. Thus, the most common diverticula are acquired or pulsion diverticula.

- Because of segmentation, the sigmoid generates pressures so high that the effect of a smaller radius is overcome resulting in total tension in the wall of the sigmoid colon being higher than the rest of the colon and thus the sigmoid has the highest risk of diverticulum formation.
- It is hypothesized that at least a part of fiber's protective effect is a result of stool bulking which maintains a larger lumen, prevents segmenting contractions, and decreases high pressures.
- Complementary to these theories of pathogenesis is the consistent colonic wall muscle abnormality associated with sigmoid diverticular disease. Both the circular and longitudinal muscle wall is typically thickened resulting in a reduction in the size of the lumen and a shortening of the sigmoid.
- Cellular hypertrophy, cellular hyperplasia, and elastosis have all been described. Elastosis seems to precede the development of diverticulosis. It is not found in any other inflammatory conditions of the colon.
- Pain associated with diverticular disease may be related to muscle spasm as well as inflammation. Perforation can occur in the absence of inflammation and may be secondary to the extremely high intraluminal pressure.

D. Etiology

- Pathophysiologic studies reveal that complications do not occur until there is microperforation through the wall of a diverticulum into the pericolic tissue.
- The perforation might be small and cause a microabscess, develop into a phlegmon, or form into a large abscess. Free perforation occurs rarely, but fistulization does frequently occur, most often to the bladder.
- The original communication with the lumen of the bowel is usually rapidly obliterated by the inflammatory process.
- Recent clinical investigations have shown that disturbances in cholinergic activity may contribute to diverticular disease. Cholinergic stimulation in patients with diverticular disease leads to unsynchronized slow waves of relatively low frequency as opposed to bursts of action potentials normally associated with peristalsis.

E. Epidemiology

Diet

- Large cohort and case-control studies in the United States and Greece have shown that diets high in red meat and low in fruit and vegetable fiber increase diverticular symptoms by as much as threefold.
- Vegetables and brown bread have been shown to be protective.
- Fiber may be protective by increasing stool weight and water content which decrease colonic segmentation pressures and transit times.
- Fiber, through the process of fermentation, also provides short-chain fatty acids to the colonic epithelial cells, an important source of fuel and mucosal health.

Age and Sex

- Female patients present with complications requiring surgery an average of 5 years later than males. Men have a higher incidence of bleeding and women a higher incidence of fistula. Younger men present with fistula and older men bleeding. Young females present with perforation whereas older females with chronic disease and stricture.
- Overall, patients younger than age 50 present more often with chronic or recurrent diverticulitis.
- More patients at younger and younger ages are being diagnosed with diverticular disease.

Nonsteroidal Inflammatory Drugs

- Nonsteroidal inflammatory drugs (NSAIDs) have been linked to increased rates of complications related to diverticular disease. The plausible mechanism of action is indirect through known inhibition of cyclooxygenase and resultant decreased prostaglandin synthesis in the gut. Prostaglandins are important in the maintenance of mucosal blood flow and an effective colonic mucosal barrier.
- A direct mechanism also exists through mucosal damage caused by NSAIDs which leads to increased translocation of toxins and bacteria.

Immunocompromise

- The use of corticosteroids is associated with a higher risk of perforation and more severe inflammatory complications. The postulated mechanism is immunosuppressive and antiinflammatory effects hinder confinement of perforation in its early stages.

Opiates

- The use of opiate pain medications has been shown to increase intracolonic pressure and slow intestinal transit, both risks for complications of diverticular disease. Case series have shown high percentages of patients with perforation taking opiate analgesics.

Smoking

- A recent large case-control study showed that smokers had three times the risk of developing complications from diverticular disease than did nonsmokers. However, a large cohort study involving more than 46,000 men in the United States did not find this same association.

Alcohol

- A Danish cohort study showed the risk of diverticulitis was three times higher in female alcoholics than the general population and two times higher in male alcoholics. However, the data may be biased because of dietary and smoking habits associated with alcoholics.

F. Clinical Manifestations

Clinical Patterns

- Diverticular disease may be classified into diverticulosis (asymptomatic) and diverticulitis (symptomatic) (Table 18.1).
- Diverticulosis refers to the presence of diverticula with no related symptoms. This applies to the vast majority (80–90%) of patients with diverticular disease.

Table 18.1. The classification of diverticular disease.

Diverticulosis		Asymptomatic
Diverticulitis		
Noninflammatory		Symptoms without inflammation
Acute		Symptoms with inflammation
Simple		Localized
Complicated		With perforation
Chronic		Persistent, low grade
Atypical		Symptoms without systemic signs
Recurring, persistent		Symptoms with systemic signs (may be intermittent)
Complex		With fistula, stricture, obstruction
Malignant		Severe, fibrosing

- Diverticulitis can be subclassified into noninflammatory, acute (simple or complicated), chronic (atypical or recurring/persistent), and complex disease.

Noninflammatory Diverticular Disease

- Noninflammatory diverticular disease describes those patients with symptoms of diverticulitis but without associated inflammation. The diagnosis is made at the time of elective operation when no inflammatory changes are found in the specimen. This has been reported in 15–35% of resections.

Acute Diverticulitis

- Acute diverticulitis is heralded by signs and symptoms of acute inflammation and may be simple (limited to the colonic wall and adjacent tissues) or complicated (with perforation). Simple acute disease is usually accompanied by systemic signs of fever and leukocytosis whereas complicated acute disease may have the added signs of tachycardia and hypotension.
- A common classification for diverticulitis with perforation was first described by Hughes et al. in 1963 and slightly revised and popularized by Hinchey et al. in 1978. Stage I diverticulitis is a localized pericolic or mesenteric abscess, stage II is a confined pelvic abscess, stage III is generalized purulent peritonitis, and stage IV is generalized fecal peritonitis (Fig. 18.1).

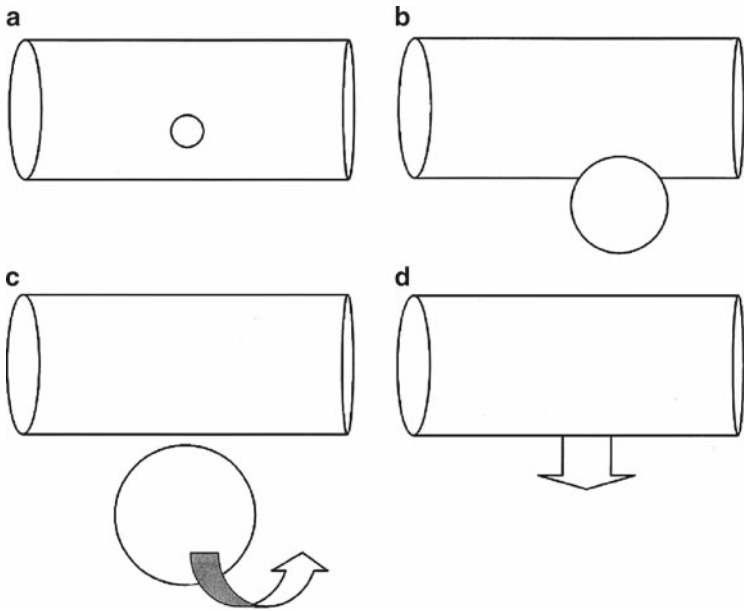


Fig. 18.1. Diagrammatic representation of classification system for diverticular abscesses in which the cylinders represent the colon, the circles an abscess, and the arrows perforation. (a) Hinchey stage I: localized pericolic or mesenteric abscess. (b) Hinchey stage II: confined pelvic abscess. (c) Hinchey stage III: generalized purulent peritonitis resulting from perforation of an abscess. (d) Hinchey stage IV: generalized fecal peritonitis secondary to free colonic perforation.

Chronic Diverticulitis

- Patients with chronic diverticulitis remain symptomatic (left lower quadrant pain) despite standard treatment. It is considered atypical if systemic signs never develop.
- With systemic signs, chronic disease may manifest as recurring, intermittent episodes of acute disease or as persistent, symptomatic low-grade disease.
- This is frequently associated with the presence of a phlegmon.

Complex Diverticular Disease

- Complex diverticulitis refers to disease in those patients who manifest sequelae of chronic inflammation including fistula, stricture, and obstruction.

G. Natural History

- The natural history of diverticular disease is one of increasing risk with increasing age and a diet low in fiber and high in red meat.
- The number and size of diverticula may increase with age; however, progression from one segment of bowel to another does not typically occur.
- The most common location for complications is in the sigmoid colon. It is unusual for complications to develop in the proximal colon after resection of the diseased sigmoid colon.
- Most patients who develop a first episode of symptomatic diverticulitis have been asymptomatic until 1 month before presentation. Most will respond to bowel rest and antibiotics as an outpatient. It is difficult to reliably estimate how many outpatients will have recurrent episodes because outpatient data are generally not reflective of a primary care population.
- It has been reported that up to 10% of patients with a first episode who have responded to outpatient management will develop recurrent or persistent symptoms which will require hospitalization.
- The interval between acute events may be prolonged (median 5 years). After a second hospital admission, up to 70% will continue with symptoms and more than half of those that require a third admission will do so within 1 year.
- The more complicated the attack, the higher the risk of recurrence.
- It has been estimated that up to 1% of all patients with diverticulosis will eventually require operative intervention. However, with an increasing overall number of individuals affected with diverticulosis and better antibiotics for managing infections, this estimate may now be too high.

H. Presenting Symptoms

- Patients with acute diverticulitis typically complain of left lower quadrant abdominal pain. However, in a patient with a

redundant sigmoid colon, an inflamed segment might present with pain in the right lower quadrant, thus complicating the differential diagnosis with appendicitis.

- The pain is generally constant in nature, not colicky. Radiation may occur to the back, ipsilateral flank, groin, and even down the leg. The pain may be preceded or accompanied by episodes of constipation or diarrhea. It often is progressive in nature if appropriate treatment is not instituted.
- Nausea and vomiting are unusual in the absence of obstruction, although secondary ileus with abdominal distention is common in more severe cases.
- Bleeding is not a typical associated finding, and, if present, suggests an alternative diagnosis (e.g., cancer).
- Symptoms of dysuria or urgency suggest possible bladder involvement because of an adjacent inflammatory mass or a colovesical fistula.
- Pneumaturia, fecaluria, or passage of gas and stool through the vagina suggest a colovesical or colovaginal fistula, respectively.
- Fever is common and proportional to the amount of inflammatory response present. A high fever suggests a perforation with abscess or peritonitis.

I. Physical Findings

- Patients presenting with acute diverticulitis will be tender to palpation in the left lower quadrant and left iliac region. There may be limited rigidity or localized guarding to deeper palpation.
- With resolution of the acute phase, palpation may reveal a mass in the left lower quadrant.
- A positive psoas sign and/or obturator sign may reflect retroperitoneal and/or pelvic involvement of the inflammatory process.
- In the event of a gross perforation with development of fecal or purulent peritonitis, the area of tenderness will spread throughout the abdomen. Guarding will become prominent and the abdominal wall will become rigid.

J. Complications

Bleeding

- Bleeding is not recognized as a feature of diverticulitis. Bleeding related to diverticulosis is discussed in Chap. 20 (Lower Gastrointestinal Hemorrhage).

Perforation

- Gross perforation can occur at two levels. If an abscess forms and then ruptures, purulent peritonitis is the result. If a large perforation occurs through the diverticulum directly into the peritoneum, fecal peritonitis is the result.
- Mixed fecal and purulent peritonitis may result from the rupture of an abscess which has an ongoing communication with the bowel lumen.
- Clinically, the presentation is that of either abrupt onset of abdominal pain for a free perforation or an abrupt exacerbation of progressive localized pain in the case of a ruptured abscess.
- A pneumoperitoneum is typically seen on abdominal films or computed tomographic (CT) scan.
- Rapid progression to diffuse abdominal pain and rigidity can be expected.

Abscess

- Small abscesses less than 1 cm in diameter will frequently resolve with antibiotic therapy.
- Larger abscesses may require drainage. CT-guided percutaneous drainage is the preferred approach when possible because it can convert the high risks of an urgent operation to a much safer elective operation.

Fistula

- The incidence of fistulization reported in the literature ranges from 5 to 33%.
- Colovesical fistula is the most common fistula associated with diverticular disease and diverticular disease is the most common cause of colovesical fistula.

- Other relatively common fistulas associated with diverticular disease are colocutaneous, colovaginal, and coloenteric.
- Most patients who develop a colovaginal fistula have had a previous hysterectomy. Other fistulas have rarely been described and include colocolic, ureterocolic, colouterine, colosaphingeal, coloperineal, sigmoido-appendiceal, colovenous, and even fistulas to the thigh (a variant of a colocutaneous fistula).
- The diagnosis of a diverticular fistula is generally clinical. Many fistulas will not be directly identifiable by imaging studies.
- Gas seen in the bladder on a CT scan in a patient who has not had their urethra or bladder instrumented is the most sensitive/common finding with a colovesical fistula.
- The primary aim of a diagnostic workup is not to see the fistula but to determine the etiology [diverticulitis, cancer, inflammatory bowel disease (IBD), etc.] so that appropriate therapy can be initiated.

Stricture

- The development of a phlegmon with repeated attacks of acute disease or long-term persistent disease may result in a stricture.
- It is necessary to rule out carcinoma as the true cause of the stricture. Colonoscopy is the first choice to help make this distinction; however, it is not uncommon for associated bowel angulation and fixation to prevent endoscopic visualization.
- Contrast studies may assist the evaluation in such instances but resection may be necessary to make a diagnosis.

Obstruction

- On rare occasions, complete obstruction may occur. If caused by diverticular disease, most patients will respond to initial medical management allowing an elective resection at a later date.
- Persistence of an obstruction may require a Hartmann's procedure or primary anastomosis with proximal diversion for management.

Ureteral Obstruction

- The ureter is infrequently involved with diverticular disease. When involved, it is most frequently the left ureter.

- A stricture may occur but compression is more common. This can result from retroperitoneal fibrosis secondary to diverticular inflammation.

Phlegmon

- A phlegmon represents an inflammatory mass. It may or may not be associated with a central abscess.
- A phlegmon can significantly complicate the technical aspects of resection.
- Many phlegmons will resolve with antibiotic therapy.
- If resection is planned because of recurrent episodes of disease, it is best to treat the acute phlegmon, to resolution if possible, before resection.
- On occasion, operation becomes necessary in the face of an acute phlegmon.

Saint's Triad

- Saint's triad is a described association of diverticulosis, cholelithiasis, and hiatal hernia. Although it has been suggested that the triad occurs in 3–6% of the general population, it is of unknown clinical significance and likely represents the normal concomitant distribution of these common maladies.

H. Diagnostic Tests

Endoscopy

- Endoscopy in the face of acute diverticulitis must be undertaken with extreme caution because of risk of gross perforation and decreased chance of success for complete colonic evaluation.
- It can provide important information before operation but will change acute management in less than 1% of cases.
- Generally, in the absence of an urgent indication, colonoscopy should be delayed until resolution of the acute episode is complete.

Abdominal X-rays

- When used, plain films of the abdomen should be done supine and upright/left lateral decubitus because the primary value is to rule out pneumoperitoneum or to assess for a possible obstruction. However, either of these two complications can also be assessed with CT scan, so in many centers, the plain abdominal film is rarely used.

Contrast Studies

- Barium or water-soluble contrast studies have proponents for their use but CT scan offers an examination of much broader scope in one evaluation making it the preferred imaging study in many centers.
- Contrast studies have been shown to identify fistulas, most often colovaginal or coloenteric.
- Some clinicians prefer the anatomic view of the entire colon provided by BE because it distinguishes the extent of diverticulosis throughout the colon and can assess for stricture and colonic length. In most centers, contrast studies, if used at all, are used in a limited manner to evaluate the anatomy of the colon before an operation.

CT Scan

- An important advantage to a CT scan is the ability to document diverticulitis, even if uncomplicated, when the diagnosis is in doubt.
- It has been demonstrated that CT can recognize and stratify patients according to the severity of their disease. It can distinguish uncomplicated disease with predictably short length of stay from complicated disease as defined by abscess, fistula, peritonitis, or obstruction and a predictably long length of stay.
- It also provides information about extracolonic pathology and anatomic variation useful for surgical planning.
- Early CT-guided drainage of abscesses allows downstaging of complicated diverticulitis to convert an otherwise urgent or emergent operation with attendant increases in morbidity and mortality to the safety of an elective operation.

Ultrasonography

- Transrectal ultrasound (TRUS) may prove to be a useful adjunct in selected cases of rectosigmoid diverticulitis and perirectal involvement by diverticular disease in centers where CT scanning is not readily available.

Magnetic Resonance Imaging

- Preliminary studies using magnetic resonance imaging colonography have shown a high correlation with CT findings in patients with diverticular disease without exposure to ionizing radiation.
- These comprehensive three-dimensional models, rather than BE, may have a role in presurgical planning with concurrent assessment of the residual colon.

I. Differential Diagnosis

- The differential diagnosis for diverticular disease includes IBS, carcinoma, IBD, appendicitis, bowel obstruction, ischemic colitis, gynecologic disease, and urologic disease. Of these, IBS is perhaps the most difficult to differentiate in many patients.

Irritable Bowel Syndrome (IBS)

- The distinction between noninflammatory diverticular disease and IBS relies on the diagnostic acumen of the clinician and the long-term outcomes of resection.
- Because of the prevalence of diverticular disease, many patients with IBS will have concomitant diverticular disease. However, because diverticular disease is usually asymptomatic, the presence of diverticulosis in these patients will often not be the source of their symptoms but rather just a source of confusion in the differential.
- It is helpful to be familiar with the Rome II criteria (Table 18.2) for the diagnosis of IBS in order to sort through this differential.

Table 18.2. The Rome II criteria for IBS

IBS can be diagnosed based on at least 12 weeks (which need not be consecutive) in the preceding 12 months, of abdominal discomfort or pain that has two of three of these features:

1. Relieved with defecation; and/or
2. Onset associated with a change in frequency of stool; and/or
3. Onset associated with a change in form (appearance) of stool.

Symptoms that cumulatively support the diagnosis of IBS:

1. Abnormal stool frequency (>3 stools per day or <3 stools per week)
2. Abnormal stool form (lumpy/hard or loose/watery stool)
3. Abnormal stool passage (straining, urgency, or feeling of incomplete evacuation);
4. Passage of mucus
5. Bloating or feeling of abdominal distension

Red Flag symptoms that are *not* typical of IBS:

1. Pain that often awakens/interferes with sleep
 2. Diarrhea that often awakens/interferes with sleep
 3. Blood in stool (visible or occult)
 4. Weight loss
 5. Fever
 6. Abnormal physical examination
-

Colon Neoplasia

- Distinguishing diverticular disease from cancer can be difficult. Imaging techniques can provide significant diagnostic assistance, but occasionally a resection is necessary to be certain.
- Several features of BE studies support a diagnosis of diverticular disease including preservation of the mucosa, long strictures, and the presence of diverticula. A BE is preferred by some clinicians to assess the extent of the diverticulosis and evaluate the length of the colon before resection.
- Although colonoscopy can frequently resolve this issue, it is not always successful because of acute angulations or narrowing of the lumen.

- CT evaluates the entire abdomen, can identify concurrent disease, and may give clues as to the underlying colonic pathology.
- Polyps and cancer must be considered whenever a diagnostic workup for diverticular disease is begun.
- Although historically diverticular disease is not believed to have an etiologic link to colon cancer, a causal association has been identified between left-sided colon cancer and diverticulitis. In a review of 7,159 patients from the Swedish Cancer Registry, patients with diverticulitis had a long-term increased risk of left-sided colon cancer compared with patients with asymptomatic diverticulosis (odds ratio $n = 4.2$).

Inflammatory Bowel Disease

- Crohn's disease can be a particularly difficult differential to make. Both Crohn's and diverticular disease may present with similar complications including fistulas, phlegmons, and abscesses. Rectal involvement, anal disease, extracolonic signs, and bleeding suggest Crohn's.
- Recurrent "diverticulitis" requiring a repeat resection should always raise the question of possible Crohn's disease.
- Ulcerative colitis is rarely a significant differential problem because bleeding is not a prominent symptom of diverticulitis and a simple endoscopic examination showing inflammation within the rectum should suffice to rule out diverticular disease.

Other Colitides, Appendicitis, Gynecologic and Urologic Disease

- Endoscopy can be an important adjunct in differentiating IBD, ischemic colitis, and other forms of colitis although caution must be used in the acute setting.
- A major advantage of the CT scan is the ability to evaluate for many of the other potential differentials including appendicitis, gynecologic and urologic disease.

Associated Conditions

- There is such a high incidence of diverticulosis among patients with autosomal dominant polycystic kidney disease that some consider it an extrarenal manifestation. These patients undergoing renal transplantation are at particularly high risk for devastating

infectious complications because of their immunocompromised state.

- Many transplant centers recommend prophylactic sigmoid resection in those polycystic kidney patients scheduled for transplantation with a documented history of diverticulitis.

J. Uncommon Presentations

Diverticulitis in Young Patients

- Young patients with diverticular disease are usually male, obese, and have a higher incidence of right-sided diverticulitis.
- Young patients undergoing operation are frequently misdiagnosed preoperatively with appendicitis being the most common misdiagnosis.
- Historically, diverticular disease in patients younger than 50 years of age has been described as more virulent and with more serious complications. Many recommend that patients younger than age 50 have an elective resection after a single episode of acute disease. Recent evidence is mixed.
- In some series, young people present with more severe disease at first presentation but less frequently have a resection at that time. Reasons for this include missed diagnoses and rapid response to therapy. With fewer resections for more complex disease, a higher percentage of young patients return with delayed complications and the appearance of more aggressive disease. Elective resection after the first episode of diverticulitis is thus advised.
- Others have recommended elective resections at a younger age to avoid the increased morbidity and mortality associated with urgent or emergent surgery in the elderly (0% vs. 34.9%).
- There is evidence that diverticular disease in young patients is changing. It is not as rare as it used to be and continues to become more common. Recent evidence suggests there is not increased risk of complications from diverticular disease in the young. Based on these findings, resection after a single episode of diverticulitis is not recommended.
- Data are difficult to interpret because the presentations of diverticular disease are so varied and most studies are small and retrospective with risks of unrecognized selection bias. However, it does seem that diverticular disease is more common

in young patients than generally recognized. Obesity may be a risk factor, probably related to diet.

- The issue of male predominance could be a result of missed diagnoses in females.
- Current recommendations for resection are based on the predicted risk of developing a serious complication that would lead to emergency surgery with increased morbidity and mortality and frequent use of colostomy in this setting.
- Age alone does not seem to be a reliable factor. The use of CT to identify “severe” or “complex” diverticular disease seems most promising.
- The risk of complications within 5 years of a first attack of diverticulitis exceeds 50% if CT shows severe diverticulitis at the initial episode.
- Severe findings are defined as abscess and/or extraluminal air and/or extraluminal contrast.
- In a recent study, the incidence of remote complications was the highest (54% at 5 years) for young patients with severe diverticulitis on CT and the lowest (19% at 5 years) for older patients with mild disease.

Rectal Diverticula

- Rectal diverticula are rare. They are typically true diverticula because they include the muscular layer of the rectum in their wall, and are frequently solitary. Inflammation can generally be managed with antibiotics.

Cecal and Right-Sided Diverticulitis

- Right-sided diverticular disease is much more common in the Far East than in the West, representing 35–84% of diverticula in that region.
- Patients present an average of 20 years younger than with sigmoid diverticulitis.
- It is estimated that 13% of patients with cecal diverticulosis develop diverticular inflammation.
- Cecal diverticulitis can be graded according to the extent of the inflammation. Grade I disease refers to an easily recognizable projecting inflamed cecal diverticulum. Grade II is an inflamed

cecal mass. Grade III encompasses a localized abscess or fistula. Grade IV is a free perforation or ruptured abscess with diffuse peritonitis.

- Cecal diverticulitis is correctly diagnosed preoperatively only 5% of the time. Appendicitis is the preoperative diagnosis in more than two-thirds of cases.
- If a correct diagnosis of uncomplicated cecal diverticulitis can be made preoperatively, then antibiotics and treatment similar to left-sided disease is appropriate. This is rare, however.
- When discovered intraoperatively, the options for treatment include:
 - Appendectomy, nonresection of the diverticulum and postoperative antibiotic therapy.
 - Appendectomy with diverticulectomy for Grade I and identifiable Grade II disease. For not readily identifiable Grade II, Grade III, and Grade IV disease, failed treatment, or when cancer is a consideration, right hemicolectomy is the procedure of choice. Appendectomy should always accompany nonresection or diverticulectomy whenever the base of the appendix is not inflamed. This is to avoid confusion at a later date.

Giant Colonic Diverticulum

- Giant diverticula of the colon are rare entities associated with sigmoid diverticular disease. They are generally pseudo-diverticula with inflammatory rather than colonic mucosal walls.
- Diagnosis is by plain film of the abdomen which shows a large, solitary, gas-filled cavity. Communication with the colon can be demonstrated with contrast enema.
- The differential includes congenital duplication of the colon, cholecystenteric fistula, colonic volvulus, emphysematous cholecystitis, infected pancreatic pseudocyst, pneumatosis cystoides intestinalis, Meckel's diverticulum, intraabdominal abscess, giant duodenal diverticulum, dilated intestinal loop, gastric dilatation, tuboovarian abscess, and mesenteric cyst.
- The treatment of choice is resection of the diverticulum and adjacent colon at time of diagnosis if the patient is symptomatic.

Diverticular Disease of the Transverse Colon

- This is an exceedingly rare condition. Clinical presentation most often mimics appendicitis, cholecystitis, or, less frequently, ischemic or Crohn's colitis.
- Treatment parallels that of sigmoid diverticulitis; however, resection is usually performed because a preoperative diagnosis is more difficult and a carcinoma frequently cannot be ruled out.

K. Treatment

Medical and Dietary Management

- The primary management of asymptomatic diverticular disease is diet. The goal of dietary manipulation is to increase the bulkiness of stool thus increasing lumen size, decreasing transit time, and decreasing intraluminal pressures. This decreases segmentation which has been described as a significant factor in the development of diverticular disease.
- The ideal amount of fiber is not known; however, the recommended daily amount is 20–30 g. In general, fiber can be obtained by consuming foods high in fiber or through supplementation with one or more of a large variety of bulk laxatives.
- Epidemiologic evidence strongly suggests a diet high in fiber can reduce the risk of developing diverticulosis. What is less clear is whether a high fiber diet can prevent diverticulitis and its complications in patients who already have diverticulosis. Recent evidence is building in support of this concept.

Acute Diverticulitis

- In the absence of systemic signs and symptoms (high fever, marked leukocytosis, tachycardia, and hypotension), most patients experiencing symptoms of diverticulitis will respond to a regimen of bowel rest and antibiotics as outpatients.
- Diet is usually restricted to low residue or clear liquids during the acute illness but with resolution of the acute symptoms, a high fiber diet should be instituted.
- There is no need to restrict the ingestion of seeds or hulls because there are no data to substantiate this practice.
- Appropriate antibiotics should be instituted to include coverage of Gram-negative and anaerobic bacteria. The most predominant

organisms cultured from acute diverticular abscess and peritonitis include the aerobic and facultative bacteria *Escherichia coli* and *Streptococcus* spp. The most frequently isolated anaerobes include *Bacteroides* spp. (*B. fragilis* group), *Peptostreptococcus*, *Clostridium*, and *Fusobacterium* spp.

- Signs of more advanced disease including marked leukocytosis, high fever, tachycardia, or hypotension as well as a physical examination demonstrating more advanced intraabdominal pathology, dictate a need for inpatient management.
- Patients admitted for inpatient care will usually undergo a baseline CT scan which can confirm the diagnosis, rule out potential alternative diagnoses, and evaluate for complicated disease that would require a change in initial management.
- Antibiotics should be administered via an intravenous route. Generally the patient will be placed NPO (nothing by mouth) until there is evidence that clinical progress is being made and surgery will not be necessary.
- The diet is then gradually advanced from clear liquids and then to low residue for a variable period of time before reinstituting a high fiber diet.
- Symptoms should improve within 24–72 h. Failure to improve should prompt further diagnostic workup including repeat CT scan and reevaluation of the need for alternative interventions such as operation or abscess drainage.
- Worsening of the patient's clinical condition, particularly progression to generalized peritonitis, should prompt urgent operative management.

Surgical Management

- The goal should always be to manage a complex patient in a way that will maximize the opportunity to avoid emergency surgery in favor of an elective resection.
- Surgical options include primary resection with anastomosis with or without proximal diversion, resection with proximal colostomy, and oversewing of the rectal remnant (Hartmann's procedure) or mucous fistula (Mikulicz operation), simple diversion with drainage of the affected segment, diversion with oversewing of the perforation site, and, rarely, subtotal colectomy. Adjunctive measures include on-table lavage and the option of a laparoscopic approach.

- For the most part, today's discussions revolve around the relative merits of a one-stage versus a two-stage approach in acute cases requiring urgent or emergent surgery. The three-stage approach is unlikely to be used except in the most extreme cases of medical instability.

Intraabdominal Abscess

- For a patient found to have an abscess, there is significant clinical evidence supporting the advantages of percutaneous drainage and the conversion of an emergent operation with its attendant increased morbidity and mortality to the relative safety of elective operation.
- An abscess not responding to medical management should be drained percutaneously or transrectally as appropriate to its location (Fig. 18.2).
- If drainage cannot be accomplished nonoperatively or if drainage is performed but fails to resolve systemic signs and symptoms, operation is indicated.
- Generally, the clinical scenario in this situation would be that of an advanced Hinchey class II. Although it is possible that intraoperative findings would support a resection with primary anastomosis with or without proximal diversion, it is more likely that a Hartmann's resection will be required.

Indications for Surgery for Acute Disease

- The indications for surgery of acute disease include:
 - failure to respond to nonoperative management including a persistent phlegmon, failure of percutaneous or transrectal drainage of an abscess or increasing fever, leukocytosis, tachycardia, hypotension, signs of sepsis, or a worsening physical examination;
 - free perforation with peritonitis;
 - obstruction that does not resolve with conservative therapy.
- Perforation without peritonitis may not require operation (Fig. 18.3).

Surgical Procedures

- For acute disease, the choice of operation is highly dependent on the degree of inflammatory response encountered at the time of operation. Because most acute disease can be managed

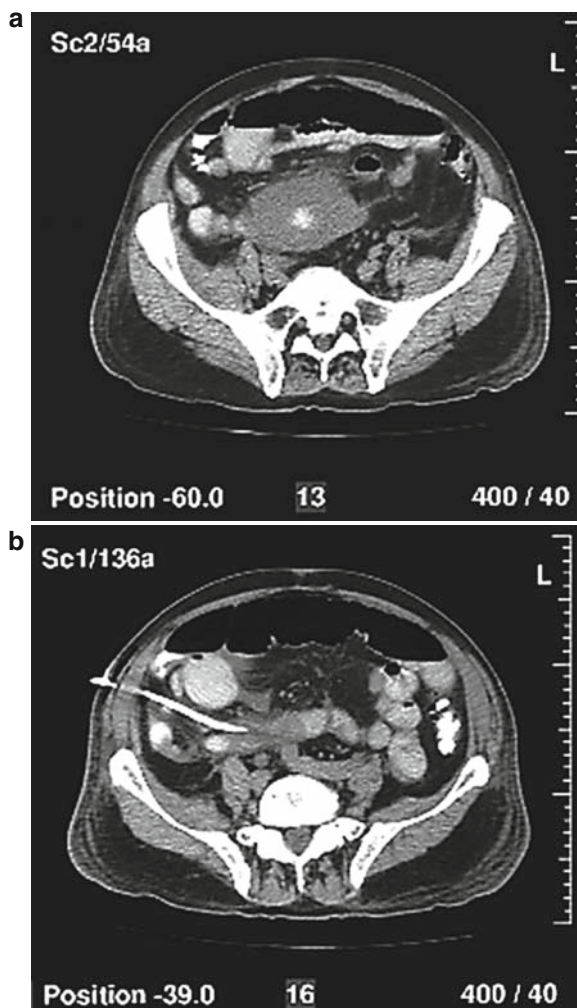


Fig. 18.2. (a) A centrally located pelvic diverticular abscess. (b) The same abscess after CT-guided percutaneous drainage.

nonoperatively (including the percutaneous drainage of most abscesses), the fact that an operation has become necessary suggests rather advanced pathology and the need to be conservative.

- *In general*, most Hinchey class I and some class II disease can be managed with a one-stage procedure (resection and

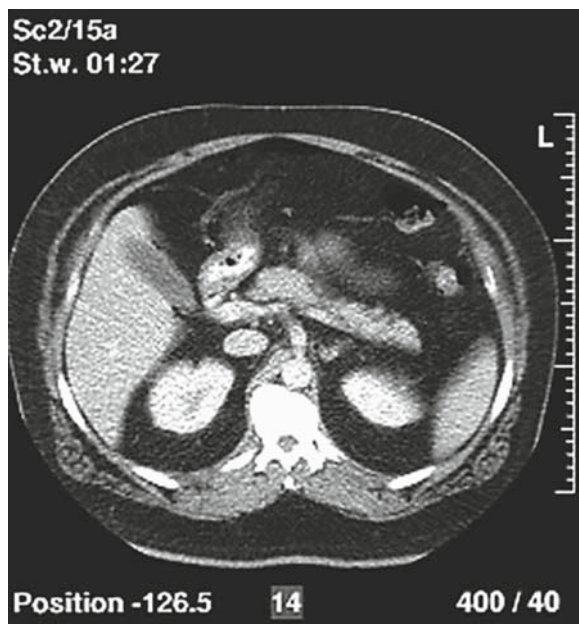


Fig. 18.3. This CT scan shows a small pneumoperitoneum anteriorly. There was not physical evidence of peritonitis. This patient was managed nonoperatively with intravenous antibiotics.

anastomosis) if the patient is stable, the extent of contamination is limited, and adequate bowel preparation is possible, recognizing, however, that the necessity of mechanical bowel preparation in elective colon resections has been recently questioned. Proximal diversion may be appropriate.

- Most cases of Hinchey class III and IV disease will require a two-stage approach.
- A major disadvantage of a two-stage procedure is that 35–45% of patients never have their colostomy closed. Women are more likely than men to not have closure.
- In patients with preexisting incontinence, a Hartman's pouch should be the procedure of choice.
- For patients who do not undergo closure of their stoma, it is critical that their rectal stump undergo scheduled surveillance for neoplasia as the remaining rectum has the same risk for neoplasia as the remainder of the colon.

Complications

- Predictors of complications from resection for diverticular disease include advanced age (older than 70–75 years), two or more comorbid conditions, obstipation at initial examination, the use of steroids, sepsis, obesity, and emergent rather than elective resection.
- Complications of resection include anastomotic leak and hemorrhage. The prevalence of leak from a low intraperitoneal anastomosis is generally considered to be between 2 and 5%. Such leaks can lead to localized or systemic sepsis without an abscess, an abscess with or without sepsis, peritonitis, and stricture.
- The diagnosis is dependent on a high index of suspicion on the part of the surgeon and quick response to any unusual signs of sepsis. Fever, vague abdominal pain, diarrhea, obstructive symptoms, oliguria, prolonged postoperative ileus, and sepsis all should raise the concern of a leak.
- The diagnosis is usually confirmed by water-soluble contrast enema and/or CT scan with intravenous, oral, and rectal contrast.
- A contained leak without an abscess can usually be managed with intravenous antibiotics and close observation.
- Free extravasation of contrast, failure to respond to treatment within 24–48 h, or initial severe sepsis or peritonitis requires exploration with resection of the anastomosis and proximal diversion.
- Repair of the anastomosis with proximal diversion is usually unsatisfactory because of the high risk for recurrent leak in this inflammatory setting.
- A leak that results in an abscess can generally be managed with percutaneous or transrectal drainage.
- A colocutaneous fistula related to a diverticular resection will usually respond to nonoperative measures. Provided that there is no distal obstruction or foreign body and that Crohn's was not the cause of the original symptoms, spontaneous closure should be anticipated.
 - Important steps to take to facilitate this closure include drainage of any undrained abscess, attention to nutritional needs, and appropriate wound care.
- Stricture is an unusual complication related to diverticular resections unless the underlying process is Crohn's disease.

In the rare instance when stricture does occur, the likely etiologies include ischemia or localized sepsis caused by confined leak. Such strictures can usually be managed by dilatation with a hydrostatic balloon or rigid proctoscopy but occasionally will require a formal restapling or resection.

- Ureteral injuries are reported to occur in 1–10% of abdominal surgeries. Early identification of any injury is the key to preventing significant morbidity.
 - Although ureteral stents have not been shown to decrease the rate of injury, they do improve intraoperative identification of the ureters and the early identification of any ureteral injury.
 - The decision to place ureteral stents before operation should be a function of clinical suspicion and the extent of retroperitoneal inflammation on CT scan.

Indications for Surgery for Recurring and Chronic Disease

- Patients with multiple, recurrent episodes of acute diverticulitis documented by CT scan should be considered for resection.
- Patients with complicated diverticulitis should be considered for resection after one attack.
- The ultimate goal is to perform an operation electively rather than as an emergency.
- It is now doubtful that age itself should be a primary consideration in the decision to operate. The literature is mixed with proponents of a more aggressive approach to the disease in young patients and those that believe age alone does not significantly increase risk.
- CT evidence of complicated or “severe” disease has been one of those criteria that have shown some promise in predicting risk. Abscess, extraluminal air, and extraluminal contrast have been associated with an increased risk of poor outcome from medical management regardless of age.
- Another approach is to identify specific groups of patients (other than age) who are at increased risk. Immunocompromised patients are one group that is at particular risk for poor outcome. The risk is attributable to a higher incidence of free perforation and more severe inflammatory complications when perforation does occur.
- Patients with autosomal dominant polycystic kidney disease undergoing renal transplant are a very high risk group.

Prophylactic resection in such patients with a history of any diverticulitis is recommended.

- Recent data have suggested that the recommendation for resection after two episodes of diverticulitis treated as an inpatient may result in too many patients undergoing resection thereby increasing the total cost of health care.
 - Performing resection after the third episode of diverticulitis results in significant cost savings.
 - Performing resection after four documented episodes rather than after two results in fewer deaths, fewer colostomies, and additional cost savings of more than \$5000 per patient in those younger than 50.
 - Others question the role of elective resection at all because of the high success rate of nonoperative management and the large percentage of patients presenting with urgent surgical disease that have no previous history of diverticulitis.

Surgical Procedures

- Patients undergoing resection for chronic disease will almost always be candidates for single-stage resection with primary anastomosis.
- Additionally, patients returning for closure of a colostomy after initial diversion and drainage, diversion with oversew of perforation, or diversion with resection via either Hartmann's or a Mikulicz procedure, can all typically be managed with one additional operation only.

Complications

- The complications related to operation for chronic disease in many ways parallel those already discussed for acute disease.
- In addition, a noted complication of operating on chronic disease is failure to achieve symptomatic relief. This usually results from a missed diagnosis of Crohn's disease or IBS. Any "recurrence" of symptoms after resection for chronic diverticulitis should raise the suspicion of this possibility.
- The presence of functional bowel symptoms preoperatively in this group of patients has been associated with poorer functional results postoperatively.

Management of Fistula

- The general principle of management is resection of the colon, usually with primary anastomosis.
- Treatment of the other involved organ/site varies:
 - For the bladder, simple drainage of the bladder with an indwelling urethral catheter for 5–7 days is advised.
 - No treatment of the vagina is required in most circumstances.
 - Cutaneous fistulas will usually close by delay or secondary intention.
 - Enteric fistulas require repair or resection of the involved small bowel or colon.
- If there is any question of cancer, an en bloc resection of a portion of the involved organ must accompany the resection.
- Occasionally nonoperative management is appropriate when symptoms are minor or when the patient is at otherwise too great a risk for other health reasons.
- The use of long-term suppressive antibiotic therapy in selected patients with colovesical fistula has been shown to eliminate symptoms and prevent complications related to the fistula until death from other causes.

Techniques for Appropriate Resection

- The practice parameters of the American Society of Colon and Rectal Surgeons set out several general recommendations regarding resection of diverticular disease. For elective resections, all thickened, diseased colon, but not necessarily the entire proximal diverticula-bearing colon, should be removed.
- All of the sigmoid colon should be removed. When anastomosis is elected, it should be made to normal rectum and must be free of tension and well vascularized.
- The single most important predictor of recurrence after sigmoid resection for uncomplicated diverticulitis is an anastomosis to the distal sigmoid colon rather than the rectum.

Laparoscopic Surgery

- Higher conversion rates are associated with more complex disease. Recurrence rates match those for open procedures, and length of stay is shorter and complications fewer. As data

continue to accumulate, it seems that laparoscopic surgery will have a significant role in the management of diverticular disease.

Appendix: Practice Parameters for the Treatment of Sigmoid Diverticulitis

Prepared by The Standards Task Force, The American Society of Colon and Rectal Surgeons.

The initial evaluation of a new patient with suspected acute diverticulitis should include a problem-specific history and physical examination; a complete blood count, urinalysis, and plain abdominal radiographs may be useful in selected clinical scenarios. Computerized tomography scan of the abdomen and pelvis is usually the most appropriate imaging modality in the assessment of suspected diverticulitis. Contrast enema x-ray, cystography, ultrasound, and endoscopy are sometimes useful in the initial evaluation of a patient with suspected acute diverticulitis.

Nonoperative treatment typically includes dietary modification and oral or intravenous antibiotics. Radiologically guided percutaneous drainage is usually the most appropriate treatment for patients with a large diverticular abscess.

After resolution of an initial episode of acute diverticulitis, the colon should be adequately evaluated to confirm the diagnosis. Colonoscopy or contrast enema x-ray (probably with flexible sigmoidoscopy) is appropriate to exclude other diagnoses, primarily cancer, ischemia, and inflammatory bowel disease.

Urgent sigmoid colectomy is required for patients with diffuse peritonitis or for those who fail nonoperative management of acute diverticulitis. The decision to recommend elective sigmoid colectomy after recovery from acute diverticulitis should be made on a case-by-case basis. Elective colon resection should typically be advised if an episode of complicated diverticulitis is treated nonoperatively. The resection should be carried proximally to compliant bowel and extend distally to the upper rectum. When a colectomy for diverticular disease is performed, a laparoscopic approach is appropriate in selected patients.

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19. Colonic Volvulus

A. Introduction/Historical Perspective

- Volvulus of the bowel refers to a twisting or torsion of the intestine about its mesentery.
- Volvulus of the colon usually occurs in the sigmoid or cecum, but may involve any segment of colon.
- In the United States, volvulus represents a rare cause of intestinal obstruction, encompassing less than 5% of large bowel obstructions. However, worldwide it is a much more common form of large bowel obstruction, representing more than 50% of the cases in some countries.
- With widespread use of flexible endoscopy, many authors have reported successful detorsion and decompression of all forms of colonic volvulus using the colonoscope or flexible sigmoidoscope. Because of high recurrence rates, these endoscopic methods are currently recommended as definitive treatment only for very high-risk individuals who are too ill to undergo surgery, and as a temporizing measure until eventual surgery under more controlled conditions for all other patients.
- The differential diagnosis of colonic volvulus encompasses any cause of colonic distention. This includes all of the mechanical as well as the nonobstructive causes.
 - Mechanical causes include colonic and extracolonic neoplasms, as well as benign entities such as diverticulitis and inflammatory bowel disease.
 - Nonobstructive causes include colonic pseudo-obstruction (Ogilvie's syndrome), and various intraabdominal processes that may result in an intestinal paralysis.

B. Cecal Volvulus

Incidence and Epidemiology

- Worldwide, cecal volvulus accounts for 40–60% of all colonic volvuli.
- It remains, however, an uncommon cause of intestinal obstruction.
- Most reported cases occur in younger individuals with a predilection for females.

Pathogenesis/Etiology

- True cecal volvulus is actually an axial torsion of the cecum, terminal ileum, and ascending colon about its mesentery (Fig. 19.1A).
- A variant, cecal bascule (Fig. 19.1B), occurs when the cecum folds anteriorly over the ascending colon without an axial twist. This represents approximately 10% of cases of cecal volvulus.
- There is a high rate of prior abdominal operations in patients who subsequently develop cecal volvulus, and previous surgery has been considered to be a potential causative factor.

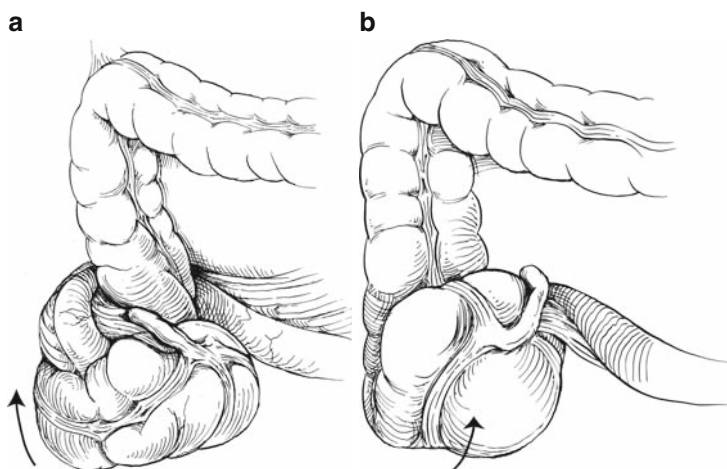


Fig. 19.1. (a) Schematic illustration of a cecal volvulus. (b) Schematic illustration of a cecal bascule.

- A clear prerequisite is a mobile cecum and ascending colon. A congenital component involves lack of fixation of the right colon, which then assumes an intraabdominal position.
- Prior abdominal surgery with colonic mobilization, recent surgical manipulation, adhesion formation, congenital bands, distal colonic obstruction, pregnancy, pelvic masses, extremes of exertion, and hyperperistalsis have all been implicated.
- During abdominal surgery, excessive mobilization or manipulation of the cecum and ascending colon or placement/withdrawal of packs may precipitate postoperative volvulus. Previous reports of cecal volvulus reveal that 30–70% of patients had undergone prior surgery.
- Displacement of the cecum by an enlarged uterus or pelvic mass may also promote volvulus. In fact, several series report that 10% of patients with cecal volvulus are pregnant at the time of presentation.

Clinical Presentation

- Symptoms and signs of cecal volvulus are that of small bowel obstruction. The majority of patients present with abdominal pain, distention, constipation, nausea, and vomiting.
- The presentation may be that of an acute obstruction or one of an intermittent or recurrent pattern.
- Acute volvulus results in a closed loop cecal obstruction and distal small bowel obstruction. This may progress to a more fulminant presentation when ischemia and gangrene develop.

Diagnosis

- The diagnosis is most often made on the basis of the combination of clinical presentation and plain abdominal films or barium enema.
- Plain films may identify the classic coffee bean deformity directed toward the left upper quadrant (Fig. 19.2A). Barium enema may reveal a “bird’s beak” or column cut-off sign in the right colon (Fig. 19.2B).
- Although barium enema is of clear value when the diagnosis is in question, in obvious cases, performance of this study may needlessly delay surgical therapy. It therefore should not be routinely used.

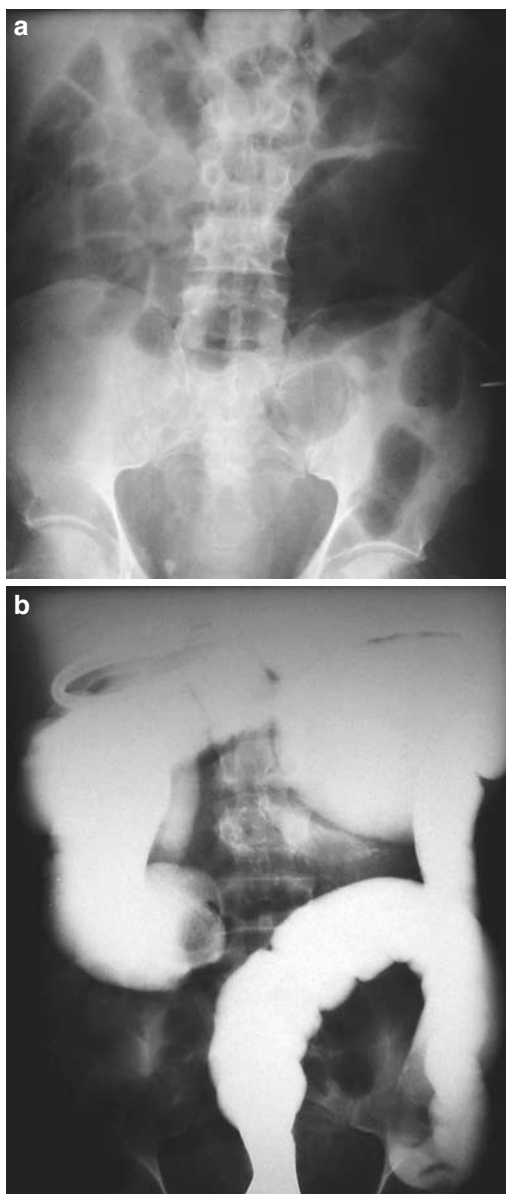


Fig. 19.2. (a) Plain abdominal X-ray of a cecal volvulus with a “coffee bean” deformity evident in the left upper quadrant. (b) Barium enema study of a cecal volvulus revealing a bird’s beak deformity.

Treatment/Outcome

- Laparotomy remains the primary treatment modality for cecal volvulus.
- Both radiographic and endoscopic reduction have been reported. Whereas radiographic attempts at reduction are generally believed to carry a high risk of perforation, other modalities have been used as temporizing measures.
- Although significantly less efficacious than in the treatment of distal volvulus, colonoscopic reduction of cecal volvulus has been reported with some success.
- The relatively high rates of ischemic changes found with cecal volvulus has tempered enthusiasm for non-operative detorsion.
- In general, the majority of individuals undergo surgical intervention with a clear diagnosis of cecal volvulus, for complete bowel obstruction, or for an acute surgical abdomen.
- When viable bowel is encountered, although resection is the preferred option, other alternatives exist. These include detorsion alone or combined with some fixation procedure. Fixation options include cecopexy and/or cecostomy. Appendicostomy has also been reported.
- Generally, fixation is accomplished by cecopexy and/or cecostomy. Cecopexy is performed by elevating a lateral peritoneal flap along the entire length of the ascending colon, and suturing the flap to the serosa of the anterior colonic wall, thereby placing the ascending colon in a partially retroperitoneal location, and eliminating the excess mobility (Fig. 19.3).
- An advantage of tube cecostomy is that it not only anchors the cecum, but also provides a vent for the distended colon.
- Cecopexy, and cecostomy all carry similar recurrence rates of 12–14%
- Resection, however, carries virtually no risk of recurrence and is not associated with a higher rate of postoperative complications when compared with cecopexy alone.
- After resection, primary anastomosis can usually be safely performed. However, in the face of gangrenous bowel, end ileostomy may be a safer procedure.

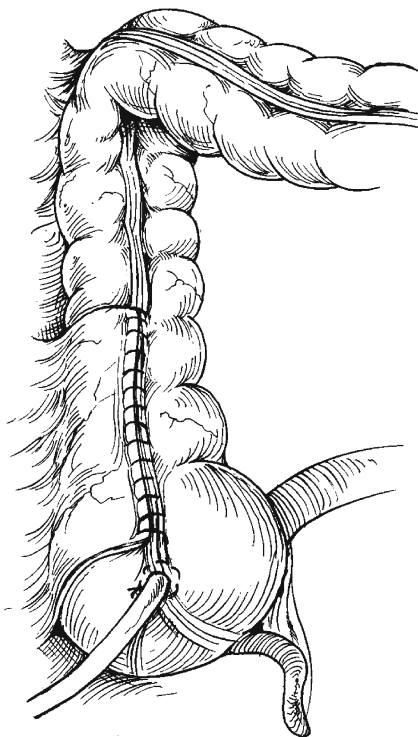


Fig. 19.3. Colopexy and cecostomy for cecal volvulus.

C. Transverse Colon Volvulus

Incidence and Epidemiology

- Volvulus of the transverse colon is an exceptionally rare finding. It is estimated to represent from 1 to 4% of all forms of colonic volvulus
- This form of volvulus tends to occur more often in the young, with most series showing a peak incidence in the second through fourth decades of life. There is a twofold to threefold female predominance.

Pathogenesis/Etiology

- Although anatomic factors are key to the development of transverse colon volvulus, physiologic, rather than congenital,

factors seem to have a crucial role in the development. These patients frequently have a history of chronic constipation and/or laxative abuse, previous abdominal surgery, a diet high in fiber, recurrent distal obstruction, and institutionalization.

- Specific factors that may increase the risk of occurrence are a redundant or elongated transverse colon with narrow mesenteric attachments, narrowed distance between the flexures, and an absence or paucity of fixation of the mesentery.

Clinical Presentation

- Transverse colon volvulus presents as a large bowel obstruction.
- Presentation may be as a subacute recurring process or may take a more fulminant course.
- The diagnosis is therefore usually made at the time of exploration.
- Plain films may reveal a distended proximal colon with decompressed distal bowel and two distinct air-fluid levels representing two limbs of the volvulized transverse colon. This has been described as a bent inner-tube appearance with the apex pointing inferiorly.
- Barium contrast studies, if performed, will demonstrate a bird's beak deformity at the distal transverse colon.

Treatment/Outcome

- Although successful endoscopic decompression has been reported, surgical intervention is the recommended treatment modality.
- Based on literature from surgical detorsion, it is assumed that endoscopic treatment will lead to a high rate of recurrence, and may therefore be best reserved for those high-risk individuals who show no signs of compromised bowel. However, colonoscopy may serve to confirm intestinal viability and allow for a less emergent definitive procedure to be performed.
- Operative procedures include detorsion with or without colopexy, and resection.
- Most authors recommend either segmental transverse colectomy or extended right colectomy as definitive treatment.

- Clearly, in the presence of nonviable bowel, resection is mandatory.
- As in cecal volvulus, the decision regarding primary anastomosis versus diversion is made during surgery, taking into account the severity of the disease process and the patient's overall condition.
- When viable bowel is encountered, several different colopexy procedures have been reported. These include suture of the greater omentum, transverse mesocolon, or transverse colon itself to the anterior abdominal wall and/or pelvis, and the U colopexy reported by Mortensen. In this procedure, after reduction and needle decompression of the volvulus, the redundant U-shaped loop of transverse colon is sutured to the adjacent limbs of ascending and descending colon (Fig. 19.4).
- Recurrence from either detorsion or colopexy has been reported to range from 30 to 75%, whereas resection eliminates virtually all risk of recurrence. Mortality, however, from resection has been reported to be as high as 33%.

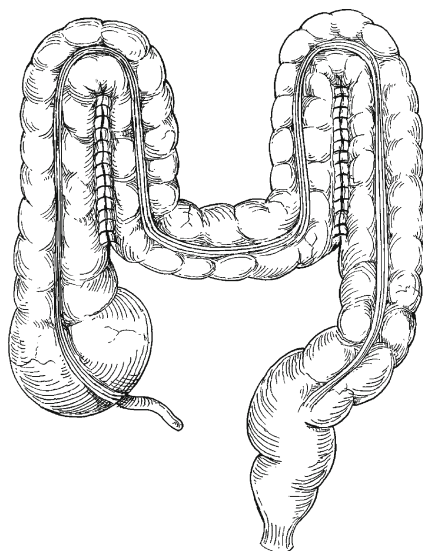


Fig. 19.4. Parallel coloplasty as described by Mortensen.³¹

D. Splenic Flexure Volvulus

Incidence and Epidemiology

- Volvulus of the splenic flexure of the colon is the rarest form of colonic volvulus. It is estimated to represent 1–2% of all cases of colonic volvulus.

Pathogenesis/Etiology

- The infrequency of this form of volvulus is believed to be the result of multiple attachments of the splenic flexure, and the retroperitoneal position of the descending colon.
- Up to two-thirds of patients have had prior abdominal surgery.

Clinical Presentation

- As in transverse colon volvulus, the presentation may be acute and fulminant, or a more chronic or subacute event.
- Four features have been described radiographically that may suggest splenic flexure volvulus:
 - A markedly dilated air-filled colon with an abrupt termination at the splenic flexure;
 - Two widely spaced air-fluid levels, one in the cecum and the other in the transverse colon;
 - An empty descending and sigmoid colon;
 - A bird's beak obstruction at the splenic flexure on contrast enema examination (Fig. 19.5).

Treatment/Outcome

- Although colonoscopic and fluoroscopic decompression have been reported, most reports have identified surgery as the primary mode of management.
- However, the recurrence rate after detorsion alone, whether performed surgically, endoscopically, or fluoroscopically, is approximately 20–25%.
- As a result of these high recurrence rates, nonoperative decompression/detorsion should be reserved for extremely high-risk patients who are not candidates for surgical intervention, or as a temporizing measure before a semi-elective definitive resection.



Fig. 19.5. Barium enema study of a chronic splenic flexure volvulus. Arrows indicate the point of rotation and bird's beak deformity.

- Surgical options include resection with or without stoma formation, or detorsion with or without colopexy.
- Segmental resection may be considered; however, the majority of these patients will have an associated redundant, dilated colon and a history of chronic constipation. Therefore, these patients may be better served by undergoing an extended resection with an ileosigmoid or ileorectal anastomosis.
- Stomas should be reserved for cases involving gangrenous bowel with perforation and peritoneal contamination, or for other high-risk cases.

E. Sigmoid Volvulus

Incidence and Epidemiology

- Although it is the most common form of volvulus seen, volvulus of the sigmoid colon is not very common in the United States and Western Europe, accounting for less than 10% of all cases of large bowel obstruction.
- In some regions of Asia, Africa, and other less-developed portions of the world, however, the situation is significantly different.

In these areas, sigmoid volvulus accounts for 20–50% of all the cases of intestinal obstruction.

- Overall, there is a substantial male predominance, especially in developing nations. However, sigmoid volvulus is the most common cause of intestinal obstruction in pregnancy, accounting for nearly 45% of all intestinal obstructions in this group of women.
- The reasons for geographic differences in incidence are thought to be primarily related to diet. In the West, relatively lower amounts of fiber are consumed, resulting in a much higher incidence of colorectal cancer and diverticular disease, which are the more common etiologies for colonic obstruction in these areas.

Pathogenesis/Etiology

- Any condition that results in an elongated colon predisposes to the development of volvulus. In order for volvulus of any part of the intestinal tract to occur, there must be a long redundant, mobile segment, with a relatively narrow mesenteric attachment, such that the sites of fixation at each end are relatively close together.
- The sigmoid colon is the ideal location for this configuration: the sigmoid can be extremely redundant and mobile and the sites of fixation at the descending-sigmoid junction and the rectosigmoid junction are often in close proximity to each other.
- In the West, the typical patient with sigmoid volvulus is an elderly institutionalized male, often receiving psychotropic medications, who is usually extremely constipated. Other factors that have been implicated are laxative abuse, previous abdominal surgery, and diabetes.
- Gross features of the sigmoid colon include progressive widening and eventual loss of taenia coli, absence of appendices epiploicae, and a thickened narrowed fibrous mesentery.
- The rotation may be either clockwise or counterclockwise. Once the rotation has reached 360 degrees, a closed loop obstruction occurs.
- Hyperperistalsis and fluid secretion into the closed loop add to increased pressure and tension. Eventually, as blood flow is compromised, ischemia and necrosis develop.
- In the face of a competent ileocecal valve, perforation is more common in the cecum.

Clinical Presentation

- As previously described, the patient is typically a male nursing home resident, on psychotropic medications, with a history of chronic constipation. These patients may not complain of pain, but rather a caregiver notices an extremely long interval between bowel movements, associated with significant abdominal distension.
- It has been reported that 40–60% of patients will give a history of having had similar episodes.
- On presentation, the distension is often dramatic. Unlike the patient with fecal impaction, the rectal ampulla is empty.
- Plain abdominal films typically show massive colonic distension, with or without small bowel dilatation (depending on the competence of the ileocecal valve). The very large sigmoid loop will be orientated toward the right upper quadrant. The adjacent walls of the sigmoid will appear to be thickened, arising out of the left lower quadrant, giving the classical “bent inner tube” sign (Fig. 19.6A).
- Plain abdominal X-rays alone are diagnostic in 60–75% of cases. However, the massive distension may, occasionally, make the diagnosis difficult to establish with certainty. In those cases, a contrast enema should be obtained. This study will show the obstruction at the rectosigmoid junction, with the classical bird’s beak configuration (Fig. 19.6B).
- The addition of barium enema to the plain abdominal X-rays may increase the diagnostic yield to near 100%.
- The major diagnosis from which sigmoid volvulus must be distinguished is colonic obstruction caused by neoplasm.
 - Usually the abdominal X-rays can distinguish one from the other; however, in the presence of truly massive distension, differentiation may be difficult.
 - At the time of attempted sigmoidoscopic detorsion, the obstructing neoplasm will hopefully be visualized and the true diagnosis will be apparent.
- The other condition that may cause clinical confusion is colonic megacolon associated with abnormal colonic motility. This condition also presents in elderly, constipated nursing home patients. The X-rays can look remarkably similar. Because rectal tube decompression will generally rapidly and successfully relieve the distension associated with this form of megacolon, distinction from volvulus can be difficult.

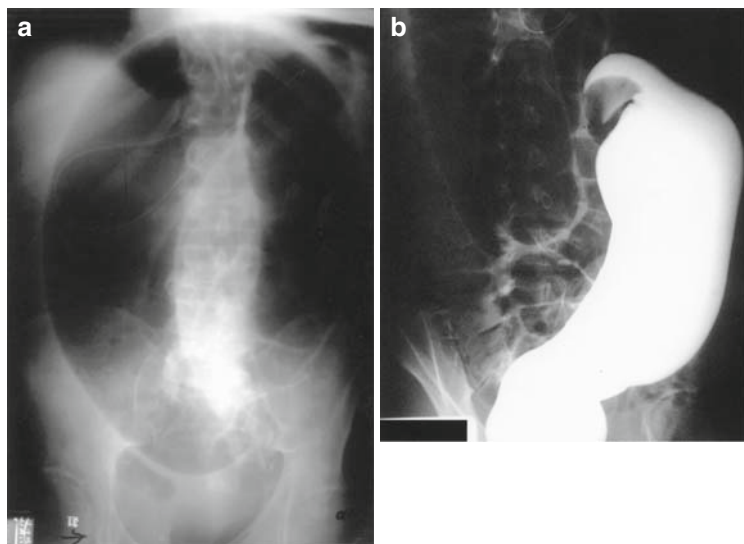


Fig. 19.6. (a) Plain abdominal X-ray of a sigmoid volvulus indicating the “bent inner tube” sign. (b) Barium enema study of a sigmoid volvulus indicating the bird’s beak deformity and complete obstruction to retrograde flow of contrast.

Treatment/Outcome

- The patient with sigmoid colon volvulus should be hydrated and resuscitated.
- The mainstay of emergency therapy has generally been detorsion and decompression.
- Detorsion of sigmoid volvulus has been described using several techniques, including rigid proctoscopy, flexible sigmoidoscopy or colonoscopy, blind passage of a rectal tube, and use of a column of barium during barium enema examination. Successful decompression using one of these techniques is generally reported in the range of 70–80%.
- A significant concern is that the sigmoid may already be gangrenous.
- If ischemic mucosa is visualized, attempts at detorsion should be immediately abandoned and operative intervention should be undertaken emergently.
- For this reason, the authors strongly recommend using only those detorsion techniques that visualize the mucosa before

detorsion. Attempts at detorsion via blind passage of a rectal tube should be avoided.

- The major complication associated with attempted detorsion is inadvertent perforation. This is more likely in the presence of gangrene, but can occur with viable bowel as well.
- Once decompression has been accomplished, there is usually forceful evacuation of flatus and stool (frequently all over the clothes and shoes of an unsuspecting novice) and visible deflation of the patient's abdominal distension.
- A rectal tube should then be gently inserted into the colon to a point proximal to the site of the twist (which is usually within 20 cm of the anus). The tube should then be fixed in place, to allow continued decompression and prevention of recurrence.
- A plain abdominal film should be obtained to document decompression and the patient should be admitted to the hospital.
- Successful detorsion provides the advantage of converting a surgical emergency to an elective situation.
- Over the next several days, bowel function is likely to return to normal. Medical conditions (cardiac, pulmonary, renal, etc.) should be addressed, electrolyte abnormalities should be corrected, and the patient's condition optimized.
- Colonoscopy, to rule out a proximal lesion, should be performed, and then a decision must be made. The rectal tube can be safely removed and the patient could be discharged from the hospital; however, it is well established that the rate of recurrent sigmoid volvulus is in excess of 25%. In fact, most authors document a recurrence rate of greater than 50%, and some report recurrences as high as 80–90%.
- The standard elective surgical procedure is sigmoid resection with primary anastomosis; however, a number of nonresective techniques have been described, including nonsurgical endoscopic sigmoidopexy with or without tube fixation, extraperitoneal sigmoidopexy, sigmoidopexy to the transverse colon and/or the parietes, mesosigmoidoplasty, colopexy with banding, mesenteric fixation, and laparoscopic fixation.
- Although several authors have reported excellent results using pexy without resection, others have reported recurrence rates in excess of 25%.

- The technique of mesosigmoidoplasty deserves discussion. This procedure is performed by incising the elongated sigmoid mesentery vertically along its axis. Peritoneal flaps are then created which are then approximated transversely (Fig. 19.7).
 - This procedure thereby creates a shortened, broad mesentery precluding future bowel rotation.
 - Although one author has reported a recurrence of 28%, most report recurrences of less than 2%. Mortality ranges from 0 to 7%.
- Resection with anastomosis, therefore, should currently be considered the standard of care for elective cases. However, in circumstances in which continence is an issue, an end stoma may be a better alternative.
- Laparoscopic techniques have also been applied, but in general, because the redundant distended colon obscures the working space and the incision required to deliver the specimen is also large enough to exteriorize the redundant sigmoid colon and

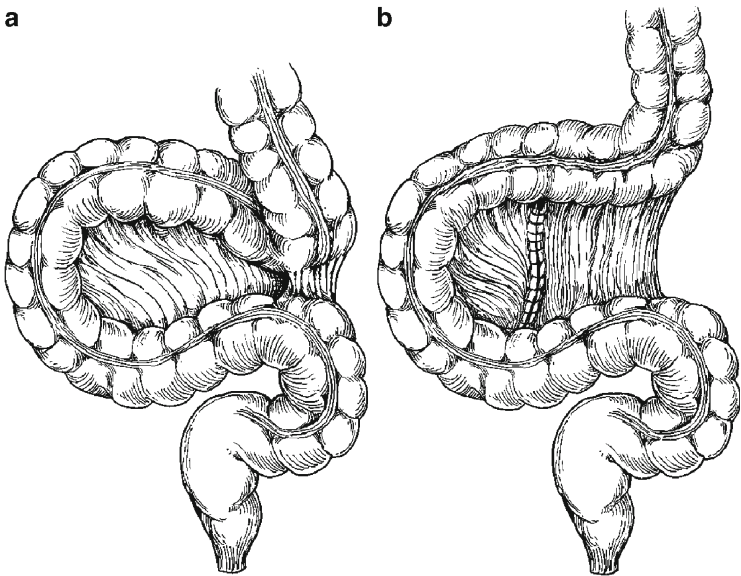


Fig. 19.7. Mesosigmoidoplasty. (a) A longitudinal peritoneal incision is made in the elongated, narrow mesentery. (b) The incision is then closed transversely, broadening the mesenteric base and shortening the height of the sigmoid loop.

perform an adequate resection and anastomosis, there is little to be gained by the use of laparoscopy.

- If decompression is not possible, if the patient has signs and symptoms of peritonitis or colonic ischemia, or if gangrenous mucosa is visualized during attempted decompression, the situation becomes a surgical emergency.
- The volvulus should be manually reduced if the bowel is viable, and the redundant, twisted sigmoid should be resected. However, when gangrenous bowel is encountered during laparotomy, detorsion should not be performed. Accumulated toxins and bacteria may be released into the circulation, resulting in sepsis and cardiovascular collapse.
- Generally, an anastomosis should be avoided if the proximal colon is massively dilated and loaded with feces.
- A single prospective, randomized trial comparing primary anastomosis to the Hartmann's procedure in 14 patients with gangrenous bowel, revealed a 50% anastomotic leak rate. In addition, mortality was more than double in those patients in whom an anastomosis was performed (33 vs. 13%).
- Overall mortality rates for the treatment of sigmoid volvulus range from 14 to 45%.
- Elective surgery, after detorsion, is currently associated with mortality rates below 10%, despite the fact that these are generally patients with multiple comorbidities.
- Finally, operative detorsion with or without pexy carries a similar mortality to elective resection and anastomosis (8–14%). Therefore, one must consider the overall risk of recurrence as well as the risk of mortality.
- As expected, any nonresectional procedure carries a substantial risk of recurrence. For decompression alone it ranges from 25 to 70%, whereas detorsion, with or without pexy, has been associated with recurrence rates of 23–40%.
- Most authors indicate that the risk of recurrence after resection approaches zero.
- The only prospective randomized trial comparing elective resection and primary anastomosis with mesosigmoidoplasty confirms these findings. None of the resected patients and 29% of the plastied patients experienced recurrence. However, there was no mortality in the plasty group as compared with 10% in the resection group.

F. Ileosigmoid Knotting

Incidence and Epidemiology

- Ileosigmoid knotting, also called compound volvulus, is a rare form of volvulus in the West. It is, however, comparatively more common in certain areas of Africa, Asia, and the Middle East. In particular, large series are reported from Turkey, Russia, Scandinavia, Uganda, and India.
- The geographic distribution corresponds with regions of the world where diets high in bulk and carbohydrates are consumed with large volumes of liquid. The incidence is highest in groups in which one single large meal is consumed daily.

Pathogenesis/Etiology

- Theories of the pathogenesis of ileosigmoid knotting focus on a large volume diet high in bulk and carbohydrates, associated with large volumes of concomitant liquid ingestion. This may lead to an elongated abnormally mobile small intestinal mesentery, in addition to a long narrow pedicled sigmoid mesentery (Fig. 19.8).

Clinical Presentation

- The presentation of ileosigmoid knotting is one of acute onset, often with a fulminant course.
- At surgery, gangrenous intestine is found in 70–100% of cases.
- Clinically, the patient's condition presents as a small bowel obstruction, but radiographic evaluation is more consistent with a large intestinal obstruction.

Treatment/Outcome

- Because of the high incidence of ischemia and gangrene at the time of presentation, after an initial period of rapid resuscitation and antibiotic administration, patients should be taken for emergent abdominal exploration.

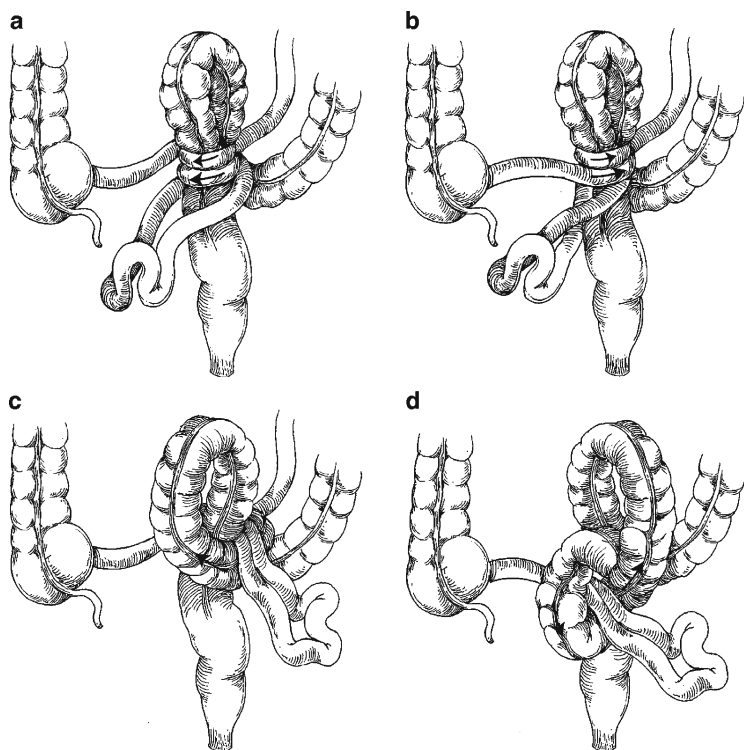


Fig. 19.8 Ileosigmoid knotting: these schematic illustrations indicate the four forms of knotting. The active ileum may rotate around the sigmoid colon in either a clockwise (a) or counterclockwise (b) direction. Much more infrequently, the sigmoid colon may act as the active loop and rotate in either a clockwise (c) or counterclockwise (d) direction around the ileum.

- Because of the high likelihood of gangrenous bowel, most authors advocate en bloc resection of both segments of intestine without attempts to untwist the bowel.
- Although most perform a primary ileoileal or ileocolic anastomosis in patients with gangrenous small bowel, a Hartmann's procedure is usually performed when the sigmoid is found to be nonviable.
- Overall surgical mortality generally ranges from 30 to 50%.

20. Lower Gastrointestinal Hemorrhage

A. Introduction

- Lower gastrointestinal hemorrhage refers to a spectrum of intestinal bleeding that arises distal to the ligament of Treitz. It may range from occult bleeding or occasional spotting of blood to massive lower intestinal hemorrhage.
- True massive intestinal hemorrhage typically involves hemodynamic compromise or acute symptomatic anemia.
- Multiple sources define massive bleeding to include patients with an acute drop in their hematocrit to less than 30%, patients with transfusion requirements (up to 3–5 units of blood/blood products), or orthostasis requiring resuscitation.
- Melena typically suggests bleeding from a more proximal source in the colon or small intestine.
- Hematochezia suggests left colonic, rectal, or anal sources.
- Overall, it is believed that upper sources may present with lower gastrointestinal bleeding symptoms in 10–15% of cases.
- Most often the intestinal bleeding resolves spontaneously often while undergoing supportive hospital care.
- In clinical scenarios in which the bleeding resolved spontaneously, the diagnostic evaluation may only unmask potential sources. Without associated attached clot or active bleeding, the true site of hemorrhage may never be elucidated.
- Current treatment regimens incorporate remediating the impact of long-term anticoagulants and antiplatelet agents for underlying cardiovascular conditions. Hemorrhage in these patients proves more life-threatening.

B. Etiologies

- Common causes for lower gastrointestinal hemorrhage include colonic diverticula, angiodysplasia, ischemic colitis, and inflammatory bowel disease. Hemorrhage may also stem from intestinal tumors or malignancies.
- Unusual causes include nonsteroidal antiinflammatory drug (NSAID)-related nonspecific colitis, Meckel's diverticulum, and anorectal diseases.

Diverticular Disease

- The precise mechanism of diverticular hemorrhage is unknown.
- It is generally accepted that thinning of the media in the vasa recta predisposes to intraluminal rupture: focal injury may occur from trauma related to a fecalith.
- It is unclear how frequently diverticula are the true cause of hemorrhage.
- Diagnostic evaluations, such as colonoscopy, often do not identify a precise source for the hemorrhage without the presence of witnessed bleeding or an adherent clot.
- Despite being considered a major source for colonic hemorrhage, bleeding from diverticula is a relatively rare event affecting only 4–17% of patients with diverticulosis.
- In most cases, bleeding ceases spontaneously, but in 10–20% of cases, the bleeding continues unabated in the absence of intervention.
- The risk of rebleeding after an episode of bleeding is approximately 25% but increases to 50% among patients who have had two or more prior episodes of diverticular bleeding.
- Right sided colonic diverticula occur less frequently than left sided or sigmoid diverticula but are thought to be responsible for a disproportionate incidence of diverticular bleeding. This finding is not well established, however, and there is often difficulty distinguishing between bleeding from an arteriovenous malformation or angiodysplasias and bleeding from diverticulosis.
- Operative management of diverticular bleeding is indicated when bleeding continues unabated and is not amenable to angiographic or endoscopic therapy.

- It also should be considered in patients with recurrent bleeding localized to the same colonic segment.
- In a stable healthy patient, the operation consists of a segmental bowel resection (usually a right colectomy or sigmoid colectomy) followed by a primary anastomosis.

Angiodysplasia

- Angiodysplasias are thin-walled arteriovenous communications located within the submucosa and mucosa of the intestine.
- Angiodysplasias may be congenital or, more typically, acquired.
- In the acquired form, distortions of the postcapillary venules may arise as a degenerative lesion associated with increases in intraluminal pressure. The intraluminal pressure occurs from loss of the precapillary sphincter and a resultant increased pressure transmitted through the capillary bed into the venules. As these vessels respond to the arterial flow, it results in thickening and ectasia. The vessels eventually entangle as tufts within the submucosa and erode into the mucosa proper.
- No one is quite certain precisely why angiodysplasias occur. Current hypotheses suggest a loss of vascular integrity related to loss of transforming growth factor (TGF) β signaling cascade or from a deficiency in mucosal type IV collagen.
- Angiodysplasias are uncommon before age 60, increase with age, and are associated with aortic stenosis (Heyde's syndrome), chronic renal failure, and von Willebrand's disease.
- Osler-Weber-Rendu (hereditary hemorrhagic telangiectasias) is a hereditary condition with telangiectasias of the lung, nervous system, skin, and intestine.
- When angiodysplasias are noted during angiography or colonoscopy, unless a hemorrhagic blush is seen during the angiogram or colonoscopy, it is difficult to accurately accuse this malady as the source of hemorrhage.
- Angiography remains the gold standard for the diagnosis of angiodysplasia.
- In the arterial phase, the radiographic findings of angiodysplasia demonstrate early venous filling which normally occurs in later phases.
- When angiography identifies a bleeding angiodysplasia, treatment with embolization therapy or directed infusion of vasopressin will decrease or stop the bleeding.

- Colonoscopy has increased as a screening agent for colorectal cancers as well as a diagnostic or therapeutic means for the investigation for colorectal bleeding. The following characteristics of angiodysplasia may be noted:
 - Angiodysplasias appear on the mucosal surface as a cherry red lesion that is typically flat. The lesions are greater than 2 mm in size and have a “fern-like” appearance.
 - It is important to identify angiodysplasias during scope insertion. Occasionally, the inexperienced endoscopists may attribute colonoscopic suction trauma to an angiodysplastic area.
 - Since colonoscopy has become more frequent, both left and right sided lesions are found to occur.

Other Causes of Lower Gastrointestinal Hemorrhage

- Most of the other etiologies that cause lower gastrointestinal bleeding (Colonic ischemia, inflammatory bowel disease, and colonic malignancies) are not associated with massive hemorrhage or acute symptomatic anemia.
- Typically, ischemic colitis presents with the abrupt onset of abdominal pain, followed by colic and a mucoid, bloody diarrhea.
- Inflammatory bowel disease, Crohn's, and ulcerative colitis present with a change in stool patterns. Patients develop diarrhea followed by hematochezia or melena.
- Colorectal carcinomas are associated with exophytic, ulcerative lesions that may bleed insidiously. Only rarely does the malignant process proceed to acute, symptomatic hemorrhage.
- Gastrointestinal stromal tumors (GIST) involve the small intestine. As these lesions enlarge, they surpass their blood supply, become ischemic, ulcerate and bleed.
- Meckel's diverticulum occur in the distal ileum. Ectopic gastric mucosa produces which ulcerates the adjacent intestinal wall.
- NSAIDs can cause a localized mucosal injury which frequently bleeds
 - The terminal ileum and cecum may serve as a reservoir and harbor these agents long enough to establish the mucosal defects.
 - Diaphragm-like strictures are pathognomonic for NSAID injuries and may result from a healing ridge related to repeated injuries from the agents.

Occult Hemorrhage

- One study noted occult bleeding in no more than 5% of all patients admitted with lower gastrointestinal massive hemorrhage.
- These patients may harbor angiodysplasias in the small intestine or right colon.
- Patients in this situation may benefit from small bowel contrast radiography or capsule endoscopy.
- Additionally, selective angiography with cecal magnification may reveal small angiodysplasias.

C. Initial Assessment, Resuscitation, and Stabilization

- Initial placement of large bore vascular access is followed by administration of intravenous fluids.
- Further hemodynamic monitoring requires cardiac rhythm monitoring and placement of a urinary catheter.
- A nasogastric tube screens for the presence of upper gastrointestinal sources for bleeding.
- Kovacs and Jensen noted 17.9% of lower gastrointestinal hemorrhage presentations involved an upper gastrointestinal source.
- The treatment goals for resuscitation are to restore volume and, replete red blood cell deficiencies for their impact on oxygen delivery.
- In addition, all coagulopathies require reversal. Patients require laboratory profiles that include a complete blood count, serum electrolytes, a coagulation profile, and a type and hold for packed red blood cells. (Crossmatch for patients with massive hemorrhage)
- The initial specific diagnostic evaluation begins with a digital anorectal examination and anoscopy. A rigid proctosigmoidoscopy will allow the examiner to evacuate the rectum of blood and clots.
 - A complete mucosal assessment serves to exclude internal hemorrhoids, anorectal solitary ulcers, neoplasms, and colitis.

- If subsequent surgery becomes necessary, this evaluation of the rectum and anorectal function greatly aids in surgical decisions. A normal anorectal examination also allows the surgeon to consider a primary rectal anastomosis as a treatment possibility.
 - Identifying an anorectal source of bleeding during this examination, often times permits therapy to control the hemorrhage.
- Once the resuscitation demonstrates a stable patient, the next phase of the diagnostic evaluation ensues.
- Colonoscopy and angiography offer diagnostic and therapeutic intervention whereas nuclear scanning is purely diagnostic.
- Decisions as to which test to use depend on the clinical judgment, local expertise, severity of the event, and the current activity of the hemorrhage.
- It may be helpful to subdivide patients into three general clinical categories based on the history, physical, and the initial laboratory data. Is the hemorrhagic event (1) minor and self-limited, (2) major and self-limited, or (3) major and ongoing?
 - Major ongoing hemorrhage requires prompt intervention with angiography or surgery.
 - Minor, self-limited may undergo a colonic lavage and colonoscopy within 24 h.
 - Major, self-limited hemorrhage is more controversial. These patients need a diagnostic test to determine if they require prompt therapy or observation.
- Radionuclide imaging
 - Radionuclide imaging (Fig. 20.1) detects the slowest bleeding rates. It is able to detect rates of 0.1–0.5 mL/min, making more sensitive than angiography.
 - Unfortunately, the nuclear scanning cannot reliably localize the site of hemorrhage
 - The more frequently preferred agent for lower gastrointestinal hemorrhage radionuclide scanning is the pertechnetate-tagged RBC scans. The tagged RBC scans may cover a period of hours and allow for reimaging within 24 h.
 - Current reports suggest accuracies ranging from 24 to 91%.
 - If the nuclear scan demonstrates an immediately positive blush (within the first 2 min of scanning), it is highly predictive of a positive angiogram (60%).

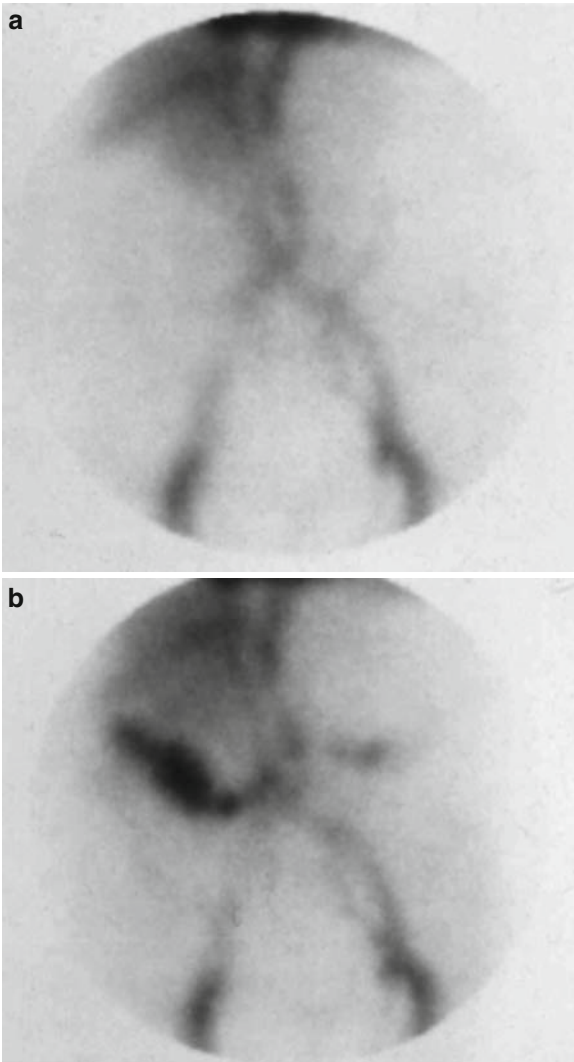


Fig. 20.1. Selected images from a ^{99m}Tc -labeled RBC gastrointestinal bleeding study in a patient with known diureticulosis. Images acquired at 1 min (**a**) and 14 min (**b**). Abnormal increased isotopic activity developed in the proximal transverse colon, which progressed antegrade to the descending colon.

- If the initial images do not demonstrate a blush, the study is highly predictive of a negative angiogram (93%) and the need for surgery is decreased to 7%.

- Thus, if the nuclear scan is negative, it provides objective evidence that the patient is not actively bleeding and may be evaluated by colonoscopy

Colonoscopy

- Many authors believe that colonoscopy has clearly demonstrated the highest efficacy and should be the first study in patients with major bleeding that appears self-limited.
- Whether colonoscopy should be undertaken emergently depends on the general ability to maintain a stable patient.
- Patients with extremely brisk hemorrhage require a prompt angiogram. Colonoscopy in such patients proves difficult to prep with lavage and the acute exsanguination may limit intraluminal visualization to deploy all the therapeutic options except for the most experienced endoscopists.
- If the patient appears stable with self-limited hemorrhage, colonoscopy is the preferred diagnostic study.
- Longstreth reported that 80.8% of their patients had colonoscopy after electrolyte-polyethylene glycol solution purge, usually within 24 h of admission.
- The Longstreth Kaiser Permanente study demonstrated a broad scope of etiologies (see Table 20.1).
- Once the endoscopist highlights a bleeding source, the region of the intestine should be tattooed to mark the site with India ink. In such patients, if the hemorrhage continues and fails

Table 20.1. Final diagnosis in patients hospitalized for acute lower gastrointestinal hemorrhage.

	n (%)
Colonic diverticulosis	91 (41.6)
Colorectal malignancy	20 (9.1)
Ischemic colitis	19 (8.7)
Acute colitis, unknown cause	11 (5.0)
Hemorrhoids	10 (4.6)
Postpolypectomy hemorrhage	9 (4.1)
Colonic angiodysplasia	6 (2.7)
Crohn's disease	5 (2.3)
Other	22 (10.1)
Unknown	26 (11.9)
Total	219 (100)

medical management, the tattoo greatly assists the surgeon in localizing the hemorrhage.

- Therapeutic endoscopic options include thermal agents such as heater probes, bipolar coagulation, and laser therapy. Injection therapy primarily uses topical and intramucosal epinephrine. Mechanical therapy includes endoscopically applied clips and detachable snares.

Angiography

- Angiography is diagnostic and therapeutic in the treatment of intestinal hemorrhage.
- Angiography is helpful in three different types of hemorrhage. First, acute, major hemorrhage with ongoing bleeding requires emergency angiography. Second, patients with an early blush during nuclear scintigraphy may benefit from therapeutic angiography. Finally, angiograms may define a potential source for hemorrhage in occult and recurrent gastrointestinal hemorrhage.
- To appreciate an angiographic blush of contrast, the study requires a hemorrhage rate of at least 1 mL/min.
- Generally, reports demonstrate yields that range from 40 to 78%.
- Angiography provides highly accurate localization of the site of bleeding (Fig. 20.2) and the angiographic blush may suggest a specific etiology, but it lacks the accuracy of colonoscopy.
- In therapeutic angiography hemorrhagic site may receive highly selective, intraarterial vasopressin infusion.
- Vasopressin controls bleeding in as many as 91% of patients. However, bleeding may recur in as many as 50% of patients once the vasopressin is tapered.
- Angiographic technology also allows for arterial embolization to control hemorrhage. Superselective mesenteric angiography with microcatheters allows for embolization of the vasa recta of the intestine, vessels as small as 1 mm.
- Embolization therapy provides immediate arrest of the bleeding. Embolization uses a combination of agents to control bleeding including Gelfoam pledgets, coils, and polyvinyl alcohol particles.
- Data suggest that angiodysplasias have multiple feeding vessels which make embolization difficult and may contribute to recurrence.



Fig. 20.2. Angiogram demonstrating extravasation (hemorrhage) in cecum.

Operative Therapy

- Surgical therapy for massive lower intestinal bleeding is rare, often definitive, and associated with significant mortality.
- If the patient is hemodynamically unresponsive to the initial resuscitation, then radiographic, radionuclide, and endoscopic evaluations are usurped by the need for urgent surgery.
- Other patients may have the site of hemorrhage localized, yet the available therapeutic interventions fail to control the bleeding.
- Bender noted a reduced mortality (7%) for patients requiring less than ten units of blood. The mortality increased to 27% for patients in excess of ten units.

- Therefore, once a patient reaches 6–7 units during the resuscitation and the hemorrhage remains ongoing, surgical intervention becomes eminent.
- All patients require an open laparotomy with a thorough examination of the entire intestine.
- The first objective at operation focuses on the location of the intraluminal blood with the hope of segmentally isolating the possible sources of bleeding. If the colon visually appears filled with blood and the small intestine remains spared, the surgeon must still examine the entire abdomen and then focus on colonic sources of bleeding. If the small bowel contains blood, then the operative team has a larger area of concern that needs inspection.
- Palpation of the intestine may demonstrate etiologies such as a Meckel's diverticulum, ileitis, colitis, or a GIST.
- Intraoperative endoscopy is a technically difficult endeavor. A team approach with two surgeons or the availability of an experienced endoscopist is important to identify the elusive lesions causing the hemorrhage.
- If the source of bleeding cannot be found, and it appears to arise from the colon, the surgeon should perform a subtotal or total colectomy. Stable patients will tolerate a primary ileosigmoid or ileorectal anastomosis in this circumstance.
- Unstable patients require an end ileostomy with closure of the rectal stump or a mucous fistula. Once stable, the patient may return for ileostomy closure.
- The rectum and sigmoid colon require reexamination endoscopically to assure no bleeding persists.
- The key concerns with operative management are, first, a delay in the decision to operate until the hemorrhage reaches a critical point beyond ten units of blood. This seems to contribute to the high mortality rate. Second, mortality rates for patients requiring urgent surgery consistently reach a range hovering between 10 and 35%.
- The rates of recurrence increase if a surgeon elects to perform a limited right or left colectomy without precise localization of the hemorrhage. Limited segmental colectomies continue to have high mortality rates and excessive persistent bleed rates of 20%. A total colectomy offers the same mortality with a lower chance of recurrent or persistent hemorrhage.

D. New Frontiers

- Horton and Fishman commented about the advanced imaging within computerized tomography. Current thinly sliced, fast image acquisition combined with three-dimensional software packages has revolutionized the imaging of the vascular tree. However, these procedures are diagnostic, not therapeutic.
- Magnetic resonance angiogram creates images using the bright signal from blood. The three-dimensional images are reconstructed using computerized imaging to project a two-dimensional image that mimics a conventional angiogram. Further improvement develops from contrast-enhanced magnetic resonance angiography (CEMRA). With current techniques, the resultant images are not as specific or as refined as an angiogram.
- Wireless capsular endoscopy is an ideal diagnostic adjunct for patients with occult hemorrhage.
- The evaluation and management of lower gastrointestinal hemorrhage remains a challenge for surgeons. An algorithm summarizing the management is provided in Fig. 20.3.

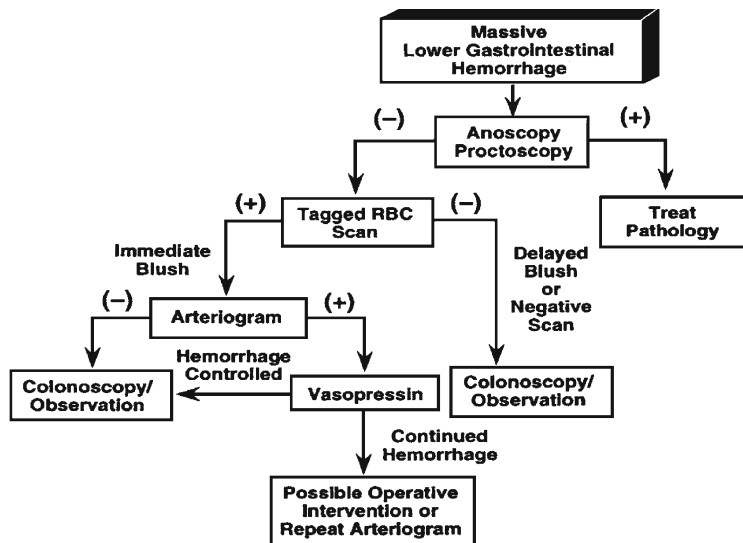


Fig. 20.3. Algorithm for the management of lower gastrointestinal hemorrhage.

21. Endometriosis

A. Introduction

- Endometriosis is a disease characterized by the presence of endometrial glands and stroma outside the uterine cavity. It is one of the most common conditions requiring surgery for women during their reproductive years.
- The degree of symptoms varies widely and does not always correspond to the extent of pathology encountered at surgery.
- Diagnosis is typically made or confirmed at laparoscopy or during laparotomy.
- Colon and rectal surgeons often become involved in the management of patients with intestinal endometriosis. This involvement may occur as a result of a combined procedure with a gynecologist or in management of an endometrioma masquerading as a neoplastic or inflammatory lesion.

B. Epidemiology

- The true prevalence of endometriosis is unknown.
- Various authors have estimated that up to 15% of all women of reproductive age and one-third of infertile women have endometriosis.
- Although endometriosis is primarily a disease of the reproductive years, the widespread use of exogenous estrogens and increasing obesity in our society have made it more prevalent in postmenopausal women.
- Conversely, there is a decrease in the incidence of the disease when women use oral contraceptives or experience multiple pregnancies.

- There is no racial predilection for endometriosis other than in Japanese women, who have double the incidence of the disease compared with Caucasian women.

C. Etiology

- The precise etiology that completely explains the cause and pathogenesis of endometriosis is unknown. The two most popular theories as to etiology are coelomic metaplasia and the implantation of viable endometrial cells from retrograde menstruation through the fallopian tubes.
- The vast majority of endometriosis occurs in the pelvis, but the entire peritoneum and abdominal cavity is at risk.
- Retrograde menstruation through the fallopian tubes and into the peritoneal cavity remains the most plausible explanation for the distribution of endometrial implants.
- Whereas retrograde menstruation is very common, occurring in virtually all women, endometriosis affects only a small minority.
- Several studies indicate a possible genetic aspect to endometriosis. Simpson et al. demonstrated that the disease seems to occur more frequently within families. He found a 7% relative risk for blood relatives of affected individuals as opposed to a 1% relative risk for nonblood controls.

D. Clinical Manifestations

- The most common sites where endometriosis occurs are summarized in Table 21.1. The most frequent of these are in the pelvis. Potential sites of implantation in the abdomen include the appendix, small bowel, and diaphragm.
- Because the majority of women have disease confined to the pelvis, the most common presenting complaints relate to menstrual irregularities, pelvic pain, and infertility.
- Ovarian hormones to varying degrees influence all endometrial tissue, and many of the clinical manifestations of endometriosis reflect the changing concentration of these hormones during a typical menstrual cycle.

Table 21.1. Sites and incidence of endometriosis.

Common	Less common	Rare
Ovaries 60–75%	Appendix 2%	Diaphragm
Uterosacral ligaments 30–65%	Ureter 1–2%	Inguinal canal
Cul-de-sac 20–30%	Terminal ileum 1%	Liver
Uterus 4–20%	Bladder <1%	Spleen
Rectosigmoid colon 3–10%	Abdominal scars <1%	Kidney

Pelvic Pain and Dysmenorrhea

- Pain is the most common symptom of endometriosis, affecting up to 80% of patients subsequently diagnosed with the disease.
- Endometriosis has been discovered in 30–50% of women undergoing laparoscopy for pelvic pain.
- Pelvic pain associated with endometriosis presents as dysmenorrhea, dyspareunia, or chronic noncyclic pelvic pain.
- Total lesion volume does seem to correlate directly to the degree of pain.
- Symptoms are related to the depth of penetration of the lesion, the type of lesion, and its location. Implants involving the uterosacral ligaments and rectovaginal septum are most frequently implicated.
- The pain is typically most intense just before menstruation and lasts for the duration of menstruation.
- Dysmenorrhea occurs in most women with endometriosis.
- Dyspareunia, deep pelvic pain with vaginal penetration, is usually a symptom of advanced endometriosis.
- The pathophysiology of pain arising from endometriosis is not completely clear. Pain may occur from the cyclic growth and subsequent increase in pressure within the capsule surrounding the implant.
- Adhesions, very common in endometriosis, may also be associated with pain.

Infertility

- Reports comparing rates of endometriosis for women undergoing elective laparoscopic sterilization versus laparoscopy for infertility have demonstrated a fourfold or greater increase in the infertile group.
- In women with known endometriosis, the infertility rate is 30–50%.

- There is little disagreement that moderate to severe disease with mechanical distortion of the fallopian tubes, ovaries, and peritoneum can potentiate infertility.

Intestinal Symptoms

- Although some women with intestinal endometriosis may be asymptomatic, some degree of intestinal complaints is typically found in those women with moderate to severe disease.
- Bowel involvement occurs in 12–37% of cases of endometriosis, and depending on the site of involvement, the symptoms of endometriosis may vary somewhat.
- In patients with intestinal endometriosis, the rectosigmoid is involved in more than 70%, followed by the small bowel and appendix.
- Rectosigmoid disease often results in alterations in bowel habits such as constipation, diarrhea, a decreased caliber of the stool, tenesmus, or, rarely, rectal bleeding. Such symptoms appear more often around the time of menses.
- Colonic endometriosis can present with obstruction and may be difficult to differentiate from other causes of large bowel obstruction, such as Crohn's disease or neoplasm.
- Intestinal perforation may occur with endometriosis.
- For those patients with asymptomatic intestinal endometriosis, the natural history seems to be benign.
- The clinical significance of appendiceal endometriosis is less than that involving the small bowel and colon.

Malignant Transformation

- Malignant transformation of endometriosis is an uncommon complication of the disease. Almost 80% of the tumors are ovarian and two-thirds are endometrioid carcinomas.

E. Diagnosis

Physical Examination

- Patients with mild cases of endometriosis may have a normal physical examination and the diagnosis may not even be suspected unless the patient undergoes laparoscopy.

- For patients with pelvic pain, careful bimanual and rectal examination may reveal nodularity or induration especially in the uterosacral ligaments or cul-de-sac of Douglas.

Laboratory Evaluation

- CA-125, an antigen expressed on tissues derived from human coelomic epithelium, is increased in women with moderate to severe endometriosis. However, the sensitivity and specificity of this test is poor because the antigen may be mildly increased in other diseases and within the normal range in women with mild endometriosis.

Endoscopy

- Because the lesions begin on the outside of the intestine, endoscopic evaluation of the large bowel is often normal except in severe disease or infiltrating nodular endometrial implants.
- Infiltration of the submucosa, although uncommon, may produce nodularity and distortion of the overlying mucosa. These findings may be difficult to visually differentiate from Crohn's disease, ischemia, or malignancy.
- Rarely is the diagnosis of endometriosis definitively confirmed by endoscopy or from endoscopic biopsies. Colonoscopy is, however, useful in excluding colon cancer from the differential diagnosis, especially in older patients presenting with a rectosigmoid mass while on hormone replacement.
- Rigid proctoscopy is very helpful in predicting the depth of rectosigmoid involvement in patients with severe endometriosis of the cul-de-sac of Douglas.

Imaging Techniques

- Transvaginal ultrasound has been used for several years to evaluate ovarian endometriomas. It is a sensitive test and in experienced hands provides specificity greater than 90% for ovarian endometriosis.
- Ultrasound of the pelvis, however, is not very sensitive in detecting focal nonovarian endometrial implants.
- Endorectal ultrasound is a potentially valuable tool to determine rectal wall invasion by endometrial implants in the cul-de-sac.

- The only real concern in evaluating patients having cul-de-sac endometriosis by endorectal ultrasound is the significant discomfort experienced by the patient when rectal distention from the balloon probe compresses the implant.
- Barium enema examination is another imaging technique often obtained by gynecologists for the intestinal complaints associated with deep pelvic endometriosis.
- There is no standard CT appearance for a mass caused by endometriosis to clearly differentiate it from pelvic masses attributable to other causes.
- When pelvic endometriosis is strongly suspected, MRI is more useful than CT scanning because of the benefit of imaging in multiple planes and the lack of ionizing radiation. MRI is rarely used, however, as an initial study in women with pelvic pain because of the higher cost, patient discomfort (claustrophobia), and the length of the scanning.

Laparoscopy

- The diagnosis of endometriosis usually requires direct visual and/or tactile assessment of the abdomen and pelvis. Laparoscopy is currently the initial approach to many patients suspected of having endometriosis, and has revolutionized both its diagnosis and treatment.
- The timing of laparoscopy in relation to the menstrual cycle is unimportant except in patients being evaluated for infertility.
- The accuracy of laparoscopy is completely dependent on the surgeon's visual evaluation of the abdomen and pelvis.
- The classic implant is nodular with a variable degree of fibrosis and pigmentation. The color may be black, white, brown, blue, or even red. The appearance of the lesion may be vesicular, papular, or hemorrhagic.

F. Treatment

- Treatment options for women with endometriosis are currently based on the severity and type of symptoms.
- With improvements in laparoscopic techniques and equipment in the past decade, notably the development of laparoscopic

laser techniques, many if not most early endometrial lesions can now be ablated at the time of diagnosis.

- Even complex excisional surgery involving the bowel and ureter can be performed safely via a laparoscopic approach in many patients.

Medical Management

- Medical therapy is designed to treat the symptoms of endometriosis, notably pelvic pain.
- Because pelvic pain may have causes other than the endometriosis seen during laparoscopy, a trial of ovarian suppression with a 3-month course of either danazol or a GnRH-a is often used to help determine the contribution of the pain from the endometrial implants.
- Most patients will have cessation of pain from endometriosis in the first month of amenorrhea.
- In limited disease, medical therapy is comparable with surgery in terms of relief of symptoms, recurrence of disease, and subsequent pregnancy rates.
- No current hormonal regimen can completely eradicate these lesions, and upon cessation of therapy, the lesions may again become symptomatic.

Oral Contraceptives

- These agents result in the induction of pseudo-pregnancy with hyperhormonal amenorrhea.
- The usual treatment regimen consists of daily administration of a tablet for 6–9 months.

Danazol

- Danazol lowers peripheral estrogen and progesterone levels by a direct effect on ovarian steroidogenesis and pituitary production of follicle-stimulating hormone (FSH) and luteinizing hormone (LH).
- The side effects of danazol necessitate discontinuation in less than 5% of patients for short courses, but is poorly tolerated for long-term suppression.

Gonadotropin-Releasing Hormone Agonists

- The introduction of GnRH-a as a new treatment modality for endometriosis has improved results, primarily by a reduction in side effects.
- Continuous administration of GnRH-a completely suppresses pituitary release of FSH and LH.
- Administered either by injection or intranasally beginning in the mid-luteal phase of the menstrual cycle, the current recommended length of therapy is 6 months.
- Pain relief is complete in more than 50% of women and significantly decreased in more than 90%.
- Laparoscopic evaluation after 6 months of treatment indicates resolution or a significant decrease in size of the lesions in the majority of patients. Studies comparing danazol and GnRH-a indicate similar clinical efficacy.
- Up to 90% of patients will experience hot flashes, night sweats, vasomotor instability, atrophic vaginitis, migraines, or depression.

Surgical Management

- Currently, surgery is considered conservative only when reproductive potential is preserved. Therefore, the major goal of surgical therapy for endometriosis is to completely excise or ablate the endometrial implants.
- Secondary goals include preservation of ovarian function and minimizing postoperative adhesion formation. These patients are operated upon in concert with gynecologists experienced with treating ovarian endometriosis to completely remove all gross disease, restore normal anatomy, and optimize fertility.

General Principles

- Removal of the lesions requires sharp excision or vaporization with electrocautery and/or the CO₂ laser.
- Laparoscopic hydrodissection is very useful in identifying normal surrounding tissue.
- All patients undergoing surgery for advanced endometriosis, either by an open or laparoscopic approach, should have a full mechanical and antibiotic bowel preparation.

Rectovaginal Endometriosis

- Endometriosis of the cul-de-sac of Douglas that extends into the rectovaginal septum is the most common site of intestinal involvement and may require intestinal resection.
- These lesions are often deep fibrotic nodules that extend from the posterior vagina and anterior rectum to the uterosacral ligaments.
- Small superficial lesions involving the intraperitoneal rectum may be vaporized with the CO₂ laser or electrocautery.
- Surgical treatment of the deeper lesions is more controversial. There has been a shift to more aggressive therapy, usually in conjunction with gynecologists who remove endometrial deposits on the ovaries and fallopian tubes
- Excision of the implant either with a disc of rectal wall or a formal anterior resection is recommended for women with symptoms related to the endometriosis.
- Care must be taken to avoid penetration of the vaginal wall with possible injury to the cervix, especially in women desiring eventual pregnancy.
- Disc excision of the anterior rectal wall, by either laparoscopic or open technique, is performed for single lesions usually less than 3 cm in diameter (Fig. 21.1).

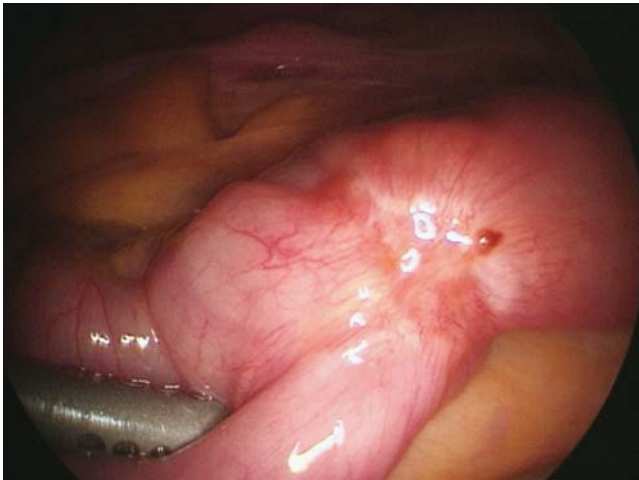


Fig. 21.1. Disc excision of the endometrial implant.

- Segmental resection of the rectosigmoid is performed for larger lesions or when neoplasia is a concern.

Small Bowel and Appendiceal Endometriosis

- Superficial small bowel implants may be treated with sharp excision, electrocautery, or the laser.
- Deeper implants may require small bowel resection, and, if within 5 cm of the ileocecal valve, may need an ileocecectomy.
- Appendiceal endometriosis is treated with appendectomy.

Results After Surgical Therapy

- Recurrence of endometriosis after surgical excision is difficult to assess because of a wide variability in the operative approach to endometriosis by various authors and the obvious need for postoperative laparoscopy to document asymptomatic recurrence.
- Studies suggest a histologically confirmed rate of recurrent endometriosis of approximately 19%.

Combined Medical and Surgical Therapy

- Combination therapy either pre- or postoperatively has been used for several years, although with a paucity of prospective, randomized data to conclusively prove long-term improvement in recurrence and symptoms.
- The rationale for preoperative medical therapy conducted over a period of 3–6 months is principally to decrease the inflammation and possibly the size of the endometrial implants. Presumably, this therapy will allow easier excision with diminished adhesion formation. Medical therapy may also reduce the vascularity of endometrial implants.
- A current use of combined therapy, after laparoscopic confirmation of advanced pelvic endometriosis, is a 3- to 6-month course of a GnRH-a before definitive surgery for virtually all patients able to tolerate the medical therapy.

22. Colon and Rectal Trauma and Rectal Foreign Bodies

A. Colon Injuries

- Despite the dramatic reduction of colon-related mortality from about 60% during World War I to about 40% during World War II to about 10% during the Vietnam War and to lower than 3% in the last decade, the colon-related morbidity remains unacceptably high.
- The abdominal sepsis rate has remained at about 20% in most prospective studies in the last decade (Table 22.1).
- No other organ injury is associated with a higher septic complication rate than the colon.

Epidemiology

- The vast majority of colon injuries are caused by penetrating trauma.
- In American urban centers, firearms are by far the most common cause of injury.
- In anterior abdominal stab wounds, the colon is the third most frequently injured organ after the liver and small bowel and an injury is found in about 18% of patients undergoing laparotomy.
- In posterior stab wounds, the colon is the most frequently injured organ and is injured in about 20% of patients undergoing laparotomy.
- In gunshot wounds, the transverse colon is the most frequently affected segment.

Table 22.1. Incidence of abdominal septic complications in colon injuries (prospective studies).

Author	Number of patients	Abdominal sepsis (%)
George et al.	102	33
Chappuis et al.	56	20
Demetriades et al.	100	16
Ivatury et al.	252	17
Gonzalez et al.	114	24
Demetriades et al.	297	24
Overall	921	22

- In stab wounds, the left colon is the most frequently injured segment, probably because of the predominance of right-handed assailants.
- Blunt trauma to the colon is uncommon and is diagnosed in about 0.5% of all major blunt trauma or in 10.6% of patients undergoing laparotomy. Most of these injuries are partial thickness and only 3% of patients undergoing laparotomy have full-thickness colon perforations.
- Traffic trauma is the most common cause of blunt colon injury.
- Seatbelts increase the risk of hollow viscous perforations and the presence of a seatbelt mark sign is a predictor of hollow viscous injury.

Diagnosis

- The diagnosis of colon injury is almost always made intraoperatively.
- A rectal examination may show blood in the stool, especially in cases with distal colon or rectal injuries.
- The colon can reliably be evaluated by soluble enema studies or abdominal computed tomography (CT) scan with soluble rectal contrast. Retroperitoneal gas or contrast extravasation are diagnostic and an exploratory laparotomy should be performed.
- The diagnosis may be suspected by the presence of free gas or thickened colonic wall on the routine abdominal CT scan.

Table 22.2. AAST colon injury scale.

Grade	Injury description
I	(a) Contusion or hematoma without devascularization (b) Partial thickness laceration
II	Laceration $\leq 50\%$ of circumference
III	Laceration $> 50\%$ of circumference
IV	Transection of the colon
V	Transection of the colon with segmental tissue loss

- Intraoperatively, every paracolic hematoma caused by penetrating trauma should be explored and the underlying colon should be evaluated carefully.
- Paracolic hematomas caused by blunt trauma should not undergo routine exploration unless there is evidence of colon perforation.

Colon Injury Scale

- The American Association for the Surgery of Trauma (AAST) developed a grading system for organ injuries in order to have objective criteria for the classification of the severity of the injury and enable reliable comparisons of results.
- The AAST Colon Injury Scale is shown in Table 22.2.

B. Operative Management

Historical Perspective

- The policy of mandatory colostomy for all colon injuries remained the unchallenged standard of care until the late 1970s. Stone and Fabian reported the first major scientific challenge of this policy in 1979. In a prospective, randomized study, which excluded patients with hypotension, multiple associated injuries, destructive colon injuries, and delayed operations, the authors concluded that primary repair was associated with fewer complications than colostomy. The exclusion criteria were perceived as risk factors for anastomotic leak and were absolute indications for diversion.

- In the 1990s and 2000s, primary repair became the standard of care in most cases although there is still some skepticism by many surgeons, especially in the presence of certain risk factors such as destructive colon injuries, severe contamination, multiple injuries, and delays in treatment.
- The recent reported experience deals mostly with civilian trauma. Military combat injuries have different mechanisms of injury, potential delays in evacuation and management, and challenges in postoperative management. Civilian trauma principles may not be appropriate to military trauma.

Nondestructive Colon Injuries

- There is now enough class I evidence (prospective, randomized studies) supporting primary repair in all nondestructive colon injuries (injuries involving <50% of the bowel wall and without devascularization) irrespective of risk factors.
- Overall, collective review of all available prospective, randomized studies (class I evidence) identified 160 patients with primary repair and an incidence of 13.1% of abdominal sepsis complications. In the group of 143 patients treated with diversion, the abdominal sepsis complication rate was 21.7% (Table 22.3).

Destructive Colon Injuries

- The available prospective, randomized studies, which include only a small number of cases, recommend resection with anastomosis irrespective of risk factors.
- In view of the lack of large prospective studies in the literature, the AAST sponsored a prospective multicenter study to evaluate the safety of primary anastomosis or diversion and identify independent risk factors for colon-related complications in patients with destructive colon injuries requiring resection.
- Multivariate analysis identified three independent risk factors for abdominal complications: severe fecal contamination, >4 units of blood transfusions within the first 24 h, and single-agent antibiotic prophylaxis. If all three risk factors were present, the incidence of abdominal complications was about 60%, if any two factors were present the complications rate was 34%, if only one factor was present this figure was about 20%, and with no risk factors it was 13%.

Table 22.3. Primary repair versus diversion: prospective, randomized studies with no exclusion criteria.

Study	Primary Repair		Diversion	
	Number of patients	Abdominal septic complications (%)	Number of patients	Abdominal complications (%)
Chappuis et al.	28	4 (14.3)	28	5 (17.9)
Sasaki et al.	43	1 (2.3)	28	8 (28.6)
Gonzalez et al.	89	16 (18)	87	18 (21)
Total	160	21 (13.1)	143	31 (21.7)

Table 22.4. AAST colon resection study: comparison of abdominal complications between primary anastomosis and diversion in high- and low-risk patients.

Patient population	Primary anastomosis: abdominal complications (%)	Diversion: abdominal complications (%)	Adjusted relative risk (95% CI)	P value
All patients	22	27	0.81 (0.55–1.41)	.69
Low-risk patients	13	8	1.26 (0.21–8.39)	.82
High-risk patients	28	30	0.90 (0.53–1.40)	.67

^aHigh-risk patients were those with PATI >25 or severe fecal contamination or 6 h from injury to operation or transfusion of >6 units of blood pre-/intraoperatively systolic blood pressure ≤90 mm Hg. Low-risk patients were those without any of the above risk factors.

- Multivariate analysis showed that the adjusted relative risk of abdominal complication in patients with primary anastomosis or diversion was similar, in both the low-risk and high-risk patients (Table 22.4). The study concluded that “In view of these findings and the fact that colon diversion is associated with worse quality of life and requires an additional operation for closure, colon injuries requiring resection should be managed by primary repair, irrespective of risk factors.”
- The only conditions for which there is agreement for colostomy are the presence of severe colon edema or a questionable blood supply of the colon. In these situations, at least theoretically, a diversion procedure might be a safe option.

Risk Factors for Abdominal Complications

- The abdominal complication rate in colon injuries is very high, with a sepsis rate of about 20% (Table 22.1).

Left Versus Right Colon Injuries

- No clinical or experimental study has ever demonstrated any healing differences between the two sides of the colon or any evidence that the two anatomic sides should be treated differently.

Associated Abdominal Injuries

- Class I and II studies have shown that although multiple associated intraabdominal injuries are significant risk factors for intraabdominal sepsis, the method of colon management does not affect the incidence of abdominal sepsis.
- The current class I and II literature supports primary repair or resection and anastomosis in patients with severe or multiple associated abdominal injuries.

Shock

- There is now sufficient class I and II evidence that preoperative or intraoperative shock is neither an independent risk factor for abdominal sepsis nor a contradiction for primary colon repair or anastomosis.

Blood Transfusions

- In a large prospective AAST study of 297 patients with penetrating destructive colon injuries requiring resection, blood transfusion was the most critical independent factor for abdominal sepsis [adjusted relative risk (RR), 2.0; 95% confidence interval (CI), 1.31–2.83; $P = 0.001$]. However, the method of colon management did not influence the complication rate in this group of patients and primary anastomosis was recommended.

Injury Severity Score

- The ISS is not an independent risk factor for abdominal sepsis and high ISS (>15) is not a contraindication for primary repair or anastomosis.

Fecal Contamination

- All prospective, randomized studies and recent large prospective observational studies have shown that the method of colon management in this group of patients does not influence the septic complication rate and recommended primary repair or anastomosis.

Specific Associated Abdominal Injuries

- There is class III evidence that the combination of colon injuries with pancreatic or ureteric injuries is associated with an increased incidence of septic complications. However, there is no evidence that the presence of any of these injuries is a contraindication for primary repair or anastomosis.

Time from Injury to Operation

- The length of delay of surgical repair over which the septic complication rate increases is not well defined. Some studies suggest >6 h whereas others >12 h as the critical delays associated with an increased risk of infections.
- The degree of contamination is much more important than the delay in surgical management and the time delay in itself should not be used as a criterion for primary repair or diversion.

Retained Missiles

- Missiles, which passed through the colon and remained lodged in the tissues, are not associated with increased risk of local sepsis and they should be removed only if it is technically easy and does not prolong the operation.

Anatomic Location of Colon Injury

- There is a plethora of classes I, II, and III evidence that the incidence of complications is similar in right and left colon injuries.

Temporary Abdominal Wall Closure

- Damage control laparotomy and temporary abdominal wall closure with prosthetic material seem to be associated with increased incidence of abdominal septic complications.
- There is no literature addressing the optimal management of colon injuries in this group of patients.
- Some authors prefer primary repair or resection and anastomosis, to avoid a colostomy near an open abdomen.

Anastomotic Leaks

- Colon leaks remain the most serious complication in repaired or anastomosed colons.
- The overall incidence of suture line failures is fairly low.
- In a collective review of 35 prospective or retrospective studies with 2,964 primary repairs, Curran reported 66 (2.2%) leaks.
- The leak rate after resection and anastomosis is significantly higher than in simple repairs.
- The risk factors for anastomotic leak are not well defined. It seems that colocolostomies are associated with a higher incidence of anastomotic leaks than ileocolostomies.
- A multicenter prospective AAST study reported a leak rate of 4.2% for ileocolostomies and 8.9% in colocolostomies. The leaks occurred in patients with or without multiple blood transfusions, severe contamination, and multiple associated injuries. No significant independent risk factors could be identified.
- The prognosis of anastomotic leaks is usually good and most of the patients can safely be managed nonoperatively with low-residue diet.
- In most cases, the leak results in a fecal fistula, which heals spontaneously within a few days. In other cases, the leak results in a local abscess, which can be drained percutaneously.
- In some patients, the colonic leak causes severe intraabdominal sepsis and a proximal diversion procedure may be required.
- Reexploration of the abdomen and creation of fecal diversion with or without resection of the leaking colon should be reserved only for patients with generalized peritonitis or failed percutaneous drainage.

C. Technique of Colon Repair

- In nondestructive injuries, repair of the injured colon should be performed after debridement of the perforation.
- The method of anastomosis, hand-sewn or stapled, does not influence the incidence of abdominal complications or leak rate and it should be surgeon's preference.
- Further protection of the anastomosis with adjacent omentum is recommended whenever possible.

D. Rectal Injuries

- Because of the paucity of class I and class II data, no consensus has been achieved with respect to the optimal management of rectal trauma.

Anatomy

- The anatomy of the rectum makes it difficult to apply the principles of colon trauma management.
- The rectum is easily accessible from the anus, with the anterior peritoneal reflection only approximately 6 cm from the anal verge. This results in a not uncommon finding of intraperitoneal injury from rectal foreign bodies.

Epidemiology

- For the various anatomic reasons, injuries to the rectum occur infrequently, and are usually the result of penetrating trauma.
- In most series, gunshot and shotgun wounds account for 80–85% of injuries, and stab wounds for 3–5%.
- Other causes include iatrogenic injuries from urologic and endoscopic procedures, sexual misadventure, and anorectal foreign bodies.
- Rectal injuries have been reported in nearly 2% of all pelvic fractures.

Diagnosis

- The diagnosis of intraperitoneal rectal injury, similar to colonic injuries, is almost always made intraoperatively.
- Extraperitoneal rectal injuries may not always be as obvious.
- The cornerstone for diagnosing an extraperitoneal injury is the combination of a digital rectal examination and rigid proctoscopy. In most series, the diagnostic accuracy of the digital rectal examination and rigid proctoscopy ranges from 80 to 95%.
- In hemodynamically stable patients with a mechanism suspicious for a rectal injury (gluteal, perineal, and transpelvic gunshot wounds, pelvic fractures, and foreign body insertion), a digital rectal examination and a rigid proctoscopy must be

performed and in the appropriate cases further evaluation by means of a contrast study should be considered.

Rectal Organ Injury Scale

- The grading system developed by the AAST for rectal injuries (Table 22.5) is similar to that of colonic injuries (Table 22.2).

E. Operative Management

Historical Perspective

- Presently there is no acceptable gold standard for the treatment of rectal injuries, because most studies have been unable to demonstrate any advantage of the various treatment options.

Intraperitoneal Injuries

- Several studies indicate that injuries to the intraperitoneal rectum can be managed similar to left colon injuries with primary repair without the need for colostomy.

Extraperitoneal Injuries

Fecal Diversion with Colostomy

- Since World War II, the mainstay of management of extraperitoneal injuries has been proximal colostomy. The only controversial aspect has been whether to perform a loop colostomy versus an end colostomy.

Table 22.5. AAST rectal organ injury scale.

Grade	Injury description
I	(a) Contusion or hematoma without devascularization (b) Partial-thickness laceration
II	Laceration ≤50% of circumference
III	Laceration >50% of circumference
IV	Full-thickness laceration with extension into the perineum
V	Devascularized segment

- Rombeau et al. demonstrated that a properly constructed loop colostomy, supported by a solid rod above the level of the skin, achieves complete fecal diversion.
- The authors believe that the type of colostomy should be dictated by the operative findings. Extensive destruction of the rectum that requires a resection may best be served with a Hartmann's procedure, whereas injuries that are not repaired or require limited dissection may be addressed by a loop colostomy.

Presacral Drainage

- In a series of 48 patients, 23 randomized to presacral drainage and 25 randomized to no drainage, no difference in pelvic sepsis was encountered. This represents the first and only class I study involving rectal injuries.

Distal Rectal Washout

- The authors do not recommend distal bowel irrigation. There is no proven benefit, and it may be associated with a high risk of infection because of spillage of intraluminal contents out of unrepaired rectal injuries.

Rectal Repair

- Even when repair is performed, no outcome advantage has been proven.

Miscellaneous Options

- Although extremely rare, abdominoperineal resection has been described for patients with severe bleeding, massive tissue loss, or devascularizing injuries.
- In a prospective study of 20 patients with extraperitoneal rectal injuries, laparoscopy (to rule out an intraperitoneal injury), followed by a diverting loop sigmoid colostomy without laparotomy yielded excellent results.

Associated Injuries

- Associated injuries are often seen with rectal injuries and have been reported to occur in as many as 77% of cases.
- Genitourinary, and in particular bladder injuries, are the most frequently seen associated injuries, occurring in 30–64% of cases.

F. Wound Management

- The incidence of wound sepsis in patients with colon or rectal injury is high.
- In a prospective study of 100 patients with gunshot wounds and routine skin closure, the wound infection rate was 11%.
- Primary wound closure in the presence of severe fecal spillage is a significant risk factor for wound sepsis and fascia dehiscence.
- This high-risk group of patients is best managed by delayed primary closure of the skin 3–5 days postoperatively.

G. Antibiotic Prophylaxis

- In view of the high incidence of septic complications in patients with colon injuries, appropriate antibiotic prophylaxis is critical. It is a standard practice to cover against both aerobes and anaerobes.
- The issue of antibiotic coverage in colon injuries merits further investigation. The authors' current choice is ampicillin/sulbactam prophylaxis in all suspected abdominal hollow viscous injury.
- There is now class I evidence that 24-h prophylaxis is at least as effective as prolonged prophylaxis for 3–5 days, even in the presence of major risk factors for abdominal sepsis, such as colon injury, multiple blood transfusions, and high Abdominal Trauma Index.
- With respect to rectal injuries, no study has addressed the type or length of antibiotic therapy. In the available studies that have even mentioned antibiotics, length of therapy has been at least 2 days using single or double agents covering both aerobes and anaerobes. It is the authors' preference to use ampicillin/sulbactam for prophylaxis in all patients with rectal injuries.

H. Trauma Ostomy Complications

- When deciding about the method of management of a colon or rectal injury, the surgeon should take into account the problems related to the creation of a stoma and later on the complications associated with the subsequent operation for colostomy closure.

- The morbidity of colostomy closure is significant. In a collective review of 809 colostomy closures in trauma patients during the period 1970–1990, the overall incidence of colon-related complications was 13.1% (major complications 5.3%; minor complications 7.8%).
- The timing of colostomy closure does not seem to have an important role in the incidence of complications.
- The optimal time for colostomy closure should be individualized and time should be allowed for wound healing and nutritional recovery. This might require only a few weeks for some patients or many months in severely injured patients.

I. Rectal Foreign Bodies

- Rectal foreign bodies represent an uncommon cause of rectal injury, accounting for <5% of cases. More often, patients present to the hospital with a retained foreign body.
- Most objects can be safely removed in the emergency department; however, a small percentage of patients will require general anesthesia and operative management with or without laparotomy.
- The only independent risk factor for operative intervention was if the foreign body was located in the sigmoid colon (odds ratio, 2.25; 95% CI, 1.1–4.4; $P = 0.04$).
- Patients with a history of retained foreign body who present with peritonitis should be taken directly to the operating room.
- Without peritonitis, patients should have an attempt at retrieval at the bedside. If unsuccessful, patients should be taken to the operating room with an attempt at transanal extraction under intravenous sedation.
- If transanal extraction is unsuccessful, then a laparotomy should be performed to maneuver the foreign body into the rectum for transanal removal. If this is unsuccessful, then a colostomy may be necessary for foreign body retrieval.

23. Colorectal Cancer: Epidemiology, Etiology, and Molecular Basis

A. Epidemiology

- Colorectal cancer (CRC) is a disease with a major worldwide burden. It is the fourth most frequently diagnosed malignancy in both sexes with almost 1 million people developing CRC annually. CRC is the third most common cause of cancer death in the world, responsible for 630,000 deaths annually.
- In the United States, CRC is the third most common cancer in men and women and the second most common cause of cancer death overall.
- The worldwide incidence of CRC is increasing.
- Before 1985, the age-adjusted incidence of CRC in the United States had been increasing; however, since this time, the rates have declined an average of -1.6% per year (Fig. 23.1). This reduction has been mainly confined to the Caucasian race and is largely limited to a decrease in the incidence of distal cancers.
- The recent decrease in incidence in the United States may be attributable to screening, specifically screening with flexible sigmoidoscopy, although other factors are likely to have influenced this trend.
- Currently, the overall probability of an individual developing CRC in United States over a lifetime is almost 6%.
- From a population perspective, age is the most important risk factor for CRC. CRC is predominantly a disease of older individuals; 90% of cases are diagnosed over the age of 50. The risk of CRC continues to increase with age (Fig. 23.2).

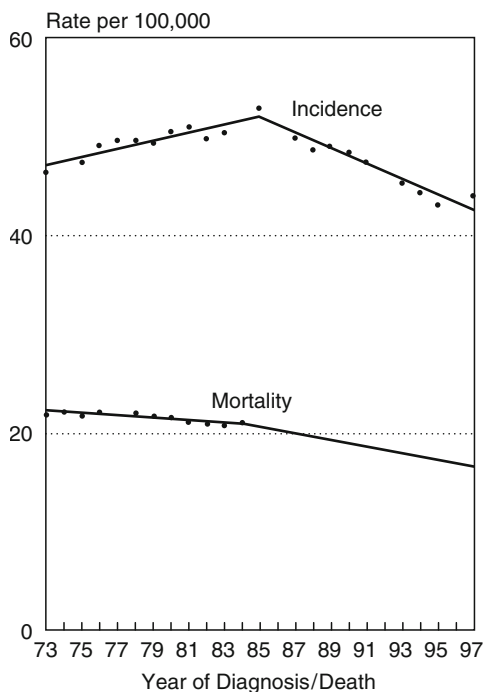


Fig. 23.1. CRC incidence and death rates in the United States 1973–1997. (From Ries et al. Copyright © 2000 American Cancer Society. Reprinted by permission of Wiley-Liss, Inc., a subsidiary of John Wiley & Sons, Inc.)

- The incidence per 100,000 people aged 80–84 is more than seven times the incidence in people aged 50–54.
- In the United States the risk of CRC differs by gender. The incidence of CRC is more than 40% higher in men than women.
- The ratio of colon to rectal cancer differs in the United States by gender; the ratio of colon to rectal cases for women is 3:1 as compared with 2:1 for males.
- Race and ethnicity influence CRC risk; Ashkenazi Jewish individuals seem to be at a slightly increased risk of CRC. At least part of this increased incidence may be attributable to a higher prevalence of the I1307K mutation of the adenomatous polyposis gene, a mutation that confers an increased risk of CRC development.

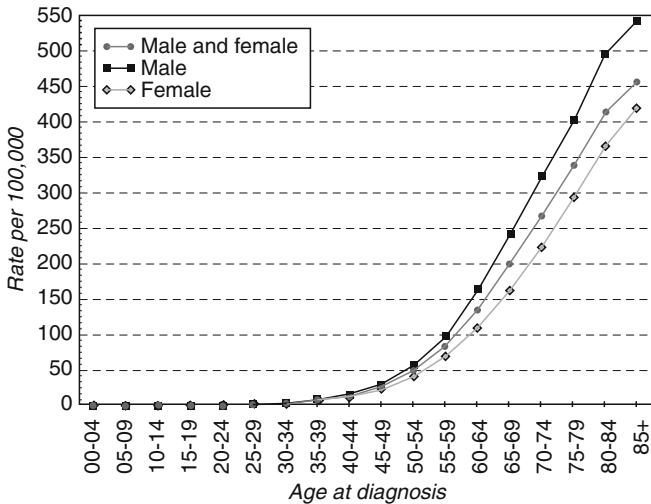


Fig. 23.2. Age-specific incidence rates in the United States. Age-specific incidence both genders – *circles*. Age-specific incidence in males – *squares*. Age-specific incidence in females – *diamonds*. [Generated from the Surveillance, Epidemiology, and End Results (SEER) Program (<http://www.seer.cancer.gov>) SEER*Stat Database: Incidence – SEER 9 Regs Public-Use, Nov 2002 Sub (1973–2000), National Cancer Institute, DCCPS, Surveillance Research Program, Cancer Statistics Branch, released April 2003, based on the November 2002 submission.]

- In the United States, the incidence of CRC is higher in African-Americans of either gender as compared with Caucasians (Table 23.1).
- In African-Americans, the increased rate of cancer is predominantly attributable to a higher rate of proximal cancers.
- The Surveillance Epidemiology and End Results registry (a National Cancer Institute population-based cancer registry representing 14% of the population in the United States) reports cancer incidence and stage over time (Table 23.2). Between 1992 and 1999 for all patients diagnosed with CRC, 38% of patients were diagnosed with localized disease, 38% with regional disease, and 19% with metastatic disease. Five percent of patients were unstaged. As a proportion of total cases, African-Americans were more likely to present with advanced

Table 23.1. Incidence and mortality rates^a for CRC by site, race, and ethnicity, United States 1996–2000.

		Caucasian	African-American	Asian American and Pacific Islander	American Indian/Alaska Native	Hispanic/Latino
Incidence	Male	64.1	72.4	57.2	37.5	49.8
	Female	46.2	56.2	38.8	32.6	32.9
Mortality	Male	25.3	34.6	15.8	18.5	18.4
	Female	17.5	24.6	11.0	12.1	11.4

Source: Adapted from Jemal et al.¹¹ with permission from Lippincott Williams & Wilkins.

^aPer 100,000 age-adjusted to the 2000 United States standard population.

Table 23.2. Stage at diagnosis.

	Caucasians	African-Americans
Localized	38	34
Regional	38	36
Distant	19	24
Unstaged	5	7

disease; 24% of African-Americans have metastatic disease at presentation. Rates of metastatic disease have fallen over time, most notably for CRC of the distal colon and rectum in Caucasians.

- There is substantial geographic variation in the incidence of CRC, with relatively high rates in North America, Western Europe, and Australia and relatively low rates in Africa and Asia (Fig. 23.3).
- Mortality from CRC is declining in the United States.
 - Improvements in surgical and medical treatments likely explain some of the change particularly that identified before 1985. More recently, the reduced mortality rate is likely secondary to the reduced incidence of CRC.

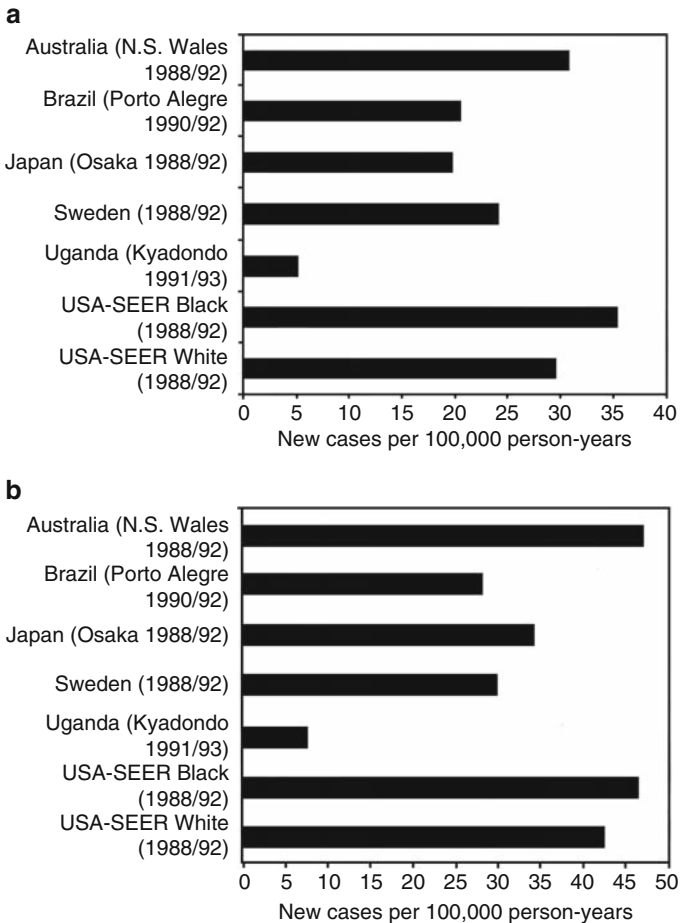


Fig. 23.3. **(a)** Age-standardized (to the world population) incidence rates of cancer of the large bowel among females. **(b)** Age-standardized (to the world population) incidence rates of cancer of the large bowel among males. (Reprinted from Lagiou.¹⁵ Copyright © 2002 by Oxford University Press, Inc. Used by permission of Oxford University Press, Inc.)

- African-Americans have the highest mortality rate from CRC in the United States (Table 23.1). The reasons for the higher mortality rate are likely multifactorial including the higher incidence of CRC, and the differences in stage distribution.

B. Etiology

Dietary Constituents and Supplements

- The relationship between diet and CRC risk is at best unclear. Studies in this area are difficult to conduct, because exposures tend to be multifactorial and change over time with our diet. In addition, because colorectal carcinogenesis is a multistep process, a number or combination of exposures may be necessary, and genetic susceptibility is likely to have a role.
- Although it can be stated that an individual with no other risk factors for CRC who ingests a diet that is high in fiber, fruits, and vegetables and low in animal fat and red meat will be on average at lower risk of CRC than an individual who eats a diet low in fiber, fruits, and vegetables and high in animal fat and red meat, it is difficult to determine with certainty which dietary components or combinations are responsible for the decreased risk.

Dietary Fat

- Dietary fat, particularly saturated animal fat has been implicated in carcinogenesis in the colon and rectum.
- However, dietary fat consumption is related to a number of other factors that may influence cancer risk, including other dietary factors such as dietary fiber and micronutrient consumption, as well as life-style factors such as exercise and alcohol consumption. Therefore, ecologic comparisons between countries are subject to a substantial risk of confounding.
- The evidence that red meat consumption is associated with CRC is in general more compelling than the evidence of an association with dietary fat. Given the lack of evidence for an independent association of dietary fat with CRC, it is unlikely that the animal fat in red meat is responsible for the association between red meat and CRC.

Red Meat

- There are a number of potential carcinogenic mechanisms unrelated to fat content that may result in a causal relationship between red meat ingestion and CRC.

- Red meat is high in iron, a prooxidant. Dietary iron may increase free-radical production in the colon, and these free radicals may cause chronic mucosal damage or promote other carcinogens.
- In humans, red meat ingestion stimulates production of *N*-nitroso compounds in a dose-response manner. Because many *N*-nitroso compounds are known carcinogens, this is a potential mechanism for an association between red meat and CRC.
- Formation of heterocyclic amines and polycyclic aromatic hydrocarbons in meat by cooking over an open flame or cooking until well done may be an important factor because these compounds are carcinogenic in animal models.
- Many epidemiologic studies have been conducted to determine the effect of ingestion of red meat on CRC risk.
- A daily increase of 100 g of red meat (3.5 ounces) was associated with a 12–17% increased risk of CRC. The risk was substantially higher with the ingestion of processed meat.
- Of note, individuals that consume diets high in red meat generally consume diets low in other dietary factors, such as antioxidants that may themselves be important in colorectal carcinogenesis. It is therefore difficult to rule out the possibility that the apparent effect of red meat on development of CRC may be confounded or modified by other dietary or lifestyle factors.

Fruit and Vegetable Intake

- Fruits and vegetables are a source of antioxidants, including carotenoids and ascorbate. Other bioactive constituents in fruits and vegetables that may protect against carcinogenesis include the indoles and isothiocyanates.
- More recent data, however, have not demonstrated a convincing link between vegetable or fruit intake and a reduced risk of CRC.
- The Cancer Prevention Study II also demonstrated a non-statistically significant trend for a higher colon cancer risk in men with the lowest vegetable consumption and women with the lowest fruit consumption.

- Overall, the evidence for an association between fruit and vegetable intake and the risk of CRC is inconsistent. Given this lack of concordant data, it is unlikely that a large number of cases of CRC can be attributed directly to a lack of fruit or vegetables, or that major additional interventions to increase consumption would lead to a substantial reduction in the incidence of CRC.

Fiber

- The data regarding the association between fiber and CRC risk are conflicting.
- Several mechanisms have been proposed for the protective effects of fiber: fiber may increase intestinal transit and therefore reduce the length of exposure of the colon to carcinogens, and fiber may dilute or absorb various potential carcinogens, particularly bile salts. In addition, products of fiber degradation and fermentation in the colon (such as butyrate) may also have a role.
- Overall, there has been little consistent evidence that a high fiber intake is associated with a decreased risk of CRC.
- Dietary interventions to increase fiber intake have proven unsuccessful in reducing the risk of colorectal neoplasia.
- There is currently no evidence from randomized studies to suggest that increased dietary fiber intake will reduce the incidence or recurrence of adenomatous polyps within a 2- to 4-year period.

Calcium

- Substantial epidemiologic and experimental evidence exists to support the beneficial effect of calcium on the prevention of colorectal neoplasia.
- Calcium has the capacity to bind and precipitate bile acids and may directly influence mucosal cell proliferation.
- More recently, large observational studies have supported a modest effect of calcium in the prevention of CRC, particularly calcium supplementation.
- Although the effect of calcium may be modest, given that CRC is a common disease, the overall impact of optimizing calcium intake from a population standpoint could be substantial.

Folate

- Folate, a B vitamin, is important for normal DNA methylation. Methylation is important in the regulation of cellular gene expression.
- Folate deficiency may lead to cancer through disruption of DNA synthesis and repair, or loss of control of proto-oncogene activity.
- There are 11 prospective studies that have evaluated the influence of folate on CRC risk in North American and European populations. In an unpublished metaanalysis of these data, a 20% reduction in the risk of CRC was found in those with the highest folate ingestion as compared with those with the lowest level of ingestion.

Alcohol

- Alcohol ingestion has a possible role in colorectal carcinogenesis.
- Alcohol may alter folate absorption, increasing CRC through reduction of folate bioavailability. Acetaldehyde, a product of alcohol metabolism may have a role, and alcohol may also contribute to abnormal DNA methylation directly.
- Thus, the totality of the evidence indicates that a high level of alcohol intake (two or more drinks per day) is associated with an increased risk of CRC.

Aspirin and Nonsteroidal Antiinflammatory Drugs

- There is considerable observational evidence that the use of aspirin or other nonsteroidal antiinflammatory drugs (NSAIDs) has protective effects at all stages of colorectal carcinogenesis (aberrant crypt foci, adenoma, carcinoma, and death from CRC).
- The mechanism of antineoplastic action of NSAIDs is incompletely understood but it is believed that both cyclooxygenase (COX)-dependent and COX-independent pathways may be important.
- Overall, the data evaluating the effect of nonaspirin NSAIDs is more limited than that for aspirin.
- The results of ongoing trials evaluating the effects of NSAIDs on CRC development are necessary before the widespread usage of NSAIDs as a chemopreventive agent for this disease.

Hormone Replacement Therapy

- Observational studies have demonstrated an association between hormone replacement therapy (HRT) in women and a reduction in both incidence and mortality from CRC.
- Possible mechanisms for the effect of HRT include a reduction in bile acid secretion (a potential promoter or initiator of CRC), as well as estrogen effects on colonic epithelium, both directly and through alterations in insulin-like growth factor with the use of estrogens.
- A metaanalysis of 18 observational studies of postmenopausal HRT demonstrated a 20% reduction in incidence of CRC in women who had taken HRT as compared with those that had never taken HRT.
- Overall, there seems to be a consistent reduction in the risk of CRC with the use of HRT. However, given the potential adverse effect of HRT, this should not be used as a primary preventive strategy for CRC.
- Interestingly, some authors have found that the influence of estrogen on CRC risk is related to microsatellite instability (MSI) – the presence of estrogen seems to protect against MSI whereas lack of estrogen in older women increases the risk of development of an MSI-positive tumor.

Obesity

- Obesity seems to increase the risk of colon cancer in men and premenopausal women.
- One of the proposed mechanisms for the association is the relative insulin resistance found in many obese patients. Insulin resistance results in hyperinsulinemia and increased activity of IGF (insulinlike growth factor) peptides. High IGF-1 levels are associated with cell proliferation and may increase the risk of colonic neoplasia.

Physical Activity

- More than 50 studies have been conducted to evaluate the influence of physical activity on CRC risk. Overall, the literature is relatively consistent with respect to the effect: greater physical activity (occupational, leisure, or total activity) is associated

with a reduced risk of CRC. The effect is relatively small; the estimated increased risk of colon cancer in the sedentary ranges from 1.6 to 2.0.

- The amount of physical activity required to have an effect is substantial – risk reduction is estimated to occur with 3.5–4 h of vigorous activity (running) per week but requires 7–35 h of moderate activity (walking at a brisk pace) per week.
- The biologic mechanisms that explain the relationship between physical activity and CRC risk are unclear.
- The mechanism is almost certainly multifactorial. Nonetheless, for a host of health-related reasons, frequent moderate to vigorous physical activity can be recommended to most patients without hesitation.

Smoking

- In a review of the literature conducted in 2001, 21 of 22 studies evaluating the relationship between cigarette smoking and colorectal adenoma were positive, smokers demonstrating a two- to threefold increase of adenoma risk as compared with nonsmokers.
- Most studies demonstrated an effect at relatively high levels of smoking (20 or more cigarettes per day). In the studies reviewed, the CRC risk was 1.4- to 2-fold higher in smokers than in nonsmokers.
- Smoking may modify the effect of micronutrients on CRC risk. In a randomized, controlled trial of antioxidants including β -carotene, or vitamin C and E supplementation in the prevention of recurrence of colorectal adenomas, among subjects who neither smoked nor drank alcohol, β -carotene was associated with a substantial reduction in the risk of recurrent adenoma (RR = 0.56). This effect was significantly attenuated in participants who were either smokers or drinkers. For participants who were both smokers and drank alcohol, β -carotene supplementation actually resulted in a doubling of the risk of recurrent adenoma formation.
- A large study found that patients with MSI-positive tumors were more likely to smoke more than 20 cigarettes a day, and had smoked for longer period of times than controls or patients with MSI-negative tumors.

Cholecystectomy

- Abnormal bile acid metabolism may predispose both to CRC and cholelithiasis.
- Studies in this area are difficult, because dietary and lifestyle factors related to cholelithiasis may confound the relationship between gallbladder disease and CRC risk.
- Two recent large prospective cohort studies have been conducted to evaluate this relationship. In a long-term follow-up study of 278,460 patients after cholecystectomy followed for up to 33 years, a significantly increased risk of small bowel malignancies and proximal colonic malignancies was found as compared with the general population. No association was found with more distal bowel cancer.

Inflammatory Bowel Disease

- Patients with long-standing inflammatory bowel disease (IBD) are known to be at an increased risk of CRC, although it is difficult to precisely estimate the risk.
- Extent of disease does seem to have a significant influence on CRC risk in UC.
- In a Swedish population-based cohort of 3,117 patients with UC, less extensive disease was associated with a lesser risk of CRC. As a ratio of the observed incidence and expected incidence, the increased risk of CRC in this cohort was 1.7 for those with ulcerative proctitis (95% CI, 0.8–3.2); 2.8 for those with left-sided colitis (95% CI, 1.6–4.4); and 14.8 for those with pancolitis (95% CI, 11.4–18.9).
- Other factors that may modify the risk of CRC in patients with UC but are currently not proven include age at onset of UC, family history of CRC, and the related diagnosis of primary sclerosing cholangitis.
- The relationship between Crohn's disease and the development of CRC has been less consistently demonstrated.
- The risk of development of CRC seems to be significantly increased in patients with extensive Crohn's colitis. The magnitude of increased risk seems similar to that of UC; however, in population-based studies, particularly those more recently published, a less dramatic effect is seen.

- Regardless, the effect of Crohn's disease on development of CRC requires further investigation.

Family History

- Individuals with a family history of CRC are at an increased risk of themselves developing CRC.
- In a metaanalysis of 27 observational studies that have evaluated the risk of family history on development of CRC, individuals with a first-degree relative with CRC had a 2.25 RR (95% CI, 2.00–2.53) of developing CRC as compared with those without a family history.
- The risk increased if more than one first-degree relative had CRC (RR = 4.25) or if a relative was diagnosed before the age of 45 (RR = 3.87).
- The RR of CRC was also increased if a first-degree relative had a history of a colorectal adenoma (RR = 1.99).
- The clustering of risk in families may be attributed to an inherited susceptibility, common environmental exposures, or a combination of both factors. The influence of a more distant family history of CRC on individual risk has not been determined with certainty.
- Some of the increased risk attributed to family history is due to inheritance of known susceptibility genes, such as mutations in the adenomatous polyposis coli gene, *p53* gene, or in MMR genes, particularly *MSH2*, *MLH1*, and *MSH6* and these are discussed in detail elsewhere in this text.
- Importantly, the majority of cases of CRC cannot be attributed to known genetic defects even when associated with a family history of CRC.
- Recognized genetic syndromes account for only a small proportion of all cases of CRC.
- Despite the importance of family history on risk of CRC, up to 25% of individuals with a first-degree relative with confirmed CRC do not report having such a family history, and even those that do report a history may not be aware of the increased risk associated with this. This fact has important implications for assessment of family history as well as patient and family counseling.

Other Risk Factors

Radiation

- Cases of rectal carcinoma have been reported in individuals who have undergone radiation for pelvic malignancies, primarily cervical cancer and prostate cancer.
- The cancers occur in the radiated field, tend to be associated with radiation changes to the adjacent rectal mucosa, and are more likely to be of mucinous histology than typical sporadic cancers, thereby strengthening the likelihood of a causal association. Nevertheless, the vast majority of individuals undergoing radiation for pelvic malignancies will not develop rectal cancer.

Ureterosigmoidostomy

- Formation of a ureterosigmoidostomy has been associated with an increased risk of carcinoma in the area of the ureterosigmoid anastomoses.
- The estimated increase ranges from 100 to 7,000 times the risk in the normal population and up to 24% of patients with a ureterosigmoidostomy will develop neoplasia at the anastomosis.
- The average latency period from formation of the ureterosigmoidostomy to development of malignancy is 26 years.
- Although the cause of this dramatic increased risk is not known, it seems to require the exposure of colonic mucosa to the mixture of urine and feces.
- Fortunately, with several options for urinary diversion, this procedure is now rarely performed.

Acromegaly

- Acromegaly, a rare endocrine syndrome resulting from secretion of excess growth hormone from a pituitary neoplasm has been found to be associated with an increased risk of CRC in several studies.
- The magnitude of the risk is unclear, with reports ranging from nonsignificant increases in risk to an RR of 18.3.
- Patients with acromegaly have increased levels of circulating IGF-1, and this may be responsible for the increased risk of colorectal neoplasia identified in these patients.

C. Molecular Basis

- Defects in genes that code for important proteins in the regulation of the cell cycle seem to be critical for carcinogenesis.
- Hanahan and Weinberg have described six alterations in regulatory mechanisms that seem constant in most cancers from the several hundred genetic mutations that have been identified in cancer cells (Fig. 23.4):
 1. Self-sufficiency in growth signals. Ordinarily, cells must receive growth signals to actively proliferate, assuring that cellular proliferation occurs only when necessary to maintain homeostasis. To proliferate autonomously, cancer cells must lose this need for exogenous growth signal.
 2. Insensitivity to antigrowth signals. Normally, there are numerous growth-inhibitory signals that function within

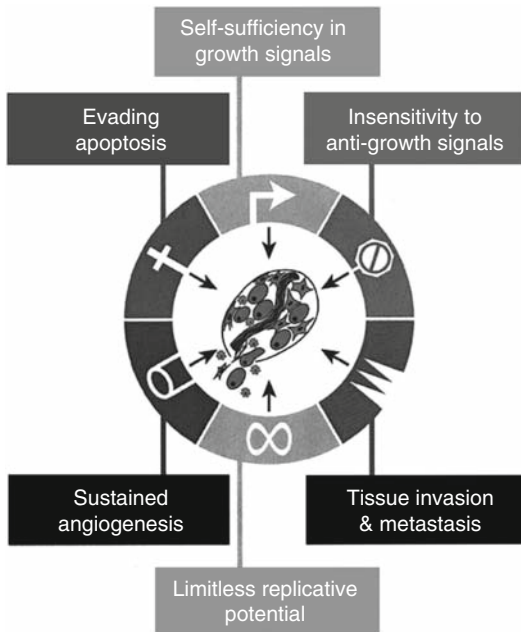


Fig. 23.4. Alterations in regulatory mechanisms important for carcinogenesis. (Reprinted from Hanahan and Weinberg,¹⁴³ copyright © 2000, with permission from Elsevier.)

a cell to maintain the cell in a quiescent and/or differentiated state. Cells with neoplastic potential must develop mechanisms to evade these antigrowth signals, enabling proliferation and dedifferentiation.

3. Evading apoptosis. Development of cancer requires not only a loss of control over cellular proliferation, but also a loss of control over programmed cell death (apoptosis). Apoptosis normally occurs in response to the cellular environment and is likely a major mechanism whereby cells that have acquired significant genetic mutations are destroyed. Tumor cells must circumvent apoptosis (either at a regulatory level or at an effector level) to continue to develop and proliferate.
 4. Limitless replicative potential. Many cells are able to replicate only a finite number of times preventing clonal expansion of any given cell. Even after acquiring independence from normal signals for cellular growth and death to develop into clinically significant cancer, cancer cells must gain unlimited capacity for replication. Intrinsic limits to proliferation must be evaded.
 5. Sustained angiogenesis. Virtually all cells must reside within 100 μm of a capillary to supply the cell with oxygen and nutrients required for functioning. Angiogenesis in normal tissue is closely regulated, and balancing of inducers and inhibitors of angiogenesis is an essential component of homeostasis. For neoplastic cells to develop into clinically significant cancer, they must develop the ability to induce and sustain angiogenesis, circumventing these homeostatic mechanisms to provide an adequate blood supply to support their ongoing growth.
 6. Development of ability to invade and metastasize. For cancer cells to develop the ability to invade other tissue and metastasize, a number of changes must occur. Normally, cells in tissue adhere to each other. A loss of this normal cell to cell adhesion must occur in the cancer microenvironment to permit metastasis to occur. In addition, the cancer cells must develop methods of modifying new environments to support continued growth.
- Although all six alterations in cell regulation are required for the development of clinically significant cancer, the sequence

of events and mechanisms are variable. The sequence of genetic mutations (or alterations) is less important than the accumulation of mutations, although some mutations tend to occur early in the neoplastic process and are termed initiators, whereas others tend to occur later and are termed promoters.

- In addition, certain genetic mutations (somatic or inherited) may be particularly critical and affect cell regulation in several important ways. Many such critical genes belong to two broad categories of genes involved in carcinogenesis: oncogenes and tumor suppressor genes.
- Additionally, caretaker genes that function to prevent the accumulation of somatic mutations are also critical to colorectal carcinogenesis. Abnormalities in caretaker genes greatly increase the risk of cancer development, independent of environmental influence.
- Of note, although the role of genes in carcinogenesis is described, in reality it is the protein products of the genes that are directly involved in changes in cell regulation.
- Mutations in oncogenes result in an abnormal gain or excess of a particular protein function. An oncogene product when expressed in a given cell (or when the product is expressed at the wrong time in the cell cycle, expressed with an enhanced function, or expressed in larger quantities than normally present) contributes to development of critical alterations in the mechanisms of cell regulation.
- Mutations causing such expression behave in a dominant manner, i.e., mutation of only one of the two alleles present is required to produce activation and phenotypic expression and promote carcinogenesis.
- The *ras* oncogene is the most frequently mutated oncogene identified in CRCs. The *K-ras* proto-oncogene, located on the short arm of chromosome 12 (12p) is mutated in approximately half of all CRCs.
- The *K-ras* gene product seems to be involved in the transduction of exogenous growth signals. Point mutations in the *K-ras* gene lead to a function gain, conferring a growth advantage to the cells.
- Other oncogenes that are frequently identified in sporadic colon cancer include *c-myc* and *c-erbB2*.
- Tumor suppressor genes normally inhibit cellular proliferation or promote apoptosis. When gene expression is lost, there is a

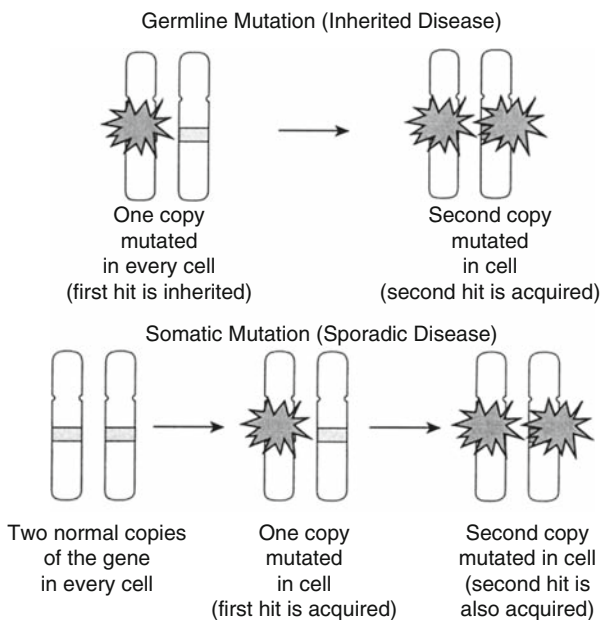


Fig. 23.5. Loss of suppressor-gene function. (Reprinted from Calvert and Frucht with permission from Annals of Internal Medicine.)

loss of this normal inhibitory control of the cell cycle. In general, gene expression is lost only when both alleles of the gene are inactivated [Knudson's two-hit theory of carcinogenesis (Fig. 23.5)], either through inherited mutation, somatic mutations, or both.

- There are a number of tumor suppressor genes that have been found to have an important role in CRC carcinogenesis, including the *APC*, *DCC*, *p53*, and *MCC* genes.
- The adenomatous polyposis coli (*APC*) gene located on the long arm of chromosome 5 (5q), is considered a gatekeeper gene of colorectal carcinogenesis as mutations in the *APC* gene seem to be initiators of this disease.
- Mutations in the *APC* gene have been found in 50% of sporadic adenomas and in 75% of sporadic cases of CRC.
- FAP, discussed in detail in Chap. 26, results from inheritance of a germline mutation in the *APC* gene.
- Mutations involve base-pair mutations, insertions or deletions that result in the formation of a stop codon, halting protein

synthesis leading to formation of a truncated or shortened protein product that affects the function of the protein.

- Although only a single abnormal allele is inherited in FAP, sporadic mutations are always acquired resulting in the formation of hundreds to thousands of colonic adenomas and ultimately carcinoma.
- The APC protein normally regulates the *Wnt* (wingless signaling pathway), an important pathway in cell regulation and development, through modulation of beta-catenin – a critical protein in the *Wnt* pathway.
- Normally, the protein product of the *APC* gene binds beta-catenin intracellularly forming a multiprotein complex that inhibits beta-catenin function. The increased functional levels of beta-catenin that result from alterations in APC protein product function leads to cell proliferation, and enhances cell to cell adhesion, limiting cell migration. Thus, hyperproliferating cells accumulate and aberrant crypt foci, the earliest phase of colorectal neoplasia.
- The *p53* gene, located on the short arm of chromosome 17 (17p) is an important gatekeeper gene for carcinogenesis – it is the most frequently mutated gene in human cancers.
- Normally, by slowing the cell cycle, *p53* facilitates DNA repair during replication. When repair is not feasible, *p53* induces apoptosis.
- Inactivation of *p53* is found in up to 75% of sporadic colorectal tumors; however, the mutation seems to occur late in the tumorigenic sequence.
- Thus *p53* gene mutations do not seem to be initiators of carcinogenesis but act as key limiting factors for malignant transformation.
- In addition, *p53* expression may be an independent prognostic marker in patients with CRC.
- Most studies demonstrate a lower survival rate in patients with advanced cancers that are *p53* negative as compared with those whose tumors express *p53* gene product particularly in those who receive chemotherapy.
- The “deleted in colorectal cancer” (*DCC*) gene was identified on the long arm of chromosome 18 (18q). Mutations in this gene have been found in the majority of CRCs.
- The gene product of *DCC* is a transmembrane protein that is important in cell–cell adhesion, and therefore inactivation of

DCC may enhance the metastatic potential of CRC through changes in adhesion.

- Similar to *p53*, patients who have *DCC*-positive tumors may have a better prognosis than those with *DCC*-negative (mutated) tumors.
- Because millions of base-pairs must be replicated during mitosis, errors in DNA replication occur and must be corrected by caretaker genes. The MMR system has a critical function in the detection and correction of errors in DNA replication, maintaining DNA integrity. MMR genes function as spell checkers – base-pair mismatches are identified, excised, and the correct sequence is synthesized and replaced.
- Lack of MMR function results in an accumulation in errors in DNA replication, increasing the probability that a mutation in an important gene in cell regulation will occur, will be preserved, and carcinogenesis will thus be initiated or promoted.
- Defects in the MMR system are identified by the detection of microsatellite instability. Microsatellites are small regions of DNA located throughout the genome that do not code for individual genes.
- Microsatellites are particularly susceptible to MMR gene defects, thus in cases of CRC attributable to MMR gene mutations, microsatellite replication errors accumulate, leading to detectable differences in the pattern of microsatellites in the tumor and in normal tissue; this is termed microsatellite instability (MSI).
- The National Cancer Institute recommends the testing of five microsatellite sequences to determine the MSI status of a tumor. If two or more of the five sequences demonstrate MSI, the tumor is designated MSI-high (MSI-H). If only one of the five sequences demonstrates changes in tumor microsatellite markers, the tumor is designated MSI-low (MSI-L). If no markers are changed, the tumor is microsatellite stable.
- Approximately 15% of CRC is MSI.
- MSI-H tumors are more likely to be high-grade, right-sided, mucinous, and have tumor-infiltrating lymphocytes. In addition, MSI tumors may have a better prognosis than microsatellite stable tumors, but may be less responsive to chemotherapy.
- A number of MMR genes (*MLH1*, *MSH2*, *MSH3*, *MSH6*, and *PMS1*) have been identified. Germline mutations in the *MLH1* and *MSH2* genes are responsible for the majority (>90%)

of cases of the hereditary nonpolyposis colorectal cancer (HNPCC) syndrome (discussed fully elsewhere in the text), whereas approximately 5–10% of HNPCC cases are attributable to mutations in the *MSH6* gene.

- In their landmark article, Vogelstein et al. (Fig. 23.6) described the pathogenesis of colon cancer as one that follows a predictable sequence of events, from adenoma to carcinoma, with histologic changes developing as genetic mutations are acquired over time.
 - Initially, a mutation in a gatekeeper gene such as the *APC* gene occurs resulting in proliferation of the colorectal mucosa and leads to the first histologically detectable event, the aberrant crypt focus. In aberrant crypt foci, the crypts have larger diameters than normal and stain more darkly with methylene blue.
 - With additional genetic changes, cells within the aberrant crypt become dysplastic and an adenoma forms.

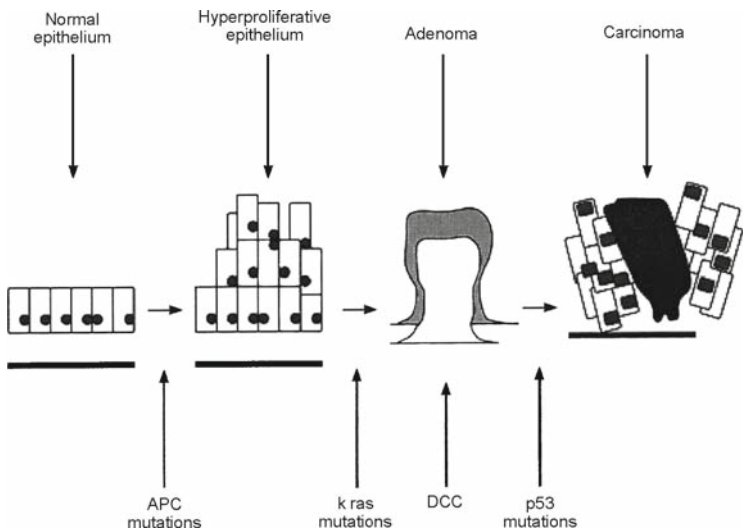


Fig. 23.6. The adenoma to carcinoma sequence of colorectal carcinogenesis. (Reprinted from Hardy RG, Meltzer SJ, Jankowski JA. ABC of CRC. Molecular basis for risk factors. *Br Med J* 2000;321:886–889, with permission of the BMJ Publishing Group.)

- Further genetic alterations are acquired, resulting in an increase in the size of the adenoma. However, the majority of adenomas do not develop into carcinoma.
 - Therefore, additional genetic alterations are required before the severity of dysplasia increases, and eventually, particularly with mutations in tumor promoters such as *p53*, carcinoma develops. This pathway to carcinogenesis is termed the chromosomal instability pathway.
 - Tumors forming through this pathway demonstrate extensive cytogenetic abnormalities, such as aneuploidy, and visible chromosomal losses and gains.
- CRC most frequently demonstrates chromosomal instability, indicating this is the most common genetic cause of colorectal carcinogenesis.
- Although MSI-H tumors may arise from adenomas, there is increasing evidence that sporadic MSI-H tumors also arise from hyperplastic polyps and serrated adenomas.
- Serrated adenomas are polyps that in the past would have been classified as hyperplastic polyps but have architectural features both of hyperplastic polyps and cytologic features of classic adenomas.
- Because only 70% of all colorectal carcinomas are believed to arise from classic adenomas, serrated adenomas may be the precursor lesion for a substantial number of cancers. However, the risk associated with serrated adenomas, in terms of progression to cancer, is unknown and currently under investigation.
- Development of CRC in UC represents a third pathway to the carcinogenesis in the colon. Most cancers develop in UC without a precursor polyp and therefore a direct dysplasia to carcinoma sequence is postulated. Genetically, cancers associated with UC seem to be heterogenous; aneuploidy and disruption of *p53* may occur as early events, however MMR genes may also be affected.

24. Screening for Colorectal Neoplasms

A. Introduction

- Evidence is mounting that colorectal adenocarcinoma can be prevented by detecting and removing adenomatous polyps, and that detecting early-stage cancers reduces mortality from the disease.
- Both polyps and early-stage cancers are usually asymptomatic; cancers that have grown large enough to cause symptoms have a much worse prognosis.
- Most people will be of average risk and require screening for colorectal cancer and polyps beginning at age 50. However, a substantial number of people are at increased risk because of an inherited predisposition to the disease and need screening or treatment as early as puberty.
- Germline and somatic truncating mutations of the adenomatous polyposis coli gene are thought to initiate colorectal tumor formation in familial adenomatous polyposis (FAP) and sporadic colorectal carcinogenesis, respectively. Genetic testing for FAP can help guide surveillance and treatment of patients at risk for the disease.
- Hereditary nonpolyposis colorectal cancer (HNPCC) is thought to be the result of DNA mismatch repair deficiency, and genetic testing for HNPCC may ultimately prove to have clinical value for patients in HNPCC families.

B. Classification of Risk and Screening Recommendations

- The cornerstone in determining a patient’s risk for developing colorectal cancer is the family history. Failure to properly investigate a patient’s family history of colorectal neoplasia can lead to inappropriate and inadequate treatment of both the patient and at-risk family members.

Average Risk

- As can be seen in Table 24.1, the majority of patients who develop colorectal cancer have no identifiable risk factors.
- Specifically, average-risk persons have no symptoms associated with colorectal cancer, no personal history of colorectal cancer or adenomatous polyps, no family history of colorectal neoplasia, no inflammatory bowel disease, and no unexplained anemia.
- Screening recommendations (Table 24.2): The AHCPR panel recommended that average-risk persons should undergo one of the following screening regimens, beginning at age 50:
 - Fecal occult blood testing annually
 - Flexible sigmoidoscopy every 5 years
 - Fecal occult blood testing annually and flexible sigmoidoscopy every 5 years
 - Air contrast barium enema every 5–10 years
 - Colonoscopy every 10 years
- Several large randomized controlled trials have shown that annual or biennial testing for fecal occult blood with complete diagnostic evaluation of the colon (primarily with colonoscopy) for patients with a positive FOBT reduces mortality from colorectal cancer.

Table 24.1. Patients with colorectal cancer.

75%	Average risk (sporadic)
15–20%	Family history of colorectal cancer
3–8%	HNPCC
1%	FAP
1%	Ulcerative colitis

Table 24.2 Screening for colorectal cancer and polyps.

Risk category	Screening method	Age to begin screening
Average risk	Choose one of the following: FOBT annually ^a Flexible sigmoidoscopy every 5 years ^a FOBT annually flexible sigmoidoscopy every 5 years Air contrast barium enema every 5–10 years ^b Colonoscopy every 10 years	50 years
Family history	Choose one of the following: 1. Colonoscopy every 5 years 2. Air contrast barium enema every 5 years ^b	40 years, or 10 years before diagnosis of the youngest affected family member, whichever is earliest 21 years
HNPCC	Colonoscopy every 1–3 years Genetic counseling Consider genetic testing	
FAP	Flexible sigmoidoscopy or colonoscopy every 1–2 years Genetic counseling Consider genetic testing	Puberty
Ulcerative colitis	Colonoscopy with biopsies for dysplasia every 1–2 years	7–8 years after the diagnosis of pancolitis; 12–15 years after the diagnosis of left-sided colitis

^aThe American Cancer Society recommends the combination of yearly FOBT and flexible sigmoidoscopy as preferable to either examination alone

^bRigid proctoscopy is recommended as an adjunctive examination to allow adequate visualization of the distal rectum. Furthermore, flexible sigmoidoscopy may be necessary to more completely evaluate a tortuous or spastic sigmoid colon

- However, because of the lack of sensitivity of FOBT, the American Cancer Society recommends combining annual FOBT with flexible sigmoidoscopy every 5 years rather than using FOBT alone as a screening method.
- A major drawback to using FOBT as a screening technique is poor compliance. Only 38%–60% of the patients in prospective trials completed all the planned FOBT tests, and use of FOBT in the general population is estimated to be lower than in the research environment.
- The restriction of frequently ingested foods and medications, combined with the natural aversion to stool sampling, makes annual FOBT unappealing to many persons.
- FOBT should not be confused with random stool guaiac testing, which is the analysis of stool found on digital rectal examination for blood. The lack of adequate diet and medication restriction before the test, potential for trauma to the anal canal during digital rectal examination, and the inability to reliably obtain stool from the distal rectum make the test unreliable. To date, random stool guaiac examination has not been demonstrated to have benefit in screening for colorectal cancer.
- The effectiveness of sigmoidoscopy as a screening tool depends on its ability to detect cancers and adenomatous polyps in the distal colon. If adenomatous polyps are found at flexible sigmoidoscopy, colonoscopy should be strongly considered because almost one-third of such patients will have neoplastic lesions in the proximal colon.
- The efficacy of sigmoidoscopy in reducing mortality from colorectal cancer has never been proven by a randomized, controlled trial, although case-control studies have shown a benefit.
- The American Cancer Society recommends combining flexible sigmoidoscopy every 5 years with annual FOBT, rather than using flexible sigmoidoscopy alone as a screening method. Although this combined approach may detect more proximal neoplasms than flexible sigmoidoscopy alone, 15–25% of patients with negative flexible sigmoidoscopy and negative FOBT will have neoplastic lesions in the proximal colon at colonoscopy, calling the rationale for this approach into question.
- The efficacy of barium enema in preventing colorectal cancer mortality has never been evaluated in a controlled trial, but can be inferred from the fact that detecting polyps and early-stage cancers by other methods reduces the incidence and mortality from colorectal cancer.

- Air contrast barium enema will detect 50–80% of polyps <1 cm, 70–90% of polyps >1 cm, and 50–80% of Stage I and II adenocarcinomas.
- Single column barium enema is less sensitive and should be combined with flexible sigmoidoscopy if used as a screening tool.
- Rigid proctoscopy should be considered as an adjunct examination because the balloon on the enema catheter often prevents adequate imaging of the distal rectum.
- Another major limitation of barium enema as a screening method is that patients usually require colonoscopy if lesions are detected.
- Colonoscopy is the only screening technique that allows the detection and removal of premalignant lesions throughout the colon and rectum, and is the final common pathway for any positive screening test.
- It remains the gold standard to evaluate the colonic mucosa.
- The ability of colonoscopy to reduce colorectal cancer mortality has been demonstrated indirectly through studies showing that detecting and removing polyps reduces the incidence of colorectal cancer and that detecting early cancers lowers the mortality from the disease.
- Compliance with screening colonoscopy may be superior to that of other methods because no confirmatory examinations are required, and thus, patients are subjected to a single bowel preparation.
- *CT colography (virtual colonoscopy)* was developed in an attempt to increase compliance with colorectal cancer screening, based on the impression that persons would be more inclined to have a “scan” than a “scope.”
 - The technique involves thin-section computed tomography (CT) with three-dimensional computer reconstructions to examine the colonic mucosa (Fig. 24.1a, b).
 - Although the technique has the advantages of being noninvasive and not requiring sedation, a vigorous oral laxative preparation is required, because adherent stool is difficult to differentiate from neoplasia on CT. In addition, a rectal catheter and air insufflation is used to distend the colon.
 - CT colography may ultimately prove to be as reliable as colonoscopy in detecting colorectal neoplasia.

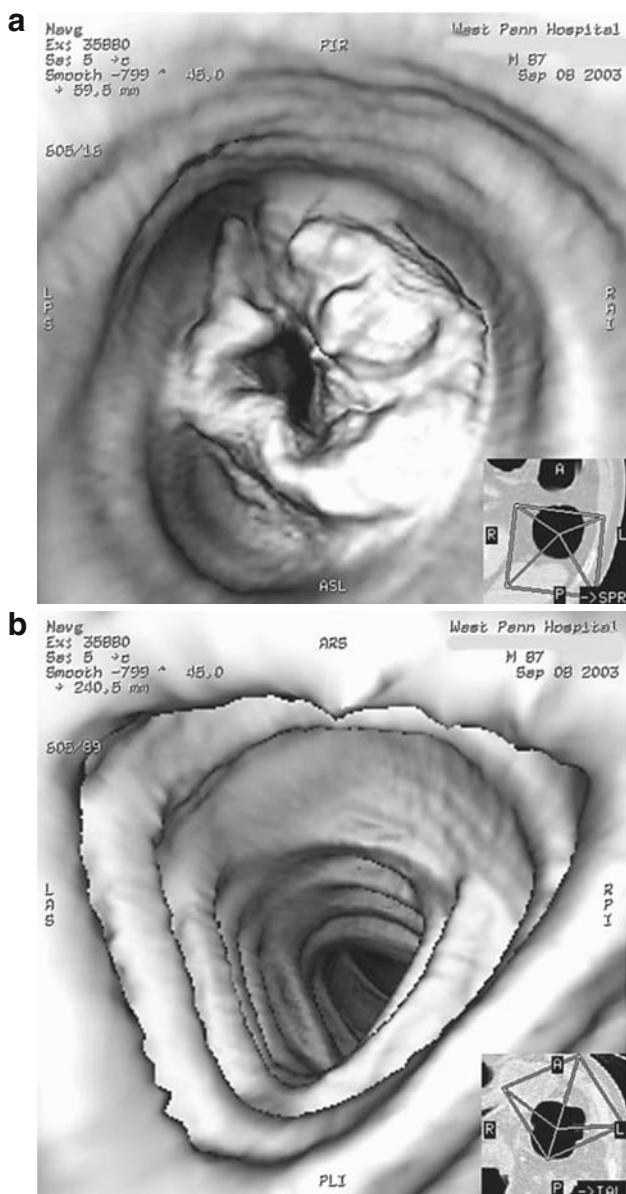


Fig. 24.1. (a) CT colography of an 87-year-old patient with a large tumor of the splenic flexure who could not undergo colonoscopy. The circumferential cancer can be seen occupying the lumen of the colon. (b) This image is of the transverse colon proximal to the cancer.

- Regardless of its accuracy, CT colography suffers (as does contrast enema) from the disadvantage that biopsies cannot be obtained and positive findings require endoscopic confirmation.
- As of January 2004, the Centers for Medicare and Medicaid Services guidelines for reimbursement for colorectal cancer screening are as follows (excerpted from their Web site, <http://www.cms.hhs.gov/medlearn/refcolcn.asp>):
 - FOBT: once every 12 months
 - Flexible sigmoidoscopy: once every 48 months
 - Colonoscopy: once every 24 months if the patient is at high risk for colon cancer; and once every 10 years (but not within 48 months of a screening sigmoidoscopy) if the patient is not at high risk for colon cancer
 - Double contrast barium enema: physician can decide to use instead of a sigmoidoscopy or colonoscopy
- Screening colonoscopy every 10–15 years beginning at age 50 may ultimately prove to be the most cost-effective method of screening average-risk persons for colorectal cancer.

Personal History of Adenomatous Polyps or Adenocarcinoma

- A personal history of adenomatous polyps or colorectal adenocarcinoma places a person at higher than average risk for the development of metachronous neoplasms. Surveillance colonoscopy is thus recommended by virtually all consensus groups.
- A rational surveillance strategy should take into account the patient's age, comorbid conditions, life expectancy, completeness of prior examinations, pattern of neoplastic growth, and histologic features of previously resected neoplasms. For instance, a 60-year-old patient in good health who undergoes colonoscopic polypectomy of a single small tubular adenoma should probably undergo surveillance colonoscopy in 3–5 years. A patient in good health who is found to have adenomas that are multiple, large, or dysplastic on initial screening colonoscopy should be considered for colonoscopy at an earlier interval, such as 6–12 months. However, a 90-year-old patient with severe comorbidities and limited life expectancy would not benefit as much from early surveillance, because removal of premalignant lesions will probably not alter lifespan or quality of life.

- Patients who undergo curative resection of colorectal adenocarcinoma should undergo regular surveillance colonoscopy to detect new metachronous primary neoplasms. The recommendation of the Standards Task Committee of the American Society of Colon and Rectal Surgeons is for initial postresection colonoscopy at 1 year, followed by colonoscopy every 3–5 years thereafter, depending on the pathology found at the preceding colonoscopic examination.
- The purpose of the colonoscopy is not specifically to look for tumor recurrence at the anastomotic suture line, because suture line recurrence in the absence of unresectable extraluminal disease is extremely uncommon, but rather to search for new primary neoplasms.

Family History of Colorectal Cancer or Adenomatous Polyps

- A family history of colorectal cancer or adenomatous polyps increases the risk of developing colorectal cancer. In general, closer familial relationships to affected relatives, younger age of onset, and larger numbers of affected relatives increase the risk. A careful family history should always be obtained to exclude one of the better-defined inherited colorectal cancer syndromes, such as HNPCC or FAP.
- *Screening recommendations:* The AHCPR panel recommended that patients with first-degree relatives with colorectal cancer or adenomatous polyps begin screening for colorectal neoplasia at age 40, or 10 years before the age at diagnosis of the affected relative, whichever is earliest.
- Those patients whose first-degree relatives developed colorectal cancer before age 50 may be at higher risk, and complete colonic evaluation with colonoscopy should be strongly considered.
- Patients with a second-degree relative with colorectal cancer, or relative with adenomatous polyps diagnosed over age 60, may be screened as an average-risk person.

Hereditary Nonpolyposis Colorectal Cancer

- Patients with HNPCC (Lynch Syndrome) typically develop cancer between age 40 and 50 and most tumors occur proximal to the splenic flexure.

- “Nonpolyposis” refers to the distinction between HNPCC and FAP (in which patients have hundreds of polyps), but is somewhat misleading because patients with HNPCC develop adenomatous polyps.
- The progression from adenoma to carcinoma seems to be accelerated in HNPCC patients as compared with patients with sporadic cancers, and there is a tendency to develop multiple colorectal cancers in HNPCC.
- Patients with HNPCC are also at high risk for cancers of other organs, especially the ovary and uterus.
- The ability to conclusively identify gene carriers is not yet fully developed, thus the penetrance of colorectal cancer in gene carriers can only be estimated (about 90%). In addition, some patients in HNPCC families who do not have identifiable germline mismatch repair gene mutations will develop colorectal cancer. For these reasons, the diagnosis of HNPCC in a family remains clinical.
- The Amsterdam criteria (colorectal cancer in three or more family members; two generations affected; one affected person a first-degree relative of another; and one cancer diagnosed before age 50) are the strictest criteria and have the highest concordance with known mismatch repair gene mutations.
- These criteria were originally developed for research purposes, to standardize the definition of HNPCC. However, they fail to identify patients who may be affected with HNPCC but do not fit the strict criteria because of unknown or abbreviated family histories, as well as patients with a personal or family history of extracolonic malignancies associated with HNPCC.
- A recent National Cancer Institute working group acknowledged the shortcomings of the Amsterdam criteria as clinical guidelines and published recommendations to expand the clinical suspicion of HNPCC to a broader range of patients
- Microsatellite instability has been reported in 85–90% of HNPCC colorectal cancers. Detection of this phenotype has been proposed as a screening method to trigger germline mutational analysis in kindreds with uncertain family histories. However, microsatellite instability is also found in approximately 15% of sporadic cancers, and has not been universally found to be predictive of familial cancer.
- At present, the “true” definition of HNPCC remains uncertain. Neither refined clinical criteria nor germline mutational analysis

has provided a model of the syndrome that is predictive of phenotype in all cases. Clinically, the absence of microsatellite instability or mismatch repair gene mutation does not negate a family history that suggests an autosomal dominant predisposition to developing colorectal cancer. At-risk family members still require aggressive screening.

- *Screening recommendations:* Expert panels convened by the AHCPR and the Cancer Genetics Studies Consortium recommend that persons who are members of a family that fits clinical criteria for HNPCC undergo colonoscopy at age 20–25, and repeat colonoscopy every 1–3 years.
 - The short time interval between colonoscopies results from the accelerated adenoma to carcinoma progression thought to occur in HNPCC.
 - Patients and their family members should be referred for genetic counseling.
 - Germline testing for mismatch repair gene mutations can be considered, but because the predictive value of such testing is only 30–50%, colonoscopy should be performed regardless.

Familial Adenomatous Polyposis

- Patients with FAP develop hundreds of adenomatous polyps as early as puberty, and will ultimately develop colorectal cancer, usually by age 40.
- Patients with FAP are also prone to develop a variety of extra-colonic tumors, notably duodenal adenomas and carcinomas, and desmoid tumors.
- FAP mutations do occur spontaneously, accounting for patients who are diagnosed with the disease without a family history of FAP.
- Attenuated FAP is a rare variant of the disease, with polyps and cancers developing later in life.
- The most frequently used genetic test for FAP is an assay for a truncated protein product of the mutated adenomatous polyposis coli gene. Because only about 80% of families with FAP will have a mutation that produces a truncated protein, the predictive value of testing at-risk family members is greatest if the proband (affected relative) has a positive test.

- *Screening recommendations:* Patients with a family history of FAP should undergo flexible sigmoidoscopy or colonoscopy at puberty. Lower endoscopy should be repeated every 1–2 years. Genetic testing should be considered, especially in large pedigrees where genotyping might be more cost effective than repeated endoscopy. If the proband has a positive truncated protein assay, at-risk relatives who test negative may be screened as average-risk persons.
- Because of the socioeconomic, medicolegal, and emotional issues surrounding genetic testing, it cannot be emphasized enough that genetic testing for FAP should be done after genetic counseling and informed consent.
- Patients should also undergo screening upper endoscopy for duodenal adenomas.

Inflammatory Bowel Disease

- Patients with ulcerative colitis have an increased risk of developing colorectal cancer. This risk begins approximately 7–8 years after diagnosis in patients with pancolitis, and 12–15 years after diagnosis in patients with limited left-sided colitis.
- There may be an increased risk of colorectal cancer in patients with Crohn's colitis, although this is less well defined.
- *Screening recommendations:* It is common practice for patients with ulcerative colitis to undergo screening colonoscopy with multiple random biopsies looking for dysplasia every 1–2 years, beginning 7–8 years after diagnosis in patients with pancolitis and 12–15 years after diagnosis in patients with left-sided colitis.

C. Future Directions

- Until recently, screening for colorectal cancer has not received much publicity in the United States, despite colorectal cancer being the second leading cause of cancer-related death in this country, and despite having a well-defined, identifiable, and treatable precursor lesion (the adenomatous polyp). Both health care professionals and the public need to become more aware of the potential benefits of colorectal cancer screening.

- As the genetics of inherited colorectal cancer syndromes become better understood, it will be possible to conclusively identify high-risk populations. It is of paramount importance that screening efforts be directed toward these populations. Genetic counselors are invaluable resources, both to counsel family members and to help direct genetic testing.

25. Polyps

A. Introduction

- The word polyp refers to a macroscopically visible lesion or mass projecting from an epithelial surface.
- Polyps may be classified as neoplastic or nonneoplastic.
 - Neoplastic polyps encompass epithelial tumors such as adenomas, polypoid adenocarcinomas, and carcinoid tumors, as well as nonepithelial lesions such as lipomas, leiomyomas, and lymphomatous polyps.
 - Nonneoplastic polyps include hamartomas, hyperplastic polyps, and inflammatory polyps.
- Colorectal polyps may be further classified on the basis of clinical information as sporadic or hereditary, the latter category making up the polyposis syndromes discussed in Chap. 26.

B. Adenomas

- The adenoma, a benign neoplasm of the epithelium, is the most common and most important colorectal polyp.
- Adenomas may be single or multiple, sporadic or hereditary.
- Adenomas are dysplastic and premalignant. Most adenocarcinomas arise from adenomas, and the removal of adenomas has been shown to be effective in decreasing the incidence of colorectal cancer. It is the relationship between adenomas and adenocarcinomas that confers upon adenomas their tremendous clinical significance.

Clinical Presentation

- Most adenomas are clinically silent and are found by screening or by investigation of symptoms unrelated to the adenoma.
- Large colonic adenomas may cause gross bleeding or may cause anemia secondary to occult blood loss.
- Large rectal adenomas, in addition to bleeding, may cause mucus discharge, tenesmus, and urgency.
- Colonoscopy is the most accurate test for polyps.
- Computed tomography (CT) colonography (virtual colonoscopy) has a sensitivity for adenomas >1 cm of approximately 90% and for adenomas 0.6–0.9 cm of approximately 80%. The false-positive rate is 17%.
- Virtual colonoscopy may be particularly useful in the evaluation of patients with incomplete colonoscopy.

Pathology

- Small adenomas are usually sessile (broad-based) and redder than the background mucosa. As polyps enlarge, some become pedunculated (attached to the bowel wall by a stalk of submucosa lined by normal mucosa) and some remain sessile, diffusely carpeting the bowel wall.
- The distribution of adenomas in the National Polyp Study was cecum 8%, ascending colon 9%, hepatic flexure 5%, transverse colon 10%, splenic flexure 4%, descending colon 14%, sigmoid 43%, and rectum 8%.
- The likelihood of synchronous sporadic adenomas when one adenoma was found approached 40%.
- There are three main histologic subtypes of adenomas: tubular, villous, and tubulovillous. Tubular adenomas exhibit dysplastic tubules in $\geq 80\%$ of the lesion. Villous adenomas have dysplastic villous fronds in $\geq 80\%$ of the lesion. The finger-like villi are actually elongated crypts with a length that is more than twice the length of normal crypts. Tubulovillous adenomas have $>20\%$ tubular and $<80\%$ villous formation.
- In the National Polyp Study, of 3,358 sporadic colorectal adenomas, 87% were tubular, 5% villous, and 8% tubulovillous.
- In adenomas, cellular proliferation is not limited to the lower half of the tubule, as in normal colonic epithelium, and the normal process of cellular maturation and differentiation from

the basal zone of the crypt to the surface of the lesion does not occur.

- Adenomas can be graded by the degree to which epithelial growth is disturbed.
 - Mild dysplasia is characterized by tubules that are lined from top to bottom by epithelium that is morphologically similar to the normal basal proliferative zone. The nuclei are enlarged, oval, hyperchromatic, and normally oriented. There is a slight excess of mitotic figures but the architecture is not disrupted.
 - In moderate dysplasia, the nuclear features are more advanced, cellular polarity is less preserved, there is nuclear stratification, and glands are more crowded.
 - In severe dysplasia, there are large vesicular nuclei, irregular, and conspicuous nucleoli, scalloped nuclear membranes, and increased nuclear to cytoplasmic ratio. Nuclear polarity is disrupted and marked cellular pleomorphism and aberrant mitoses are present. Structural alterations include budding and branching tubules, back-to-back arrangement of glands, and cribriform growth of epithelial cells in clusters and sheets; mitotic figures are numerous. The terms carcinoma in situ and intramucosal carcinoma are often used to describe these severely dysplastic adenomas, but these terms are potentially misleading because these lesions do not have metastatic potential.
- Although the lymphatics of the colon and rectum are closely associated with the muscularis mucosa, only lesions that have invaded through the muscularis mucosa have the potential to metastasize.
- The dominant risk factors for invasive carcinoma, that is, cancer cells invading beyond the muscularis mucosa, are polyp size and villous histology.

Epidemiology

- Colonoscopy-determined prevalence rates in asymptomatic average risk individuals older than 50 years range from 24 to 47%.
- The prevalence rate approximately doubles from age 50 to 60, but does not clearly continue to increase with age, unlike the incidence of colorectal cancer.

- Higher prevalence rates have been identified in men, with a 1.5 relative risk compared with age-matched women.
- A multicentered screening colonoscopy study examined the risk of colorectal adenomas in a cohort of individuals with one affected first-degree relative with sporadic colorectal cancer and found the odds ratio to be 1.5 for adenomas, 2.5 for large adenomas, 1.2 for small adenomas, and 2.6 for high-risk adenomas.
- The prevalence of adenomas is higher in relatives of individuals with colorectal cancer or adenoma at a young age, and in individuals with multiple relatives with cancer or adenomas.
- The incidence of adenomas at intervals ranging from 6 months to 4 years in postpolypectomy surveillance colonoscopy studies varies from 30 to 50%.
- Judged by repeat endoscopy, including studies with same-day back-to-back colonoscopies, the miss rate for adenomas ≥ 1 cm is approximately 5%, for adenomas 6–9 mm is approximately 10%, and for adenomas ≤ 5 mm approaches 30%.
- Incidental polyps are distributed more proximally, consistent with the observation that miss rates for adenomas are higher in the proximal colon.
- More important than the overall incidence rate is the incidence rate for advanced adenomas, defined as polyps ≥ 1 cm in size or containing high-grade dysplasia, or containing appreciable villous tissue.
- The incidence rate for advanced adenomas ranges from 6 to 9% and is closely related to the findings at initial colonoscopy.
- Three or more polyps at the initial colonoscopy has been shown to increase the risk of subsequent advanced adenomas, and in the National Polyp Study, age >60 years plus a family history of a parent with colorectal cancer was also a predictor of incident advanced adenomas.
- The cumulative incidence of advanced adenomas at 3 and 6 years of follow-up in the National Polyp Study in the highest risk group (three or more adenomas at baseline, or age ≥ 60 years plus a parent with colorectal cancer) were 10% and 20%, respectively.
- The lowest risk group (only one adenoma and age <60 years at baseline) had an incidence of advanced adenomas of $<1\%$ at both 3- and 6-year follow-up.

- The 5-year incidence of advanced adenomas in individuals with a previously negative colonoscopy is also <1%.
- Aggressive adenomas have been recognized in hereditary non-polyposis colorectal cancer, a condition in which patients may go from a normal colonoscopy to an established cancer in 1–3 years. These cancers show a phenotype called microsatellite instability (MSI), a feature that is also present in 15% of sporadic cancers. Sporadic cancers with high-frequency MSI (MSI-H) may have developed rapidly.

Adenoma–Carcinoma Sequence

- The prevalence of sporadic adenomas in the general population ≥ 60 years is approximately 30–40% but the lifetime risk of developing colorectal cancer in Western countries is 6% by age 85; this observation suggests that only a few adenomas become adenocarcinomas.
- A mathematical model suggested that it takes 2–3 years for an adenoma ≤ 5 mm to grow to 1 cm, and another 2–5 years for the 1-cm adenoma to progress to cancer.
- For a lesion ≥ 1 cm, the cancer probability is 3%, 8%, and 24% after 5, 10, and 20 years, respectively.
- Overall, the yearly rate of conversion from adenoma to carcinoma has been estimated to be 0.25%, but the risk is higher for polyps >1 cm (3%) for villous adenomas (17%) and for adenomas with high-grade dysplasia (37%).
- In a study that analyzed 7,590 adenomatous polyps to determine risk factors for high-grade dysplasia or invasion, size was the strongest predictor. The percent of adenomas with high-grade dysplasia or invasive cancer based on the size of the polyp was: < 5 mm, 3.4%; 5–10 mm, 13.5%; and >10 mm, 38.5%. Villous change, left-sided lesions, and age ≥ 60 years were also associated with advanced histologic features; no invasive cancer was found in polyps ≤ 5 mm.
- On a molecular level, a simplified view of the traditional pathway from adenoma to adenocarcinoma is as follows: adenoma development is dependent on an individual epithelial cell having both copies of the *APC* gene deactivated. This feature seems to allow for mutations in additional oncogenes, the key targets being *K-ras*, *DCC*, *P53*. The accumulation of molecular abnormalities is associated with the development of invasive

cancer. This pathway is the predominant pathway of colorectal carcinogenesis and is what is seen in familial adenomatous polyposis.

- In hereditary nonpolyposis colorectal cancer (HNPCC), patients inherit a mutated copy of a DNA mismatch repair (MMR) gene. When the second copy is inactivated, loss of MMR function results in the development of mutations throughout the gene. The accumulation of mutations is associated with the rapid evolution of adenocarcinoma, often without a recognizable precursor lesion.
- When there is a precursor lesion for an HNPCC cancer, it is often a typical adenoma, but hyperplastic polyps and mixed polyps with distinct components of hyperplastic and adenomatous polyps have been implicated in some HNPCC cancers.

Management

- When an adenoma is found, every effort should be made to do a complete colonoscopy to the cecum because of the high rate of synchronous neoplasms in patients with adenomas and adenocarcinomas.
- Multiple studies support the recommendation that villous polyps regardless of size and adenomas >1 cm are important markers for the presence of advanced adenomas and carcinoma in the proximal colon.
- The majority of colorectal polyps are treated by endoscopic snare polypectomy; polyp removal is performed using electrocautery snare.
- Almost all polyps can be safely endoscopically removed, but if the polyp appears to be malignant, snare polypectomy may not be possible, and is generally inadvisable.
- Malignancy should be suspected in the setting of irregular surface contour, ulceration, friability, firm or hard consistency, thickening of the stalk, and nonlifting with submucosal injection (a feature of submucosal invasion or fibrosis from previous attempts at polypectomy).
- It is particularly important that if polypectomy is performed for a suspicious polyp, the site of the polyp should be precisely localized by tattooing the bowel wall with India ink or similar dye.

- Some large polyps may not be amenable to polypectomy and are treated by colon resection; in these instances, a conventional oncologic resection should be done.

Rectal Adenomas

- Sessile villous adenomas are usually encountered in the rectum and the larger lesions may not be amenable to snare polypectomy. Local excision or rectal resection may be required.
- For lesions in the lower half of the rectum, endoanal excision is generally performed.
- For more proximal lesions, transanal endoscopic microsurgery (TEM) may be appropriate.
- Larger lesions that extend too proximally for endoanal excision will usually be best managed by anterior resection.
- Preoperatively, the lesion should be evaluated with respect to the risk of containing invasive cancer. The best clinical clue to the presence of invasion is firmness on digital rectal examination, although previous attempts at removal can produce fibrosis. Endoanal ultrasound and magnetic resonance imaging may be helpful, but sensitivity with respect to a small focus of submucosal invasion is low.
- When invasive cancer is present, treatment will be determined primarily by the level and size of the lesion, the depth of mural penetration, and by any evidence of lymphatic metastases.
- More proximal rectal lesions will usually be treated by anterior resection. Selected small proximal lesions may be managed by TEM. More distal lesions will need either resection or local excision.
- If biopsy of a hard area reveals a poorly differentiated cancer, a resectional approach is recommended. Even small rectal cancers that are not poorly differentiated carry a risk of lymph node metastases.

Surveillance

- After polypectomy of large or multiple adenomas (three or more) or advanced adenomas, cancer risk is increased three- to fivefold.

- The National Polyp Study determined that colonoscopy performed 3 years after initial polypectomy protects patients as well as more frequent examinations.
- Recommendations for surveillance postpolypectomy are based on the estimated risk of metachronous neoplasia:
 - After colon clearance, first follow-up colonoscopy in 3 years (for most patients).
 - First follow-up colonoscopy in 5 years for low-risk patients [fewer than three small (<1 cm) tubular adenomas, no significant family history of colorectal cancer or adenomas].
 - If first follow-up examination is negative, second follow-up colonoscopy in 5 years.
 - Earlier follow-up colonoscopy for selected patients with multiple or large sessile adenomas.
 - Individualize for age and comorbidity. (After removal of a small tubular adenoma, no follow-up may be indicated in elderly patients, or for those individuals with significant comorbidity, or the first follow-up can be delayed for 5 years.)
- For large sessile polyps (>3 cm), there is a significant recurrence rate after endoscopic polypectomy. There should be close follow-up, for example, every 3–6 months in the first year, every 6–12 months in the second year, and yearly to the fifth year.

The Malignant Polyp

- Polyps with cancer cells penetrating the muscularis mucosa are malignant polyps. Invasion is invariably limited to the submucosa. In terms of TNM classification, these are T1NxMx lesions.
- Malignant polyps (T1 lesions) account for 2–12% of polyps in colonoscopic polypectomy series.
- The risk of malignancy related to adenoma size in one large series was 0.6–1.5 cm, 2%; 1.6–2.5 cm, 19%; 2.6–3.5 cm, 43%; and >3.5 cm, 76%.
- The clinical decision to proceed with further treatment, such as resection or local excision, depends on the estimated risk of lymph node metastases and the patient's general condition.

- The main determinant of the risk of lymph node metastasis is the depth or level of invasion of cancer within the polyp. Haggitt's classification of malignant polyps (Fig. 25.1) is based on the level of invasion:
 - Level 0: Noninvasive (severe dysplasia)
 - Level 1: Cancer invading through the muscularis mucosa but limited to the head of a pedunculated polyp
 - Level 2: Cancer invading the neck of a pedunculated polyp
 - Level 3: Cancer invading the stalk of a pedunculated polyp
 - Level 4: Cancer invading into the submucosa of the bowel wall below the stalk of a pedunculated polyp. All sessile polyps with invasive cancer are level 4
- The stalk of a pedunculated polyp is covered by normal mucosa and has a central core of submucosa. A line drawn at the junction of normal and adenomatous epithelium is the transition

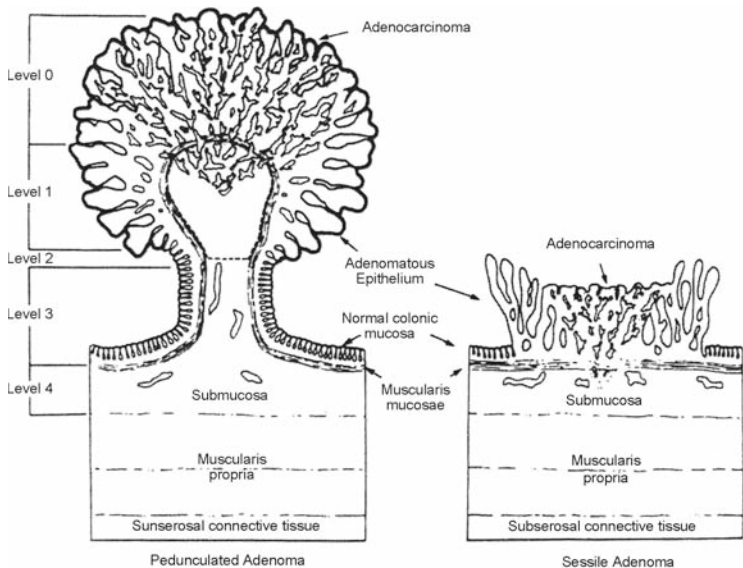


Fig. 25.1. Anatomic landmarks of pedunculated and sessile malignant polyps. (Reprinted from Haggitt et al. copyright 1985, with permission from the American Gastroenterological Association.)

between the stalk and the head of the polyp. The junction zone is called the neck.

- Kudo has stratified the depth of submucosal invasion into three levels (Fig. 25.2):
 - SM1: Invasion into the upper third of the submucosa
 - SM2: Invasion into the middle third of the submucosa
 - SM3: Invasion into the lower third of the submucosa
- Haggitt levels 1, 2, and 3 are SM1; Haggitt level 4 may be SM1, SM2, or SM3.
- The risk of lymph node metastases is <1% for pedunculated polyps with Haggitt level 1, 2, or 3. The risk of lymph node metastases for Haggitt level 4 lesions, pedunculated or sessile, ranges from 12 to 25%.
- Factors reported to be associated with an increased risk of lymph node metastases include lymphovascular invasion, poor differentiation, gender, extensive budding, microacinar structure, flat or depressed lesions, and SM3 level of invasion.
- The rate of lymph node metastases from rectal lesions is not different than from colon lesions. However, T1 lesions in the distal third of the rectum have been found to have a higher risk of lymph node metastases than more proximal rectal lesions. This finding is consistent with the high local recurrence rates, in the range of 5–28%, which have been observed after full-thickness local excision of T1 lesions of the distal rectum.

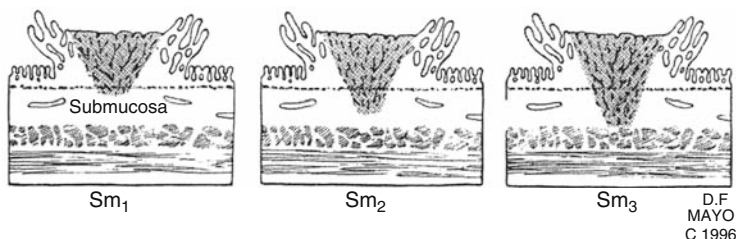


Fig. 25.2. Depth of submucosal invasion in sessile malignant polyps. Sm_1 invasion into upper third; Sm_2 invasion into middle third; Sm_3 invasion into lower third. (Reprinted from Nivatvongs S. Surgical management of early colorectal cancer. Surg Clin North Am 2000;82:1052–1055, copyright 2000, with permission from Elsevier.)

- A positive polypectomy margin should not be considered an adverse risk factor for recurrence – in general, this should be regarded as inadequate treatment. A distance of 2 mm beyond the deepest level of invasion is needed to consider the margin clear.
- In view of the risk of lymph node metastases of < 1%, pedunculated polyps with invasion to Haggitt levels 1–3 are safely treated by snare polypectomy. Level 4 pedunculated lesions are treated as sessile lesions.
- Sessile lesions that are snared in one piece and have a margin of at least 2 mm are considered adequately treated.
- If a piecemeal polypectomy was performed, margins cannot be adequately assessed and further treatment is needed.
- High-risk sessile lesions such as lesions with SM3, lymphovascular invasion, poor differentiation, and those in the lower third of the rectum should have an oncologic resection.
- Nivatvongs's summary of the indications for oncologic resection are presented in Table 25.1.

Table 25.1. Summary of malignant colorectal polyps that should have an oncologic bowel resection.

A. Lesions in colon
(a) Pedunculated Haggitt level 4 with invasion into distal third of submucosa, or pedunculated lesions with lymphovascular invasion
(b) Lesions removed with margin <2 mm
(c) Sessile lesions removed piecemeal
(d) Sessile lesions with depth of invasion into distal third of submucosa (Sm ₃)
(e) Sessile lesions with lymphovascular invasion
B. Lesions in middle third and upper third rectum
Same as lesions in colon
C. Lesions in distal third rectum
(a) Pedunculated Haggitt level 4 with invasion into distal third of submucosa, or pedunculated lesions with lymphovascular invasion
(b) All sessile lesions

An alternative may be a per anal full-thickness excision plus chemoradiation

Source: Reprinted from Nivatvongs S. Surgical management of early colorectal cancer. Surg Clin North Am 2000;82:1,052–1,055, copyright 2000, with permission from Elsevier.

- Close endoscopic follow-up is required to look for local recurrence. A reasonable schedule is to examine the polypectomy site in 2–3 months and then every 6 months for the first 2 years; complete colonoscopy is done in the third year, and then at 3-year intervals.

Specific Adenomas

Flat and Depressed Adenomas

- Some adenomas display a flat or depressed growth pattern and are not elevated above the mucosal surface; they are not “true polyps.”
- They are most readily identified by chromoendoscopy, a technique in which the mucosa is sprayed with indigo carmine dye.
- The incidence of flat and depressed adenomas in three Western population studies was approximately 20%, and these lesions contained cancer more often than polypoid adenomas.
- Twenty-nine percent of flat lesions >1 cm contained either high-grade dysplasia or cancer.
- Because of the risk of cancer, these small lesions should be removed, either by endoscopic polypectomy or by operative resection.

Serrated Adenomas

- The serrated adenoma is a more recently recognized histologic phenotype of sporadic adenoma. Serrated adenomas are uncommon, accounting for approximately 0.5–1.3% of colorectal polyps. Initially, serrated adenomas were described as hyperplastic polyps that contained adenomatous features.
- It is unclear whether serrated adenomas develop in association with hyperplastic polyps or develop *de novo*.
- The serrated polyps include the mixed polyp, in addition to the hyperplastic and serrated adenoma. The mixed polyp is recognized by distinct areas of hyperplastic and adenomatous morphology.
- The relationship between hyperplastic polyps, serrated adenomas, and cancer is not clear. In one report, 5.8% of colorectal cancers were associated with an adjacent serrated adenoma and some serrated adenomas harbor high-grade dysplasia. A review concluded that the risk of high-grade dysplasia was the

same in serrated adenomas as in the more common adenomatous phenotypes.

C. Nonneoplastic Polyps

Hyperplastic Polyps

- Hyperplastic polyps are the result of a failure of programmed cell death.
- Mature goblet cells are the main cellular component of hyperplastic polyps, whereas adenomatous crypts have reduced numbers of goblet cells.
- Hyperplastic polyps are the most common polyps found on flexible sigmoidoscopy. The true ratio of hyperplastic polyps to adenomas approximates 1:1.
- Most hyperplastic polyps are small (<3–5 mm in diameter), pale, usually located in the rectosigmoid region, and are almost always asymptomatic.
- Chromoendoscopy can improve the endoscopist's ability to distinguish hyperplastic from adenomatous polyps.
- Data conflict as to whether hyperplastic polyps found on a screening examination represent an increased risk of future neoplasia.
- A report using data from two large chemoprevention studies demonstrated that hyperplastic polyps were not predictive of an increased risk of developing adenomatous polyps on follow-up colonoscopy.
- Hyperplastic polyps have been implicated in some colorectal cancers, especially in HNPCC.
- A strong association of MSI-H cancers with residual adenomas has not been observed.
- Sporadic adenocarcinomas arising through the defective MMR pathway (MSI-H adenocarcinoma) occur in older patients (>70 years), have a female gender bias, and are predominantly located in the right colon. The vast majority lack *APC* mutations. These MSI-H cancers can be associated with large hyperplastic polyps, and analysis of these combined lesions demonstrates that both the cancer component and the hyperplastic polyp epithelial cells lack *hMLH1* expression.

- Hyperplastic polyps may serve as fertile soil for gene-specific hypermethylation leading to knockout of *hMLH1* and loss of DNA MMR function.
- Carriers of hyperplastic polyps clearly at increased risk for colorectal cancer are those with the hereditary syndrome of hyperplastic polyposis.
- The syndrome is thought to be very rare.

Hamartomas

- Juvenile polyps are hamartomas, localized overgrowths of normal mature cells.
- Most juvenile polyps are round, pink, smooth, and pedunculated, although some are small and sessile.
- The muscularis mucosa does not participate in the formation of a juvenile polyp, and the unique potential of these lesions to twist and “auto-amputate” has been ascribed to the absence of supporting muscle fibers.
- Most juvenile polyps present in childhood, but they may present in infancy or in adulthood. Usually, only one or two polyps are found.
- Symptoms include rectal bleeding, mucus discharge, diarrhea, and abdominal pain, intussusception and prolapse of a polyp through the anus.
- Treatment is snare polypectomy.
- Numerous hamartomatous polyps are present in juvenile polyposis syndrome, Peutz-Jeghers syndrome, Cowden disease, and Cronkhite-Canada Syndrome.
- Although sporadic hamartomatous polyps are not dysplastic and are not believed to be premalignant, the syndromes of hamartomatous polyposis have a significant rate of cancer development.

Inflammatory Polyps

- Inflammatory or pseudopolyps (a misnomer) are associated with colitis, most often ulcerative colitis and Crohn’s disease, but can result from any form of severe colonic inflammation.
- The inflammatory polyp is a remnant or island of normal or minimally inflamed mucosa.

- The presence of inflammatory polyps in inflammatory bowel disease is not associated with dysplasia or cancer risk.
- Inflammatory polyps are almost always multiple.
- Treatment is directed at the underlying bowel disease.

Lymphoid Polyps

- Benign enlargements of lymphoid follicles may produce polyps that are usually seen in the rectum. The overlying mucosa is normal.
- The lesions are typically multiple; their cause is unknown.
- Histologic criteria for establishing the benign nature of lymphoid polyps have been described: lymphoid tissue is entirely within the mucosa and submucosa; there is no invasion of the muscularis propria; at least two germinal centers must be seen; if the specimen does not include the muscle coat and no germinal centers are seen, then the diagnosis of lymphoid polyp cannot be made.

26. Polyposis Syndromes

A. Familial Adenomatous Polyposis

- Familial adenomatous polyposis (FAP) is an autosomal dominantly inherited condition caused by mutation of the *APC* gene, which occurs with a frequency of about 1:10,000.
- Mutation of this tumor suppressor gene results in a generalized disorder of tissue growth regulation and a range of clinical manifestations, principally the formation of multiple gastrointestinal adenomas and carcinomas, but also a variety of extraintestinal abnormalities.
- In the past, FAP accounted for about 1% of all colorectal cancers, but an understanding of its inheritance, surveillance of at-risk family members, and the introduction of prophylactic large bowel resection have resulted in this contribution now being in the region of 0.05% in countries where such services are available.
- Patients with a firm diagnosis of FAP or in whom it is suspected, together with their family, should be referred to a polyposis registry.

B. Polyposis Registries

- The aim of polyposis registries is to provide counseling, support, and clinical services for families with FAP. This includes thorough pedigree analysis and identification of at-risk family members, who are offered clinical surveillance and genetic testing so that those affected can be offered prophylactic surgery.
- Some registries also coordinate postoperative surveillance and provide a focal point for audit and research.
- Observational studies suggest that the introduction of registries, together with the use of prophylactic surgery, has led to increased

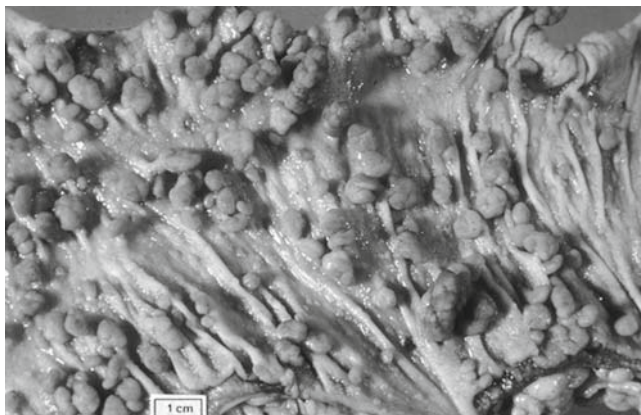


Fig. 26.1. The large bowel in classical familial adenomatous polyposis.

life expectancy and a dramatic reduction in the incidence of colorectal cancer in FAP.

C. Features of FAP

The Large Bowel

- The cardinal manifestation of FAP is the development of more than 100 colorectal adenomatous polyps, which inevitably progress to carcinoma if not removed (Fig. 26.1).
- Polyps usually appear in adolescence, with colorectal cancer diagnosed at an average age of about 40 years.
- Although most patients have a family history of FAP, about 25% do not, their disease being attributable to a new mutation. These individuals usually present with a symptomatic colorectal cancer or, more rarely, with anemia, rectal bleeding, or mucous discharge caused by benign polyps.

Extracolonic Manifestations

- The extracolonic manifestations of FAP are shown in Table 26.1. Two of these, duodenal cancer and desmoid disease, have

Table 26.1. Extracolonic features of FAP.

System	Feature	Frequency (%)
Upper gastrointestinal tract	Upper gastrointestinal adenomas	95
	Upper gastrointestinal carcinoma	5
	Fundic gland polyps	40
Connective tissue	Osteomas (especially jaw)	80
	Desmoids	15
Dental	Unerrupted and supernumerary teeth	17
Cutaneous	Epidermoid cysts	50
Endocrine	Adrenocortical adenomas	5
	Papillary thyroid carcinoma	1
Hepatobiliary	Biliary tract carcinoma	<1
	Hepatoblastoma	<1
Central nervous system	CHRPE	75
	Tumors (especially medulloblastoma)	<1

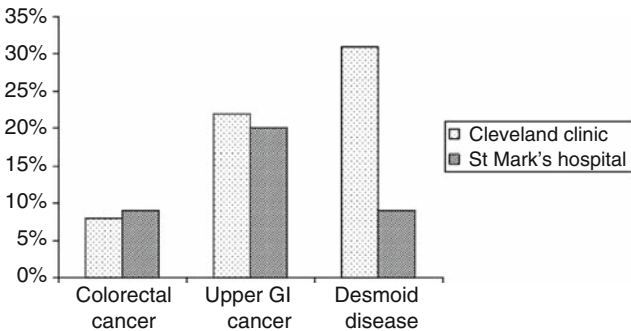


Fig. 26.2. FAP-related cause of death in patients after prophylactic colectomy.

now emerged as the major sources of morbidity and mortality, exceeding colorectal cancer as cause of death (Fig. 26.2).

- Other features may be a useful clue in diagnosis. Congenital hypertrophy of the retinal pigment epithelium (CHRPE), a patchy fundus discoloration, was considered a potential screening tool before advances in genetics. Isolated CHRPE is seen in normal people, but the presence of more than four is a specific phenotypic marker present in two-thirds of FAP families.

D. Genetics

The APC Gene

- In both FAP and the majority of sporadic colorectal cancers, mutation of the *APC* gene is one of the earliest events.
- More than 500 germline mutations causing FAP have been identified, almost all resulting in truncation of the APC protein product.
- Mutations have been found between codons 168 (exon 4) and 2,839 (exon 15), but most are between codons 168 and 1,640 (exon 15) in the 5' half of the coding region, with a particular concentration at two "hotspots," codons 1,061 and 1,309.

The APC Protein

- *APC* is ubiquitously expressed, but the mRNA is found at particularly high levels in normal colonic mucosa and in many epithelia is only found when cell replication has ceased and terminal differentiation is established.
- The 300-kDa APC protein is found in the cytoplasm and has sites of interaction with a range of other proteins including β -catenin and the cytoskeleton.
- APC binds and down-regulates cytoplasmic β -catenin, preventing its translocation to the nucleus. Abnormal APC protein fails to do this, so that β -catenin is free to enter the nucleus and form a complex which results in specific transcription of cell cycle stimulating DNA sequences, and hence proliferation.

Genotype-Phenotype Correlation in FAP

- There is evidence of correlation between the position of the germline *APC* mutation (genotype) and some aspects of the phenotype in patients with FAP (Fig. 26.3).
- Mutation at codon 1,309 is associated with particularly large numbers of colonic polyps, and between codon 1,250 and 1,464 with earlier onset of, and death from, colorectal cancer.
- Mutations located 5' of codon 160 and 3' of codon 1,597 have been identified in a form of FAP with attenuated colonic polyposis, which accounts for about 10% of those affected.

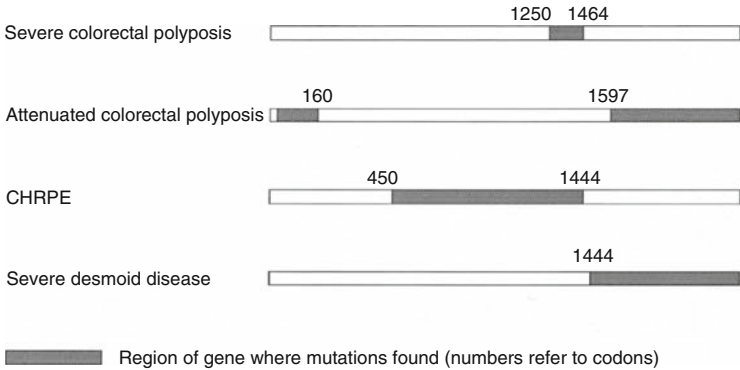


Fig. 26.3. Schematic representation of the *APC* gene showing genotype-phenotype correlations.

- CHRPE occurs only with mutation between codons 450 (exon 9) and 1,444, and desmoids occur in individuals with any mutation, but the presence of a germline mutation 3' of codon 1,444 can be associated with highly penetrant desmoid disease.
- However, identical *APC* mutations may be associated with diverse phenotypes, suggesting that other genetic modifiers are involved and that environment probably also has some influence.

MYH Polyposis

- An autosomal recessive form of familial adenomatous polyposis, caused by mutation in the MutY homolog (*MYH*) gene, has recently been described.
- Whereas many of the individuals identified with biallelic *MYH* mutations had fewer than 100 polyps, some had many hundreds, and thus a genuine clinical diagnosis of FAP.
- This discovery has major implications for genetic counseling, because, for the first time, an autosomal recessive form of FAP has been identified. This diagnosis should be considered in families in which no *APC* mutation has been identified, the mode of inheritance is not clearly autosomal dominant, or polyp numbers are low.

E. Clinical Variants of FAP

Attenuated FAP

- A group of patients have been described who develop fewer than 100 colorectal polyps (usually between one and 50), at a greater age (34–44 years) than in “classical” FAP, but who may still exhibit extracolonic manifestations and carry a germline *APC* mutation.
- Colorectal cancers also occur correspondingly later (mean 56 years) in this group, and with incomplete penetrance.
- The polyps have a rather different distribution, being more frequently found proximal to the splenic flexure, and their number varies significantly between family members, some of whom may have hundreds of adenomas.
- This feature can result in diagnostic confusion because the clinical picture is very similar to HNPCC, and indeed the first kindreds described were thought to have a form of HNPCC before they were identified as carrying *APC* mutations.
- A number of distinct mutations have been identified in individuals with attenuated FAP (AFAP); the mutations are clustered in exons 3 and 4, at the 5′ end of the gene, and also at the 3′ end of exon 15.
- The main consequence of the attenuated phenotype is that it causes diagnostic difficulty. Because the polyps are predominantly right sided, the disease may be missed by flexible sigmoidoscopy.
- A careful search (including upper gastrointestinal endoscopy) for extracolonic features of FAP, dye-spray colonoscopy to confirm polyp number, and testing of tumor or polyp tissue for microsatellite instability and mismatch repair immunohistochemistry may be helpful.
- Once the diagnosis is confirmed, management is essentially the same as for FAP with a more classic phenotype, although ileorectal anastomosis (IRA) is probably reasonable in most patients.

Gardner’s Syndrome

- Gardner described the association between FAP and epidermoid cysts, osteomas and “fibromas,” later found to be desmoid

tumors in 1953. The term “Gardner’s syndrome” was only later used to describe colorectal polyposis occurring with these extracolonic manifestations.

- Gardner’s syndrome is now considered to be genetically indistinct from FAP, and systematic examination has revealed that most patients with FAP have at least one extraintestinal feature.
- Although it is of historical interest, the term Gardner’s syndrome is no longer considered a genetic or clinically entity and should be regarded as obsolete.

Turcot’s Syndrome

- This syndrome is the association between colorectal adenomatous polyposis and central nervous system tumors.
- About two-thirds of families have mutations in the *APC* gene, with cerebellar medulloblastoma as the predominant brain tumor.
- Most of the other third, including Turcot’s original family, seem to be variants of HNPCC with glioblastoma as the predominant brain tumor, and multiple (but fewer than 100) colorectal adenomas.

F. Diagnosis

Genetic Testing

- Genetic testing should be preceded by thorough counseling, with the provision of written information about the process and consequences, and should only be done once informed consent has been obtained.
- The implications with respect to confidentiality, employment, insurance, and other financial issues vary from country to country, but must be discussed before testing.
- The first step in the process is mutation detection.
- If mutation detection has been successful, at-risk family members can be offered predictive testing with a high degree of accuracy. This testing is generally done between the ages of 12 and 15 years, when the individual is old enough to take part in genetic counseling. There is no need for testing to be

done earlier, because the disease does not usually become clinically manifest and treatment is rarely indicated before the mid-teens.

- In the event of negative predictive testing (i.e., an individual does not possess the family mutation), that person can be discharged from further surveillance and be reassured that they do not have FAP. This approach reduces the costs and risks associated with endoscopic surveillance, as well as removing the anxiety of living with a potential diagnosis of FAP.
- A positive test result allows optimal surveillance and prophylaxis to be targeted to those individuals who need it, and knowledge of the site of mutation can aid decision making with regard to prophylactic surgery.

Clinical Surveillance

- In kindreds in whom mutation detection has not been performed or has not been informative, at-risk individuals should be offered regular clinical surveillance.
- This surveillance starts at the age of 12–14 years, when adenomas would be expected to develop. Although there have been reports of polyps and even cancers occurring earlier than this, they are very rare.
- Clearly, anyone at risk of FAP should undergo colonoscopy if they become symptomatic.
- Surveillance is initially by flexible sigmoidoscopy, because it is well tolerated and most polyps are in the left colon and rectum. If surveillance continues, colonoscopy should then be performed commencing at approximately age of 20, alternating with flexible sigmoidoscopy so that one or the other examination is done each year.
- The vast majority of individuals with FAP will develop polyps by the age of 30, but there is no consensus regarding the age at which surveillance can cease. It should certainly continue until the age of 40 years, and longer in families in which the disease tends to manifest late.
- The use of a dye-spray technique, together with multiple biopsies to identify microadenomas, can be very helpful in identifying FAP and avoiding an underestimate of the polyp burden.

G. Management of the Large Bowel

Timing of Prophylactic Surgery

- Once FAP has been diagnosed, the aim is to perform prophylactic surgery. Invasive cancer is very rare in patients younger than the age of 18 years, and usually causes symptoms.
- Patients with severe polyposis (more than 1,000 colonic or more than 20 rectal polyps), or those people who are symptomatic, should have surgery as soon as possible.
- In those individuals with milder disease, it can usually be delayed until an educationally and socially convenient time (e.g., a long school vacation).
- In these circumstances, annual colonoscopy is recommended to monitor disease, but the aim should be to avoid delay, so that most will have surgery between the ages of 16 and 20, which is well before invasive disease usually develops.

Choice of Operation

- The surgical options for the management of this condition are proctocolectomy with end ileostomy (with or without Koch pouch), colectomy with IRA or proctocolectomy with ileal pouch anal anastomosis (IPAA).
- In most cases, the choice is between the latter two options, and is a matter of considerable ongoing debate, the essence of which is the balance between functional results and morbidity of surgery on the one hand and prevention of cancer on the other.
- Both procedures can be performed with laparoscopic mobilization, so that a midline laparotomy is not essential, a cosmetic improvement with potentially great appeal to essentially healthy young people undergoing this surgery.
- Both the IRA and the IPAA can be performed by laparotomy, laparoscopy, laparoscopic or hand-assisted procedures. The only proven benefit of the minimally invasive approaches is superior cosmesis as compared with laparotomy.
- IRA is more straightforward to perform, and requires only one procedure, and is usually associated with a shorter hospital stay and fewer complications. The risks of erectile and ejaculatory dysfunction caused by nerve damage during pelvic dissection

are significantly reduced, as is the significant reduction in fecundity observed in women after IPAA. In addition, bowel frequency and soiling are less.

- For a teenager facing prophylactic surgery, these functional factors are of great significance, particularly when most cancer risk is a few decades away and later conversion to a pouch is usually possible.
- The main disadvantage of IRA is that follow-up studies have shown a 12–29% risk of developing a cancer in the retained rectum within 20–25 years, the risk being dependent on age, rather than time since surgery.
- High-density (more than 1,000) colonic polyposis is associated with a cancer risk double that in milder disease, and also with severe polyposis in the rectum after IRA, leading to frequent need for completion proctectomy. FAP attributable to mutation in exon 15G, which includes the frequently mutated codon 1,309, consistently results in this severe colorectal phenotype. In this group, there is a high rate of subsequent proctectomy if IRA is done as the first-line procedure.
- IPAA has the attraction of entirely removing the colon and rectum; complication rates and functional results have improved with experience.
- Surveillance of ileoanal pouches from various centers has shown adenomas in up to 53%, and even some cancers.
- IRA is a reasonable and safe option today in young patients, particularly children and teenagers without 1,309 mutation or severe polyposis, and is strongly indicated if there are fewer than five rectal polyps.
- Most individuals presenting over the age of 25 years and those with severe polyposis or known to carry a mutation in codon 1,309 should be advised to undergo IPAA.
- But there are other issues: pouch surgery in young men has an approximately 1% risk of damage to erection, ejaculation, and bladder function; in women fertility is compromised. In addition, some families prefer a certain operation, regardless of the medical advice they have received.

Postoperative Surveillance

- After IRA, the retained rectum should be examined, ideally using a flexible sigmoidoscope, every 6–12 months, the interval depending on the severity of disease.

- In about two-thirds of patients, rectal adenoma regression is seen in the first few years after IRA.
- Polyps larger than 5 mm should be removed; repeated fulguration can result in scarring, making future surveillance difficult and unreliable.
- If severe dysplasia or uncontrolled polyposis develops, completion proctectomy with or without ileoanal pouch formation is indicated.
- In patients who have had IPAA, the pouch should be examined by flexible endoscopy annually, and a careful digital examination of the anorectal transition zone should be performed.

Chemoprevention

- In placebo controlled trials, both the nonsteroidal antiinflammatory drug (NSAID) sulindac and the COX-2 inhibitor celecoxib have reduced the number and size of colorectal adenomas.
- There are circumstances, for example, when completion proctectomy is impossible because of desmoid disease, or while awaiting surgery that must otherwise unavoidably be delayed, or in patients with a very high family risk of desmoid disease, when the use of such agents has a definite place.

H. Upper Gastrointestinal Polyposis

- Fundic gland polyps, which are areas of cystic hyperplasia, are found in about 50% of individuals with FAP. These polyps have a very low malignant potential, but gastric adenomas, dysplasia, and invasive carcinoma have been described.
- Prospective studies have demonstrated that more than 95% of individuals with FAP have duodenal adenomas, which tend to occur about 15 years later than large bowel polyps.
- Adenomas are found throughout the small intestine, but most are at or just distal to the ampulla of Vater.
- Duodenal or periampullary cancer occurs in approximately 5% overall, at an average age of 50 years.

Surveillance of the Duodenum

- Duodenal adenomas may be clearly defined polyps or more confluent areas, and biopsies of macroscopically normal mucosa may reveal microadenomas.

Table 26.2. Scoring of polyp features in Spigelman staging for duodenal adenomas.

Points allocated	No. of polyps	Size of polyps (mm)	Histology	Dysplasia
1	1–4	1–4	Tubular	Mild
2	5–20	5–10	Tubulovillous	Moderate
3	>20	>10	Villous	Severe

Table 26.3. Derivation of Spigelman stage from scores.

Total points	Spigelman stage	Suggested interval to next duodenoscopy (years)
0	0	5
1–4	I	3–5
5–6	II	3
7–8	III	1
9–12	IV	1

- In contrast to the situation in the large bowel, only a minority of these will progress to invasive carcinoma, but when they do the prognosis is very poor.
- To stratify the severity of duodenal polyposis, the Spigelman staging was developed and has been widely adopted (Tables 26.2 and 26.3).
- A prospective 10-year follow-up of Spigelman's original cohort has identified a 36% risk of developing invasive carcinoma in those with stage IV disease at the start of the study, and a 2% risk in those with stage II or III disease.
- Examination of the duodenum using both forward- and side-viewing scopes, together with multiple biopsies, starting at the age of 25 years, is recommended.

Management

- Management of severe duodenal polyposis is difficult, but the outcome once invasive carcinoma has developed is poor.
- Sulindac can result in regression of small polyps, but has little effect on larger ones.
- Duodenectomy, whether by a classical Whipple's procedure or using pylorus or pancreas preserving techniques, has been

considered a last resort because of its significant morbidity and mortality. However, given the very poor prognosis once neoplasia becomes frankly invasive, the high rate of diagnosis of invasive disease which was preoperatively thought to be benign, and the limitations of other options, it should be seriously considered for advanced premalignant disease.

I. Desmoid Disease

- Desmoids are locally invasive, nonmetastasizing clonal proliferations of myofibroblasts.
- The importance of desmoid disease lies in its significant contribution to disease-related mortality in FAP. Overall mortality ranges from 10 to 50%, and desmoids can also contribute to death from other causes by making surgery for rectal or upper gastrointestinal malignancy difficult or even impossible.
- Ten to fifteen percent of patients with FAP develop desmoid, with a peak incidence at around 30 years, 2–3 years after surgery. Whereas sporadic desmoids are considerably more common in females than males, this difference is less marked in the setting of FAP.

Clinical Features

- Desmoids occurring in association with FAP typically arise within the abdomen (70%), especially in the small bowel mesentery, and in the abdominal wall (15%), although many other sites have been described.
- Mesenteric desmoids (Fig. 26.4) can be either well-defined mass lesions, or a more diffuse fibromatous infiltration. Encasement or compression of the mesenteric blood vessels can result in ischemia and perforation of the bowel, and makes resection hazardous.
- A desmoid tumor can also cause direct compression of bowel and ureters. The presence of a desmoid may preclude adequate mesenteric length to fashion an IPAA.
- Trauma (particularly in the form of surgery) and estrogens have both been implicated in the etiology of these lesions, although they can occur spontaneously.

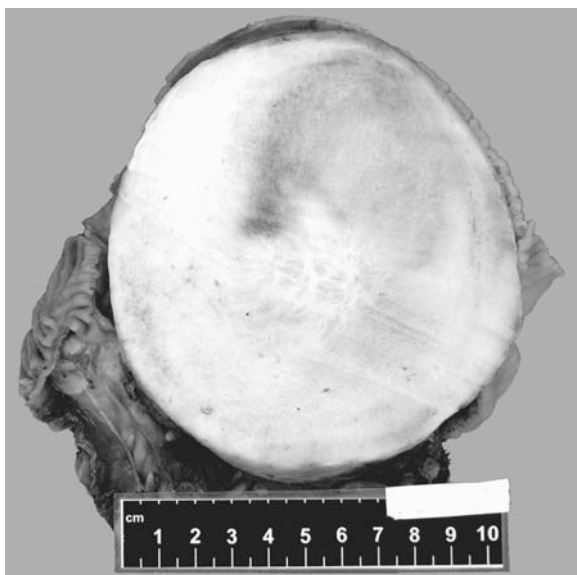


Fig. 26.4. Desmoid tumor arising in the small bowel mesentery.

- There is evidence for some degree of genotype-phenotype correlation. Desmoids have been reported to occur more frequently in patients with germline mutations located toward the 3' end of the gene.
- Desmoid natural history is very variable, about 10% resolving spontaneously, 10% growing rapidly and relentlessly, and the remainder either showing cycles of growth and resolution or remaining stable.

Investigation

- Computed tomographic scanning is the mainstay of investigation, allowing imaging and measurement of the desmoid itself, as well as demonstrating the relationship to other structures such as the ureters and bowel.
- Magnetic resonance imaging (Fig. 26.5) may have a place, and there is some evidence that T2-weighted signal intensity correlates with subsequent growth. Because only a small proportion of desmoids grow and cause significant clinical problems, the ability to predict such progression might be very useful.

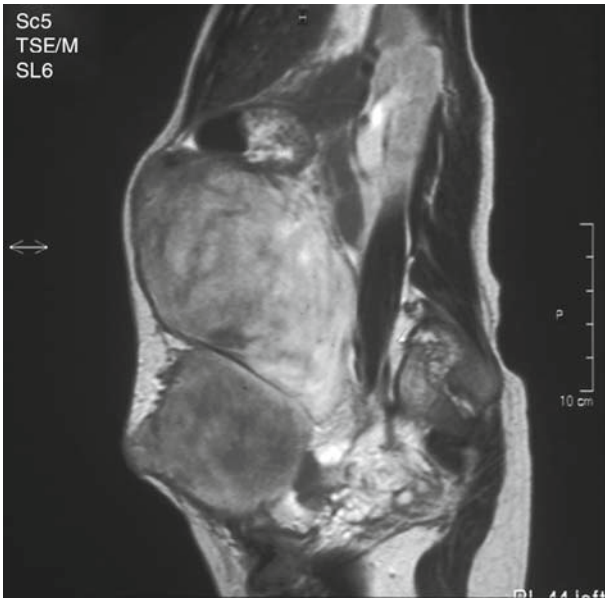


Fig. 26.5. MRI scan showing intraabdominal desmoid tumor.

- Because desmoid disease frequently causes ureteric compression, regular ultrasound monitoring of the kidneys permits timely intervention.

Management

- The treatment of desmoids is controversial, empirical, and often difficult.
- Surgery is widely accepted as the first-line treatment for troublesome extraabdominal and abdominal wall desmoids. Recurrence is common (20–50%), but complications are few.
- Within the abdomen the situation is very different, because the majority lie in the small bowel mesentery, encasing the mesenteric vasculature. The result is a high perioperative mortality rate (usually from hemorrhage) and substantial morbidity, particularly because of extensive loss of small bowel.
- Ureteric obstruction is best managed with stents, and proximal defunctioning may be required in some patients with bowel obstruction or perforation.

- Various medical treatments have been reported, the most widely used being NSAIDs (particularly Sulindac) and anti-estrogens (tamoxifen or toremifene).
- Cytotoxic chemotherapy has been used in irresectable or aggressive desmoid disease, and objective remissions have been noted with a variety of different agents. There have been several encouraging reports of an anti-sarcoma regimen consisting of doxorubicin and dacarbazine in the treatment of life-threatening intraabdominal desmoid disease and more recently a less toxic combination of vinblastine and methotrexate has produced some responses.
- One proposed treatment protocol for intraabdominal desmoid suggests initial treatment with sulindac 150–200 mg twice daily. If growth continues, tamoxifen (80–120 mg per day) is added. If progression is rapid or relentless, chemotherapy is considered.

J. Peutz-Jeghers Syndrome

- This syndrome, which has an incidence in the region of 1 in 200,000, consists of perioral, buccal, and occasionally genital melanin pigmentation together with gastrointestinal hamartomatous polyposis.
- Pigmentation can also be seen on the lips and sometimes on the eyelids, hands and feet, or be absent altogether. It usually appears in early childhood and tends to fade in the late twenties.
- The polyps occur predominantly in the small intestine (78%), but are also found in the stomach (38%), colon (42%), and rectum (28%).
- They are hamartomas with a characteristic branching morphology, containing smooth muscle. Adenomatous change with dysplasia and progression to invasive adenocarcinoma has been observed.

Inheritance

- Peutz-Jeghers is autosomal dominantly inherited with high penetrance, and is caused by mutation of *LKB1* (also known as *STK11*) on chromosome 19p13.3, which encodes a serine-threonine kinase of unknown function.

- Mutation of *LKB1* is only found in about 50% of cases, and has been formally excluded in some, suggesting that other genes are responsible in a proportion of cases.

K. Clinical Issues

Polyp-Related Complications

- The most common clinical problems in Peutz-Jeghers syndrome are anemia caused by chronic blood loss from large polyps and small bowel obstruction, caused by intussusception with a polyp at the apex.

Risk of Malignancy

- Follow-up studies have shown that individuals with this syndrome are at increased risk of developing a range of malignancies at a particularly young age. Indeed, by the age of 57 years, approximately half of all patients in one series had died of cancer, of which about half were gastrointestinal.
- It is estimated that there is a 50-fold excess of gastrointestinal cancer in Peutz-Jeghers syndrome, resulting in a lifetime risk of approximately 20% of colorectal cancer and about 5% of gastric cancer, as well as breast, pancreatic (30% lifetime risk), ovarian sex-cord tumors (10% of females), feminizing Sertoli cell testicular tumors in prepubertal boys, and cervical malignancies.

L. Management

Gastrointestinal Surveillance

- Two or three yearly gastroduodenoscopy and colonoscopy with polypectomy are recommended, with barium study (and increasingly capsule endoscopy) of the small intestine at the same interval.
- Hemoglobin should be checked annually. Small bowel polyps causing symptoms or anemia, or measuring more than 1.5 cm, should be removed at laparotomy with intraoperative enteroscopy.

Laparotomy in Peutz-Jeghers Syndrome

- The technique of laparotomy with intraoperative enteroscopy was introduced to reduce the repeated emergency laparotomies and small bowel resections undertaken on these patients.

Extraintestinal Surveillance

- Mammography in premenopausal woman lacks sensitivity, but there is little evidence to support ultrasound or MRI as alternatives.
- Testicular tumors tend to occur in prepubertal boys, and it would seem sensible to encourage regular examination.
- Women should undergo standard cervical and breast screening according to nationally agreed protocols.
- It is important that clinicians caring for these patients are aware of the high cancer risk, and maintain a high index of suspicion.

M. Juvenile Polyposis

- Juvenile polyps are hamartomas that lack smooth muscle histologically, having poor anchorage to the bowel wall, and not infrequently becoming detached and being passed anally.
- Solitary juvenile polyps may affect up to 2% of children and adolescents, but have little or no malignant potential.
- Juvenile polyposis is characterized by the finding of multiple juvenile polyps in the large bowel, although the stomach (and perhaps small intestine) is affected as well in about 50%.
- Most affected individuals develop 50–200 polyps, but some have very few.
- Adenomatous dysplasia occurs in up to half of these, which may then progress to invasive adenocarcinoma.
- Other morphologic abnormalities including macrocephaly, mental retardation, cleft lip or palate, congenital heart disease, genitourinary malformations, and malrotations are found in 10–20%.

N. Genetics

- This syndrome is genetically heterogeneous, with three separate genes currently implicated.
- Mutations have been identified in affected individuals in *SMAD4* which lies on chromosome 18q21 and is a known tumor suppressor gene, implicated in sporadic colorectal carcinogenesis.
- Recently, germline mutations of *BMPRIA* on 10q22, which encodes a protein involved in the same signaling pathway, have been found in a further 15%.
- *PTEN* mutations have also been reported in so-called “juvenile polyposis,” but it is as yet unclear whether these are genuine cases, or in fact Cowden syndrome, or even whether this syndrome is simply a clinical variant of juvenile polyposis.

O. Cancer Risk and Management

- The cumulative risk of colorectal cancer has been estimated at 30–50%, and 10–20% in the upper gastrointestinal tract.
- First-degree relatives of affected individuals should be screened by colonoscopy from around the age of 12 years if asymptomatic and five yearly thereafter.
- In most cases, the polyps can be controlled by regular endoscopic polypectomy, with both upper gastrointestinal endoscopy and colonoscopy recommended at least every 2 years. In cases in which polyps are either too numerous or too large to be managed in this way, colectomy and IRA or restorative proctocolectomy is advised.
- Affected individuals should also undergo upper gastrointestinal surveillance from the age of 25 years.

P. Other Juvenile Polyposes

Cowden Syndrome

- This is autosomal dominantly inherited and attributable to mutation of the *PTEN* gene, which encodes a protein tyrosine phosphatase involved in inhibiting cell growth.

- It is characterized by macrocephaly (30%), trichilemmomas (which are considered pathognomonic), and both benign and malignant neoplasms of the thyroid, breast, uterus, and skin. The hamartomas occur in the mouth as well as other parts of the gastrointestinal tract, resulting in a nodular appearance of the buccal mucosa.

Bannayan-Riley-Ruvalcaba Syndrome

- The juvenile polyps (50%) are associated with characteristic pigmented penile macules, macrocephaly, mental retardation (50%), lipomatosis, and hemangiomas. *PTEN* mutations have also been identified in this syndrome.
- The risk of colorectal cancer is not clear.

Q. Metaplastic Polyposis

- Metaplastic (hyperplastic) polyps are the most common lesions observed in the large bowel, being found in 40% at the age of 50 years. Their significance is unclear and there is much controversy surrounding their potential as precursors of adenomas and carcinoma.
- There is increasing evidence of correlation between numbers of metaplastic polyps and adenomas and cancer risk.
- In addition, metaplastic polyposis, a loosely defined entity in which multiple hyperplastic polyps are seen, does appear to be associated with an increased risk of colorectal cancer, often with microsatellite instability.

R. Cronkhite-Canada Syndrome

- This is a very rare condition with onset in adulthood and no evidence of an inherited predisposition. The disease is characterized by gastrointestinal hamartomatous polyposis together with ectodermal abnormalities including alopecia, onychodystrophy, and hyperpigmentation of the skin of the face and eyelids. The gastric mucosa resembles Ménétrier's

disease, and malabsorption and protein loss can lead to anemia, diarrhea, weight loss, edema, and tetany. Hypokalemia can also be a feature.

- Multiple juvenile-type polyps, with marked inflammatory features, are found in the duodenum in 75% of cases, the small intestine in 50%, and occasionally in the stomach and large bowel. Adenomatous change is seen and gastrointestinal cancer has been reported in about 10%.
- Management is essentially supportive, with aggressive fluid resuscitation and nutrition.

27. Colon Cancer Evaluation and Staging

A. Introduction

- Colorectal cancer is the third most common cancer affecting persons in the United States.
- Overall, approximately 38% of newly diagnosed patients with colorectal cancer in the United States will die of their disease.

B. Clinical Presentation

- Most importantly, colon cancers are diagnosed in patients who are asymptomatic, who undergo surveillance, or who are investigated for other problems such as anemia.
- In symptomatic patients, the most common presenting symptoms are abdominal pain, change in bowel habits, rectal bleeding, and occult blood in the stool. These symptoms frequently mean that the tumor is more advanced than it is in asymptomatic patients.
- Abdominal pain is the most common presenting symptom of colon cancer.
- In the early phases or stages of colon cancer without evidence of obstructive symptoms, the pain can be vague, dull, and poorly localized.
- With progression of the disease and a larger growing mass or a mass causing obstruction, symptoms of intestinal obstruction may eventually occur. This type of pain is characterized by crampy, colicky pain, often postprandial in nature.
- A change in bowel habits is the second most common symptom of colon cancer.

- In early lesions the change may be minor, with only a change in stool frequency. There can be changes in size, shape, and/or consistency of bowel movements. Characteristic changes include narrowing of the stool, irregular shape, and typically looser or diarrheal stool.
- Right-sided tumors occur where the bowel lumen is larger and the stool is liquid. Symptoms occur later, but on the left side where the stool is more solid and the lumen narrower, symptoms occur at an earlier stage.
- Rectal bleeding may be present in as many as 25% of patients with colon cancer.
- Bright red rectal bleeding is more consistent with a more distal location of a cancer. The mistake of attributing rectal bleeding to hemorrhoids even in a young population can lead to serious and at times fatal delays in the diagnosis of a colon cancer.
- Almost all patients, regardless of age, who present with rectal bleeding should undergo colonoscopic evaluation. In a series of 570 patients, 50 years of age or younger with rectal bleeding who underwent endoscopic evaluation, there was a 17.5% incidence of colorectal neoplasm.
- Patients with a positive stool guaiac test for occult blood performed for routine screening have a 5.1% chance of having an invasive cancer and a 24% chance of having a benign polyp.
- There has been a proximal shift overall of colon cancers with more tumors identified in the proximal colon. The Lahey Clinic reported a 10-year representative anatomic site distribution in which the cancer was located in the right colon in 18%, the transverse colon in 9%, the descending colon in 5%, the sigmoid colon in 25%, and the rectum in 43%.

C. Staging and Prognostic Factors

Evolution of Staging Systems

- The TMN staging system is the preferred method of colorectal cancer staging although both the Dukes' and modified Dukes' staging systems are still used.

Current Staging Systems

- The TNM classification is the system developed by the American Joint Committee on Cancer (AJCC) and the International Union Against Cancer (UICC). It utilizes three descriptors based on each letter in the name, T for tumor depth, N for nodal involvement, and M for metastases. Based on a combination of T, N, and M for any given tumor, an overall stage from Stage I to IV can be determined.
- The T stage can be divided into seven possible categories based on the depth of invasion. Tis, carcinoma in situ, represents a non-malignant tumor, T1 has invasion into the submucosa, T2 has invasion into the muscularis propria, T3 has invasion into the subserosa or nonperitonealized pericolic or rectal tissue (through the bowel wall). T4 has invasion of other organs or structures.
- The T3 category can be further subdivided by the depth of penetration into the muscularis propria.
- The N stage can be divided into three categories. N0, with no lymph node involvement, N1 with 1–3 lymph nodes involved, and N2 with 4 or more lymph nodes involved.
- The M stage is only divided into two categories, either no metastases (M0) or distant metastases (M1).
- Typically, the combination of T, N, and M will lead to one of four stages based on the combination of findings.
 - Stage 0 is Tis, N0, and M0.
 - Stage 1 is T1 or T2, N0, M0.
 - Stage 2 is T3 or T4, N0, M0.
 - Stage 3 is Any T, N1 or N2, and M0.
 - Stage 4 is Any T, Any N, and M1.
- In the most recent AJCC/UICC Definitions, Stage II and III are subdivided into two Stage II categories: Stage IIA (T3, N0, M0) and Stage IIB (T4, N0, M0); and three Stage III categories: Stage IIIA (T1 or T2, N1, M0), Stage IIIB (T3 or T4, N1, M0), and Stage IIIC (Any T, N2, M0).

D. Clinical Prognostic Factors

Age

- As with many cancers, colon cancer incidence increases with increasing age. Most series report a mean age in the sixth decade for nonhereditary colon cancer.

- Patients with familial adenomatous polyposis (FAP) will present with colon cancer in their mid to late 30s if colectomy is not performed before this age.
- Patients with hereditary nonpolyposis colorectal cancer (HNPCC) can present at any age but tend to have colon cancer between the ages of 40 and 60, significantly younger than individuals with nonhereditary colon cancers.

Symptoms

- Obstruction and perforation are poor prognostic signs often associated with advanced disease. In addition, because patients are operated on in an urgent manner, their operative morbidity and mortality are increased.
- Patients with a perforated cancer have a 9% operative mortality compared with obstructed cancer patients which have a mortality rate of 5%.

Blood Transfusion

- Blood transfusions can cause immunosuppression in the post-operative period which may allow for an inability to combat tumor cells shed at the time of surgery and theoretically lead to a worse prognosis.
- Chung et al. reviewed 20 papers, representing 5,236 patients supporting the hypothesis that perioperative blood transfusions are associated with an increased recurrence and death from colon carcinoma.

Adjacent Organ Involvement

- Local extension of colon carcinoma can involve any structure or organ adjacent to the primary tumor.
- It occurs in 5–12% of colorectal cancers. All tumors with local extension would be considered T4.
- For right colon cancers, the most frequently involved structures are the liver, duodenum, pancreas, and abdominal wall.
- Izbicki et al. reported on 83 patients with colorectal cancer undergoing extended en bloc resections. Comparing extended to nonextended resections; mean survival of both groups was

approximately 45 months conferring the benefit of extended resections when necessary to achieve R0 resections.

E. Histologic/Biochemical/Genetic Factors

Histologic Grade

- Broders described classifying adenocarcinomas by the degree of differentiation.
- Three grades are used and include Grade 1 with well-differentiated features, Grade 2 moderately differentiated, and Grade 3 poorly differentiated.
- The vast majority of colon cancers are moderately differentiated (Grade 2) with preservation of gland-forming architecture.
- The degree of differentiation corresponds to prognosis. Poorly differentiated tumors have a worse prognosis stage for stage compared with better differentiated tumors.

Mucin Production and Microsatellite Instability

- Microsatellite instability, known as MSI, is associated with HNPCC.
- MSI is an alteration in mismatch repair genes which are important to repairing errors in replication. When altered, they can lead to colorectal cancer.
- Because there is loss of one of the two alleles in HNPCC, these patients tend to present earlier in life, with multiple colonic and extracolonic cancers.
- Many HNPCC cancers are mucin producing which when present have a better prognosis compared with non-mucin-producing tumors in these patients.

Signet-Cell Histology

- Signet-ring or signet-cell tumors have a worse prognosis in many intestinal cancers. Signet-cell tumors tend to be of a more advanced stage when discovered.
- In a comparison between signet-ring and non-signet-ring colon cancers, it has been noted that patients with signet-ring cancers

were younger, had more advanced stages, and an increased incidence of liver metastases. In addition, the rate of curative resection was lower at 35% compared with 79%.

Venous Invasion

- Blood vessel invasion has been linked with poor prognosis both independently as well as with its association with lymph node metastasis.
- Venous invasion in colon cancer occurs in 42% of patients and increases with increasing grade and stage. Patients with blood vessel invasion had a 74% survival compared with those without it at 85%. In those patients with both intramural and extramural vascular invasion, the prognosis was even worse at 32%.

Perineural Invasion

- The growth of tumor along perineural spaces is known as perineural invasion and, similar to venous invasion, it increases with increasing grade and stage of the tumor.
- Numerous studies have confirmed poorer prognosis when perineural invasion is noted.

Lymph Node Involvement

- Lymph node metastasis has been long understood to be one of, if not the most, important prognostic factors in colon cancer outcome.
- It has been reported by Scott and Grace that, if 13 lymph nodes are not recovered, adequate staging cannot be performed.
- The main determinant for an adequate lymph node harvest is surgical but a variety of means to enhance the yield have been developed and include fat clearance with xylene, other chemicals, and polymerase chain reaction techniques. Using these techniques, more lymph nodes, or lymph nodes not found by standard techniques, can be discovered, improving the accuracy of staging and allowing for better prognosis and application of adjuvant treatment.

Carcinoembryonic Antigen

- Carcinoembryonic antigen (CEA), a glycoprotein absent in normal colonic mucosa but present in 97% of patients with colon cancer.
- CEA increase correlates with either disease that has metastasized to the liver or with very large tumors.
- It is not useful for screening but can be used to follow patients with colon cancer.
- A CEA of greater than 15 mg/mL predicts an increased risk of metastases in otherwise apparently curable colon cancer.
- A normal preoperative CEA may become increased with metastatic disease.

Sentinel Node

- The idea of a sentinel lymph node being present and if identified be able to predict lymph node metastases has become standard of care in breast cancer and melanoma. Its application to colon cancer is in its infancy and may be less important in colon cancer than these other malignancies.

DNA Ploidy

- Normal cells are made up of diploid cells. Tumors can maintain normal diploid cells or can be aneuploid. Numerous studies show that nondiploid tumors have a worse prognosis and correlate with more advanced Dukes' stage.

F. Spreading Patterns

Intramural Spread

- Intramural spread is the tumor spreading along the bowel wall either proximally or distally in one of the bowel wall layers. Like rectal cancers, colon cancer rarely spreads this way.
- In a study of 42 colorectal cancers of which 64% were colonic, the maximum extent of intramural spread was 2 cm. This finding supports the practice of excising 5 cm or more of colon on either side of a tumor to decrease the risk of anastomotic recurrence.

Transmural Spread

- Almost all colon cancers start as a mucosal lesion and then penetrate a variable degree into deeper layers of the colonic wall.
- Transmural spread is the mechanism that produces T4 tumors.

Margins

- The acceptable bowel wall margins are dictated by three issues: first, thickness of penetration of the bowel wall margin and the risk based on the distance of local tumor spread intramurally.
- The “ideal extent of a bowel resection is defined by removing the blood supply and the lymphatics at the level of the origin of the primary feeding arterial vessel.”

Radial Margins

- It has been shown that positive circumferential margins in rectal cancer are associated with local recurrence rates as high as 85%.
- In colon cancer, the radial margins are less important with the exception of T4 tumors where en bloc resection is required.

Transperitoneal/Implantation

- Tumors with serosal involvement can shed viable tumor cells which can spread throughout the peritoneal cavity and implant on a variety of structures. Usually, tumors will implant on the ovaries, omentum, serosal, or peritoneal surfaces. When widespread, this is known as carcinomatosis.
- When localized to the ovaries which occurs in 3–5% of patients, bilateral oophorectomy should be performed.

Lymphatic

- Lymphatic invasion is the most common mechanism leading to metastatic disease.
- Lymphatics exist within the colonic wall and lymphatic invasion correlates with the depth of penetration of colon cancers.
- T1 tumors have a risk of lymph node involvement up to 9%, T2 up to 25%, and T3 up to 45%.

- The lymphatic drainage goes along the venous drainage of the colon, ultimately coursing through the portal vein and into the liver. Metastatic liver disease is believed to occur typically as a result of lymphatic spread.

Hematogenous

- Hematogenous spread of colon cancer is less common than lymphatic spread. Hematogenous spread will bypass the liver and allow tumor cells to go peripherally into the systemic circulation.
- This is thought to be the mechanism for the development of pulmonary metastases.

Detection and Management of Synchronous Lesions

- Synchronous polyps and cancers occur in patients with colon cancer. Most colon cancers are diagnosed by colonoscopy and the remainder of the colon is evaluated at the same time by colonoscopy.
- However, if an obstructing lesion is noted that will not allow a colonoscope to pass, evaluation of the more proximal colon may be jeopardized. Alternatives to evaluating the remainder of the colon in these instances include contrast enemas, virtual colonoscopy, or intraoperative colonoscopy at the time of resection.
- When a colon cancer is diagnosed by colonoscopy, synchronous cancers occur in 6% or fewer of patients. When present, it should raise the suspicion of possibly HNPCC which is associated with synchronous colon cancer.
- When synchronous colon cancer is diagnosed, a subtotal colectomy should be considered

Distant Metastatic Disease

- Distant metastatic disease associated with colon cancer is almost always either liver or lung metastases.
- The search for liver and lung metastases can be accomplished by a variety of imaging studies including ultrasound, computed tomography (CT) scan, magnetic resonance imaging (MRI), chest X-ray, and positron emission tomography (PET) scans.

Liver Metastases

- CT scan is the most frequently used method to preoperatively and postoperatively determine the presence or absence of liver metastases associated with colon cancer.
- There are numerous advantages to cross-sectional imaging such as CT over ultrasound and include the ability to find abdominal wall or contiguous organ invasion as well as liver metastases.
- Standard CT scan is 64% sensitive in identifying liver lesions larger than 1 cm.
- MRI of the liver has been poorly studied and is used less often in the evaluation of liver metastases.

Lung Metastases

- Lung metastases occur in 3.5% of patients with colon cancer.
- CT scan clearly has advantages over plain radiographs and can identify and characterize lung pathology better than plain X-rays. Given that most patients will undergo CT imaging of the abdomen before surgical intervention, the addition of imaging of the chest via CT seems reasonable.
- One must be careful about the amount of intravenous contrast administered when simultaneously scanning multiple regions such as chest, abdomen, and pelvis.

PET Scans

- PET scans are currently approved only for patients with suspected metastatic disease and not for the use in primary staging of colon cancer.

Appendix: Practice Parameters for the Detection of Colorectal Neoplasms

Prepared by The Standards Committee, The American Society of Colon and Rectal Surgeons

Drs. Clifford L. Simmang and Peter Senatore, Project Directors; Ann Lowry, Chair; Terry Hicks, Council Representative; Marcus Burnstein, Frederick Dentsman, Victor Fazio, Edward Glennon, Neil Hyman, Bruce Kerner, John Kilkenny, Richard Moore, Walter Peters, Theodore Ross, Paul Savoca, Anthony Vernava, W. Douglas Wong

Colorectal cancer is the most preventable visceral cancer, and its incidence makes it one of the most important. The lifetime probability of an individual developing colorectal cancer is 5–6%, translating into an estimated 133,500 new cancers of the colon and rectum diagnosed annually. It is further estimated that 54,900 people will die of their cancer each year. Although the incidence was relatively stable during the last half of the twentieth century, there seems to have been a decrease during the past decade. Mortality is also decreasing, which suggests greater awareness of the disease and improved detection. Nevertheless, 65% of patients present with advanced disease. It is also reported that when the disease is localized, the 5-year survival rate is approximately 90% for colon cancer and 80% for cancer of the rectum. Most cases are diagnosed after 50 years of age. Although the results of some investigations have not demonstrated a reduction in mortality with screening, those statistics do not reflect the number of patients who are spared from death by early detection and endoscopic removal of polyps, which blunts the adenoma-to-carcinoma sequence.

A consortium of five medical societies (American College of Gastroenterology, American Gastroenterological Association, The American Society of Colon and Rectal Surgeons, American Society for Gastrointestinal Endoscopy, and Society of American Gastrointestinal Endoscopic Surgeons) responded to a request for a proposal from the Agency for Health Care Policy and Research to develop national guidelines for colorectal cancer screening. An interdisciplinary panel of 16 health care professionals from the fields of medicine, nursing, consumer advocacy, health care economics, behavioral sciences, and radiology evaluated the currently available evidence for colorectal cancer screening and made

recommendations for physicians and the public. The panel studied 3,500 peer-reviewed published articles and analyzed 350 articles in detail specifically assessing the following (1) performance of screening tests; (2) effectiveness of screening tests; (3) acceptability to patients; (4) cost effectiveness; and (5) outcome. A computer simulation of the consequences of conducting the various screening strategies in the population was done to determine the risks and benefits of each test. The guidelines made recommendations for people in two groups: average individuals and individuals at increased risk for developing colorectal cancer. All screening strategies, including annual fecal occult blood testing, screening sigmoidoscopy every 5 years, screening by both annual fecal occult blood testing and flexible sigmoidoscopy (every 5 years), double contrast barium enema every 5–10 years, and colonoscopy every 10 years were found to have a net benefit. The panel analyzed an Office of Technology Assessment study for screening average-risk individuals, which demonstrated that costs associated with colorectal cancer screening are within the range of cost effectiveness frequently accepted for other tests, such as mammography.

Recently revised colorectal cancer screening guidelines from the American Cancer Society have been announced. The new guidelines divide the population into three categories – average, moderate, and high risk – with specific recommendations for each. The American Society of Colon and Rectal Surgeons endorses the colorectal cancer screening guidelines by the American Cancer Society, which were based in part on “Colorectal Cancer Screening and Surveillance Clinical Guidelines and Rationale” published by the consortium and specialty societies and discussed above. Guidelines governing the detection of colorectal neoplasms as set forth by The American Society of Colon and Rectal Surgeons Task Force are presented in Table 27.1.

Low-Risk Individuals

For low-risk asymptomatic persons, screening should begin at the age of 50. Low-risk or average-risk patients are those who are asymptomatic, age 50 or older, have a family history of colorectal cancer limited to non-first-degree relatives, and no other risk factors (65–75% of people). Annual digital rectal examination should be performed. In addition, fecal occult blood testing (FOBT) should be performed annually. Yearly testing is chosen because the randomized trials show that yearly testing is more effective for decreasing mortality than testing every 2 years. Rehydration improves the sensitivity of the test at the

Table 27.1. Screening guidelines.

Risk	Procedure	Onset (age, years)	Frequency
I. Low or average: 65–75%	Digital rectal exam and one of the following:	50	Yearly
A. Asymptomatic: no risk factors	Fecal occult blood testing and flexible sigmoidoscopy	50	FOBT yearly, flex-sig every 5 years
B. Colorectal cancer in no first-degree relatives	Total colon exam (colonoscopy or double contrast barium enema and proctosigmoidoscopy)	50	Every 5–10 years
II. Moderate risk: 20%–30% of people			
A. Colorectal cancer in first-degree relative, age 55 or younger, or two or more first-degree relatives of any age	Colonoscopy	40 or 10 years before the youngest case in the family, whichever is earlier	Every 5 years
B. Colorectal cancer in a first-degree relative older than age 55	Colonoscopy	50 or 10 years before the age of the case, whichever is earlier	Every 5–10 years
C. Personal history of large (>1 cm) or multiple colorectal polyps of any size	Colonoscopy	1 year after polypectomy	If recurrent polyps, 1 year If normal, 5 years
D. Personal history of colorectal malignancy, surveillance after resection for curative intent	Colonoscopy	1 year after resection	If normal, 3 years If still normal, 5 years If abnormal, as above

(continued)

Table 27.1. (continued)

Risk	Procedure	Onset (age, years)	Frequency
III. High risk (6–8% of people)			
A. Family history of hereditary adenomatous polyposis	Flexible sigmoidoscopy; consider genetic counseling; consider genetic testing	12–14 (puberty)	Every 1–2 years
B. Family history of hereditary nonpolyposis colon cancer	Colonoscopy; consider genetic counseling; consider genetic testing	21–40	Every 2 years
		40	Every years
C. Inflammatory bowel disease			
1. Left-side colitis	Colonoscopy	15th	Every 1–2 years
2. Pancolitis	Colonoscopy	8th	Every 1–2 years

FOBT fecal occult blood testing; *Flex-sig* flexible sigmoidoscopy

expense of specificity. Dietary avoidance of rare meat, turnips, melons, horseradish, salmon, and sardines can decrease the rate of false-positive test results. Aspirin and other nonsteroidal drugs should also be avoided. Diagnostic workup of positive FOBT results should include an evaluation of the entire colon. Double-contrast barium enema can examine the entire colon with relatively high sensitivity and specificity for large polyps (>1 cm) and cancers and is less expensive than colonoscopy. However, it is not possible to biopsy or remove neoplasms during the same procedure, so that patients with abnormalities must undergo an additional examination by colonoscopy to establish the diagnosis and provide treatment. Adding flexible sigmoidoscopy to double-contrast barium enema increases sensitivity, but the magnitude in clinical importance of the additional sensitivity is uncertain. For these reasons, colonoscopy, which can examine the entire colon with few false-negative or false-positive findings and can provide definitive treatment of polyps and some cancers during the same procedure, is

usually chosen. For patients who have negative FOBT results, flexible sigmoidoscopy performed every 5 years is recommended. A 5-year interval is chosen because of the observation that few polyps arise and progress to advanced cancer in a 5-year period. If a polyp is identified, it should be biopsied. If the pathologic diagnosis is a hyperplastic polyp, then no additional evaluation is required. If the pathologic diagnosis is an adenoma, then colonoscopy should be recommended.

Colonoscopy permits visualization of the entire colon directly, along with detection and removal of polyps and biopsy of cancers throughout the colon. It can be considered for screening of average-risk individuals. An interval of 10 years has been chosen for asymptomatic, average-risk people because of strong direct evidence that few clinically important lesions are missed by this examination and that it takes an average of approximately 10 years for an adenomatous polyp, particularly one <1 cm in diameter, to transform into invasive cancer. In addition, a controlled trial has shown a very low incidence of advanced adenomas during surveillance follow-up colonoscopy after an initial examination with negative results. Indirect evidence from the National Polyp Study indicates that few polyps will arise and progress to advanced cancer in less time in patients with no special risk factors.

Moderate-Risk Individuals

Patients at moderate risk for cancer are those who have one or more first-degree relatives with colorectal cancer or personal history of colorectal neoplasia (20–30% of people).

Colorectal Neoplasia in a Close Relative

People with a first-degree relative (sibling, parent, or child) who has a colorectal cancer or adenomatous polyp should be offered the same options as average-risk people, but with several important differences. Those people with two or more affected close relatives or with an affected close relative younger than age 55 are at even further increased risk, and surveillance should begin at the age of 40 years or 10 years before the youngest case in the family, whichever is earlier. Colonoscopy is the recommended procedure of choice in this situation. If colorectal cancer is detected in a close relative older than age 55, then screening should begin with colonoscopy at the age of 50 or 10 years before the age of the case, whichever is earlier.

Patients with Other Risk Factors

Patients with prior endometrial, ovarian, or breast cancer and those who have had pelvic radiation, could be followed up according to the guidelines established for patients with a family history of colon cancer. Patients with a ureterocolonic anastomosis should be followed up yearly with flexible sigmoidoscopy as a minimum and colonoscopy if the area of anastomosis cannot be visualized by sigmoidoscopy. Total colonic examination may be recommended for patients with acromegaly, *Streptococcus bovis*, *Streptococcus sanguis*, or a *Clostridium septicum* bacteremia, schistosomiasis, extramammary perianal Paget's disease, and dermatomyositis.

Polyp Surveillance

For patients who have had a neoplasm identified by sigmoidoscopic examination, a biopsy should be performed. If the pathologic finding is an adenoma, then a colonoscopy should be performed. For a polyp detected during a barium enema examination, a colonoscopy is the recommended procedure. Colonoscopy can directly inspect the entire colon for the presence of synchronous lesions and allow the removal of polyps or biopsy of a larger neoplasm. If a large (>1 cm) polyp is removed, or if multiple polyps of any size are identified and removed, colonoscopy should be repeated 1 year later. If a single, small (<1 cm), tubular adenoma is identified and removed, colonoscopy should be repeated in 3–5 years. If the results of this examination are normal, then colonoscopy should be repeated every 5 years. The finding of an adenoma at any of the follow-up examinations may prompt yearly colonoscopy until the colon is again cleared of polyps. Studies may need to be repeated when the entire colon is not visualized, when there is poor preparation or spasm, when polypectomy is deemed incomplete or complications ensue that require intervention, when there is diagnostic uncertainty, or when tumor debulking is necessary. If the pathologic diagnosis of the initial polyp is a hyperplastic polyp, no diagnostic studies are required at this time and the patient should continue appropriate screening evaluation.

If a polypectomy is performed for curative intent of an invasive cancer, follow-up colonoscopy should be performed in 6–12 months. If these examination results are normal, colonoscopy should be repeated every 3–5 years as long as the colon remains clear. If, between total colonoscopic examinations, it is necessary to visualize high-risk sites, such as those from which a large, sessile polyp has been removed from the rectum in a piecemeal manner, sigmoidoscopy is a viable alternative.

Personal History of Colorectal Malignancy

When the colon has been cleared by barium enema or colonoscopy before resection for cancer, colonoscopy or barium enema is performed again approximately 1–3 years after surgical resection. If the colon was not cleared before surgical resection, colonoscopy or barium enema is recommended in 3–6 months. If the follow-up examination results are normal, it is repeated in 3 years and if they are still normal, the interval between colonic surveillance can be extended to every 5 years.

High-Risk Individuals

Patients at high risk for developing colorectal cancer are those with a hereditary or genetic predisposition for development of colorectal cancer, and those patients with inflammatory bowel disease (6–8% of people).

Family History of FAP

FAP is characterized by the development of multiple (more than 100) adenomatous polyps in the colon and rectum. Inheritance is by an autosomal dominant manner with high penetrance.

It is recommended that endoscopic examination of the rectum and sigmoid colon be performed every 12 months beginning at the age of puberty (12–14 years). For those patients with familial adenomatous polyposis who have undergone a total abdominal colectomy with an ileorectal anastomosis, it may be desirable to examine the rectum every 6–12 months.

Definitive data regarding appropriate duration of screening is not available. As a general guideline, intense surveillance could change to routine screening at age 40 in families with uniformly severe disease. In families with variability in the severity of polyposis, screening should continue until age 60, although the interval might be increased to 2 years after age 40.

People with a family history of FAP should also be considered for genetic counseling and consider genetic testing to see if they are gene carriers. A negative genetic test result rules out FAP only if an affected family member has an identified mutation. Gene carriers or indeterminate cases should be offered flexible sigmoidoscopy as recommended above. If polyposis is present, colonoscopy is not a reliable screening test for malignancy and prophylactic surgery is indicated, preferably before the patient is 20 years old. If genetic test results are negative, screening should be the same as for low-risk individuals.

Family History of HNPCC

HNPCC is an autosomal dominant disease characterized by early-onset colorectal tumors, primarily in the right colon, that are frequently associated with other cancers. A common standard for the diagnosis of HNPCC, referred to as the Amsterdam criteria, is the existence of three or more relatives with colorectal cancer, one of whom is a first-degree relative and involves at least two generations, with one or more cases diagnosed before the age of 50. The Amsterdam criteria have been criticized as being too rigid, failing to take into account small families where a dominant pattern of inheritance may not be obvious and extracolonic cancers that make up the syndrome of HNPCC. When a strong family history is present, the possibility of HNPCC must be considered.

People with a family history of colorectal cancer in multiple close relatives and across generations, especially if the cancers occurred at a young age, should receive genetic counseling and consider genetic testing for HNPCC. When performed, genetic test results are positive in approximately 80% of these families. It is recommended that individuals considering genetic testing be counseled regarding the unknown efficacy of measures to reduce risks and associated issues and that care for individuals with cancer-predisposing mutations be provided whenever possible within the context of research protocols designed to evaluate clinical outcomes.

Endoscopic examination should begin between the ages of 20 and 25 years or at least 10 years younger than the family member who had colorectal cancer. The endoscopic procedure of choice is colonoscopy and this should be performed every 2 years until the age of 40 years. After the age of 40 years, colonoscopy should be performed annually. Unless genetic testing results are negative, surveillance should be performed as long as the patient's overall medical condition warrants it. Colonoscopy is selected because the cancers and precursor adenomatous polyps are both predominantly proximal to the splenic flexure.

Inflammatory Bowel Disease

Ulcerative Colitis

The increased risk of developing colorectal cancer in patients with inflammatory bowel disease is well established, with a lifetime incidence of 6% in patients with ulcerative colitis (UC). Up to 1% of all cases of colorectal cancers seen in the general population may be associated with inflammatory bowel disease. The risk of developing colorectal cancer is

low until 8 years of disease duration, after which the risk increases exponentially to reach as high as 56 times that of the general population by the fourth decade of disease. The degree of risk also depends on extent of involvement and age of onset. The strongest predisposing factor for cancer is the anatomic extent of the inflammation, with patients at most risk if they have pancolitis or ulceration extending proximally to the splenic flexure and least risk if the disease is limited to the rectum and sigmoid colon. Because the risk of developing dysplasia or cancer increases with longer disease duration, efficient surveillance calls for more frequent testing as the risk increases with duration. It is common practice to perform surveillance colonoscopy every 1–2 years after 8 years of disease in patients with pancolitis or after 15 years in patients with colitis limited to the left colon. Ulcerative proctitis does not need extraordinary cancer surveillance.

Crohn's Disease

Patients with Crohn's disease have a 20-fold increased risk of colon carcinoma over the general population; however, less than the increased risk seen with UC. Compared with sporadic colorectal cancer, colorectal cancers in Crohn's disease occur at an earlier age (48 vs. 60 years), are more often located in the right colon, and are more frequently multiple. In particular, sites of stricture and fistula formation seem particularly prone to the development of carcinomas. It is clear that Crohn's disease warrants attention to risk of cancer; however, evidence for the most appropriate surveillance program is lacking. We recommend a moderate program, such as recommended for left-sided UC with surveillance colonoscopy every 1–2 years after 15 years of disease.

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28. Surgical Management of Colon Cancer

A. Preoperative Preparation

- Planning an operation for a patient with colon cancer requires the surgeon to have as much understanding as possible of the tumor's location in the bowel, the stage of the cancer, and the patient's physiologic status.
- Localization of the tumor and the histopathology are important data elements that allow preoperative selection of an operative plan and selection of the optimal resection margins.
- The presence of a lesion at watershed areas of vascular supply such as the hepatic and splenic flexures may require more extensive resection of colonic length for a safe and complete oncologic procedure. An extended right or left colectomy may be indicated to remove all contributing vascular supplies.
- In addition, information consistent with the hereditary non-polyposis colon cancer (HNPCC) (right-sided lesion, Crohn's-like inflammatory response, young patient, and positive family history) would support the resection of the abdominal colon rather than a simple segmental resection.
- This diagnosis may also be supported by special stains of the biopsy specimen which demonstrate microsatellite instability, the hallmark of the disease which develops from mutations in the DNA mismatch repair system.
- Colonoscopy is widely used today and represents the optimal means of diagnosing the lesion, identifying location, providing histopathologic material, and tattooing for intraoperative localization when required.

- Contrast enema is another means of localizing the lesion anatomically which should be considered to localize a lesion when colonoscopy fails to clearly define the portion of bowel involved.
- Computed tomography (CT) allows the localization of larger lesions, identification of local organ invasion, and provides important staging information regarding the presence of extra-colonic disease, particularly liver involvement.
- Although positron emission tomography has recently been approved for colon cancer staging, in isolation its role in assessing the majority of primary, curable lesions remains speculative.
- More recent prospective, randomized studies have questioned the additional benefit of luminal preparation, compared with the use of appropriate intravenous antibiotics administered in a timely manner.
- A mechanical bowel preparation is still advantageous for laparoscopic colectomy because the reduction in stool volume within the colon makes manipulation of the bowel easier with the small instruments and reduces the size of the extrac-tion site.

B. Surgical Technique

Right Colectomy

- The key to an oncologically safe and effective resection of a colon cancer requires clear lateral margins, resection of the locoregional lymph node bearing mesentery for both cure and staging, and fashioning of an accurate and well-vascularized anastomosis. Therefore, a right colectomy is required for a tumor at any location in the ascending colon.

Extended Right Colectomy

- An extended right colectomy should be performed for any lesion involving the transverse colon including the hepatic and splenic flexure (see Fig. 28.1).

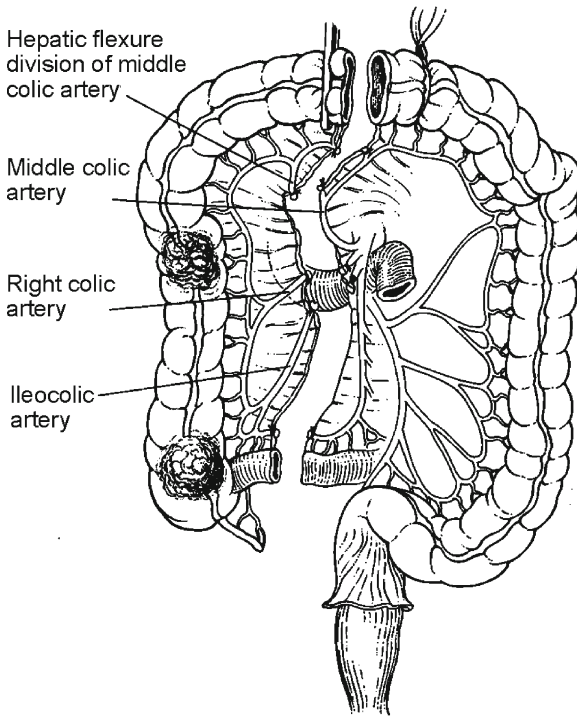


Fig. 28.1. The drawing demonstrates the appropriate levels for vascular ligation and colonic transition for a right hemicolectomy. Notably, the transverse colon is divided just to the right of the main trunk of the MCA, although the right branch of the MCA may be taken, if required. The middle colic vessels are demonstrated and may be ligated during the performance of an extended right hemicolectomy. This leaves the descending colon in place supported by the left colic artery.

Left Colectomy

The Lateral Approach

- An incision is made first at the attachments of the sigmoid colon at the pelvic brim and then along the left gutter medial to the white line of Toldt. An areolar tissue plane is found between the mesentery of the left colon and retroperitoneal

structures which can be bluntly dissected as far as the midline. The splenic flexure is mobilized with this plane as the guide. Finally, the medial incision is made along the base of the left colon mesentery to expose the IMA and IMV.

Sigmoid Colectomy

- High ligation of the IMA (Fig. 28.2) is necessary when performing a sigmoid colectomy to remove all of the lymphatic drainage, and more importantly to ensure construction of a tension-free anastomosis.

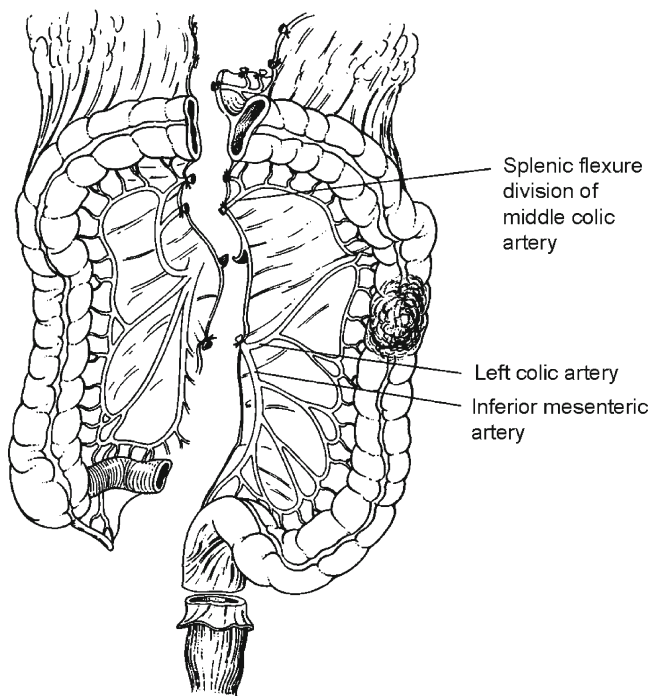


Fig. 28.2. The small bowel mesentery is mobilized to the right upper quadrant to expose the origin of the IMA located just caudal to the third portion of the duodenum. An incision running along the base of the left colic and sigmoid mesentery from the sacral promontory to the ligament of Treitz, exposes the aorta, bifurcation of the common iliac arteries, and IMA vein. The IMA is ligated and divided proximal to the take-off of the left colic artery. The left branch of the middle colic vessels will require ligation and division for a formal left colectomy.

- The ascending branch of the left colic artery should be preserved to allow retrograde blood flow via the marginal artery from the middle colic arterial supply. The splenic flexure should be released to avoid anastomotic tension. The sigmoid colon is mobilized to the level of the middle colic vessels medial to lateral or lateral to medial and the proximal rectum is mobilized from the sacral promontory. The patient is always in modified lithotomy position to allow transanal access for the anastomosis.
- An end-to-end circular stapled anastomosis can be performed between proximal left colon and rectum, after dividing the rectosigmoid junction with a transverse linear stapler.
- A leak test with air insufflation of a submerged anastomotic segment should be performed in all cases using either an endoscope or bulb syringe.

Total Abdominal Colectomy with Ileorectal Anastomosis

- This procedure may be required for circumstances in which the patient has been diagnosed with HNPCC, attenuated familial adenomatous polyposis, metachronous cancers in separate colon segments, and frequently in acute malignant distal colon obstructions with unknown status of the proximal bowel.
- The terminal ileum should be sufficiently mobilized to allow easy reach to the rectum.
- A circular stapled end-to-end anastomosis or functional end-to-side/side-to-side anastomosis are both appropriate.

C. Special Circumstances

Acute Obstruction

- The associated bacterial overgrowth coupled with possible impairment of blood flow in the proximal bowel, have been the primary factors that have classically dictated resection and proximal diversion.
- On-table colonic lavage has been advocated as an alternative means of dealing with the obstructed colon.

- A complete resection of the tumor and obstructed proximal bowel with primary ileocolic anastomosis has been shown to be safe and carry low leak rates.

Prophylactic Oophorectomy

- A randomized trial of prophylactic oophorectomy has shown no benefit to survival.
- In general, prophylactic oophorectomy is not performed.

Colon Cancer and Abdominal Aortic Aneurysm

- A survey of general surgery program directors revealed that vascular surgeons preferred to repair the aneurysm first, whereas the nonvascular surgeons preferred colectomy.
- The primary risk is that performing either operation first may cause complications that significantly delay the second procedure.
- In all likelihood, the best guidance suggests that any aneurysm >6 cm should be repaired first or synchronously in the face of an associated colon cancer to avoid the risk of rupture.
- Endoluminal grafting of an appropriate aneurysm may eliminate the majority of these quandaries in the future.

Synchronous Management of Colon Cancer and Liver Metastases

- The potential benefit of simultaneous colectomy and hepatectomy is the avoidance of two laparotomies and possible reduction in operative risk. Conversely, delayed management of colonic hepatic metastases offers the ability to accurately stage patients and avoid the risk of hepatectomy in a group of patients who will prove to have more widely metastatic disease in several months.
- Selection of patients who have limited hepatic involvement and who are positron emission tomography negative for distant disease has resulted in increased resectability and 5-year survival after hepatectomy.
- The risks of simultaneous colectomy and hepatectomy do not seem to be excessive in select patients operated by expert groups.

D. Sentinel Node Assessment

- Evaluation of the technique, including some modifications, has demonstrated false-negative rates approaching 60%, and limitations in rectal cancers.
- Therefore, at the present time, routine lymph node mapping cannot be recommended.

E. Outcome of Colectomy for Colon Cancer

- In general, the operative outcome and long-term survival after resection of curable colon cancer parallels the TNM and Dukes' stage (A1, well above 90%; B2, 65–90%; C3, 45–75%) which may be modulated by adjuvant chemotherapy.
- The impact of the surgeon's experience and the associated expertise of the institution have recently been found to have a profound effect on outcome.
- High-volume surgeons, particularly those at high-volume institutions, have demonstrated significantly lower perioperative complications and an improved survival after colectomy for colon cancer.
- A colectomy for palliation should rarely be performed and only in patients with life-threatening comorbidities or advanced incurable disease. Local extension of colon cancer may be treated with chemoradiation initially to allow eventual resection and primary anastomosis.
- Although not clearly defined, it is generally agreed that 5 cm proximal and distal bowel margins are sufficient to allow resection of mural tumor spread.
- More recent data would suggest that mural tumor migration is rarely greater than 2 cm either proximal or distal to the palpable tumor edge.

Appendix: Practice Parameters for Colon Cancer

Prepared by The Standards Practice Task Force, The American Society of Colon and Rectal Surgeons

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I. Diagnostic evaluation

II. Preoperative assessment

Guideline – Preoperative, carcinoembryonic antigen level should be obtained. Level of evidence (Class II, Grade A)

Guideline – Evaluation with preoperative CT scanning of selected patients is indicated and routine preoperative CT scanning is optional. Level of evidence (Class II, Grade B)

Guideline – Routine performance of preoperative chest X-rays is acceptable. Level of evidence (Class III, Grade C)

III. Preparation for operation

A. Informed consent

Guideline – Informed consent should be obtained preoperatively. Level of evidence (Class III, Grade C)

B. Mechanical bowel preparation

Guideline – Mechanical bowel preparation is nearly universally used in elective surgery. Level of evidence (Class II, Grade A)

Guideline – Outpatient bowel preparation is generally safe and cost effective. Level of evidence (Class II, Grade A)

C. Prophylactic antibiotics

Guideline – Prophylactic antibiotics are recommended for patients undergoing colon resection. Level of evidence (Class I, Grade A)

D. Blood cross-match and transfusion

Guideline – Blood transfusion should be based on physiologic need. Level of evidence (Class III, Grade C)

E. Thromboembolism prophylaxis

Guideline – All patients undergoing surgery for colon cancer should receive prophylaxis against thromboembolic disease. Level of evidence (Class I, Grade A)

IV. Operative issues

A. Operative technique

Guideline – The extent of resection of the colon should correspond to the lymphovascular drainage of the site of the colon cancer. Level of evidence (Class II, Grade B)

B. Synchronous colon cancer

Guideline – Synchronous colon cancers can be treated by two separate resections or subtotal colectomy. Level of evidence (Class II, Grade B)

C. Contiguous organ attachment

Guideline – Colon cancers adherent to adjacent structures should be resected en bloc. Level of evidence (Class II, Grade A)

D. Synchronous resection of liver metastases

Guideline – Resection of synchronous liver metastases may be reasonable to perform at the time of the initial colon resection. Level of evidence (Class III, Grade B)

E. Role of oophorectomy

Guideline – Bilateral oophorectomy is advised when one or both ovaries are grossly abnormal or involved with contiguous extension of the colon cancer. However, prophylactic oophorectomy is not recommended. Level of evidence (Class II, Grade B)

F. Role of laparoscopic resection

Guideline – Relative merits of laparoscopic versus open resection for colon cancer remain unproved at this time. Level of evidence (Class II, Grade B)

V. Operative issues – emergent

A. Obstructing colon cancer

Guideline – Patients with an obstructing right or transverse colon cancer should undergo a right or extended right colectomy. A primary ileocolic anastomosis can be performed in the appropriate clinical setting. Level of evidence (Class II, Grade C)

Guideline – For the patient with a left-sided colonic obstruction, the procedure selected should be individualized

from a variety of appropriate operative approaches. Level of evidence (Class II, Grade C)

B. Colonic perforation

Guidelines – The site of a colonic perforation caused by colon cancer should be resected, if at all possible. Level of evidence (Class III, Grade C)

C. Massive colonic bleeding

Guideline – Acutely bleeding colon cancers that require emergent resection should be removed following the same principles as in elective resection. Level of evidence (Class III, Grade C)

VI. Staging of colon cancer

Guideline – Colon cancers should be staged using the TNM staging system. Level of evidence (Class II, Grade B)

Guideline – To be properly evaluated, one should strive to have a minimum of 15 lymph nodes examined microscopically. Level of evidence (Class II, Grade B)

VII. Adjuvant therapy

A. Chemotherapy

Guideline – Postoperative adjuvant systemic chemotherapy has a proven benefit in Stage III colon cancer and may be beneficial in certain high-risk Stage II patients. Level of evidence (Class I, Grade A)

B. Immunotherapy

Guideline – The value of immunotherapy for colon cancer is undetermined. Its use is recommended within the setting of a clinical trial. Level of evidence (Class II, Grade C)

C. Intraperitoneal/Intraportal Chemotherapy

Guideline – Intraperitoneal and intraportal infusions of chemotherapy are recommended only in the confines of a clinical trial. Level of evidence (Class II, Grade C)

D. Radiation therapy

Guideline – The role for radiation therapy in colon cancer is limited. Level of evidence (Class II, Grade C)

29. The Preoperative Staging of Rectal Cancer

A. Introduction

- As the therapeutic options available for the treatment of rectal cancer increase, the ability to accurately preoperatively stage a rectal tumor assumes greater importance.
- The tumor-related factors of prognostic significance that are most useful in the preoperative staging of rectal cancers include the depth of penetration of the tumor through the rectal wall, the presence or absence of metastasis to the regional lymph nodes, and the presence or absence of distant metastases.
- The most frequently used modalities for the preoperative staging of rectal tumors available today are clinical examination, computed tomography (CT), magnetic resonance imaging (MRI), endorectal ultrasonography (ERUS), and positron emission tomography (PET).
- Laboratory tests including CEA (carcinoembryonic antigen) levels and liver function tests may also provide useful information in patients with rectal cancer.
- There is a small risk of metastatic spread of rectal cancer to the lung, bypassing the liver, therefore a baseline chest X-ray should also be obtained.

B. Clinical Evaluation

- Careful digital assessment of the rectal tumor may yield valuable information. Table 29.1 lists some of the important parameters

Table 29.1. Tumor characteristics to assess on digital examination.

Location
Morphology
Number of quadrants involved
Degree of fixation
Mobility
Extrarectal growths
Direct continuity
Separate

that should be recorded during the physical examination of a rectal tumor.

- Certain limitations of a digital examination must be recognized. The accurate assessment of early invasion into the rectal wall has been disappointing, especially in selecting patients for local excision of such a tumor.
- Clinical staging is more accurate in correctly assessing the stage of more advanced lesions where local excision is not an option.
- Finally, only tumors of the mid and distal rectum can be assessed by digital examination.

C. Local and Regional Staging

CT Scan

- CT scan is helpful in providing an image of the entire pelvis and the relationship of the tumor to surrounding pelvic structures especially for advanced tumors. However, CT scan has not proven to be very accurate in determining the depth of penetration of the tumor through rectal wall or assessing involved perirectal lymph node metastasis.
- The reported accuracy rate of CT scan in determining tumor penetration through the rectal wall ranges from 52to 100%.
- CT scan is unable to depict the layers of the rectal wall. Thus, for tumors that are confined to the rectal wall, CT scan cannot distinguish tumors that are confined to the submucosa from those that have breached the submucosa and involve the muscularis propria.

- In cases of advanced tumor growth, CT scan does provides valuable information about the relationship of the tumor to the surrounding viscera and pelvic structures.
- The accuracy of CT scan in determining lymph node involvement ranges from 35 to 70%. One drawback of CT scan is its inability to detect lymph nodes smaller than its resolution threshold of 1 cm. A second drawback of CT scan for the assessment of perirectal lymph node metastasis is its inability to differentiate between tumor metastasis and inflammation in enlarged lymph nodes.
- New technology such as the multidetector-row CT (MDRCT) may significantly improve the ability of CT scans to accurately determine the depth of invasion and lymph node metastasis in rectal cancer.

Magnetic Resonance Imaging

- Accuracy rates for MRI in the preoperative staging of rectal cancer have varied according to technique.
- The addition of an endorectal coil to this technique resulted in T stage accuracy rates of 66–91%. These results are listed in Table 29.2.
- In recent years, tumor involvement of the circumferential resection margin (CRM) has been identified as an important predictor

Table 29.2. Accuracy of MRI in the preoperative staging of rectal cancer.

	Year	No. of patients	T staging (%)	N staging (%)
de Lange et al.	1990	29	89	65
Chan et al. ^a	1991	12	91	75
Okizuka et al.	1993	33	88	88
Thaler et al.	1994	34	82	60
Schnall et al. ^a	1994	36	81	72
Joosten et al. ^a	1995	15	66	
Indinnimeo et al. ^a	1996	23	78	79
Hadfield et al.	1997	38	55	76
Zagoria et al. ^a	1995	10	80	
Kim et al.	2000	217	81	63
Gagliardi et al.	2002	28	86	69
Brown et al.	2003	94	85	84
Low et al.	2003	48	85	68

^aEndorectal coil used in MRI

of locoregional recurrence in rectal cancer patients undergoing a radical proctectomy with total mesorectal excision (TME).

- Postoperative radiation is not effective in reducing the risk of local recurrence in patients with a positive CRM, and a curative operation in these patients will require either tumor downstaging by preoperative chemoradiation, an extended resection, or both.
- Consequently, the preoperative assessment of the relationship of the tumor with the fascia propria of the rectum, the CRM in patients treated with TME, has become of utmost importance in deciding the type of neoadjuvant therapy and planning the surgical resection.
- The fascia propria of the rectum is well visualized by phased-array coil or endorectal coil MRI and several studies have suggested that MRI can predict with high degree of accuracy the distance of the tumor to the fascia propria of the rectum.
- Furthermore, because of its multiplanar capabilities, MRI is the most accurate imaging technique in assessing the relationship of the tumor with the levator plate and the sphincter complex.

Endorectal Ultrasound

- This approach is proving to be safe, reliable, and relatively inexpensive. It is an outpatient procedure requiring only enema preparation and no sedation or anesthesia.
- Table 29.3 lists the results of ERUS in the preoperative staging of rectal cancer. The accuracy of the ultrasound in determining the depth of penetration of the tumor through the layers of the rectal wall varied from 60 to 93%.
- Overall, 5% of the tumors were overstaged. This tendency to overstage tumors was a common finding throughout this series because of the inability to differentiate perirectal inflammation from tumor infiltration in the perirectal fat.
- Preoperative radiation of rectal cancer causes various degrees of tumor regression resulting in scarring and fibrosis that impairs ultrasound imaging interpretation.
- Endorectal ultrasonography should be performed in the patient before receiving radiotherapy in order to increase its accuracy rate.
- The accuracy in determining lymph node involvement with the ERUS varies from 68 to 83% (Table 29.3).

Table 29.3. Accuracy of ERUS in preoperative staging of rectal cancer.

	No. of patients	T staging (%)	N staging (%)
Hildebrandt and Feifel (1990)	137	88	73
Beynon et al. (1989)	100	93	83
Jochem et al. (1990)	50	80	72
Milson et al. (1990)	52	83	70
Orrom et al. (1990)	77	75	82
Goldman et al. (1991)	32	81	68
Thaler et al. (1994)	37	88	80
Starck et al. (1995)	34	88	71
Nielsen et al. (1996)	100	85	66
Massari et al. (1998)	75	91	76
Harewood et al. (2002)	80	91	82
Garcia-Aguilar et al. (2002)	545	69	64
Marusch et al. (2002)	422	63	—
Hull et al. (2004)	411	60	—

- ERUS cannot differentiate between inflammatory or neoplastic nodes.
- Several prospective studies have compared ERUS and MRI in the preoperative staging of rectal cancer. Surface coil MRI is less accurate than ERUS in assessing rectal wall invasion and is primarily used for the staging of locally advanced rectal cancers.
- ERUS has the highest sensitivity and specificity in assessing wall penetration, but MRI with endorectal coil had higher accuracy than ERUS in assessing nodal metastasis.

D. Distant Metastases

- The most common site of distant spread of rectal cancer is the liver.
- The most frequently used imaging modalities used today to detect liver metastasis are abdominal ultrasound and CT scans.
- MRI and intraoperative ultrasound are now used with increasing frequency, particularly in patients with known metastasis that are considered candidates for surgical resection.

- Studies that have investigated the use of preoperative ultrasonography and CT in the detection of liver metastases have reported an overall accuracy ranging from 66 to 90%.
- Despite refinements in enhancement techniques of CT and external ultrasounds, along with the addition of MRI, the resolution threshold for liver metastases remains at approximately 1 cm.
- Even after preoperative imaging, up to one-third of colorectal cancer patients are found at the time of surgery to have unsuspected additional liver lesions or extrahepatic metastases.
- PET scans have been shown to have higher sensitivity and specificity in detecting recurrent rectal cancer than both CT and MRI.
 - Although sensitivity and specificity in diagnosing tumor recurrence are higher for PET scans, its spacial resolution is not very accurate and therefore other studies such as MRI and/or CT scans are required to define the precise location of the tumor to important anatomic landmarks.
 - Current scanners are available that fuse CT or MR images with the PET scan images.
 - PET scans when coupled with other studies are also being used to assess the extent of pathologic response of rectal cancers that receive neoadjuvant therapy.
 - At the present time, PET scan is primarily used for the diagnosis of local and distant recurrence after curative surgery for colorectal cancer. It is also being used with increased frequency to detect distant metastasis of the time of the primary diagnosis of rectal cancer.
- Immunoscintigraphy refers to the use of radiolabeled monoclonal antibodies that bind specifically to tumors to aid in detection and diagnosis.
 - The clinical application of this technique has been limited.
 - The accuracy rate of immunoscintigraphy in detecting primary or metastatic colorectal cancers ranges from 63 to 96%.
 - There has not been a defined role for the use of preoperative or intraoperative radiolabeled immunoscintigraphy when dealing with a primary rectal cancer. Likewise, its role in management of recurrent rectal cancer has yet to be well defined.

30. Surgical Treatment of Rectal Cancer

A. Introduction

- Approximately 42,000 patients each year are diagnosed with rectal cancer in the United States. Approximately 8,500 die of this disease.
- Despite remarkable recent advances in new oncologic agents for the treatment of colon and rectal cancer, cure is almost never achieved without surgical resection.
- The current management of rectal cancer is now more varied and complex because of the new approaches with multimodal-ity therapy and the refinements in surgical techniques.

B. Evaluation of the Patient with Rectal Cancer

History

- The patient with rectal cancer usually presents to the surgeon after a definitive endoscopic diagnosis. The patient's initial complaint may have been rectal bleeding, a change in bowel habits, or a sense of rectal pressure. However, with the increase in surveillance colonoscopy, many patients are completely asymptomatic on presentation.
- Tenesmus (the constant sensation of needing to move the bow-els) is often indicative of a large cancer.
- Constant anal pain or pain with defecation suggests invasion of the anal sphincters or pelvic floor.

- Questions concerning a patient's fecal continence should also be discussed before any therapy.
- A history of significant continence problems should prompt a discussion with the patient concerning quality of life issues. Sphincter-sparing surgery in these patients, even if technically possible, often leads to significant fecal soiling and the patient may be better served with a resection and permanent colostomy.

Physical Examination and Rigid Sigmoidoscopic Examination

- A digital rectal examination (DRE) and a rigid sigmoidoscopy are essential to the surgical decision-making process.
- On DRE, fixation of the lesion to the anal sphincter, its relationship to the anorectal ring (the collection of muscles that make up the sphincters), and possible fixation to both the rectal wall and the pelvic wall can be evaluated.
- For mid rectal or upper rectal lesions, the DRE and rigid sigmoidoscopy can help determine how much normal rectum lies distal to the lower border of the tumor.
- With the combination of DRE and sigmoidoscopy at the initial visit, the surgeon can often determine whether a patient is a candidate for sphincter-sparing surgery, whether a temporary diverting ostomy is likely, and what anorectal function will be like post-treatment.

Colonoscopy

- colonoscopy should be performed before surgical resection of a rectal cancer. Colonoscopy allows for confirmation of a malignancy through biopsy and the diagnosis and possible removal of synchronous colonic lesions.
- Synchronous benign polyps have been reported in 13–62% of cases and synchronous cancers have been reported in 2–8% of cases.
- Even if a colonoscopy has been recently performed, the surgeon may still wish to perform a rigid sigmoidoscopy because flexible endoscopic estimates of the location of the lesion are often misleading. For example, because of the flexibility of the colonoscope, a lesion that is described as 15 cm from the anal verge can sometimes be as close as 5 cm from the anal verge when evaluated with the rigid scope.

However, digital rectal examination can provide the identical accurate information as long as the tumor is within reach of the digit.

Preoperative Staging

- For a basic evaluation, all patients should receive a chest X-ray or chest computed tomography (CT) scan to exclude pulmonary metastases.
- One can obtain a carcinoembryonic antigen (CEA) level. If increased preoperatively, the CEA level should decrease to the normal range after treatment. CEA can then be followed postoperatively to detect a recurrence.
- The most useful staging for rectal cancer is abdominal/pelvic imaging with CT, magnetic resonance imaging (MRI), or ultrasound (US).

C. Imaging for Rectal Cancer

- Pretreatment abdominal and pelvic imaging of the patient with rectal cancer is necessary because of the increasing value of preoperative adjuvant therapies.
- For upper rectal cancers, imaging to determine stage will seldom influence the treatment plan. Many of these patients with upper rectal tumors will benefit from an LAR regardless of the stage and may not require neoadjuvant therapy as often as low and mid rectal cancers.

CT Scans

- For rectal cancer, there may be some merit to a baseline preoperative CT scan for advanced lesions. CT scanning is quite accurate in assessing rectal tumors that have invaded adjacent organs. However, for assessment of small primary lesions, CT scanning has many limitations.
- The overall accuracy of CT scanning in determining depth of invasion is approximately 70%.
- Overall accuracy with CT scanning for assessing lymph nodes in rectal cancer is only 45%.

Endoluminal Imaging

- Endoluminal imaging in the form of endoluminal US and endoluminal MRI have become extremely useful in the accurate preoperative staging of a rectal cancer. These modalities allow for more precise determination of the depth of invasion and the presence or absence of mesorectal lymph node metastasis. The knowledge of these factors is critical in determining the sequence and type of therapy for any given rectal cancer.
- In a recent metaanalysis review, endoluminal US was found to be 95% accurate in distinguishing whether a tumor was confined to the rectal wall (T1, T2) vs. invasive into the perirectal fat (T3 or greater).
- ERUS is less useful in predicting lymph node metastases with 80–85% accuracy.
- Two methods of MRI can be used for the evaluation of rectal cancer. One can use the endorectal coil (ecMRI) or the surface coil MRI.
- In general, eMRI has been more helpful in the assessment of perirectal nodal involvement than T stage.
- Reported accuracy rates of MRI for nodal staging range from 50 to 95%.
- The ecMRI is less operator dependent and in answering the critical question of whether a patient has Stage I vs. Stage II or Stage III disease, ecMRI was 88% accurate.
- Double contrast MRI may permit more accurate T staging of rectal cancer by allowing better distinction among mucosa, muscularis, and perirectal tissues. The specificity and sensitivity of ecMRI to predict infiltration of the anal sphincter was 100% and 90%, respectively.
- Phased-array surface coil MRI may prove to be the option of choice for staging of more advanced rectal cancers. The technique has been useful in predicting the likelihood of a tumor-free resection margin by visualizing tumor involvement of the mesorectal fascia.

D. Preparation of the Rectal Cancer Patient for Surgery

Bowel Preparation

- There have been multiple recent metaanalyses that have concluded that mechanical bowel cleansing before colorectal surgery has no significant impact on perioperative infection rates. Despite these recent studies, the authors still recommend that some type of colonic cleansing occur before surgery because it is easier to manipulate the bowel if it is not filled with stool.
- Saline laxatives are often phosphate- or magnesium-based and should not be used in patients with renal failure.

Antibiotic Prophylaxis

- Most surgeons use perioperative systemic antibiotics instead of oral antibiotics for antibiotic prophylaxis. Regimens need to include coverage for both aerobic and anaerobic gut bacteria.
- For long procedures, redosing should be considered depending on the serum half-life of the antibiotics used.

Other Perioperative Issues

- Cardiac, pulmonary, and nutritional evaluations are performed when necessary.
- Perioperative systemic antibiotic coverage is expanded in patients with high-risk cardiac lesions such as prosthetic heart valves, a history of endocarditis, or a surgically constructed systemic-pulmonary shunt, and with intermediate-risk cardiac lesions such as mitral valve prolapse, valvular heart disease, or idiopathic hypertrophic subaortic stenosis.
- Oral anticoagulation is stopped, and patients are placed on intravenous anticoagulation or on Lovenox approximately 5 days before surgery.
- Depending on the individual risk of the patient and the extent of the operative dissection, anticoagulation is restarted as early as 8 h postoperatively, but without a bolus.
- Careful monitoring of the patient's hematocrit and partial thromboplastin time are necessary if early reheparinization is instituted.

E. Anatomic and Biologic Issues

Surgical Anatomy

- The NCI consensus on rectal cancer recommended localizing the tumor relative to the anal verge which is defined as starting at the intersphincteric groove.
- Another important landmark defining the upper limit of the anal canal is the anorectal ring. From the surgeon's perspective, the top of the anorectal ring is the lower limit of a distal resection margin.
- A large, full-thickness cancer needs to be located high enough above the top of the anorectal ring to allow for an adequate distal margin if sphincter preservation is contemplated. If the dissection is to be carried lower toward the dentate line, then the tumor must be confined to the mucosa, submucosa, and superficial layer of the internal sphincter.

Biologic Issues

- "Clinical" biology, means the typical pattern of growth and natural history of the spread of the disease.
- Whatever method used to study the issue, one can clearly say that the vast majority of carcinomas arise in preexisting adenomas.
- In preparing a patient for surgery, the surgeon should have the colon completely evaluated preoperatively so as to be able to operatively treat any synchronous disease that cannot be removed endoscopically.
- Rectal cancers usually proceed in an orderly march from the adjacent mesorectal nodes up the lymphatic chain to the upper extent of the mesentery along the inferior mesenteric artery (IMA) and vein systems.
- As part of a multimodality team that now treats most solid tumors, it must be emphasized to our medical colleagues that a rectal cancer is not a systemic disease from the first abnormal cell division. Aggressive local therapy in the form of an adequate resection is still the "anchor" to any therapy.

F. Surgical Procedures: Principles

- Primary resection and anastomosis without a colostomy or ileostomy is now the rule rather than the exception.
- Palliation should be the goal in a patient for whom curative resection is not possible.
- Nonoperative therapy should be considered when there is significant metastatic disease and the primary tumor is relatively small and uncomplicated. In this situation, it is likely that the patient will die of metastatic disease before a complication from the primary tumor.

Variability in Outcome Based on Surgeon and Hospital Volume

- There is a large body of evidence demonstrating significant variability among surgeons with respect to local recurrence rates for stage-matched rectal cancers.
- Hospital volume can also have an impact on colostomy rates, postoperative mortality, and overall survival.
- The ability to perform sphincter-sparing surgery is also affected by hospital volume.

Total Mesorectal Excision

- Total mesorectal excision in conjunction with an LAR or an abdominal perineal resection involves precise sharp dissection and removal of the entire rectal mesentery, including that distal to the tumor, as an intact unit.
- The rectal mesentery is removed sharply under direct visualization emphasizing autonomic nerve preservation, complete hemostasis, and avoidance of violation of the mesorectal envelope.
- Its rationale is underscored by the hypothesis that the field of rectal cancer spread is limited to this envelope and its total removal encompasses virtually every tumor satellite.
- The reduction of positive radial margins can be reduced from 25% in conventional surgery to 7% in cases resected by TME.
- The meticulous dissection, however, is not without consequence. Prolonged operative time and increased anastomotic

leak rates are noted. Anastomoses 3–6 cm from the anal verge have led up to 17% leak rates. Some centers are now routinely fashioning a protective diverting ostomy.

- After TME with its careful nerve-sparing dissection, impotence has been reported in only 10–29% of cases.
- There are well-recognized points during the rectal dissection where nerve injury can occur. The most proximal is the sympathetic nerve plexus surrounding the aorta. These sympathetic nerve trunks are also prone to injury near the pelvic brim as the bifurcate to each side of the pelvis. Intact nerves should look like a “wishbone” near the sacral promontory after a proper dissection.
- The clinical consequence of an isolated sympathetic nerve injury is retrograde ejaculation.
- In the lower part of the mid rectum, the hypogastric plexus and nervi erigentes can be injured in the anterolateral pelvis. A radial dissection well outside the lymphovascular bundle which lies adjacent to the nerve and nerve plexus can also lead to a mixed parasympathetic and sympathetic injury.
- This bundle and the nerve structure are typically located just lateral to the seminal vesicles in a man or the cardinal ligaments in a woman.
- Adjuvant therapy has recently been shown to improve the results of TME surgery.
- Adjuvant therapy should therefore be considered in patients undergoing TME surgery with Stage II and Stage III disease.
- Figure 30.1 demonstrates schematically how the dissection should proceed. Figure 30.2 shows a cross-section of the rectum, the mesorectal fat, and the associated fascia.

Distal Margins and Radial Margins

- The extent of resection margins in rectal cancer remains controversial.
- When distal intramural spread occurs, it is usually within 2.0 cm of the tumor, unless the lesion is poorly differentiated or widely metastatic.
- It seems reasonable to conclude that a 2-cm distal margin is justified over a 5-cm distal margin. Even smaller distal margins may be acceptable in certain patients for whom there is no other option for sphincter preservation. In these cases, a

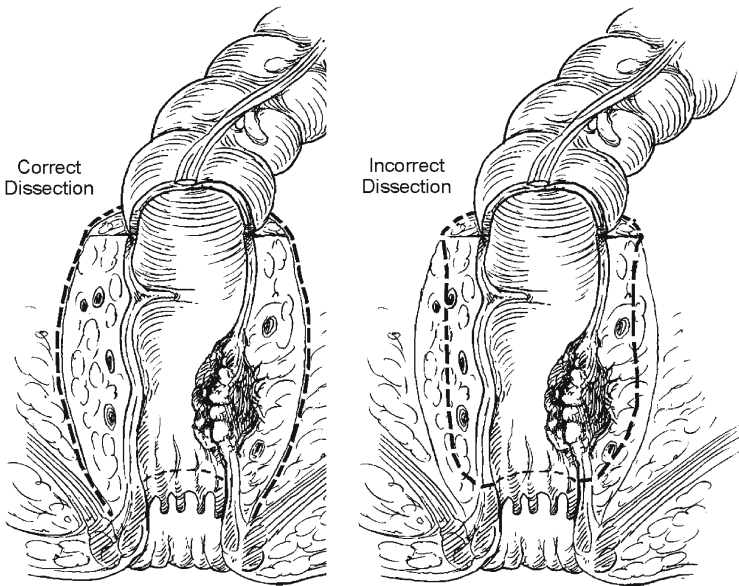


Fig. 30.1. Schematic representation of the correct TME dissection vs. an incorrect dissection. The dissection should proceed between the mesorectal fascia and the pelvic wall fascia to ensure a “complete” TME.

frozen section analysis of the distal margin must be performed to confirm a cancer-free margin.

- It is now clear that the status of the radial margin is perhaps the most critical in determining prognosis.

Selection of Appropriate Therapy for Rectal Cancer

- Presently, a surgeon has three major curative options: local excision, sphincter-saving abdominal surgery, and APR.
- Ideal candidates for local therapy that preserves anal sphincter anatomy and function include small T1 lesions (invasion only into the submucosa) and T2 lesions (invasion into the muscularis propria).
- At present, patients with T3 lesions (invasion into the perirectal fat) are not suitable candidates for local therapy and should be treated with an appropriate major resection as well as adjuvant therapy in most cases.

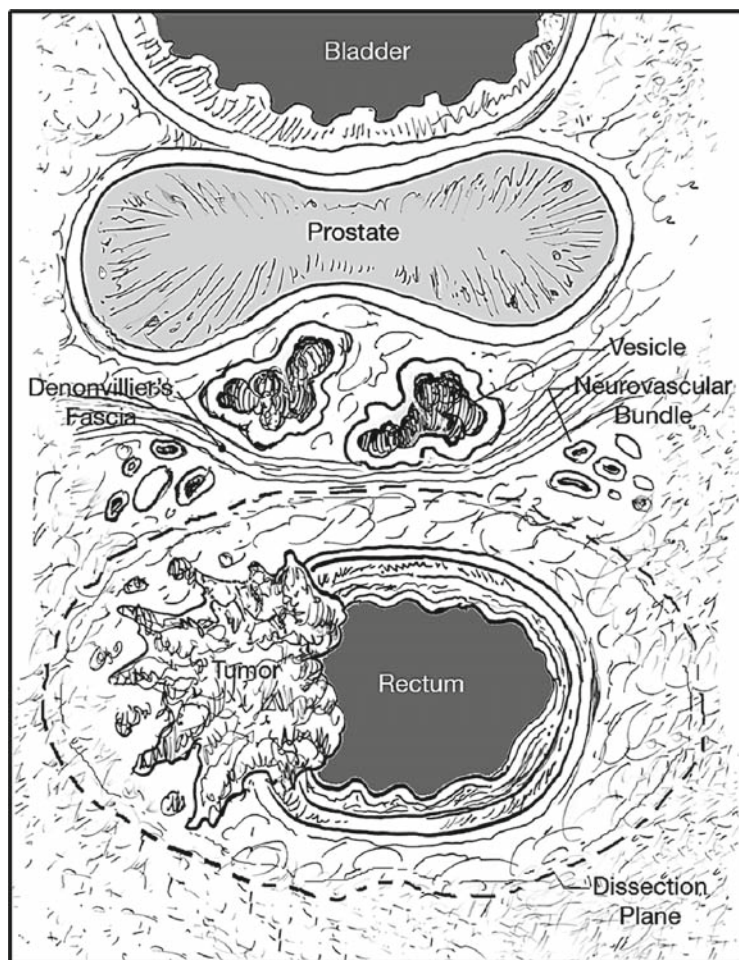


Fig. 30.2. Transverse diagram of the structures of the mid rectum. The proper dissection proceeds just outside the mesorectal fat and fascia but with sparing of the neurovascular bundle and hypogastric plexus that is located anterolaterally along the pelvic sidewall. One or both layers of Denonvillier's fascia should be included in males and the equivalent fascial dissection along the back of the vagina in females.

- Certain clinical features also may have an impact on decisions about the appropriate therapy.
 - Patients with physical handicaps may have significant difficulty in managing a stoma.

- Body habitus and patient gender influence the surgeon's ability to perform a sphincter-saving operation because of pelvic anatomy. Whereas a sphincter-saving procedure in a multiparous thin female can be straightforward, performing a low anastomosis in an obese male with a narrow pelvis can be extremely difficult.
- A history of pelvic irradiation or nonrectal pelvic malignancy can make a rectal resection and sphincter preservation more difficult.
- In summary, each patient with rectal cancer should be individually evaluated and a technical plan for their resection customized to their stage, gender, age, and body habitus (Fig. 30.3).

G. Techniques of Rectal Excision

Abdominoperineal Resection

- Candidates for an APR are patients whose tumors are either invading into the anal sphincter or are so close to the anal sphincter that a safe distal margin cannot be obtained. Also, there is a small subset of patients with mid rectal tumors but with poor continence who may benefit from an APR even though they are technically sphincter-preservation candidates. Lastly some significantly obese male patients with middle third rectal tumors may require an APR due to technical limitations.

Position

- Usually the patient is placed in the lithotomy position.

Incision and Exploration

- An APR can be performed using laparoscopic-assisted surgery. The abdominal portion of the procedure can be performed using laparoscopic techniques with extraction of the specimen through the perineum. It has yet to be shown, however, whether there is any value added with the laparoscopic-assisted approach.

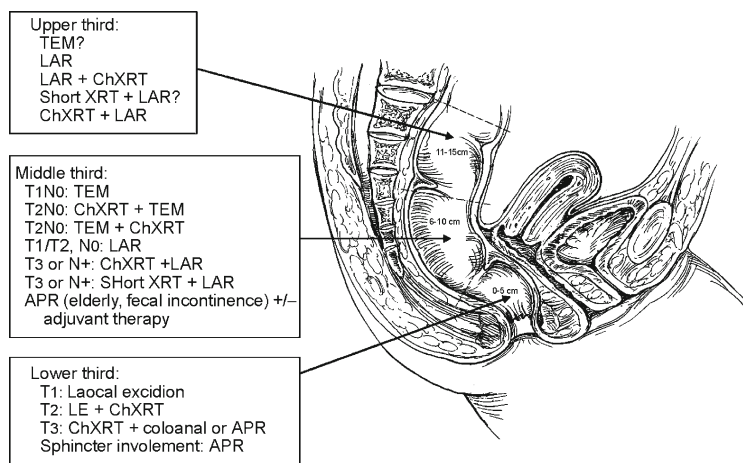


Fig. 30.3. Treatment options for rectal cancer depending on stage and location. Stage I (T1N0, T2N0 – The cancer is confined to the rectal wall and no nodes are involved)

- Distal rectal cancers: T1 (invasion into the submucosa only)
- Local excision
- Radical resection, often an APR
- Adjuvant therapy is usually not recommended.
- Distal rectal cancers: T2 (invasion into the muscularis propria)
- Local excision with preoperative or postoperative adjuvant therapy
- Radical resection without adjuvant therapy, often an APR
- Mid rectal cancer: T1
- TEM
- Radical resection, usually an LAR with low anastomosis. A temporary proximal diverting ostomy is often required.
- Adjuvant therapy is usually not recommended.
- Mid rectal cancer: T2
- TEM with either preoperative or postoperative adjuvant therapy
- Radical resection similar to a T1 cancer
- Adjuvant therapy is not recommended if a radical resection is performed but is recommended after a TEM resection.
- Upper rectal cancers: T1 and T2
- LAR

Stage II and Stage III cancers [Stage II cancers have invasion into the mesorectal fat (T3) but no involved mesorectal lymph nodes. Stage III cancers are any rectal cancer (T1, T2, or T3) but with involved lymph nodes.]

- Distal rectal cancers
- Preoperative adjuvant therapy is most often recommended followed by a radical resection, usually an APR.

- A large tumor burden, particularly multiple peritoneal implants, should lead to a reassessment of the need for resection and perhaps only a colostomy should be performed.

Mobilization

- To excise the whole pelvic mesocolon and “zone of upward spread,” the sigmoid colon and left colon need to be mobilized.

Resection and Ligation

- After mobilization of the mesentery, the bowel is divided near the sigmoid colon/left colon junction at right angles to the blood supply (Fig. 30.4).

The TME

- successful TME starts with the proper ligation of the IMA.
- As one dissects down toward the sacral promontory, the sympathetic nerve trunks are identified. The dissection plane is just anterior or medial to these nerves.
- The anterior dissection is perhaps the most difficult. In men, one should try to include the two layers of Denonvillier’s

←
Fig. 30.3. (continued)

- If preoperative imaging does not clearly define the stage of the cancer, resection can be done first followed by postoperative adjuvant therapy.
- Mid rectal cancers
- Same as above for distal rectal cancers except an LAR is usually performed instead of an APR.

- Upper rectal cancers
 - LAR, with either preoperative or postoperative adjuvant therapy
- Stage IV cancers

- Treatment for any cancer is dependent on the extent of metastasis. With better surgical and medical treatments for metastatic disease, locoregional control of the primary should be aggressive and similar to the above recommendations except in the most advanced cases.

(Key: LE, local excision; short XRT, short-course radiation therapy given two times a day for 5 days in larger fractions; ChXRT, long-course therapy given in 30 smaller fractions over 6 weeks in combination with chemotherapy).

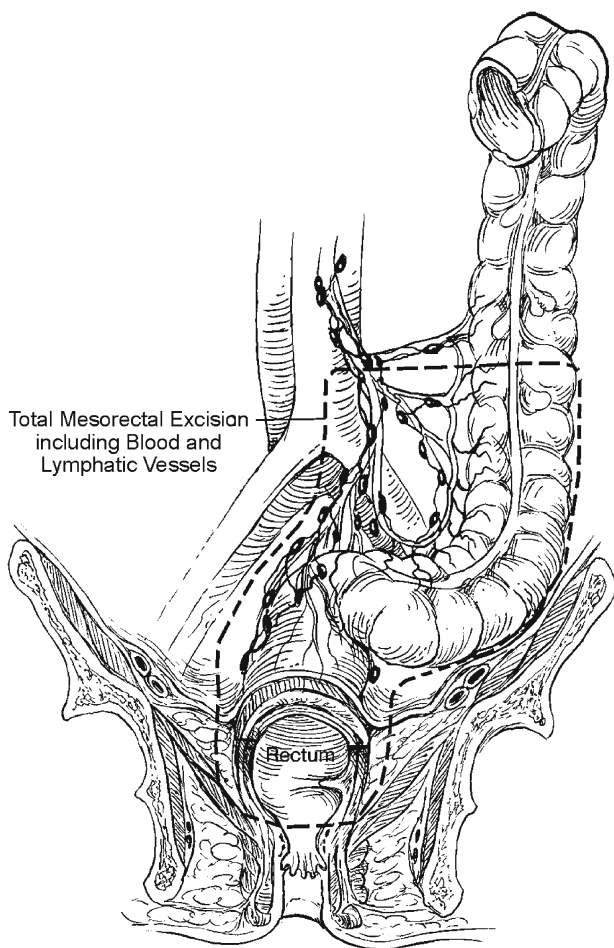


Fig. 30.4. The vascular supply of the sigmoid and rectum. A typical ligation is performed at the junction of the SHA and left colic artery. In patients with a clinical suspicion of positive nodes at the level of the IMA or if vascular mobilization is needed for the left and transverse colon, then a ligation of the IMA is performed at the aorta.

fascia. This fascia is composed of peritoneum that has been entrapped between the seminal vesicles and prostate anterior and the rectum posterior (Fig. 30.5).

- In woman, the peritoneum at the base of the pouch of Douglas is incised and the rectovaginal septum is then separated.

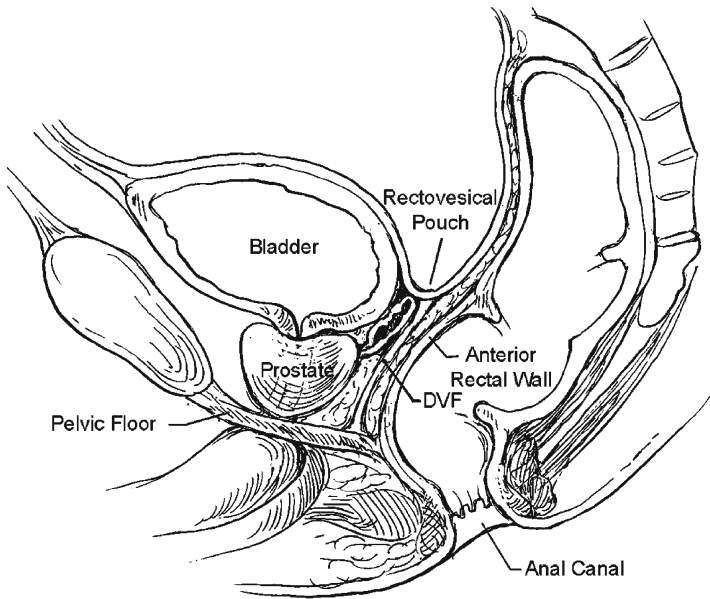


Fig. 30.5. Sagittal view of the rectum, bladder, Denonvillier's fascia, and the prostate. The dissection should proceed anterior to one or both layers of Denonvillier's fascia.

The Perineal Dissection

- The incision for the perineal dissection starts anteriorly at the perineal body, goes laterally to the ischiorectal spines, and then finishes posteriorly at the tip of the coccyx.

Closure

- With the specimen removed, attention is turned to creating an ostomy. Ideally, the patient has been preoperatively marked by a certified ostomy therapist.
- After creating the ostomy, pelvic drains may be placed. These drains keep fluid from leaking through the perineal closure and allow for better healing and a reduced risk of a perineal hernia.
- After skin closure and placement of the dressing, the ostomy is matured.

LAR with Sphincter Preservation

- Sphincter-sparing procedures for resection of mid and some distal rectal cancers have become increasingly prevalent as their safety and efficacy have been established. The advent of circular stapling devices is largely responsible for their increasing popularity and utilization.
- An LAR involves dissection and anastomosis below the peritoneal reflection with ligation of the superior and middle hemorrhoidal arteries.
- An extended LAR indicates complete mobilization of the rectum down to the pelvic floor with division of the lateral ligaments and posterior mobilization through Waldeyer's fascia to the tip of the coccyx.
- As long as the surgeon can obtain a distal margin of at least 2 cm, an anastomosis can be considered appropriate if technically feasible.
- Body habitus, adequacy of the anal sphincter, encroachment of the tumor on the anal sphincters, and adequacy of the distal margin are all factors in determining the applicability of a sphincter-sparing operation.

Coloanal Anastomosis

- The ultimate procedure in sphincter-saving operations is the ultra LAR with coloanal anastomosis. This operation preserves the sphincter mechanism in patients with very low-lying rectal cancer in whom the distal margin is at the minimally acceptable level yet adequate for cancer clearance.
- These operations are reserved for patients who have a distal rectal cancer that does not invade the sphincter musculature and in whom a standard extended LAR is technically not possible.
- The coloanal anastomosis can also be done with a colonic J pouch. Because of the larger capacity of the J pouch construction, anorectal function is improved, especially early after the surgery (Fig. 30.6).
- An alternative to the colonic J pouch is the coloplasty.
 - This technique is similar in concept to a stricturoplasty. The distal colon is divided in a longitudinal direction for 8–10 cm starting 4–6 cm from the distal edge of the pedicle.

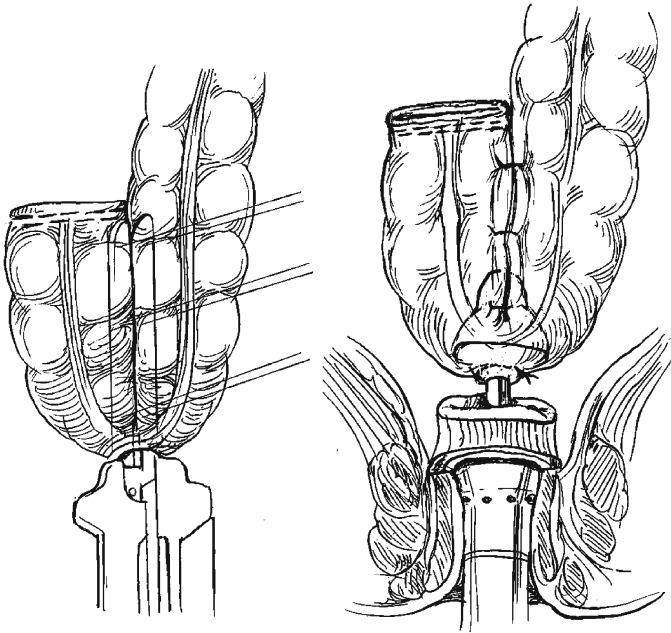


Fig. 30.6 Construction of a colonic J pouch after an ultra LAR. The distal colon pedicle is folded back on itself to make a “J.” A common channel is then created using a stapling device that will staple and divide. A larger reservoir is then created. The J pouch is then anastomosed to the anus using a circular stapler or in a hand-sewn manner.

The longitudinal incision is then approximated transversely making a larger reservoir capacity (Fig. 30.7). The technique can decrease frequency in the early postoperative period but it has been associated with an increased number of anastomotic leaks. Furthermore, a recent large multinational multicenter trial has found the coloplasty to be significantly inferior to the colonic J pouch.

- A proximal diverting stoma is advisable because of the potential for an anastomotic leak or vascular compromise of the left colon.
- Contraindications to the procedure include baseline fecal incontinence from weak anal sphincter muscles; tumor invasion of the anal sphincter musculature or rectovaginal

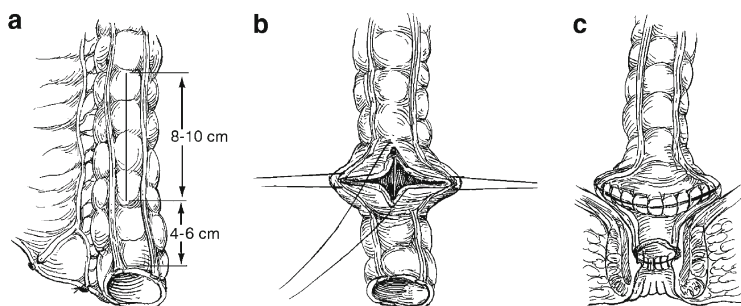


Fig. 30.7. Construction of a coloplasty. The bowel is divided in a longitudinal manner as shown and resutured transversely to create a larger reservoir capacity.

septum; tenesmus; and technical factors such as body habitus, tumor location, and tumor size.

H. Local Excision

- The complication rates, the change in body image with a colostomy, and the improvements in patient selection secondary to innovations in preoperative imaging modalities have led to a renewed interest in local excision of rectal cancers.

Preoperative Evaluation

- Proper patient selection remains the key to successful local excision of rectal cancers.
- The retrospective literature shows that there is a direct correlation between local recurrence and specific pathologic tumor features including depth of invasion, lymphatic invasion, histologic grade, and most importantly clear negative margins at the time of resection.
- A digital rectal examination should be performed to assess the distance of the tumor from the anal verge, as well as its size and mobility.
- Tumors amenable to local excision should be <4 cm in diameter and occupy <40% of the bowel circumference.

Table 30.1. Properties of distal rectal adenocarcinoma amenable to local excision for curative intent.¹²⁴

Physical features
Tumors <4 cm in diameter
Tumor <40% of bowel circumference
Tumor within 10 cm of dentate line
Tumor freely mobile on digital rectal examination
ERUS
T1, T2 lesions
No regional lymph node involvement

- Tumors <5 cm from the dentate are amenable to resection via a transanal procedure, whereas tumors in the middle third of the rectum may require a transcoccygeal approach or transanal endoscopic microsurgery (TEM).
- Immobile tumors are likely transmural, and thus not candidates for local excision.
- The overall health of the patient must be taken into account, because patients who are considered medically unfit for a major resection are often good candidates for local excision.
- Imaging is especially critical in selecting patients for a local excision. The best candidates have either a T1N0 or a T2N0 lesion.
- For the T2 lesions, local excision alone is not sufficient as therapy alone, and either preoperative or postoperative adjuvant therapy should be added.
- The selection criteria for a local excision are summarized in Table 30.1.

I. Technique

Transanal Excision

- Local excision can be accomplished via a transanal approach for the majority of low rectal cancers.
- Once adequate visualization has been obtained, traction sutures are often placed 1–2 cm distal to the tumor, and the line of dissection is marked on the mucosa using electrocautery. This line

of dissection should be approximately 1–2 cm from the border of the tumor circumferentially (Fig. 30.8a–c).

- Upon completion of this incision, the perirectal fat should be visible beneath the lesion to confirm a full-thickness excision. In anterior lesions, care must be taken not to injure the back wall of the vagina in females, or the prostate in males.
- The complications most closely associated with transanal excisions include urinary retention, urinary tract infections, delayed hemorrhage, infections of the perirectal and ischiorectal space, and fecal impactions. However, the overall incidence of these complications is quite low, and the mortality rate is 0% in most series.

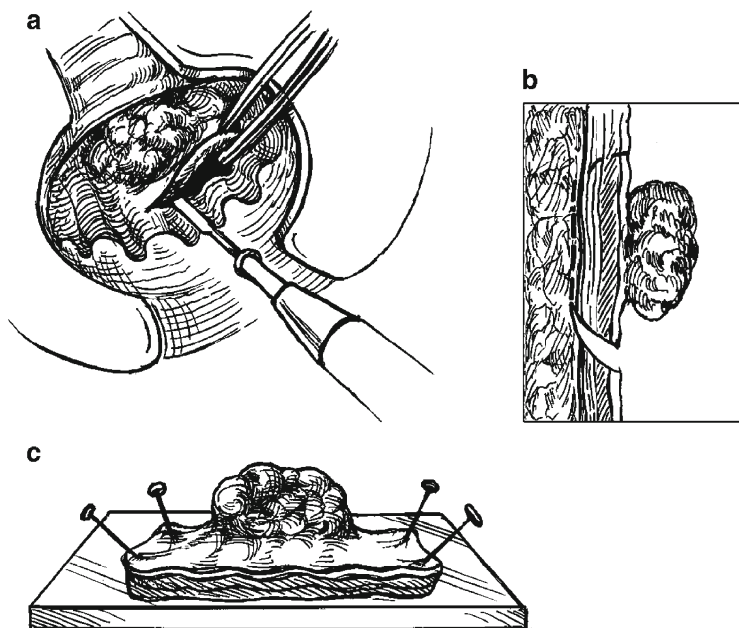


Fig. 30.8. Transanal excision. (a) A transanal excision is performed by marking out a 1 cm or greater margin around the tumor. (b) A full-thickness excision is then performed to obtain adequate radial as well as lateral margins. (c) The specimen is then oriented accurately for the pathologist.

Transcoccygeal Excision

- The transcoccygeal approach was used historically over the transanal approach for larger, more proximal lesions. It was originally popularized by Kraske who found it beneficial when operating on lesions within the middle or distal third of the rectum.
- This approach is especially useful for lesions on the posterior wall of the rectum, but can certainly be used for anterior or lateral lesions as well.
- For posteriorly-based lesions, the distal margin of the tumor can be palpated via a rectal examination, and then the mesorectum and rectum are transected at a point 1–1.5 cm distal to the tumor (Fig. 30.9).

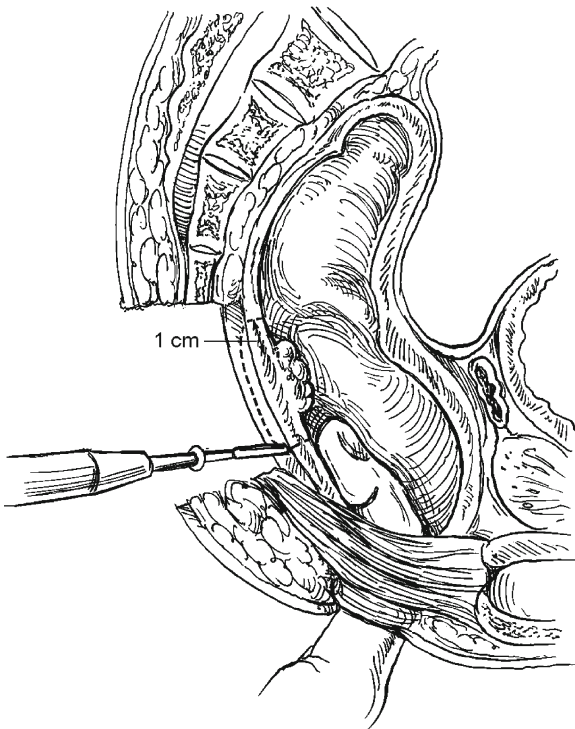


Fig. 30.9. Transcoccygeal excision. For posterior lesions using a transcoccygeal or “Kraske” approach, one can palpate the lower border of the tumor to ensure an adequate distal margin.

- For posterior lesions, the transcoccygeal approach allows for the removal of perirectal nodes that lie in the surrounding mesorectal tissue.
- An unfortunate complication of this procedure is the development of a fecal fistula that extends from the rectum to the posterior midline incision. The incidence of this complication ranges from 5 to 20%, and most heal after temporary diversion of the fecal stream via a loop ileostomy or colostomy. For this reason, the Kraske approach is used much less frequently than other methods for local treatment.

Transsphincteric Excision

- The transsphincteric approach developed by York and Mason involves the complete division of the sphincters and the posterior wall of the rectum.
- Once the lesion is removed, the rectum, sphincters, and overlying musculature are closed in a careful stepwise manner.
- This procedure has an increased risk of incontinence secondary to sphincter dysfunction. Because the exposure provided from this approach is similar to that from the Kraske procedure, which carries less of a risk of incontinence, there are very few indications for this technique.

Transanal Endoscopic Microsurgery

- The surgery is performed with the use of a special resectoscope which is 4 cm in diameter and available in lengths of both 12 and 20 cm.
- Once setup is complete, the operation proceeds in a manner similar to a transanal excision using a variety of special endoscopic instruments, which are introduced through the four ports in the working adapter.
- TEM allows for local excision of proximal rectal lesions that are not accessible via the transanal, transsphincteric, or transcoccygeal approaches.

Outcomes: Retrospective Studies

- The majority of the literature for local excision of rectal cancer comes from small retrospective reviews from single institutions.

These studies are difficult to interpret because there is no uniform approach among the reviews. The length of follow-up varies from study to study, and many combine patients with tumors of different depth, positive margins, and different forms of local therapy including snare cautery and fulguration.

- These retrospective reviews report a local recurrence rate of 5–33% and survival rates of 57–100% (Table 30.2).
- These studies demonstrate that patients with superficial tumors and negative margins at the time of resection have low recurrence rates and a very good prognosis.

Local Excision and Adjuvant Therapy

- Local recurrence continues to be a major source of morbidity and mortality after both local excisions and radical resections for rectal cancer. The major risk factors for recurrence include the depth of invasion of the primary tumor, positive surgical margins, histologic grade of the tumor, and the presence of tumor in the regional lymph nodes.
- The addition of adjuvant or neoadjuvant radiation has been shown to decrease these local recurrence rates, and there is increasing evidence that chemoradiation may have a beneficial effect on survival.
- Microscopic disease can be present in the regional lymph nodes in up to 12% of T1 lesions, 22% of T2 lesions, and 58% of T3 and T4 lesions.
- Similar to the studies for local excision alone, many of the studies involving local excision combined with pre- or postoperative chemoradiation are small retrospective single-institution studies, and thus are difficult to interpret (Table 30.3).
- Local recurrence rates are decreased when compared with local excision alone, ranging from 0 to 15% for T1 and T2 lesions, and 0 to 20% for T3 lesions.

Prospective Studies

- There are very few prospective studies that use local excision for distal rectal adenocarcinoma with or without chemoradiotherapy (Table 30.4).
 - Bleday treated 48 patients with rectal adenocarcinoma via local excision, using postoperative chemoradiation

Table 30.2. Series of local excision alone (retrospective series).

Author	No. of patients	Treatment arms	Follow-up	Recurrence local	Survival
Koscinski	58 (26 T1 and 32 T2)	47 TA, 6 TC, 5 TEM	Mean of 48 months for Stage I and 59 months for Stage II	T1, 5% T2, 28%	T1, 100% T2, 87.5%
Mellgren et al.	261 (All T1 and T2)	108 LE via TA; 153 via APR	Mean of 52.8 months	T1 estimated, 18% (LE), 0% (APR) T2 estimated, 47% (LE), 6% (APR)	T1, 72% (LE), 80% (APR) T2, 65% (LE), 81% (APR)
Horn	38 (17 T1, 14 T2, 7 requiring APR after LE)	3 endoscopic polypectomy, 35 TA, 5 salvage APR	Median of 50 mo	T1, 0% T2, 43%	T1, 100% T2, 82.6%
Gall et al.	84 (54 T1, 19 T2, 11 T3) via LE; 383 APR	16 endoscopic polypectomy, 68 LE, 383 APR	Median of 77.5 mo	T1, 11% (LE), 0% (APR) T2, 22% (LE), 5% (APR)	T1, 74% ± 15% (LE), 100%–2% (APR) T2, 68% ± 24% (LE), 76% ± 11% (APR)
Morson et al.	143 (115 T1, 20 T2, 7 T3)	143 LE; only 91 with negative margins		2/91 (2%) with negative margins 13/69 (19%) with positive margins	Corr. 5 years of 100% with negative margins Corr. 5 years of 83%–96% with positive margins
Whiteway	46 (13 T1, 18 T2, 15 T3)	46 TA and TSp; 27 for cure, 6 disseminated disease; 13 for high		Approximately 8 (17%) risk	Cancer specific survival of 87%

Source: Greenberg J, Bleday R. Local excision of rectal cancer, Clin Colon Rectal Surg 2005; 16:40–46. LE local excision; TA transanal excision; TC transcoxygeal excision; TSp transsphincteric excision

Table 30.3. Local excision plus XRT (retrospective series).

Author	No. of patients	Treatment arms	Follow-up	Local recurrence	Survival
Wong et al.	25	21 TA, 4 endoscopic polypectomy or fulguration, all got 50 Gy XRT postop	Median 72 months (minimum of 36 months)	6/25 (24%)	Crude 5-year survival 96%
Mendenhall et al.	67 (34 T1, 12 T2, 2 T3)	65 TA, 2 TC	Median 65 months (6–273 months)	T1 = 11%	T1 = 76%
Bailey et al.	63 (35 T1, 18 T2, 10 T3)	48 received 45–60 Gy XRT postop 63 LE	Median 44 months (12–130)	T2–3 = 25% 4/53 (7.5%)	T2–3 = 77% Crude 5-years survival 74.3%
Chakravarti et al.	99 (58 T1, 41 T2)	34 XRT, 45–50 Gy 52 LE alone 47 LE plus 45–64.8 Gy	Median 51 months (4–162 mo)	LE alone = 11% T1, LE + CRT = 0% T1, 15% T2	Relapse-free 5-years survival LE alone = 80% T1, 33% T2 LE + CRT = 65% T1, 76% T2
Paty et al.	125 (74 T1, 51 T2)	XRT (45 postop, 2 preop) 33 also had 5-FU 125 LE	Median 80.4 mo	T1 = 17% T2 = 26%	10-years survival of 74% for T1 and 72% for T2
Willett et al.	56 (34 T1, 22 T2)	31 received 45–54 Gy and 15 of them got 5-FU 45 TA or TSp, 10 TC, 1 fulguration, 30 received 45 Gy postop XRT. Since 1986, received 5-FU	Median 48 mo	Since 1985, 0/20 patients after chemoradiation	Actuarial 5-years recurrent-free survival of 72%

Source: Greenberg J, Bleday R. Local excision of rectal cancer, Clin Colon Rectal Surg 2005; 16:40–46.
LE local excision; TA transanal excision; TC transcoccygeal excision; TSp transsphincteric excision; Gy gray; CRT chemoradiation therapy; XRT radiation therapy

Table 30.4. Local excision plus adjuvant therapy (prospective series).

Author	No. of patients	Treatment arms	Follow-up	Local recurrence	Survival
Ota	46	LE	Median 36 months (18–73)	3/46 (6.5%)	Overall 3-years survival 93%
Bleday et al.	48 (21 T1, 21 T2, 6 T3)	Postop XRT (53 Gy) 5-FU for 7 T3's, 1 T2	Mean 40.5 months	All T3's	Overall 3-years survival 93.8%
		Postop XRT 54 Gy and 5-FU/500 mg/M ² day 1–3, 28–30 for T2, T3 lesions		4/48 (8%)	
Steele et al.	110 (59 T1, 51 T2)	Postop XRT 54 Gy and 5-FU/500 mg/M ² day 1–3, 29–31 for T2 lesions	Mean 48 months	T1, 3/59 (5.1%) T2, 7/51 (13.7%)	Overall 6-years survival 85%

Source: Greenberg J, Bleday R. Local excision of rectal cancer, Clin Colon Rectal Surg 2005; 16:40–46.

for all T2 and T3 lesions. Over a mean follow-up period of 40.5 months, we found an overall survival of 93.8%, with recurrence rates by stage of 0% for T0 lesions, 9.5% for T1 lesions, 0% for T2 lesions, and 40% for T3 lesions. Of note, local recurrence was seen in three of five patients with lymphatic invasion and two of two patients with positive margins at the time of local excision.

- Bleday concluded that surgery alone was adequate for T1 lesions, whereas T2 lesions required a combination of surgery and chemoradiation for adequate results, provided that there were negative margins and no lymphatic involvement. If either of these characteristics were present, he recommended the addition of chemoradiation for T1 lesions, and radical resection for T2 lesions.

Transanal Endoscopic Microsurgery

- Because TEM is still a relatively new technique in North America, the data supporting its use in North America are still being compiled.
- In general, these studies show survival and recurrence rates ranging from 83 to 100% and 0 to 27%, respectively.
- These rates are equivalent to those seen for transanal excision, but again comparison is difficult because of the differences in patient population, adjuvant therapy, and tumor characteristics (Table 30.5).

Recommendations

- Patient selection is arguably the most important factor for obtaining comparable oncologic results with local excision or TEM vs. APR in the treatment of low rectal cancers.
- Ideally, tumors should be <4 cm in diameter and occupy <40% of the bowel circumference.
- Tumors within 5 cm from the dentate are amenable to resection via a transanal procedure, whereas more proximal tumors may require a TEM or transcoccygeal approach if an LAR is not feasible.
- Immobile tumors are not candidates for local excision because they are likely transmural.

Table 30.5. Transanal endoscopic microsurgery.

Author	No. of patients	Treatment arms	Follow-up	Local recurrence	Survival
Lezoche et al.	35 (All T2)	All had preop 50 Gy XRT then TEM	Median 38 months (24–96 months)	1/35 (2.85%)	Probability of survival at 96 months = 83%
Farmer et al.	49 (36 Tis, 10 T1, 3 T2, 1 T3)	All TEM	Median 33 months (20–48 months)	2/49 (5.6%) 1 patient had a salvage APR	1 death from disseminated cancer. Survival = 97.9%
Azimuddin	21 (7 Tis, 9 T1, 5 T2)	All TEM	Mean 15 months	0% for T0 and T1 20% for T2	100% for all grades
de Graaf et al.	76 (32 Tis, 21 T1, 18 T2, 5 T3)	All TEM	Median 10 months, mean 13.9 months (1–52 months)	Tis = 0%, T1 = 10%, T2 = 33%, and T3 = 0%	1 patient died yielding overall survival of 98.7%

- The overall health of the patient must be taken into account, because medically unfit patients are often good candidates for local excision. Even T2 and T3 lesions in these patients can be locally excised, accepting a higher rate of local recurrence for lower rates of morbidity and mortality. In this setting, these patients should receive adjuvant chemoradiotherapy and close follow-up.
- Tumors with evidence of nodal involvement should be considered advanced disease, and should be treated with a radical resection, either an APR or LAR with low pelvic anastomosis.
- T1 lesions have a very low probability of regional nodal involvement and are excellent candidates for local excision, whereas the opposite is true for T3 and T4 lesions, which should be treated via radical resection.
- The treatment of T2 lesions is somewhat controversial. Historically, better results have been seen with APR for T2 lesions; however, local excision with postoperative chemoradiation seems to be yielding similar results. If local excision is offered to patients with T2 lesions, either preoperative or postoperative chemoradiation therapy should be part of the treatment plan.
- CT scans of the abdomen and pelvis should be obtained in order to look for any signs of distant spread. PA and lateral views of the chest are necessary for similar reasons.
- A full colonoscopy should also be performed preoperatively to assess for any synchronous polyps or carcinomas.
- Surgical margins should be 1 cm, although the key factor is a negative margin regardless of size.
- These excisions must be full thickness and include some perirectal fat. Local excisions are still considered total excisional biopsies, because final therapy awaits pathologic evaluation.
- Tumors with positive margins must be treated with additional therapy, either via reexcision, chemoradiation, or radical resection.
- Patients with high-risk T2 and any T3 lesions should undergo radical resection (Table 30.6).

Other Local Techniques

- Small rectal cancers can be treated definitively using electrocoagulation or endocavitary radiation (ecRT).

Table 30.6. Treatment recommendations after initial resection.

T stage	Low risk^a	High risk^b
T1	No further treatment	Adjuvant chemoradiation
T2	Adjuvant chemoradiation	Radical resection
T3	Radical resection	Radical resection

^aLow risk: well or moderately differentiated with no evidence of lymphatic or vascular invasion.

^bHigh risk: poorly differentiated or lymphatic invasion or vascular invasion.

- Treatment results using each technique have not been evaluated in any prospective trial; however, recent retrospective reviews conclude that these two techniques are good treatment options in carefully selected patients.

Survival After Rectal Cancer Excision

- Reports from 20 years previous have assured us that a sphincter-sparing surgical approach does not sacrifice survival in selected patients where an adequate margin can be achieved.
- Overall, 5-year survival rates after major surgery for rectal cancer are as follows: Stage I, 85–100%; Stage II, 60–80%; and Stage III, 30–50%.
- Local excision of cancers confined to the rectal wall without lymphatic or distant spread (T1 and T2N0) can achieve cure rates of 80–100%.

Laparoscopically Assisted Resections for Rectal Cancer

- In these operations, part of the procedure is done using the laparoscope and completion of the procedure is in the traditional manner.
- The main questions about laparoscopically assisted proctectomy for colorectal cancer are whether it provides the same TME specimen as traditional open techniques, and whether there is any other unique biologic alteration in the laparoscopic procedure that leads to a change in survival or in recurrence patterns.
- A randomized trial of open vs. laparoscopically assisted colon resection found no statistically significant differences in survival.

Synchronous Cancers

- Synchronous cancers of the large intestine occur with an incidence of approximately 3.5%.
- If one finds two cancers within the colon and rectum, then one must plan an approach to the surgical resection that depends on the location of the two lesions.

Extended Resection for Locally Advanced Colon or Rectal Cancer

- Carcinoma of the colon and rectum will sometimes invade adjacent organs or the abdominal wall. When this occurs, it has been shown that extended resection of the cancer along with the tissue or organ that it has adhered to can lead to a 5-year survival rate of >50%, provided the surgical margins are tumor free.
- The organs that are usually involved with adhesions from colon or rectal cancer include the uterus, small bowel, urinary bladder, and abdominal wall. In general, approximately 5% of patients will present with locally advanced lesions.

Surgical Treatment of Recurrent Colorectal Carcinoma

- Recurrent colorectal cancer affects between 12 and 50% of patients with Dukes B or C (T2N0 through T3N1) disease.
- Most often, the intent of surgery for recurrent disease is not curative, but to improve survival or palliate symptoms.
- Although 60–70% of patients who die of colorectal cancer have liver metastasis, the liver is an isolated site of recurrence in <20% of patients. Of the latter group, only 5–10% will be candidates for curative hepatic resection.

Appendix: Practice Parameters for the Treatment of Rectal Carcinoma

Prepared by the American Society of Colon and Rectal Surgeons

Preoperative Evaluation

A patient with a newly diagnosed rectal cancer requires preoperative assessment to identify tumor stage and operative risk factors that may affect the choice of the surgical procedure.

Examination

Digital rectal examination and sigmoidoscopy allow for the assessment of tumor location, size, and fixation.

Synchronous colon malignancies or coexisting adenomatous polyps should be identified preoperatively, if possible. Colonoscopy is preferred over barium enema.

Imaging Studies

Identifying the extent of local, regional, or distant metastasis may be useful if the findings would modify the approach to treatment. ERUS may be preferred to assess rectal wall penetration, MRI to evaluate perirectal tissue involvement, and CT scan to identify hepatic or pulmonary metastasis.

Laboratory Studies

Laboratory studies should be obtained as indicated by the patient's general condition and anesthetic requirements. The measurement of baseline CEA is useful if postoperative monitoring is planned.

Treatment Considerations

Where possible, the patient should participate in the treatment selection. They should understand the risks and benefits of therapy including short-term and long-term outcome and treatment alternatives.

Abdominoperineal Resection

This procedure is generally indicated for lesions of the lower one-third of the rectum or for higher lesions where tumor characteristics and anatomic factors favor such resection. Where possible, preoperative colostomy counseling is recommended.

Sphincter-Preserving Resection

These procedures are possible for the majority of patients with rectal carcinoma. The choice of the anastomotic technique should be left to the discretion of the surgeon.

Transanal Procedures

Such procedures may be performed for cure in highly selected patients with favorable tumor characteristics or for patients in need of palliative therapy. These procedures include local excision, electrocoagulation, endocavitary irradiation, and laser ablation.

Hartmann's Procedure

This procedure may be indicated for patients who present with obstructed or perforated carcinoma and for patients in whom colorectal anastomosis is clinically inadvisable.

Abdominal Transsacral Resection

The indication for this procedure has been largely supplemented by other sphincter-preserving resections. It provides adequate treatment for mid rectal cancers in the hands of surgeons experienced with this approach.

Adjacent Organ Resection

Contiguous organ resection should be considered in the absence of metastatic disease.

Palliative Surgical Procedures

Such procedures, which may include contiguous organ resection, may be indicated to alleviate or significantly reduce the patient's symptoms caused by primary or recurrent tumor.

Adjuvant Therapy

Adjuvant chemotherapy or radiation therapy, preoperatively or post-operatively, may be used in combination with surgical resection to potentially improve results for cure or for palliation.

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31. Adjuvant Therapy for Colorectal Cancer

A. Colon Cancer

Introduction

- The stage of disease at presentation remains the most important prognostic factor for colon cancer patients.
- Stage I disease carries an excellent prognosis of more than 95% 5-year survival rate, and surgical treatment alone is sufficient; adjuvant treatment is not indicated.
- In contrast, adjuvant treatment has repeatedly been shown to improve survival for Stage III disease.
- The role of adjuvant treatment for Stage II (node-negative) disease remains controversial. However, high risk stage II patients should be considered for adjuvant chemotherapy.

Adjuvant Chemotherapy for Node-Positive Disease (Stage III)

- Overall 5-year survival from curative surgery for Stage III colon cancer is 30–60%.
- Adjuvant chemotherapy improves survival by approximately 10–15%.
- The treatment options for Stage III disease include 5-Fluorouracil (5-FU)/leucovorin (LV)/oxaliplatin (FOLFOX) as the preferred choice in the United States today. A single agent (capecitabine) or 5-fluorouracil/leucovorin (5FU/LV).
- Following surgical resection, 6 months of chemotherapy is recommended for stage III disease.

- A recent European study has confirmed a significant reduction of 25% in the odds of cancer death in Stage III patients receiving adjuvant 5-FU and levamisole.
- The relative merits of levamisole and LV as modulators of 5-FU-based adjuvant chemotherapy, and the optimal duration of treatment were investigated in several studies published between 1998 and 2000.
- The survival advantage provided by LV modulation over levamisole has been confirmed.
- Based on the results of these studies, the new standard for treatment was changed to 6 months of adjuvant chemotherapy with 5-FU/LV for Stage III, node-positive disease.
- The newer chemotherapeutic agents currently under study or in use for treatment of metastatic disease (e.g., irinotecan, capecitabine, oxaliplatin) are undergoing evaluation for their usefulness in the adjuvant treatment of patients with Stage II and Stage III disease. Recent data from the multicenter international randomized MOSAIC trial have confirmed that the addition of oxaliplatin to 5-FU/LV (FOLFOX) further decreases the risk of recurrence in Stage II and Stage III disease by 23%, resulting in a significant improvement in 3-year disease-free survival.
- Several tumor characteristics such as microsatellite instability and the expression of DNA synthesis-associated enzymes have recently been found to predict chemoresistance to 5-FU and irinotecan.

Adjuvant Chemotherapy for Node-negative Disease (Stage II)

- The data from the early studies that prompted the NIH recommendation for adjuvant treatment in Stage III disease did not support a similar recommendation for Stage II disease.
- At this time, the use of adjuvant chemotherapy for Stage II node-negative disease remains an unanswered question, mainly because the overall prognosis for Stage II node-negative disease is good, and many patients would undergo unnecessary treatment.
- For the time being, patients with Stage II colon cancer at high risk for tumor recurrence might be considered for adjuvant treatment on an individual basis, or might be entered in a clinical trial.
- High risk stage II patients include T4 tumors, poor histologic grade, peritumoral lymphovascular involvement, obstruction at

the time of presentation, T3 lesions with localized perforation, close, indeterminate, or positive margins or inadequately sampled nodes.

Radiotherapy

- Two large retrospective reviews helped define the risk factors for local recurrence after surgery for colon cancer. Locoregional failure was identified in 19–46% of patients overall; at least half of local recurrences were in the original tumor bed. Only 13% of the local recurrences were surgically salvageable.
- The most important risk factors for local recurrence were (1) pathologic staging, with local recurrence rates of 35% in modified Astler-Coller Stages B3, C2, or C3 vs. 7% in Stages A, B1, and C1; (2) primary tumor localization in a fixed, nonperitonealized segment of the colon, with the highest failure rates in the cecum, descending colon, hepatic or splenic flexures, and sigmoid colon; (3) colon carcinoma complicated by perforation or obstruction, with a twofold to threefold increase in local recurrence for any given pathologic stage.
- At this time, the precise role of adjuvant radiotherapy in the treatment of colon cancer remains undefined. There are no data to support a systematic recommendation for therapy or a well-recognized adjuvant regimen.
- The potential risks of adjuvant radiotherapy for colon cancer, particularly radiation damage to surrounding organs (e.g., small bowel) are significant.
- Treatment for individuals deemed at high risk for local recurrence after curative surgery for colon cancer should be individualized.

Immunotherapy, Tumor Vaccines, and Gene Therapy

- Nonspecific immune stimulation with bacterial cell products (e.g., BCG) and cytokines (e.g., interleukin-2) has recently been superseded by more specific immune stimulation targeted against colorectal tumor-expressed antigens.
- Vaccines stimulate the immune system to recognize and act specifically against these tumor-expressed antigens, through either the humoral or cellular pathway.

- Because of its marginal efficacy, the complexity in the preparation of the vaccine, and the introduction of more effective chemotherapeutic agents, tumor cell-based immunotherapy is not frequently used in colon cancer patients.
- Gene therapy is based on the concept of transferring genetic material into target cells, which would allow for correction of genetic defects in tumor suppressor genes, inactivation of oncogenes, or insertion of treatment-sensitizing genes (such as drug-converting enzymes) or “suicide genes” into the colorectal cells.
 - Correction of p53 mutations, inactivation of k-ras gene product p21, and the delivery of prodrug converting enzymes are currently being studied.
 - The long-term potential for clinical usefulness of these techniques remains to be defined.

B. Rectal Cancer

- The modern multimodal therapy approach individualizes rectal cancer care, thus offering the best and most appropriate treatment to every single patient. Local and distant staging guides the decision for adjuvant radiotherapy and/or chemoradiotherapy and for available surgical approaches, i.e., local excision or an abdominal procedure.
- Many prospective trials have demonstrated the beneficial effect of preoperative and postoperative radiation therapy in patients with rectal cancer who had surgery with curative intent.
- The clinical benefits of radiotherapy in the treatment of rectal cancer can be broadly divided under four categories:
 - First, radiotherapy lowers local failure rates and improves survival in resectable rectal cancer
 - Second, radiotherapy allows surgery in nonresectable rectal cancer
 - Third, it facilitates sphincter-preserving procedures in low-lying rectal cancer
 - Finally, it may offer a totally curative approach without major surgery

Benefit No. 1: Radiotherapy Lowers the Local Failure Rates and Improves Survival in Resectable Rectal Cancer

- According to three recently published metaanalyses, there is no doubt that neoadjuvant treatment is superior to adjuvant treatment with regard to reduction in local failure rates and cancer-specific survival.

Neoadjuvant Therapy: Radiation Alone Vs. Chemoradiation

- The potential advantages of neoadjuvant therapy include increased tumor radiosensitivity with decreased small bowel toxicity, decreased overall radiation-associated complications, and decreased risk of tumor seeding during surgery.
- The primary disadvantage of neoadjuvant therapy is the risk for overtreatment in patients with early-stage disease.
- New imaging modalities such as endorectal ultrasound and magnetic resonance imaging now allow for increasingly precise preoperative identification of patients with T2 and T3 tumors, thus minimizing the number of patients who would be overtreated by neoadjuvant therapy.
- A short course of preoperative radiation, 20–25 Gy given over 1 week is biologically equivalent to the traditional postoperative course of 45–55 Gy given over 5–6 weeks.
- The main objection to all trials showing improvement in local recurrence and survival rates with radiotherapy, including the Swedish rectal cancer trial (SRCT), was the high rate of local recurrence in the control arm that has been attributed to non-standardized surgical technique.
- Thus, it seems that neoadjuvant radiotherapy still has a place in the treatment of rectal cancer, even when surgical technique is optimized.

Postoperative Adjuvant Therapy: Radiation Alone Vs. Chemoradiation

- The advantage of reserving adjuvant treatment for the postoperative setting is the ability to restrict its use to patients who are at identified risk for failure, based on their histopathologic staging.
- The disadvantages include the higher incidence of radiation-related complications, particularly small bowel radiation injury and a higher number of patients unable to complete the entire

course of therapy because of treatment side effects. Other reasons are the relative radioresistance of the hypoxic surgical bed and the risk for repopulation of tumor cells from surgery to the start of radiotherapy.

- Postoperative adjuvant radiation therapy alone decreases local recurrence, although not to the same extent as neoadjuvant treatment, and does not improve survival.
- Combined modality chemoradiotherapy is currently the standard postoperative adjuvant treatment for patients with Stage II and Stage III rectal cancer.

Benefit No. 2: Radiotherapy Allows Surgery in Nonresectable Rectal Cancer

- The definition of a nonresectable rectal cancer is controversial. These tumors are clinically tethered or fixed but it is often difficult to predict whether fixation is the result of fibrotic adhesions or tumor infiltration of the pelvic sidewalls or adjacent organs.
- Magnetic resonance imaging is particularly useful to determine the relationship of the tumor with the fascia propria of the rectum, and it may be the best imaging modality for the preoperative staging of patients with fixed tumors.
- Based on available data, patients with such locally advanced rectal cancer tumors benefit from preoperative radiotherapy with the aim of downsizing the tumor.
- Approximately 10–15% of all patients with rectal cancer fall into this category; half of those patients have no metastases, indicating that there is potential for a curative procedure.
- Based on tumor characteristics, surgery alone is unlikely to be curative and it is indicated to offer radiotherapy to those patients.
- It must be emphasized that short-course radiotherapy is not an option in unresectable rectal cancer; a standard dose of 45–55 Gy over 5–6 weeks must always be given.
- Radiotherapy is used to downsize tumors in this group of patients. After completion of standard-dose radiotherapy, a 6- to 8-week waiting period allows the tumor to shrink, increasing the possibility for a curative procedure.
- The role of additional chemotherapy remains unclear in this context.
- At this time, there is no good evidence supporting the use of chemotherapy in addition to radiotherapy for unresectable rectal

cancer. Despite the lack of data and scientific evidence, most radiotherapists and medical oncologists have more or less accepted the concept of using chemoradiotherapy for nonresectable rectal cancer patients.

Benefit No. 3: Radiotherapy Facilitates Sphincter-Preserving Procedures in distal Rectal Cancer

- Several series claim that preoperative radiotherapy (and preferably chemoradiotherapy) downsizes tumors to the extent that it is possible to increase the number of patients in whom the sphincters can be preserved.
- The dramatic recent changes in surgical technique (TME, staplers) and the modern approach to rectal cancer treatment may partially explain the increased rate of sphincter preservation. We now accept a 5- to 10-mm distal margin as curative procedure if a stapled anastomosis is done.
- The German trial (CAO/ARO/AIO trial), in which patients were randomized to pre- or postoperative chemoradiotherapy, has shown a clear tendency to more favorable stage in patients having had preoperative treatment compared with postoperative chemoradiotherapy.
- At this time, there is no evidence that prolonged-course radiotherapy combined with chemotherapy with delayed surgery impacts sphincter preservation. It is possible that increasing the waiting time from end of radiotherapy to surgery will achieve further downsizing, which might improve sphincter preservation.
- An important consequence of increased sphincter preservation is poor function. Poor quality of life may be the price to pay for intact sphincters: up to 20% of all patients who undergo a low anterior resection are incontinent of solid stool. This contrasts with reports that patients with a stoma had a better quality of life compared with those with an anterior resection.

Adjuvant Chemotherapy Alone in Rectal Cancer

- In contrast to colon cancer, chemotherapy alone as adjuvant treatment in rectal cancer remains questionable.
- Two large randomized trials comprising more than 4,000 patients have studied the value of chemotherapy vs. surgery

alone in colon and rectal cancer patients. Combination 5-FU/levamisole and 5-FU/LV were found to improve survival in patients with colon cancer, but showed no benefit in patients with rectal cancer.

- At this time, adjuvant chemotherapy alone is not acceptable in rectal cancer. However, postoperative chemotherapy is currently used to reduce the risk of distant relapse in patients with rectal cancer treated with pre- or postoperative chemoradiation and radical surgery.

32. Colorectal Cancer Surveillance

A. Introduction

- Rational follow-up should detect treatable recurrent cancers, identify and remove metachronous polyps, and identify possible hereditary influences in development of a colorectal cancer.
- It is clear that accurate risk stratification and patient selection are central to any program of surveillance.
- The intensity of surveillance should be proportional to the patient's risk of recurrence, and those patients unfit for further surgery because of age or comorbidity may be best served by colonoscopic follow-up only.

B. Types of Surveillance

Metachronous Colorectal Neoplasms

- Those patients who have undergone successful treatment of a colorectal malignancy have an increased risk of developing subsequent polyps or cancers compared with the rate at which an age-matched control population would develop their first colorectal neoplasm.
- The period of risk for the development of metachronous disease seems to be lifelong and cumulative.
- The risk of developing metachronous polyps ranges between 30 and 56%, and the risk of a second cancer is 2–8%.
- Because these cancers arise from adenomatous polyps, periodic colonoscopy with polypectomy should prevent the development of subsequent cancers.

- The Standards Task Force of the American Society of Colon and Rectal Surgeons (ASCRS) has recommended colonoscopic surveillance to begin 3 years after surgery assuming preoperative or intraoperative clearance was done and was negative.
- If preoperative or intraoperative clearance examination could not be done, postoperative colonoscopy within 6 months of surgery is recommended.
- Follow-up surveillance colonoscopy every 3 years can be continued for the duration of an individual's active life.
- Once the patient is older than age 80, further examinations may be of limited usefulness although exceptions can be made for individuals who are healthy and active despite their advanced age.

Recurrent Cancer

- The term "recurrent cancer" is a misnomer because the cancer does not disappear and then return. It simply progresses in sites not clinically detectable at the time of the original surgery.
- Locoregional recurrences are more common in cases of rectal cancer, and may represent inadequate tumor clearance at the time of surgery.
- Distant disease, typically in the liver or lungs, usually does not cause symptoms until the situation is quite advanced.
- Options for the detection of asymptomatic recurrences include physical examination, carcinoembryonic antigen (CEA) monitoring, colonoscopy, chest X-ray, and various scans.
- In this high technology era, careful attention to new symptoms such as abdominal pain, change in bowel habits, weight loss, or anorexia is often lacking, but such symptoms are the first sign of recurrence in many cases.
- When present, a meticulous physical examination is conducted. This should include a digital rectal and vaginal examination for patients with rectal cancer.
- CEA testing is most useful in cases in which the level was increased preoperatively but decreased to normal levels after resection. Even in cases in which the preoperative CEA level is normal, serial CEA testing is often the first indication a patient has recurrent disease.
- Endoscopic follow-up is of limited usefulness in looking for recurrences because only 2% of recurrences are visible at colonoscopy.
- Rigid proctoscopy is an alternative and, some suggest, superior way to assess a rectal anastomosis for recurrence.

- Patients with rectal cancer, especially those treated with transanal excision, may benefit from endorectal ultrasound surveillance. However, its value remains to be proven.
- Computerized tomography (CT) and magnetic resonance imaging (MRI) scanning are very sensitive ways to detect liver and lung metastases, but are not recommended as a routine screening procedure.
- Positron emission tomography (PET) scanning may become the most sensitive way to detect recurrences, but although it is becoming more widely available, data supporting its use are still lacking.
- Patients with isolated metastatic disease (fewer than eight liver metastases or one or two lobe lung involvement) may be candidates for operative treatment (see Chap. 34).

Hereditary Cancer

- Heredity is thought to be a major factor in 10–25% of colorectal cancers.
- Patients who developed their cancer before age 50 years or who have first-degree relatives who developed colorectal or associated cancers such as endometrial, ovarian, ureteral, or bladder cancer or who have multiple family members with varying cancers especially if diagnosed before 50 years of age may have a hereditary cancer.
- Thus, in addition to informing family members of their risks and need for intensive surveillance, the patient's follow-up plan may need to incorporate surveillance of other potential sites of cancer.
- Sometimes, genetic counseling and testing is useful and prophylactic surgery may be considered as in the case of hereditary nonpolyposis colon cancer syndrome.

C. Risk of Recurrence/Pattern of Recurrence

- The risk of recurrence is proportional to the stage of the original disease.
- Most Stage IV patients have undergone palliative treatment and are not candidates for surveillance unless they were treated by operative removal of metastatic disease.
- Patients with Stage I colon cancer treated by radical surgery have such a low chance of recurrent disease that routine

surveillance may not be justified. However, Stage I rectal cancer patients treated by local therapy are at significant risk of local recurrence and may deserve close follow-up.

- Patients with Stage II or III disease would seem to benefit most from close surveillance.
- Other tumor or surgery related factors such as degree of differentiation, presence of lymph node metastases, iatrogenic perforation, and poor primary tumor clearance, influence the risk of recurrence, and could be used to more accurately predict an individual patient's risk of recurrence, and guide the development of a specific follow-up program.
- To date, there is no standardized formula for doing this but an experienced clinician can individualize follow-up based on the risk of recurrence, the patient's overall health status, the patient's willingness to undergo serial testing and the ability for the patient to undergo aggressive retreatment if recurrence is identified.
- The patterns of recurrence reflect the location of the primary tumor. Rectal cancers tend to recur locally in the pelvis, but this tendency has diminished recently with improved mesorectal clearance techniques and the use of neoadjuvant chemoradiation.
- All colorectal cancers metastasize hematogenously to the liver and lungs as well as to regional lymphatics, and these areas need to be evaluated when looking for recurrent disease.
- It is well established that 60–80% of recurrences occur within 2 years of surgery, and more than 90% of recurrences are found within 5 years. Therefore, follow-up protocols should be most intensive for the first 2 years, and then taper off in frequency of evaluations over the next 3 years.
- The exception to this timing of recurrence is the patient who has had pelvic radiation. In such cases, recurrence tends to occur later so intensive surveillance may need to extend to 5 or 6 years.
- The development of symptoms at any time during follow-up should prompt a thorough diagnostic work-up and specific treatment.

D. Surveillance Effectiveness

- The utility of a surveillance program should be manifest in an improvement in survival or quality of life when compared with patients who have received little or no follow-up.

- The identification of recurrent disease does not necessarily result in improved outcomes. Only about 10% of recurrences are resectable with curative intent and chemotherapy offers little chance of cure.
- Those patients who are fortunate to have a lesion amenable to surgery are often not suitable surgical candidates as a result of age or comorbidity, and should not be subjected to intense follow-up because any information obtained cannot be acted upon.
- There is a subset of patients with resectable disease, who may benefit from radical re-resection, with 5-year survivals of 25–30% in most series. PET scanning can assist in identifying this small group of individuals.
- The results of intensive follow-up programs reported in the literature have been disappointing. A recent review summarized the results of the six randomized, prospective trials of high-intensity versus low-intensity follow-up after surgical resection with curative intent for colorectal cancer. Recurrences were not more common in the closely monitored group, but they were found earlier and were more likely to result in reoperation with curative intent. Despite this, only two of the six studies demonstrated a statistically significant improvement in overall survival as a result of intensive surveillance.
- Because of the concern that inadequate sample size was in part responsible for the negative results encountered in the above studies, three separate metaanalyses have been conducted on these data. Although this resulted in a more clearly discerned reduction in death from recurrent cancer, the reduction in absolute risk was only 7%.

E. Cost of Surveillance

- One meta-analysis evaluated the cost-associated intensive follow-up in terms of cost per year of life gained and found it to be \$6,096.
- Although these costs are significant, they seem to be below the accepted threshold of \$30,000 per year of life gained.

F. Quality of Life

- Intensive surveillance may have a negative impact on quality of life secondary to the anxiety, inconvenience, and cost associated with the testing. Conversely, intensive testing may be reassuring to patients and improve their quality of life.
- Investigators in Denmark found that although patients subjected to closer follow-up expressed greater confidence in their examinations, the increment in quality of life was marginal and did not justify the expense of follow-up.
- Additional data are needed to determine methods and settings for follow-up that maximize both survival and the quality of life.

G. Recommendations

- Virtually all patients can undergo follow-up studies that are focused on excluding hereditary cancer and on prevention of synchronous cancer by every 3- to 5-year surveillance colonoscopies to remove metachronous polyps.
- If hereditary cancer is likely, work-up appropriately and/or consider referral to experts in hereditary cancers.
- The search for treatable recurrent disease is more selective. It is helpful to first determine whether the patient has a significant risk of recurrence. If so, determine whether the patient prefers an aggressive approach to follow-up testing and whether the patient could tolerate retreatment if recurrence is identified.
- If there is a minimal risk of recurrence and/or the patient refuses or is not a candidate for aggressive follow-up, no additional testing is done.
- Patients should still undergo routine colonoscopic surveillance every 5 years to detect metachronous polyps or cancer.
- If there is a significant risk of recurrence and the patient wants aggressive follow-up and would tolerate retreatment, follow-up will include the search for recurrent disease. Typically this includes: history, physical examination, and serial testing as noted below every 3–6 months for the first 3 years, and then every 6–12 months for an additional 2 years. If pelvic radiation was used for rectal cancer, the closer interval of follow-up may need to be extended to 5 or 6 years. Careful attention to new symptoms and physical finding should be made.

- Complete colonoscopy before resection, followed by an examination 1–3 years after surgery and every 3–5 years thereafter for the duration of the patient’s productive life.
- Serial CEA testing every 3 months for the first postoperative year or two and every 6–12 months thereafter for patients who desire an aggressive follow-up protocol and would tolerate aggressive retreatment for locoregional disease or hepatic or pulmonary metastasis.
- Serial CXR every 6–12 months for patients who desire an aggressive follow-up protocol and would tolerate pulmonary resection.
- Serial proctoscopy and selective endorectal ultrasound for rectal cancer patients who desire an aggressive follow-up protocol and would tolerate aggressive radical pelvic surgery with or without additional radiation and chemotherapy.
- Based on the available evidence, there is no role for the routine use of liver function tests, hemoglobin, CT scanning, MRI, or PET scanning in asymptomatic patients.

33. Management of Locally Advanced and Recurrent Rectal Cancer

A. Introduction

- Of patients with newly diagnosed colorectal cancer who undergo surgery with curative intent, approximately 5–12% will have tumors that have spread beyond the anatomic landmarks of a standard resection due to invasion of adjacent organs or structures.
- The goal of surgery in such cases is a wide, en bloc resection of the tumor and any involved adjacent organ or structure.
- Of patients who undergo resection with curative intent and receive adjuvant therapy, between 7 and 33% develop isolated local or regional recurrences. In up to 20% of these recurrences, repeat resection can be curative.
- The most important factor that influences tumor recurrence is the stage of disease at the initial presentation. Others factors include obstruction or perforation at presentation, adjacent organ involvement, tumor aneuploidy, increased tumor grade, mucin production, or evidence of venous or perineural invasion.
- Locally advanced primary rectal cancers include tumors that are T4 N1-2 MX at the time of initial diagnosis. They are often associated with a higher rate of concurrent metastatic disease and have a poorer overall prognosis than earlier-stage disease.
- For advanced or recurrent rectal cancer, multimodality therapy incorporating radiation, chemotherapy, and surgery should be used to achieve local tumor control and to prevent or control systemic tumor dissemination, thereby improving patient tumor specific survival.

- To achieve these goals, appropriate surgery is combined with external-beam radiation therapy (EBRT), and, under ideal circumstances, intraoperative radiation therapy (IORT) and adjuvant or neoadjuvant chemotherapy.
- Patients with isolated hepatic or pulmonary metastasis from a rectal cancer are known to have reasonable survival after surgical treatment; however, survival with an isolated, untreated, locoregional, rectal cancer recurrence is quite poor.
- Most patients who develop a pelvic tumor recurrence develop disabling complications, including severe pain from bony or nervous tissue involvement, urinary obstruction, fecal obstruction or incontinence, or persistent bleeding.
- Nearly 90% of rectal cancer recurrences after surgery alone occur in the central or posterior pelvis, and 19% occur at the anastomosis.
- Stage T4 primary tumors are significantly associated with relapse in the anterior pelvic region. EBRT alone or combined with systemic chemotherapy may result in temporary improvement of symptoms, but the 5-year survival rate is less than 5%.
- Surgical palliation without the addition of systemic chemotherapy or radiation therapy adds little to the overall survival. For these patients, length of survival is perhaps less important than quality of life.
- A patient who presents with a locally advanced primary or recurrent rectal cancer must be thoroughly evaluated for the presence of extrapelvic disease. If extensive extrapelvic disease is found, the degree and scope of surgical resection should be changed from one of curative intent to palliation.
- Whether a patient is a candidate for surgery is influenced by a number of factors, including the patient's overall physical condition and comorbid diseases and the extent of spread and fixation of the rectal tumor.

Preoperative Evaluation and Patient Selection

- To be considered for a complete resection, the patient should be in generally good health. Any significant cardiac or respiratory conditions should be thoroughly evaluated and treated. Patients who are in poor health, or who will not be able to tolerate multimodality therapy combined with complete surgical resection, or have an ASA classification of IV–V are not considered acceptable surgical candidates.

- Nearly as important as their physical condition is consideration of the patient's motivation and emotional preparedness for undergoing this extensive treatment.
- If the patient is deemed an acceptable candidate for surgery, the next step is evaluation for the extent of local spread and the possibility of extrapelvic disease.
 - A detailed history should be obtained. Symptoms that may suggest metastatic disease, such as back or bone pain outside of the pelvis, new respiratory symptoms, or headaches need to be carefully examined and ruled out as being the result of metastatic disease.
 - A thorough physical examination, with particular attention placed on the rectal and vaginal examination, needs to be performed and any fixation of the tumor to rigid pelvic structures needs to be assessed.
 - Complete endoscopic evaluation of the colon needs to be performed, if technically possible, to rule out the presence of a synchronous intestinal lesion.
 - Endoluminal ultrasound of the rectum may be combined with this evaluation in cases of recurrent disease to determine if there is a discrete mass adjacent to the intestine that might be amenable to endoscopic biopsy.
 - The abdomen and pelvis need to be evaluated with a double contrast (intravenous and oral) computed tomography (CT) scan to exclude extrapelvic spread and to assess the extent of possible resection. CT scans are generally reliable for identifying the extent of disease and adjacent organ involvement but are less discriminating for predicting local tumor resectability.
 - Any suspicious hepatic lesion should be examined with ultrasound. If the lesion is worrisome for metastatic disease, it should be biopsied.
 - Questionable findings on the chest X-ray film should prompt further investigation. Any worrisome lesion that is technically accessible should be biopsied.
- Magnetic resonance imaging (MRI) might be more accurate than conventional CT scanning for detecting recurrences in the pelvis or elsewhere in the abdomen because of better image resolution.
- However, similar to CT scans, MRIs provide only anatomic details and may not be any better at distinguishing tumor recurrence from scar in a postoperative field, particularly after pelvic irradiation.

- To overcome this limitation, a metabolic-based imaging modality such as positron emission tomography (PET) should be employed to evaluate questionable changes or worrisome lesions in the pelvis that are seen on CT scans.
- Colorectal cancer is known to rapidly metabolize fluorine-18 fluorodeoxyglucose (FDG), which therefore can be used as a metabolic label to detect tumor deposits, not only in the pelvis, but throughout the entire body.
- Thus, FDG-PET is a useful tool in the postoperative patient in whom there is a suspicion of recurrence but equivocal CT findings, and in whom extensive reoperative surgery might be extremely high risk.
- There are three ways of differentiating postoperative changes from tumor. The first is to document a change in the lesion, such as increase in size over time; the second is invasion of the adjacent organs; the third is histologic evidence obtained from endoscopic, CT- or ultrasound-guided biopsies of the suspicious tissue.
- However, occasionally pelvic disease is suspected from an increasing carcinoembryonic antigen or development of symptoms without any definable anatomic change on examination. In such situations, histologic proof should be vigorously sought.
- Exploratory pelvic surgery to obtain a diagnosis should be strongly discouraged because it poses an extreme risk to the patient and makes future evaluation of the pelvis even more difficult.

B. Determining Resectability

- Locally advanced primary or locoregional recurrences of rectal cancers can extend to involve any of the pelvic organs or rigid bony structures of the pelvis. Resectability is based on the anatomic location and what other structures are fixed to the lesion.
- Identifying the anatomic extent provides a better appreciation of the scope of the required resection. For example, anterior fixed lesions may require a hysterectomy, vaginectomy, a partial or complete cystectomy, or prostatectomy, whereas lesions that are fixed posteriorly may require a sacrectomy.
- Some factors are clearly associated with an unresectable tumor (Table 33.1).

Table 33.1. Symptoms or findings suggestive of unresectability for cure.

Sciatic pain

Bilateral ureteral obstruction

Multiple points of tumor fixation to the pelvic sidewall

Circumferential involvement of the pelvic sidewall

S1 or S2 bony or neural involvement

Extrapelvic disease

- Any circumferential tumor that extends to the pelvic sidewall is considered unresectable.
- Evidence of bilateral ureteral obstruction is a very worrisome finding. Unless there is focal infiltration of the bladder trigone causing bilateral ureteral obstruction, this finding usually indicates that a bulky tumor has invaded both lateral pelvic sidewalls.
- S1 and S2 nerve root involvement or evidence of invasion of the sacral bone at the level of S1 and S2 indicates an unresectable tumor.
- A sacrectomy proximal to S2 results in sacroiliac joint instability and although internal fixation is possible, it is not warranted for cases of locally recurrent rectal cancer.
- Nerve compression symptoms may completely resolve after pelvic irradiation and chemotherapy. However, persistent buttock and perineal pain usually resulting from tumor expansion and ingrowth into unresectable structures.

C. Multimodality Therapy for Advanced or Locally Recurrent Rectal Cancer

- Surgery with curative intent is the mainstay of treatment for advanced or locally recurrent rectal cancer. However, surgery alone results in a high rate of local and distant failure.
- Although EBRT may relieve symptoms and pain resulting from a large primary or recurrent rectal tumor, it alone does not offer a significant chance of cure. However, when it is combined with sensitizing chemotherapy, the probability of achieving a resection with negative margins and the rate of local tumor control increases.

- In general, for patients who never received prior pelvic radiation therapy, a full course of EBRT (5,040 cGy) is administered with concurrent 5-fluorouracil chemotherapy.

D. Surgery

- Before surgery, the magnitude of the operation and the possible complications are discussed in depth with the patient and family members.
- Very rarely in cases of locally advanced primary rectal cancers can the sphincter mechanism be preserved.
- In addition, the resection of adjacent structures or organs and the functional implications and reconstruction alternatives, such as an ileal conduit, need to be discussed.
- Ideally, patients are admitted the night before surgery for mechanical and antibiotic bowel preparation, intravenous hydration, and instruction in preoperative incentive spirometry.
- A midline incision is usually made. Transverse abdominal incisions should be avoided because they compromise the placement of any stomas and may injure the inferior epigastric vessels, the primary blood supply of the rectus muscle. Preservation of the rectus muscle is important in case a transpelvic rectus abdominis flap is required to reconstruct the pelvic floor.
- A self-retaining retractor is placed and the small bowel is packed into the upper abdomen to facilitate pelvic exposure.
- For rectal cancer recurrences that are not fixed to any pelvic structure (F0), a completion abdominoperineal resection (APR) is required.
- For anteriorly fixed tumors there are different operations that need to be considered, whereas for a primary or recurrent posteriorly fixed tumor that is fixed posteriorly, our operation of choice is an en bloc distal sacrectomy.
- For the anteriorly fixed lesion, the choice of operation is influenced somewhat by the sex of the patient.
 - In a woman, depending on the level and extent of the tumor, the resection may require only an en bloc excision of the posterior wall of the vagina, with immediate reconstruction.
 - A man with an anteriorly fixed tumor usually needs a cystectomy or cystoprostatectomy.

- Posteriorly fixed lesions require an en bloc distal sacrectomy. The proximal extent of the resection is to S2–3.
- When the resection is limited to the S2–3 level, it is generally possible to preserve one S3 root, which is usually sufficient to preserve bladder function.
- The wound complications and breakdown in this heavily irradiated field are not uncommon and occur in as many as 65% of patients who undergo radical resection with concurrent IORT. These postoperative wounds often require transfer of nonirradiated, well-vascularized tissue like muscle flaps to heal if that transfer was not done at the initial operation.

E. Use of IORT

- In cases of close margins, known microscopically positive margins, or minimal gross unresectable disease in the pelvis or after the sacrectomy, intraoperative electron-beam radiation therapy (IORT) is used in some centers.
- Between 1,000 and 2,000 cGy is delivered, depending on the extent of margin involvement.
- At Memorial Sloan–Kettering, a combined-modality treatment protocol uses high-dose intraoperative brachytherapy (HDR-IORT). The radiation is delivered via an array of catheters that are imbedded in a flexible rubber pad. This pad is then sutured to the area of concern and other normal tissue is packed away and protected.
- One possible disadvantage with the use of the postoperative brachytherapy catheters is that it is difficult to protect normal tissue, particularly the small intestine, once the operation is complete.

F. Results of Multimodality Treatment for Advanced Primary or Locally Recurrent Rectal Cancer

- In recent reports, the combination of preoperative EBRT and total mesorectal excision surgery for resectable rectal cancer resulted in a recurrence-free rate of 94% for Stage II and 85% for Stage III tumors.

- However, more locally advanced rectal cancers often have a higher recurrence rate. Although the cause of death in these patients is usually attributable to systemic disease, a mortality rate of 16–44% has been attributed to isolated local failure.
- To better address the significant symptoms associated with advanced primary or recurrent rectal cancer and to perhaps improve survival, a number of institutions have used multimodality therapy, including preoperative chemoradiation, extensive surgery, and intraoperative-directed local radiation therapy.
- For patients with advanced primary rectal cancer, studies have shown the benefit of combined preoperative chemoradiation followed by radical surgery.
- Surgery alone has been used to treat recurrent rectal cancers.
- In most series, recurrence and survival rates for patients with recurrent rectal cancer treated with surgery alone are less than those for patients with primary advanced rectal cancer, but are still better than historical data for patients treated with palliative therapies.
- The institution with the most experience using multimodality therapy including IORT for recurrent rectal cancer is the Mayo Clinic, Rochester.
 - The 1-, 3-, and 5-year survival rates for the 304 patients were 84%, 43%, and 25%, respectively.
- Patients whose tumors can be resected with negative margins often have better outcomes. Because of this, some investigators have questioned the routine use of the intraoperative, locally directed radiation therapy.
- For now, most studies, although retrospective and often based on single institutions, suggest that combined multimodality therapy that includes IORT provides the best chance for cure for patients with locally advanced or recurrent rectal cancer.

G. Palliative Care for Advanced or Recurrent Rectal Cancer

- Patients who present with locally advanced or recurrent rectal cancer must first be evaluated with the intent to cure. An equally important consideration is palliation of symptoms if a cure does not seem to be achievable.

- Palliative interventions may be broadly classified as noninvasive, minimally invasive, and surgical. The primary noninvasive palliative option is radiotherapy.
- Minimally invasive approaches to palliation usually involve mechanical means to reduce symptoms related to pelvic tumors. These include ureteral stents to alleviate urinary obstruction and expandable metal colonic wall stents or the use of lasers to relieve rectal obstruction.
- Self-expanding metal stents (SEMS) are useful for the nonsurgical management of rectal obstructions, bleeding, and malignant fistulas.
- Endoscopic lasers are an alternative to SEMS.
 - Endoscopic laser treatments remove the tissue intraluminally by coagulative necrosis or immediate tissue vaporization, depending on the amount of energy applied.
 - Palliation of symptoms and marked improvement in quality of life is achieved after repeated laser sessions (usually 2–5) in 80–90% of patients.
 - Unfortunately, laser therapy does not seem to be a durable treatment. Effective palliation decreases as a patient survives longer; successful palliation at 1 year was only 42%.
- In appropriately selected patients with Stage IV disease and complicated or advanced rectal cancer, surgical resection of the primary tumors can achieve very reasonable oncologic results and provide good palliation of symptoms related to the tumor.

34. Colorectal Cancer: Metastatic (Palliation)

A. Introduction

- Approximately 20% of patients with colorectal cancer present with established distant metastases. In most cases, the metastases are detectable with noninvasive imaging, and patients can be assigned to AJCC (American Joint Committee on Cancer) Stage IV before any surgical intervention.
- The clinical spectrum at the time of diagnosis ranges from the asymptomatic patient with a single metastatic lesion to the rapidly deteriorating patient with colon obstruction and advanced, multi-organ metastases. It is therefore difficult to define rigid treatment algorithms that can be widely applied to all clinical settings.
- The vast majority of Stage IV patients are not curable by current treatment protocols. A recent analysis of data from the SEER (surveillance, epidemiology, and end results) population-based database estimates that the 5-year survival rate for Stage IV patients diagnosed between 1991 and 2000 was 8%.
- Systemic chemotherapy, endoscopic treatments to palliate obstruction, surgical diversion, and surgical resection all have important roles in treatment of Stage IV patients. Treatment approaches must be individualized based on the extent and resectability of local and distant disease, the presence or absence of bowel obstruction, performance status, and comorbidities.
- For patients with good performance status and minimal symptoms from their primary cancers, standard treatment is systemic chemotherapy, which is well documented to increase survival and quality of life.

- Surgical resection of the primary tumor and, when feasible, of the metastatic lesions can provide excellent palliation and can, in some cases, provide lasting cure.
- In the past decade, there has been remarkable improvement in the efficacy of chemotherapy for colorectal cancer. First-line therapy with either FOLFOX or FOLFIRI in combination with bevacizumab now yields major responses in up to 50% of previously untreated patients, and achieves minor responses or stable disease in an additional 20% of patients.
- Over the past 10 years, the median survival for patients with metastatic disease who are treated with chemotherapy has improved from 12 to 14 months to 21 months.

B. Biology of Metastatic Disease

- Metastasis is defined as the spread of malignant cells from a primary tumor to a distant organ. It is estimated that 90% of all cancer deaths are a result of metastasis.
- Metastatic foci themselves can go through the metastatic process and spread to other organs (i.e., metastases can metastasize).
- Numerous clinical and laboratory studies have attempted to define the complex process of metastasis formation. It is a multi-step process, and failure at any step results in failure of the overall process. The process relies on properties of the tumor cells, as well as the microenvironment of the primary and secondary sites. A series of major events must occur (Fig. 34.1).
- The first step is tumorigenesis, which occurs after the initial malignant transformation. The tumor proliferates into a small mass of heterogeneous cells that are of varying metastatic or malignant potential. These tumor cells undergo multiple and sequential genetic changes, characterized by the appearance of oncogenes and a decrease in tumor suppressor genes. As the tumor grows beyond 1 mm in diameter and becomes relatively hypoxic, angiogenesis is initiated. The process of tumor angiogenesis is tightly regulated by pro- and anti-angiogenic factors secreted by both the tumor and its environment. As tumors successfully grow, suppressors of angiogenesis are inhibited and pro-angiogenic factors predominate, resulting in neovascularity and further growth of the tumor. Some tumors may grow by utilizing other existing blood vessels in nearby tissues.
- In the next step, some cells will develop an invasive phenotype.

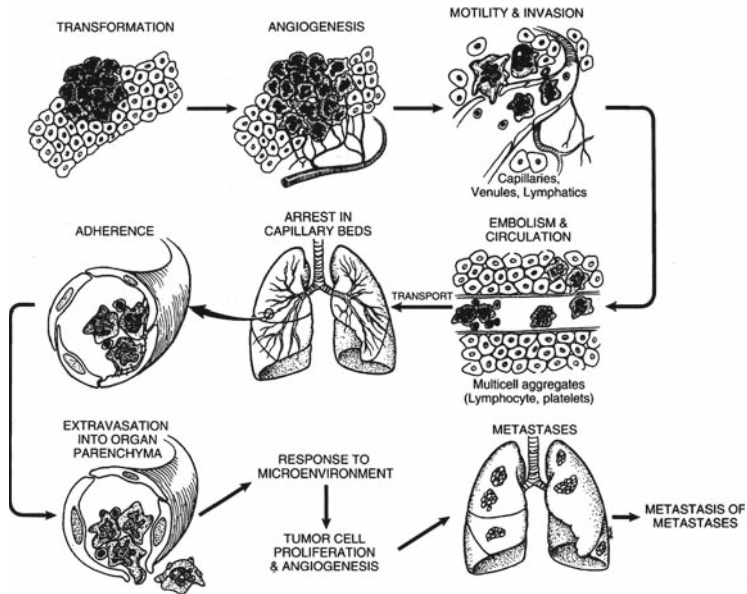


Fig. 34.1. Schematic illustrating the multistep process involved in the development of metastasis. (Reprinted from DeVita VT Jr, Hellman S, Rosenberg SA. *Cancer: Principles and Practice of Oncology*. 6th ed. copyright 2001, with permission of Lippincott Williams & Wilkins.)

- Malignant invasion is characterized by down-regulation of cell adhesion, resulting in detachment of the cell from the primary tumor mass and the extracellular matrix. Stromal invasion is accomplished through interactions with the basement membrane, including adhesion, proteolysis, and migration, ultimately resulting in detachment and invasion through the basement membrane. This invasive phenotype also enables these cells to enter thin-walled lymphatics and vasculature, allowing access to systemic circulation. The neovasculature from tumor-induced angiogenesis seems to be more susceptible to such invasion. This process of invasion is critically related to the expression (up-regulated or down-regulated) of adhesion molecules and factors influencing cell migration.
- Once inside the vascular system, cells or cell clumps (emboli) are circulated, and must survive hemodynamic filtering as well as immune surveillance. They must then arrest in a distant organ. This probably involves adhesion and/or trapping, based on size, within small capillary beds. There is likely a complex interaction between the malignant cell and the endothelium or

exposed basement membrane, allowing cell arrest. Once arrested in a tissue bed, the cells extravasate into the tissue, enabling formation of a metastatic focus.

- Paracrine growth factors, hormones, and the local tissue environment have critical roles in the ultimate outcome of extravasated cells.
- Growth in the distant organ after deposition is a major limiting factor in the formation of metastasis, and some metastatic cells can remain dormant for years. Once deposited in the distant organ, the metastatic focus, if proliferating, must again go through tumorigenesis, angiogenesis, and evasion of the immune system.
- This complex multistep process of metastasis formation is related to multiple genetic changes among malignant cells.
- It seems that there are genes specific to tumorigenesis, invasion, angiogenesis, and other steps. Recently, a number of genes have been identified that suppress metastatic potential and, by their down-regulation, affect a cell's ability to metastasize without affecting tumorigenicity. These discoveries provide a sense of the future challenge in elucidating the multiple, stepwise, and specific changes that regulate a cell's ability to metastasize. Advances in this field will have obvious and profound implications for the treatment of cancer.

C. Diagnosis/Staging

- The clinical presentation of Stage IV patients is variable. Most present with symptoms referable to the primary tumor. However, symptoms from metastatic disease, asymptomatic metastatic lesions found on imaging studies, abnormalities in routine blood work, and cancers discovered on endoscopic screening procedures may also be the first signs of disease.
- Initial staging evaluation should include colonoscopy with biopsy, and imaging of the primary tumor, liver, and lungs.
- When feasible, endorectal ultrasound or magnetic resonance imaging (MRI) is recommended for rectal cancers to document the initial T and N stage.
- Spiral computed tomographic (CT) scanning of the chest/abdomen/pelvis is a highly accurate and efficient method of detecting metastases.
- Positron emission tomography (PET) scanning detects occult disease not seen on CT scan in 20% of Stage IV patients, and should be considered if such findings might affect patient management.

- Once the extent of disease workup is complete and distant metastases have been documented, the surgeon must make three important judgments.
 - First is whether the patient is fit for aggressive treatment. Patients with poor performance status or serious cardiovascular, pulmonary, renal, neurologic, or gastrointestinal impairment may not tolerate chemotherapy or major surgery.
 - Second is whether the primary tumor presents a clinically significant risk of bowel obstruction. Symptoms, radiographic findings, and endoscopic findings are important considerations. If the proximal colon is not dilated on radiographic studies and a colonoscope can traverse the tumor, it is generally safe to begin treatment with chemotherapy.
 - The third determination is whether the patient's metastases can be surgically resected, and therefore treated with curative intent. If complete resection of all disease can be expected, then surgical intervention should assume a high priority.

D. Multidisciplinary Evaluation

- Management of patients with advanced disease is often complex, and multidisciplinary evaluation can be helpful in determining initial therapy. The surgeon and medical oncologist should evaluate the patient in consultation with a radiologist and gastroenterologist.
- For rectal cancers that are bulky or symptomatic, the advice of a radiation oncologist is often helpful.

E. Palliative Management of the Primary Cancer: Stents, Laser

- In the setting of metastatic cancer, the critical question is whether colon obstruction should be considered a contraindication for systemic chemotherapy or radiotherapy. The degree of symptoms, endoscopic findings, and radiographic findings are all relevant to this decision.
- For patients with advanced obstruction, nonresective palliative options include laser therapy, fulguration, colonic self-expanding metal stents, and creation of a diverting stoma.

- Laser therapy has been used for palliation of obstructing rectal cancers for the past two decades. In a large series of 272 patients who underwent palliative laser therapy for rectosigmoid cancers, the immediate success rate in treating obstructive symptoms was 85%.
 - However, laser therapy is practical only for treating cancers of the distal colon and rectum, and is rarely used to treat proximal lesions. In addition, multiple therapy sessions are required to achieve lasting relief of symptoms.
 - Serious complications such as bleeding, perforation, and severe pain have been reported in 5–15% of patients, especially those undergoing multiple treatments.
- Fulguration of rectal cancers is another method of opening the rectal lumen. Fulguration, in combination with endoluminal debulking, can remove a large volume of tumor; however, unlike laser therapy, this procedure requires hospital admission and regional or general anesthesia.
- Since their introduction in 1991, colonic stents have become an important method of palliation for obstruction in colorectal cancer patients, especially those with unresectable metastatic disease.
 - These self-expanding metallic stents can potentially dilate the lumen to a near-normal diameter, providing quick relief of symptoms and, in some cases, allowing endoscopic assessment of the proximal colon.
 - Stents can be placed in patients using minimal sedation, without need of prior endoscopic dilation and the concomitant increased risk of complications such as perforation or tumor fracture.
 - Moreover, these stents can be placed across relatively long lesions by overlapping stents in a “stent-within-stent” manner.
 - In a retrospective series of 80 patients who underwent colonic stent placement for malignant large bowel obstruction, stents were successfully placed in 70 patients (87.5% overall technical success rate).
 - Satisfactory symptomatic relief and clinical decompression was achieved in 67 patients (83.7% overall clinical success rate). Two perforations occurred in this series, one of which resulted in death. Other complications included stent migration resulting in expulsion, reobstruction, and intractable tenesmus. Stenting of cancers in the mid and low rectum may result in debilitating urgency and incontinence.

F. Surgical Management of the Primary Cancer: Resection

- The role of bowel resection in patients with unresectable metastases is controversial. It is important to recognize that there are no randomized data demonstrating a survival benefit for bowel resection in Stage IV patients.
- However, palliative resection of the primary tumor does provide durable local control, is generally well tolerated, and can benefit many Stage IV patients.
- Thus, standard management for patients with unresectable metastatic colorectal cancer is systemic chemotherapy. The proper use of elective colon/rectal resection in nonobstructed patients is a source of continuing debate.
 - Loss of performance status, risk of surgical complications, and delay in chemotherapy are major downsides to palliative resection.
 - Alternatively, elective operations have a far lower morbidity than emergency surgery and fear having to operate on patients who obstruct while receiving chemotherapy or who present with more advanced disease after multiple cycles of ineffective chemotherapy.
- To summarize the treatment options for Stage IV patients with unresectable metastases, treatment algorithms are shown for patients with Stage IV colon cancer (Fig. 34.2) and Stage IV rectal cancer (Fig. 34.3).

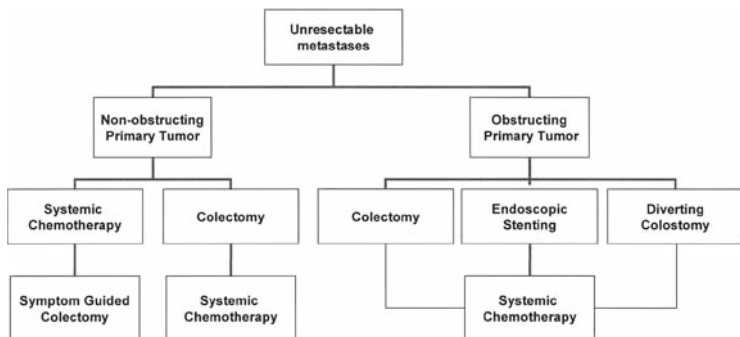


Fig. 34.2. Treatment algorithms for patients with Stage IV colon cancer: use of palliative colon resection.

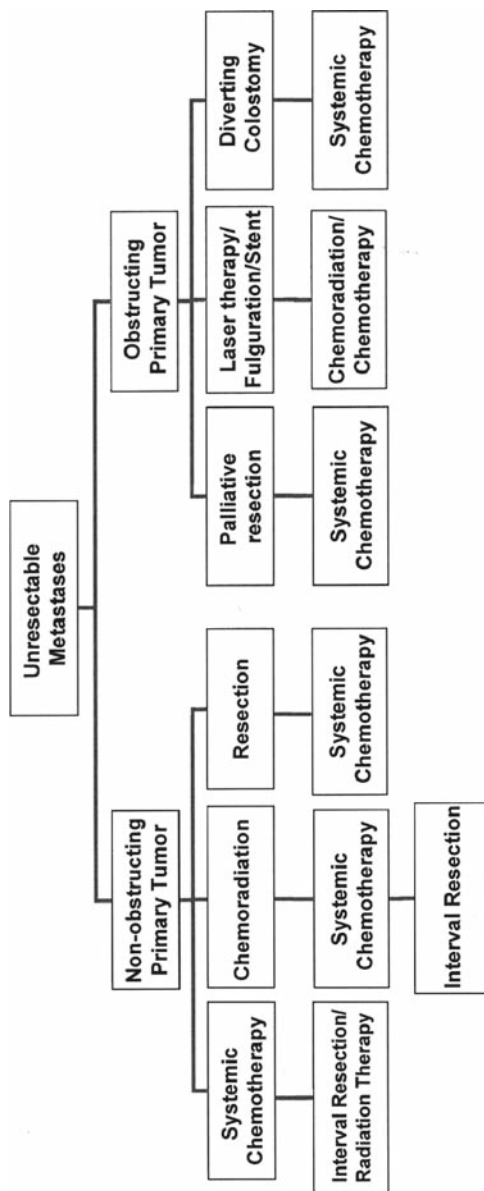


Fig. 34.3. Treatment algorithms for patients with Stage IV rectal cancer: use of palliative rectal resection.

- The major variables to consider are location of the primary tumor, degree of colon/rectal obstruction, extent of metastatic disease, and fitness of the patient for surgery.
- For patients with nonobstructing primary tumors, upfront treatment with chemotherapy is favored because, in this era of increasingly effective chemotherapy, it is important that patients be given the full benefit of aggressive systemic therapy.
- However, it should be remembered that the goal of therapy is effective palliation, and surgical resection remains the most effective and durable local treatment option.

G. Liver Metastasis

- Of the 150,000 new cases of primary colorectal cancer diagnosed in the United States each year, approximately 60% of these patients will develop liver metastases and about one-third will have disease limited to the liver.
- Overall, it has been estimated that about 10% of all patients with colorectal liver metastases are candidates for potentially curative hepatic surgery.
- Of those able to undergo complete hepatic resection, 25–35% achieve long-term survival.
- Therefore, only a small percentage of the overall number of patients with metastatic colorectal cancer are cured by liver surgery; this underlines the paramount importance of patient selection in determining optimal treatment.
- These statistics also highlight the fact that the majority of patients with liver metastases have unresectable disease, and require evaluation for chemotherapy or supportive care.

H. Natural History of Untreated Liver Metastases

- Several investigators have retrospectively studied untreated patients, documenting median survivals of 5–10 months; long-term survival was rarely seen.

Diagnosis and Patient Evaluation

- In the patient who presents with liver metastases, the first consideration must be whether he or she is a potential surgical candidate, because resection remains the only potentially curative modality.
- First, a complete evaluation of the colon via colonoscopy should be performed within a year of presentation; this addresses the issue of synchronous and metachronous colonic neoplasms, as well as the issue of local recurrence (especially in rectal cancers).
- Complete cross-sectional imaging of the abdomen and pelvis with high-quality CT is also essential, to rule out extrahepatic disease.
- The additional advantage of routine chest CT is low compared with that of a plain chest X-ray, but should be considered in high-risk cases.
- FDG (Fluoro-deoxy-glucose) PET scanning is routinely performed because of early prospective data documenting its utility.
- The information obtained from PET scanning changes management decisions in patients with recurrent colorectal carcinoma 20–50% of the time. The major strength of PET scanning seems to be the detection of occult extrahepatic disease.
- A baseline serum carcinoembryonic antigen (CEA) level should also be drawn, as it is of prognostic value, and serves as a baseline to follow after the conclusion of therapeutic interventions.
- CT scans are the most common modality used to address liver disease and, with modern dynamic helical scanning techniques, this remains the mainstay of hepatic imaging.
- In experienced hands, ultrasound is excellent at distinguishing neoplastic tumors from benign lesions such as cysts, focal nodular hyperplasia, or hemangiomas.
- Additionally, ultrasound can specifically evaluate the relationship of specific lesions to major vascular structures and the biliary tree.
- MRI is an excellent method for characterizing liver lesions. Particularly if there are multiple hepatic lesions, not all of which are suspected to be metastatic tumors, MRI can help distinguish malignant lesions from cysts, hemangiomas, and other benign lesions. MRI is also an excellent modality for evaluating relationships of tumor to the biliary tree (via magnetic resonance cholangiopancreatography – MRCP) and to hepatic vasculature.

- High-quality MRI and CT are probably equivalent for evaluating extent of liver disease, and as aids in surgical planning.
- In any patient being considered for hepatic resection, a complete medical workup should be performed to assess the patient's fitness for undergoing a major abdominal operation.

Treatment Options

Chemotherapy

- Despite many attempts to modify 5-FU with other agents, response rates generally ranged from 15 to 20%, and survival beyond 1 year was uncommon. The addition of leucovorin (5-FU/LV) and the use of infusional dosing techniques are associated with an increased response rate, and are frequently used despite no improvement in survival.
- Irinotecan (CPT-11) in conjunction with 5-FU/LV has been recently shown to be more effective than 5-FU/LV alone for treatment of metastatic colorectal cancer.
- Two randomized trials established the superiority of single-agent irinotecan over 5-FU/LV alone or best supportive care as second-line therapy.
- Additionally, two randomized trials utilizing combined irinotecan/5-FU/LV as first-line chemotherapy have shown response rates of 40%, with modestly improved survival (median 15–17 months versus 12–14 months).
- The addition of oxaliplatin has been particularly exciting because of the in vitro sensitivity seen in cisplatin-resistant cell lines, as well as its synergy with 5-FU. In a trial comparing oxaliplatin/5-FU/LV (FOLFOX) to 5-FU/LV, response rates for FOLFOX were in excess of 50% (compared with 22% for 5-FU/LV).
- Early analyses of comparisons of irinotecan/5-FU/LV to FOLFOX have so far shown FOLFOX to yield superior response rates.
- Regional hepatic therapy via hepatic artery infusional (HAI) chemotherapy has been studied since the 1970s.
- Early phase II trials of HAI FUDR or 5-FU for unresectable colorectal hepatic metastases demonstrated remarkable response rates ranging from 29 to 88%. Subsequently, ten randomized phase III trials comparing HAI chemotherapy to systemic chemotherapy have been completed (Table 34.1).

Table 34.1 Randomized trials comparing HAI to systemic chemotherapy for unresectable liver metastases.

Study group	Year	Arms	n	Percentage receiving assigned treatment	Crossover allowed	Response rate (% CR + PR)	Median survival (months)
MSKCC	1987	HAI FUDR	48	94	Yes	50 ^a	17
NCI	1987	IV FUDR	51	94		20	12
		HAI FUDR	32	66	No	62 ^a	17
NCOG	1989	IV FUDR	32	92		17	12
		HAI FUDR	67	75	Yes	42 ^a	17
City of Hope	1990	IV FUDR	76	86		10	16
		HAI FUDR	31	100	Yes	55 ^a	14
NCCTG	1990	IV 5-FU	10	100		20	12
		HAI FUDR	39	85	No	48	13
French	1992	IV 5-FU/LV	35	100		12	11
		HAI FUDR	81	87	No	44 ^a	15 ^a
English	1994	BSC or IV 5-FU	82	50 got 5-FU		9	11
		HAI FUDR	51	96	No	—	14
German	2000	BSC or IV 5-FU	49	20 got 5-FU		—	8
		HAI FUDR	54	69	Yes	43 ^a	13
MRC/EORTC	2003	HAI 5-FU/LV	57	70		45 ^a	19
		IV 5-FU/LV	57	91		20	18
		HAI 5-FU/LV	95	66	No	22	15

CALGB	2003	IV 5-FU/LV	126	87	No	19	15
		HAI FUDR	59	87		48 ^a	23 ^a
		IV 5-FU/LV	58	87		25	20

Source: Adapted from Cohen and Kemeny.
Note: Response rate calculations are based on patients who received assigned treatment. Survival based on intent-to-treat calculation.
NCI National Cancer Institute; *NCOG* Northern California Oncology Group; *NCCTG* North Central Cancer Treatment Group; *MRC/EORTC* Medical Research Group/European Organization for Research and Treatment of Cancer; *CR* complete response; *PR* partial response

^aStatistically significant ($P < .05$)

From 1987 through 1990, five trials were done comparing HAI FUDR to intravenous FUDR or intravenous 5-FU/LV. All of these trials showed significantly increased response rates, but only trials comparing HAI chemotherapy to best supportive care showed improved survival.

- One of the major lessons learned from trials evaluating HAI chemotherapy was that, although control of hepatic disease was excellent, there was significant extrahepatic failure.
- Although recent advances in cytotoxic chemotherapy for colorectal cancer over the last decade have been very exciting, the development of targeted molecular-based therapy provides even greater hope for more effective systemic treatments.

Resection

- Over the last 20 years large series have demonstrated that liver surgery can now be practiced with acceptable safety, and that patients with isolated and resectable hepatic metastases have the potential for long-term survival.
- In modern series, mortality rates for hepatectomy for metastatic colorectal cancer are uniformly 5% or less (Table 34.2). Nonetheless, morbidity for these operations remains substantial, and is usually reported between 20 and 50%.
- Major institutional and multi-institutional reviews of patients undergoing hepatectomy for metastatic colorectal cancer have now clearly documented that, in well-selected patients, 5-year survival ranges from 25 to 40%, 10-year survival ranges from 20 to 26%, and median survivals range from 24 to 46 months (Table 34.3).
- Many studies of patients undergoing liver resection for isolated hepatic metastases have evaluated prognostic factors to help select those patients most likely to benefit from hepatectomy and, conversely, to identify those unlikely to benefit.
- The two most consistent negative prognostic factors are the presence of extrahepatic disease and the inability to resect all tumor; these two factors remain contraindications to hepatectomy.
- The exception to this rule is the patient with limited pulmonary metastases or colonic anastomotic recurrence, who may undergo combined resections with some success.

Table 34.2 Surgical series of hepatectomy for metastatic colorectal cancer with 100 or more patients.

Author	No. of patients	Operative mortality (%)	1-year survival (%)	5-year survival (%)	10-year survival (%)	Median survival (months)
Adson et al.	141	2	82	25	—	24
Hughes et al.	607	—	—	33	—	—
Schlag et al.	122	4	85	30	—	32
Doci et al.	100	5	—	30	—	28
Gayowski et al.	204	0	91	32	—	33
Scheele et al.	469	4	83	33	20	40
Fong et al.	577	4	85	35	—	40
Jenkins et al.	131	4	81	25	—	33
Rees et al.	150	1	94	37	—	—
Jamison et al.	280	4	84	27	20	33
Fong et al.	1,001	3	89	37	22	42
Minagawa et al.	235	0	—	35	26	37
Figueras et al.	235	4	87	36	—	—
Choti et al.	226	1	—	40	26	46
Laurent et al.	311	3	86	36	—	40

Table 34.3. Clinical risk score^a and survival in 1,001 patients undergoing liver resection for metastatic colorectal cancer.

Score	1-year survival (%)	3-year survival (%)	5-year survival (%)	Median survival (months)
0	93	72	60	74
1	91	66	44	51
2	89	60	40	47
3	86	42	20	33
4	70	38	25	20
5	71	27	14	22

Source: Adapted from Fong et al.

^aEach of the following five risk factors equals one point: node positive primary, DFI <12 months, >1 tumor, size >5 cm, CEA >200 ng/mL. Score is total number of points in an individual patient.

- A multivariate analysis of 1,001 patients who underwent potentially curative hepatectomy, identified five factors as having the most influence on outcome. These included size greater than 5 cm, DFI of less than 1 year, more than one tumor, lymph node-positive primary, and CEA greater than 200 ng/mL. Utilizing these five factors, a risk score predictive of recurrence after liver resection (Table 34.3) has been developed.
- Recurrence after hepatectomy for colorectal metastases is common, occurring in more than two-thirds of patients.
- In patients who do recur, the liver is the most common site of recurrence and is involved approximately 45% of the time.
- Because many recurrences are isolated to the liver, repeat liver resection has been attempted by several surgeons with some success. Unfortunately, only 5–10% of patients are candidates for a second liver resection, underscoring the importance of patient selection.
- Because the majority of patients with hepatic colorectal metastases are technically unresectable, the development of more effective chemotherapy has inspired many oncologists to use a “neoadjuvant” chemotherapy strategy in an attempt to render patients resectable.
- Although resection has become the gold standard for treatment of liver metastases, other methods of tumor destruction using thermal ablation techniques have also been developed.

- More recently, radiofrequency ablation (RFA) probes have been developed that can heat liver tumors and a surrounding margin of tissue to create coagulation necrosis. RFA can be used percutaneously, laparoscopically, and at laparotomy under ultrasound, CT, or MRI guidance.
- Furthermore, RFA has low morbidity that generally ranges around 10% and is rarely serious. Although RFA can be used near blood vessels, because the heat-sink effect of blood flow protects the endothelium, major bile ducts can be seriously injured, limiting the use of RFA in central tumors situated near major bile ducts
- Perhaps the greatest application of ablative techniques will be in their use as additions to resection in patients with multiple bilobar tumors.

I. Lung Metastasis

- It has been estimated that approximately 10% of patients with colorectal cancer will develop lung metastasis. Of these, only 10% will have metastases isolated to the lung; and of those patients with isolated lung metastases, only a small proportion (probably another 10%) will be considered candidates for pulmonary metastasectomy.
- These estimates demonstrate that the majority of patients with metastatic colorectal cancer to the lung have advanced disease, and are thus treated with systemic chemotherapy or best supportive care.
- Modern series of lung resection for metastatic colorectal cancer uniformly report operative mortalities of less than 2% (Table 34.4).
- Five-year survival rates range from 16 to 64%, but generally cluster around 30–40%.
- The majority of studies that have analyzed synchronous liver and lung metastases report a uniformly poor outcome after combined resections.
- In the setting of isolated pulmonary recurrence after potentially curative partial hepatectomy, outcomes for pulmonary metastasectomy are more favorable and are similar to those for the initial hepatectomy.

Table 34.4. Outcome of patients undergoing pulmonary metastasectomy for colorectal cancer.

Author	N	Operative mortality (%)	5-y survival (%)	Significant risk factors
Mori et al.	35	—	38	None found
McCormack et al.	144	0	44	Margin
McAfee et al.	139	1	31	No. of lesions, CEA
Yano et al.	27	—	41	No. of lesions
Saclarides et al.	23	—	16	No. of lesions
van Halteren et al.	38	—	43	DFI
Shirouzu et al.	22	—	37	No. of lesions, size
Girard et al.	86	1	24	CEA, margin
Okumura et al.	159	2	41	No. of lesions, LN status
Zanella et al.	22	0	62	None found
Zink et al.	110	0	33	Size, CEA

Source: Adapted from Rizk and Downey

LN lymph nodes

J. Peritoneal Metastasis

- The peritoneal surface is involved in approximately 10–15% of patients with colorectal cancer at time of initial presentation (synchronous metastases) and in 20–50% of patients who develop recurrence (metachronous metastases).
- As a site of colorectal cancer metastasis, the peritoneal surface ranks second only to the liver.
- Peritoneal metastasis occurs by direct implantation of cancer cells via one of four mechanisms (1) spontaneous intraperitoneal (IP) seeding from a T4 colorectal cancer that has penetrated the serosal surface of the colon; (2) extravasation of tumor cells at the time of colon perforation from an obstructing cancer; (3) iatrogenic tumor perforation through an area of serosal injury or enterotomy at the time of colon resection; (4) leakage of tumor cells from transected lymphatics or veins at the time of colon resection. The risk of peritoneal metastasis is therefore highest in the setting of locally advanced cancers.

- Peritoneal metastases are clinically important because of their frequent progression to malignant ascites and/or malignant bowel obstruction.
- Preoperative detection of peritoneal metastases is not reliable.
- The extent of carcinomatosis is a major prognostic factor, and is best assessed by either laparoscopic or open exploration.
- Standard management of patients known to have peritoneal metastases at initial presentation is systemic chemotherapy.
- Although few prospective trials have been completed for colorectal carcinomatosis, the available evidence suggests a survival benefit for cytoreductive surgery and IP chemotherapy. Phase II studies report 5-year survival rates ranging between 19 and 28%. The most consistent and important prognostic factor in these studies is the ability to achieve complete resection of all gross disease.

K. Ovarian Metastasis

- Approximately 7–30% of ovarian neoplasms are metastatic cancers, the most common being colorectal and breast cancer.
- However, the risk of developing ovarian metastasis is substantially higher in woman with Stage IV disease, and approaches 90% in women with established peritoneal metastases.
- Thus, in a woman with recent diagnosis of advanced colorectal cancer, any ovarian mass should be considered a metastasis from colorectal cancer until proven otherwise.
- Most often these metastatic lesions are large, and at least half of the cases have bilateral ovarian involvement.
- Distinguishing a metastatic colorectal cancer from primary ovarian tumor is difficult by gross assessment alone, but a correct diagnosis can generally be determined through integration of clinicopathologic, immunohistochemical, and cytogenetic features. Most metastatic colorectal lesions are CK20+/CEA+/CK7- on staining, whereas primary ovarian neoplasms are CK20-/CEA-/CK7+.
- In addition, ovarian metastases are frequently resistant to systemic chemotherapy even when other sites of metastatic disease are responding. Therefore, resection of synchronous ovarian metastases should be performed when encountered

in the operating room. Bilateral oophorectomy and complete resection of gross disease is recommended.

- For women with isolated ovarian metastases, median postresection survival is 18 months.
- The role of prophylactic oophorectomy in the absence of macroscopic disease is not well defined.
- For premenopausal patients, only those with established peritoneal metastases, those with a clearly increased risk of developing ovarian carcinoma (strong family history, known carriers of breast cancer [BRCA] or hereditary nonpolyposis colorectal cancer [HNPCC] mutation), or those who have already completed their families should be considered for prophylactic oophorectomy.

L. Bone and Brain Metastases

- Bone metastases from colorectal cancer reportedly occur in 7–9% of cases, and most often present in the context of widespread metastatic disease.
- Routine diagnostic bone imaging is not indicated in colorectal cancer patients, however, unless there are specific bone-related symptoms.
- Symptomatic relief from bony metastases can usually be accomplished with radiation and medical therapy. However, pathologic fractures are best treated by operative internal fixation.
- Cerebral metastases from colorectal cancer are uncommon, occurring in 1–4% of colorectal cancer cases.
- Colorectal tumors account for approximately 3% of all metastatic brain tumors. These are generally found in the context of widespread metastases to multiple organ sites, but on rare occasion can present as an isolated brain metastasis.
- There is no role for routine brain imaging at primary presentation or at presentation with metastases elsewhere, unless there are specific neurologic symptoms.
- Once brain metastases occur, symptoms are common; palliative therapies include steroids to decrease swelling and anticonvulsants to control seizures. Definitive therapy of colorectal brain metastases usually involves surgery, radiation, or a combination of the two. For isolated, single brain metastases, resection can result in survival beyond 1–2 years.

35. Anal Cancer

A. New Anatomic Considerations

- New terminology is necessary because true anal canal lesions may have a more aggressive biology requiring chemoradiotherapy whereas lesions of the perianal skin may simply be treated with local excision. Thus, if the two classes of lesions are unwittingly grouped together, the response rates of anal cancer to chemoradiation therapy may be overstated.
- The authors have proposed a new classification that may prove more useful to all caregivers who diagnose or treat patients with anal cancers. The classification system divides the region into three easily identifiable regions: intraanal, perianal, and skin (Fig. 35.1).
 - **Intraanal** lesions are lesions that cannot be visualized at all, or are incompletely visualized, while gentle traction is placed on the buttocks.
 - In contrast, **perianal** lesions are completely visible and fall within a 5-cm radius of the anal opening when gentle traction is placed on the buttocks.
 - Finally, **skin** lesions fall outside of the 5-cm radius of the anal opening.
 - A key component of this classification system is that all clinicians, including gastroenterologists, surgeons, nurse practitioners, and medical and radiation oncologists can perform this simple examination in their offices without the aide of an anoscope or a clear understanding of the anatomic landmarks (dentate line and anal verge) of the region.

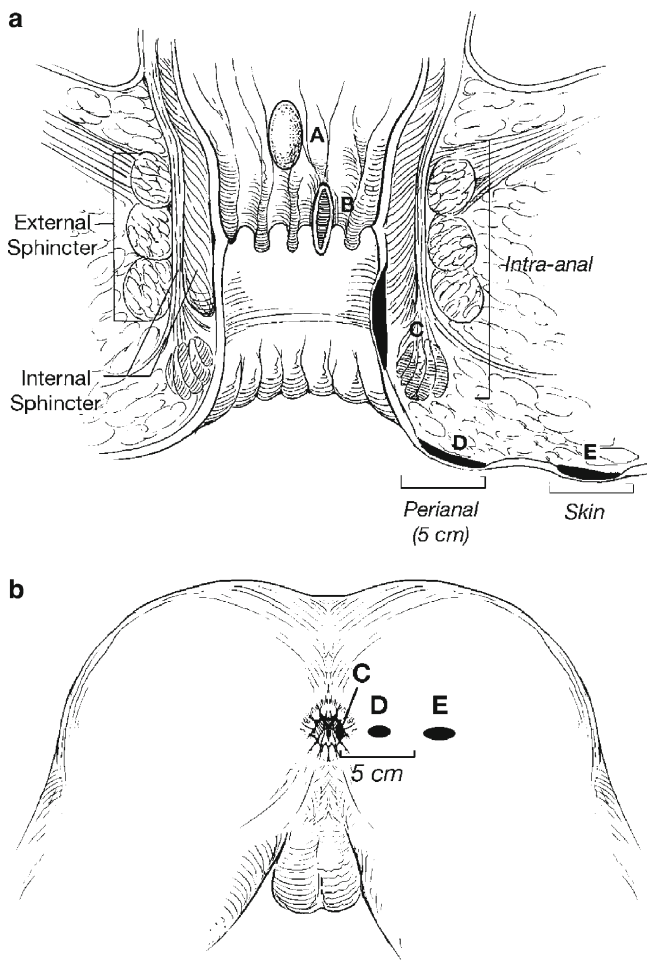


Fig. 35.1. Classification system of anal cancers (a) coronal section. (b) perianal view; (A–C) intranal (anal canal) lesions, (D) perianal (anal margin) lesions, (E) skin lesions.

- Identification of a new zone, the transformation zone, is also proposed to help clinicians and pathologists understand how intraanal SCCs may be found 6, 8, or even 10 cm proximal to the dentate line in the anatomic rectum.
 - The transition zone is a well-known region. It is an area 0–12 mm in length beginning at the dentate line where a

“transitional urothelium-like” epithelium may be found in the rectal mucosa instead of the standard columnar mucosa of the rectum.

- A “transformation zone” is a common finding in the cervix. This transformation zone, which we would propose for the anorectum, is a region in which squamous metaplasia may be found overlying the normal columnar mucosa. This immature metaplastic tissue may extend up the rectum in a fluid and dynamic manner involving at times 10 cm or more of distal rectal mucosa.
- The “transformation zone” is an important region where metaplastic tissue susceptible to human papillomavirus (HPV) infection, in particular HPV 16, may be found.

B. Terminology

- The terminology used by pathologists when reporting premalignant lesions of the anus and perineum is often confusing to the treating clinicians. The terms SCC in situ (CIS), anal intraepithelial neoplasia (AIN), anal dysplasia, squamous intraepithelial lesion (SIL), and Bowen’s disease may all be used to refer to the same histopathology.
- AIN and anal dysplasia have both historically been broken into AIN I, II, and III and low-, moderate-, and high-grade dysplasia. However, as with other pathologic staging systems, the intra- and interobserver variability are too high with this many categories.
- Therefore, it has been suggested that when referring to intraanal, perianal, and skin lesions of the buttock that the tissue be classified as normal, low-grade squamous intraepithelial lesions (LSIL), high-grade squamous intraepithelial lesions (HSIL), or invasive cancer. Throughout the remainder of the chapter we will use this terminology and avoid CIS and Bowen’s disease.

C. Lymphatic Drainage

- Lymphatic drainage above the dentate line occurs via the superior rectal lymphatics to the inferior mesenteric lymph nodes and laterally to the internal iliac nodes. Below the dentate line,

drainage is primarily to the inguinal nodes but may also involve the inferior or superior rectal lymph nodes.

D. Etiology and Pathogenesis of Anal Dysplasia and Anal SCC

- HPV is a DNA papovavirus with an 8-kb genome and is the most common viral sexually transmitted infection. The HPV is a necessary but not sufficient cause for the development of anal SCC (SCCA) and SILs.
- Although most patients clear the virus with only 1% of the patients developing genital warts with low oncogenic potential (HPV serotypes 6 and 11), an estimated 10–46% of patients will develop subclinical infections that may harbor malignant potential (HPV serotypes 16, 18, 31, 33, 35).
- Transmission is not prevented by condoms because the virus pools at the base of the penis and scrotum thus abstinence is the only effective means of prevention.
- In women, the virus may pool and extend from the vagina to the anus.
- Anoreceptive intercourse may be associated with the development of intraanal disease but the presence of condylomata or dysplasia within the anus does not mandate that anoreceptive intercourse has occurred.
- The squamous metaplastic tissue above the dentate line is a relatively “immature” incompletely developed squamous epithelium overlying the columnar epithelium and may not require trauma to disrupt an intact “barrier” making it particularly susceptible to HPV infection.
- If high-risk viral DNA eludes immune surveillance and gains access to the nucleus of replicating cells (wound repair or metaplasia), the infection can become widespread and persistent lasting for decades resulting in an increased risk of cancer.
- Cell-mediated immunity seems to be important to the cellular response prohibiting the virus from establishing a prolonged presence.
- Oncogenic viruses lead to cellular proliferation in the latency phase by interfering with cell cycle control mechanisms. Two “early region” viral genes, E6 and E7, inhibit cell cycle control resulting in increased proliferation. E7 binds directly

to the retinoblastoma (Rb) tumor suppressor protein products p105, p107, and p130 related proteins leading to a complicated cascade of events involving E2F transcription factors, cyclin complexes, and other regulatory proteins allowing the cell to progress through G1 into S phase.

- Cell cycle release by E7 allows for immortalization of the cells but is not sufficient for transformation of the infected cell. Accumulation of genetic errors seems necessary for transformation which is consistent with the clinical scenario of a longstanding low-grade infection preceding the development of malignancy.
- The genetic errors may accumulate as a result of the E6 protein which binds to p53 with E6 associated protein (E6AP) leading to degradation of the complex through the ubiquitin pathway.
- The unblocked p53 protein is an important cell cycle regulating protein that leads to cell cycle arrest and apoptosis when genetic errors have accumulated, thus allowing for DNA repair and avoidance of replication of errors.
- As the infection with oncogenic viruses persists, the anal tissues may progress through low-grade to high-grade dysplasia and cancer.
- Fortunately, the angiogenic changes associated with development of anal HSIL can also be visualized with the aid of acetic acid and Lugol's solution in the perianal skin, anus, and distal rectum through an operative microscope, colposcope, or loops in the office or operating room. Targeted destruction is safe and may result in the same decrease in anal cancer incidence as was seen with cervical cancer when cervical Pap smears and targeted destruction was introduced for cervical disease.
- The cost effectiveness of such an anal cytology screening system to prevent anal cancer has been demonstrated using an economic model in both HIV-positive and HIV-negative men who have sex with men (MSM). These studies demonstrated that screening to identify patients with HSIL to be referred for treatment would be cost effective if performed annually for HIV-positive MSM and every 2–3 years for HIV-negative MSM.
- Although the association of HPV and anal cancer is clear, the association of HIV with the development and progression of anal cancer has been hard to separate from other confounding factors.
- Thus, as might be expected, more recent studies reporting anal cancer rates in patients who are now surviving longer with effective HAART suggest an association with HIV and anal cancer.

- The increase in anal cancer and dysplasia rates is seen in HIV-positive MSM, and HIV-positive heterosexual men and women who do not report anoreceptive intercourse.
- Data are accumulating that suggest that as HIV-positive men and women live longer in the HAART era, the indolent HPV infection will result in an increased risk for the development of anal cancer and this effect will be most significant in the most immunocompromised patients.

E. Epidemiology

- The incidence of SCCA has been increasing in frequency over the last 30 years in the United States, Europe, and South America.

F. Bowen's Disease

- The term Bowen's disease is applied to SCC in situ in both keratinizing and nonkeratinizing tissues. Thus, the authors believe the term is archaic and confusing, and should be abandoned in favor of HSIL.
- Bowen's disease (HSIL) is frequently found as an incidental histologic finding after surgery for an unrelated problem, often hemorrhoids. The lesion is clinically unapparent but histologic assessment of the specimen reveals SCC in situ.
- Alternatively, patients may present with complaints of perianal burning, pruritus, or pain. Physical examination may reveal scaly, discrete, erythematous, or pigmented lesions.
- The natural history of Bowen's disease is poorly defined. In the immunocompetent, fewer than 10% will progress to cancer.
- However, in immunocompromised patients, the progression rate seems greater as evidenced by the higher rates of anal cancers observed in the HIV positive, and immunosuppressed transplant patients.
- Because we are as yet unable to identify those patients that will progress, the authors favor treatment of Bowen's disease. An exception to this recommendation would be patients with advanced AIDS with poor performance statuses despite maximal medical therapy.
- The preferred treatment is fairly controversial but should be tailored to the given patient.

- The standard recommendation for the unsuspected lesion found after hemorrhoidectomy is to return the patient to the operating room for random biopsies taken at 1-cm intervals starting at the dentate line and around the anus in a clock-like manner.
- Frozen sections establish the presence of Bowen's disease and these areas are widely locally excised with 1-cm margins.
- Large defects are covered with flaps of gluteal and perianal skin. Bowen's recurrence rates in one series were as high as 23% despite this radical approach.
 - A less radical approach involves taking patients to the operating room and with the aide of an operating microscope, acetic acid, and Lugol's solution the lesions are visualized and targeted for electrocautery destruction.
- This technique minimizes the morbidity of the procedure and saves the normal anal mucosa and perianal skin that would otherwise be sacrificed. Postoperative pain is comparable to any other perianal procedure. Finally, progression to malignant disease is much lower when compared to expectant management.
- Bowen's disease identified with the operative microscope and acetic acid may also simply be locally excised taking care to stay close to the lesion margin which is directly visualized with the operative microscope. The deep margin is kept equally close because wide local excision seems of limited benefit and increases morbidity. The resulting minimal defects heal in secondarily.
- High-risk patients, the immunocompromised, and patients practicing receptive anal intercourse should be followed with Pap smears at yearly and three yearly intervals for the immunocompromised and immunocompetent, respectively.
- Other therapeutic modalities include topical 5-fluorouracil (5-FU) cream, imiquimod, photodynamic therapy, radiation therapy, laser therapy, and combinations of the above. The reports are generally small series with limited follow-up but there may be anecdotal success with each approach and the options may be kept in mind for challenging cases.

G. SCC of the Anal Margin

- SCC arises from both the anal margin and the anal canal, although it is much less common in the former group. The distinction

between the two locations has become more important as they are increasingly considered different entities with separate treatments and prognosis.

- The anal margin is defined as the skin starting at the distal end of the anal canal to a 5-cm margin surrounding the anal verge.

Clinical Characteristics

- Tumors of the anal margin resemble SCC of other areas of skin and are therefore staged and often treated in a similar manner.
- They have rolled, everted edges with central ulceration, and may have a palpable component in the subcutaneous tissues although the sphincter complex is not usually involved.
- Patients present in the seventh decade of life with equal incidence in men and women.
- Presenting symptoms include a painful lump, bleeding, pruritus, tenesmus, discharge, or even fecal incontinence.
- In general, anal margin tumors are characterized by a delay in diagnosis because of their location and indistinct features, and SCC is no exception. Patients have been noted to have symptoms anywhere from 0 to 144 months before diagnosis (median of 3 months), and almost one-third are misdiagnosed at their first physician visit. Patients were given erroneous diagnoses of hemorrhoids, anal fissures, fistulas, eczema, abscesses, or benign tumors.

Staging

- The staging of anal margin SCC is based on size of the tumor and lymph node involvement, both of which correlate with prognosis.
- Lymphatic drainage of the anal margin extends to the femoral and inguinal nodes and then to the external and common iliac nodes.
- Lymph node involvement is associated with the size and differentiation of the tumor.
- Distal visceral metastasis at presentation is rare but should be evaluated with a computed tomography (CT) scan of the abdomen and pelvis, to assess for liver metastases, as well as the presence of nodal disease.
- These tumors are generally slow growing and histologically are well differentiated with well-developed patterns of keratinization.

- The American Joint Committee on Cancer (AJCC) staging system is described in Table 35.1.

Table 35.1. AJCC staging of SCC.

Anal margin		Anal canal
Primary tumor (T)		
Tx	Tumor cannot be assessed	Tumor cannot be assessed
T0	No evidence of primary tumor	No evidence of primary tumor
Tis	Carcinoma in situ	Carcinoma in situ
T1	Tumor ≤ 2 cm in greatest dimension	Tumor ≤ 2 cm in greatest dimension
T2	Tumor 2–5 cm in greatest dimension	Tumor 2–5 cm in greatest dimension
T3	Tumor ≥ 5 cm in greatest dimension	Tumor ≥ 5 cm in greatest dimension
T4	Tumor invades deep structures (muscle, bone, cartilage)	Tumor invades deep structures (vagina, urethra, bladder, but not sphincter)
Nodal status (N)		
Nx	Regional lymph nodes cannot be assessed	Regional lymph nodes cannot be assessed
N0	No regional lymph node metastasis	No regional lymph node metastasis
N1	Regional lymph node metastasis present	Perirectal lymph node metastasis present
N2		Unilateral internal iliac/inguinal lymph node metastasis present
N3		N1 and N2 and/or bilateral internal iliac and/or inguinal lymph node metastasis
Distant metastasis (M)		
Mx	Distant metastasis cannot be assessed	Distant metastasis cannot be assessed
M0	No distant metastasis	No distant metastasis
M1	Distant metastasis present	Distant metastasis present
Stage grouping (3b does not exist for anal margin)		
Stage 0	Tis	N0 M0
Stage 1	T1	N0 M0
Stage 2	T2,3	N0 M0
Stage 3a	T1,2,3	N1 M0 or T4 N0 M0
Stage 3b	Any T	N2,3 M0 or T4 N1 M0
Stage 4	Any T	Any N M1

Table 35.2. Results of local excision of anal margin tumors.

Author	Year	N	Local recurrence (%)	Survival (%)
Beahrs and Wilson	1976	27	0	100
Al-Jurf et al.	1979	10	50	90
Schraut et al.	1983	11	18	80
Greenall et al.	1985	31	42	68
Jensen et al.	1988	32	63	—
Pintor et al.	1989	41	—	68

Treatment Options

- Treatment of anal margin SCC traditionally consisted of surgical resection with wide local excision for smaller-sized tumors and abdominoperineal resection (APR) for larger, invasive tumors.
- However, it is well documented that wide local excision alone results in high locoregional recurrence rates (18–63%) (Table 35.2) and should be reserved for those lesions that can be excised with a 1-cm margin, are Tis or T1, and do not involve enough sphincter to compromise function.
- Since it was introduced in the early 1970s, radiation therapy has become the mainstay of therapy for SCC of the anal canal and its application to tumors of the anal margin is increasing.
- In patients with T1 or early T2 lesions, local excision or radiation therapy provides similar local control rates (60–100%), but for less favorable lesions, chemoradiation is now used as the first-line therapy using a perineal field and inguinal fields, even without clinically detectable disease in the groin.
- Pelvic lymph nodes are also treated for those patients with T3 and T4 tumors.
- Local control rates for radiation therapy reported by T stage are as follows: T1, 50–100%; T2, 60–100%; T3, 37–100% (Table 35.3).
- The absolute 5-year survival rate for patients treated with local excision or APR ranges from 60 to 100% but is lower in patients with larger tumors.
- Similarly, absolute 5-year survival in patients treated with radiation ranges from 52 to 90% with sphincter preservation in about 80%.

Table 35.3. Radiation therapy for anal margin tumors by T stage.

Author	Year	N	Local recurrence (%)			Cancer-specific 5-year survival (%)
			T1	T2	T3	
Cummings et al.	1986	29	100	100	60	—
Cutuli et al.	1988	21	50	71	37	72
Papillon and Chassard	1992	54	100	84	50	80
Touboul et al.	1995	17	100	60	100	86
Peiffert et al.	1997	32	88	73	57	89

- The use of chemoradiation specifically pertaining to SCC of the anal margin has not been well examined. However, one study did show an improvement in local control (64% vs. 88%) with the addition of 5-FU and mitomycin to radiation.
- In summary, the choice of treatment is dependent on the stage of tumor, the anticipated functional result as a result of therapy, and the risk of complications.
- Although surgery may result in alteration of sphincter function, or a permanent colostomy, radiation therapy may also cause skin changes or proctitis that produces urgency, incontinence, or the need for diversion.
- For T1 and early T2 tumors, wide local excision may be less morbid and time consuming than radiation therapy and therefore a superior choice.
- However, if the excision will result in damage to the sphincters with impairment of fecal function, radiation provides similar local control and survival.
- T2 tumors should be treated with radiation therapy to the primary lesion and inguinal fields because of poor local control with excision and the significant risk of lymph node metastasis. This treatment modality is much less morbid than resection of the primary and bilateral lymph node dissection with similar control rates.
- Those with T3, T4, or poorly differentiated tumors should receive radiation to the primary lesion and include inguinal and pelvic fields to treat regional nodes in these areas.

- APR should be reserved for those patients with persistent or recurrent disease after radiation therapy.

H. SCC of the Anal Canal

- SCC of the anal canal incorporates all large-cell keratinizing, large-cell nonkeratinizing (transitional), and basaloid histologies. The terms epidermoid, cloacogenic, and mucoepidermoid carcinoma are all encompassed in the SCC group.
- SCC of the anal canal is five times more common than SCC of the anal margin but its incidence is one-tenth that of rectal cancer.

Clinical Characteristics

- The most common presenting symptom is bleeding, which occurs in >50% of patients with many complaining of anal pain.
- Other symptoms include palpable lump, pruritus, discharge, tenesmus, change in bowel habits, fecal incontinence, and rarely, inguinal lymphadenopathy.
- Most patients are diagnosed late, with up to 55% of patients being misdiagnosed at the time of presentation.

Evaluation

- Physical examination should include a complete anorectal examination with external inspection of the anoderm, digital examination, anoscopy and proctoscopy, in addition to examination of inguinal areas.
- Careful notation should be made of the size, location, and mobility of the mass, associated perirectal lymphadenopathy, and in women, a pelvic examination should be performed to look for any associated lesions or invasion of tumor into the vagina.
- Complete examination and biopsy may require anesthesia for those patients with significant pain.
- Additional workup includes an endoanal/endorectal ultrasound to assess the depth of the tumor, presence of perirectal lymph nodes, and invasion of adjacent organs as an adjunct to the

physical examination. Ultrasound has been found to be superior to physical examination in assessing the involvement of internal and external anal sphincter muscle and perirectal lymph nodes.

- This has an impact on staging because physical examination often understages tumors.
- Inguinal nodal involvement at the time of presentation can be difficult to determine.
- Enlarged lymph nodes can be reactive to secondary inflammation in some cases and therefore should be biopsied with direct FNA (fine-needle aspiration) or ultrasound-guided FNA if detected by imaging.
- Excisional lymph node biopsy is rarely required but may be done if FNA is inconclusive.
- Positron emission tomography (PET) scans are primarily useful for assessing persistent or residual disease after treatment.
- Colonoscopy can exclude any associated lesions proximal to the anal canal.
- Lastly, an HIV test should be performed for those at higher risk. HIV-positive patients with CD4 counts <200 need better monitoring of opportunistic infections, closer attention to toxic effects of chemoradiation with possible alterations in dosage, and management of antiretroviral therapy.

Staging

- The staging of anal canal SCC is based on the size of the tumor and lymph node metastasis. The TNM (tumor-node-metastasis) staging is listed in Table 35.1.
- The risk of nodal metastasis correlates with the size, depth of invasion, and the histologic grade of the tumor.
- In a series of 305 patients with SCC, lymph node metastasis was present in 16%. Nodal metastasis by T stage was as follows: T1 (0%), T2 (8.5%), T3 (29%), T4 (35%). Lymph node metastasis occurred in 47% of patients with T4 tumors >5 cm in size.
- Inguinal metastases have been detected in 10–30% of patients at the time of diagnosis with an additional 5–22% of patients developing clinically apparent lymph node metastases over time.

- Nodal metastasis was almost double (58% vs. 30%) in those tumors invading beyond the external sphincter compared with invasion of the internal sphincter.
- Mesenteric lymph nodes are more common in tumors of the proximal anal canal (50%) than the distal anal canal (14%).
- An anatomic study of lymph node metastasis demonstrated that they most often occur above the peritoneal reflection and not in the perianal area.
- Distant visceral metastasis occurs in 10–17% of patients at presentation and can be found in the liver, lung, bone, and subcutaneous tissues.

Treatment

Surgery

- The treatment of anal canal SCC was historically operative with APR being the standard of care. Unfortunately, local recurrence rates ranged from 27 to 47% and 5-year survival was 40–70%. The presence of pelvic lymph nodes decreased the 5-year survival to <20%.

Radiation Therapy

- Primary radiation therapy is quite effective in treating SCC because this tumor is extremely radiosensitive. It can be given as external beam radiation, brachytherapy, or in combination.
- Response is dose dependent with the best chance of tumor eradication occurring with at least 54 Gy of external beam radiation (Table 35.4).
- Local control and cure can be achieved in 70–90% of selected patients with 60–70% retaining sphincter function.
- However, when tumors are larger than 5 cm or lymph nodes are involved, the cure rate decreases to 50%.

Table 35.4. Response to radiation based on dosage.

Author	Year	Local control (%)	
		<54 Gy	>54 Gy
Hughes et al.	1989	50	90
Constantinou et al.	1997	61	77

- Better results with higher doses of radiation must be balanced against the increased radiation-induced complications when more than 40 Gy is administered. Serious late complications include anal necrosis, stenosis, and ulcerations, diarrhea, urgency, and fecal incontinence, cystitis, urethral stenosis, and small bowel obstruction.
- Significant impairment of function caused by anal complications can lead to the need for a colostomy. Most studies have found a dose-dependent effect on morbidity with the requirement of a colostomy in 6–12% of patients.

Chemoradiation Therapy

- Chemoradiation has become the standard therapy for SCC of the anal canal.
- Various radiation doses (30–60 Gy) and chemotherapeutic regimens have been used with similar complete pathologic responses (45–100%) and survival rates (70–90%) (Table 35.5).
- Although much controversy existed as to the benefit of chemoradiation therapy compared with primary radiation therapy, two randomized, controlled studies have been completed which demonstrate the superiority of chemoradiation therapy using 5-FU and mitomycin C to radiation alone. Using 45 Gy with a boost for good response, both studies exhibited better local control rates with chemoradiation (Table 35.6) but no significant difference in survival.
- Although the use of mitomycin C has provided excellent results, cisplatin has gained favor because it is a radiation sensitizer, is less myelosuppressive than mitomycin C, and has been used for those patients who failed to respond to mitomycin C. However, a recent trial randomized controlled trial found no advantage to cisplatin over mitomycin C, but there was a significantly worse colostomy rate with cisplatin.
- Although the presence of inguinal metastasis at presentation indicates a worse prognosis, the overall 5-year survival is 48% (range, 30–66%).
- Surgical management with radical groin dissection can lead to significant complications and may be successful only 15% of the time.
- The management of synchronous inguinal node metastasis is not standardized and different centers will use primary radiation therapy (45–65 Gy), chemoradiation, and selective lymph

Table 35.5. SCC of the anal canal: results of combination radiation and 5-FU plus mitomycin C.

Author(s)	No. of patients	Dose (Gy)	Complete regression (%)	Follow-up (months)	5-year survival (%)
Flam et al. (1987)	30	41–50	87	9–76→	–
Nigro (1987)	104	30	93	24–132→	83
Habr-Gama et al. (1989)	30	30–45	73	12–60→	–
Sischy et al. (1989)	79	40.8	90	20–55→	–
Cho et al. (1991)	20	30	85	Av., 34	70
Cummings et al. (1991)	69	50	85–93	>36	76
Lopez et al. (1991)	33	30–56	88	Med., 48	79
Doci et al. (1992)	56	36 + 18	87	2–45	81
Johnson et al. (1993)	24	40.5–45	100	Med., 41	87
Tanum et al. (1993)	86	50	T1 ^a 97 T2 ^a 80	46% >36	72
Beck and Karulf (1994)	35	30–45	97	4–155	87
Smith et al. (1994)	42	30	T1 ^a 90 T2 ^a 87	31 31	90 87

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Comp. complete; med. median; av. average; → survival at follow-up aStage according to TNM classification

Table 35.6. Results of two randomized trials examining radiation therapy alone and radiation therapy with chemotherapy for anal canal SCC.

			Local control (%)			Overall survival (%)		
		Followup (years)	Chemo		P	Chemo		P
	N		XRT	XRT	value	XRT	XRT	Value
EORTC	110	5	50	68	.02	57	52	.17
UKCCCR	585	3	39	61	<.001	58	65	.25

node dissection followed by radiation which has been reported to maintain disease-free intervals in up to 60% of patients.

Follow-up

- No consensus has been reached on appropriate follow-up after treatment of SCC.
- It is generally agreed that early intervention for persistent disease and recurrent locoregional disease can lead to successful salvage therapy.
- Routine examination with digital rectal examination and proctoscopy every 2 months in the first year, every 3 months in the second year, and every 6 months thereafter has been recommended.
- CT scan or MRI performed after completion of chemoradiation may also be useful as a baseline for future comparison. MRI is useful for distinguishing surrounding tissues and detecting persistent or recurrent disease.

Treatment of Residual or Recurrent Disease

- Persistent or recurrent disease localized to the pelvis after chemoradiation can be treated with salvage therapy. Patients need to be restaged with a CT of the chest, abdomen, and pelvis. MRI may be useful to assess resectability of pelvic recurrence and PET scan may help to differentiate tumor from radiation-induced tissue changes or other undetectable metastases.
- APR can be performed for tumor localized to the pelvis with a 5-year survival of 24–47%.
- Morbidity for APR in this setting is significant with an increased risk of perineal wound complications. This has prompted the use of plastic surgery reconstruction using rotational or advancement flaps to promote healing.

I. Uncommon Anal Canal Neoplasms

Adenocarcinoma

- Anal canal adenocarcinomas are classified into three types. The first group may arise from the mucosa of the transitional zone in the upper canal and are indistinguishable from rectal

adenocarcinoma. The second derives from the base of the anal glands which are lined with mucin-secreting columnar epithelium. The last can develop in the setting of a chronic anorectal fistula.

- Adenocarcinomas account for 5–19% of all anal cancers, and have a more aggressive natural history than SCCs.
- The average age at presentation ranges from 59 to 71 years with equal gender distribution. Patients may present with pain, induration, abscess/fistula, or a palpable mass. Other symptoms include bleeding, pruritus, seepage, prolapse, and weight loss.
- The local disease may tend to be more advanced in those that arise in glands and fistulous tracts because these locations are outside the bowel wall and therefore the disease originates in a locally advanced location.
- Wide local excision may be feasible for those patients with a “rectal-type” tumor that is small, well differentiated, and does not invade the sphincter complex. All other tumors require APR.
- Chemoradiation alone has not been shown to be as effective for adenocarcinoma compared with SCC because of high local recurrence rates (54% vs. 18%) and poor survival rates (64% vs. 85%).
- Although no large series of patients has been treated in any uniform manner to substantiate the approach of chemoradiation therapy followed by surgery, the success of this approach for rectal adenocarcinoma would support its use.

Melanoma

- Although the anorectum is the most common site for primary melanoma of the gastrointestinal tract, it comprises only 0.5–5% of all malignancies there.
- Anorectal bleeding is the most common symptom described. However, anal pain, change in bowel habits, or tenesmus may also be reported.
- A mass in the anal canal is the most frequent sign with a high likelihood of palpable inguinal lymph nodes.
- These tumors arise from the transitional epithelium of the anal canal, the anoderm, or the mucocutaneous junction.
- Most lesions are pigmented, with early lesions appearing polypoid and larger lesions having ulcerations, raised edges, or significant growth into the rectal vault.

- An early lesion may be indistinguishable from a thrombosed hemorrhoid and some cases have been incidentally diagnosed from a hemorrhoidectomy specimen.
- Surgical management of anorectal melanoma provides the only chance for cure. However, the choice of operation continues to be controversial because the prognosis is so poor. Up to 35% of patients present with metastatic disease, and those patients with tumors >10 mm in thickness are not cured by any treatment.
- Anorectal melanoma is largely a fatal disease and so the choice of treatment has little influence on the eventual outcome. Therefore, many authors advocate local excision to spare patients the morbidity of an APR and a colostomy.

Gastrointestinal Stromal Tumors

- Gastrointestinal stromal tumors (GISTs) of the anus are extremely uncommon with only 17 cases reported in the literature up to 2003.
- GISTs are tumors of mesenchymal origin that are not derived from smooth muscle or Schwann cells. They are identified by immunohistochemical studies that stain positive for CD34 and CD117 antigens.
- Treatment involves local excision for tumors <2 cm and APR for those with larger tumors or worse pathologic features.
- The natural history of GISTs is indolent with a long latency period (> 4 years) to recurrence or metastasis, which is usually by a hematogenous route.

Small Cell Carcinoma/Neuroendocrine Tumors

- Small cell or neuroendocrine tumors comprise less than 1% of all colorectal malignancies and are extremely rare in the anal canal.

J. Uncommon Anal Margin/Perianal Neoplasms

Basal Cell Carcinoma

- The incidence of basal cell carcinomas (BCCs) of the anus, in comparison to sun-exposed areas of the body, is extremely low. It comprises about 0.1% of all BCCs diagnosed and fewer

than 200 cases of BCC have been reported on the perianal and genital area.

- Treatment is wide local excision ensuring adequate margins which is possible in lesions <2 cm.

Paget's Disease

- It is currently believed that Paget's cells represent an intraepithelial adenocarcinoma with a prolonged preinvasive phase that eventually develops into an adenocarcinoma of the underlying apocrine gland given enough time.
- This is a rare condition with fewer than 200 cases reported in the literature to date.
- Patients present in the seventh decade of life with equal distribution among men and women. The most common presenting symptom is intractable itching followed by bleeding, palpable mass, inguinal lymphadenopathy, weight loss, anal discharge and constipation.
- The lesions themselves often have an erythematous, eczematous appearance with well-demarcated borders mimicking a rash. They may look ulcerated or plaque-like with oozing or scaling. A third of cases involve the entire anus. These lesions are often misdiagnosed because of their similarity to other conditions. The differential includes Bowen's disease, Crohn's disease, condyloma acuminatum, hidradenitis suppurativa, pruritus ani, and SCC.
- Biopsy is essential to confirm the diagnosis.
- The incidence of associated visceral malignancies in perianal Paget's disease is increased with various series reporting rates of 30–50%. The most common sites include the gastrointestinal tract, anus, skin, prostate, neck, and nasopharynx. There may also be synchronous lesions in the axillary or anogenital area in patients diagnosed with perianal disease, therefore a careful survey of other sites for malignancy and secondary disease is necessary.
- The treatment for perianal Paget's disease depends on the presence of invasion and other associated anorectal malignancies. For noninvasive lesions, wide local excision is the procedure of choice. In addition to resecting the lesion with grossly negative margins, it is important to map the extent of involvement of the lesion microscopically.

- If the defect is small, the skin may be closed primarily.
- For larger lesions that require circumferential excision of the perianal skin, split-thickness skin grafts or sliding and rotational flaps may be required. Recurrence rates range from 37 to 100%.
- Patients who have an invasive component or an associated anorectal malignancy should be considered for radical excision with APR.

Verrucous Carcinoma

- The term verrucous carcinoma was initially coined in 1948 to describe a low-grade carcinoma of the oral mucosa that resembled viral warts. It has now been expanded to include those lesions described as giant condyloma acuminatum or Buschke–Lowenstein tumors.
- Although it is a well recognized entity, only 51 cases have been reported in the literature to date. HPV is frequently detected.
- These tumors are more frequently found in men with a 2.7:1 male to female ratio.
- The average age of patients is 45 years and is slowly decreasing. Patients usually present with complaint of an anal growth.
- They usually arise from the perianal skin but can also present in the anal canal and distal rectum. At presentation they tend to be quite large measuring anywhere from 1.5 to 30 cm.
- The standard treatment for verrucous carcinoma is radical local excision. For those patients with extensive deep tissue involvement, multiple fistulas, or involvement of the anal sphincter, APR is indicated.

K. HIV-related Anal Cancer

Kaposi's Sarcoma

- Although Kaposi's sarcoma is the most common cutaneous malignancy in patients with AIDS, the incidence of perianal lesions is quite small and decreasing with the increasingly effective antiretroviral therapy available today.

Lymphoma

- The incidence of non-Hodgkin's lymphoma (NHL) has been increasing in AIDS patients as treatment improves and life expectancy increases. NHL is the second most common AIDS-related neoplasm after Kaposi's sarcoma. Compared with lymphomas found in the general population, these tumors are characterized by B cells of a higher histologic grade that originates from extranodal tissue. They are also more aggressive, prone to dissemination, and resistant to treatment. Most lymphomas are found in the central nervous system and the gastrointestinal tract.
- Anorectal lymphomas are extremely rare, comprising less than 1% of all anorectal neoplasms in the general population.
- There is no role for surgical treatment. Usual chemotherapeutic agents include cyclophosphamide, actinomycin, vincristine, and corticosteroids (CHOP).

36. Presacral Tumors

A. Introduction

- The presacral or retrorectal space may be the site of a group of heterogeneous, and rare tumors that are often indolent and produce ill-defined symptoms. Because detection is often difficult and delayed, patients frequently present with tumors that have reached considerable size and involve multiple organ systems, complicating their treatment. The diagnosis and management of these tumors has evolved in recent years because of improved imaging modalities, a better understanding of tumor biology, adjuvant chemoradiation therapy, and a more aggressive surgical approach. Few surgeons have the opportunity to treat these complex lesions, and the care of these patients can be greatly optimized by an experienced, multidisciplinary team.

B. Anatomy and Neurophysiology

- The boundaries of the retrorectal region include the posterior wall of the rectum anteriorly and the sacrum posteriorly (Fig. 36.1). This space extends superiorly to the peritoneal reflection and inferiorly to the rectosacral fascia and the supralelevator space. Laterally, the area is bordered by the ureters, the iliac vessels, and the sacral nerve roots (Fig. 36.2a).
- Several important vascular and neural structures are located in this area and injury to them may have important physiologic rectoanal sequelae, as well as neurologic and musculoskeletal consequences. If all sacral roots on one side of the sacrum are sacrificed, the patient will continue to have normal anorectal

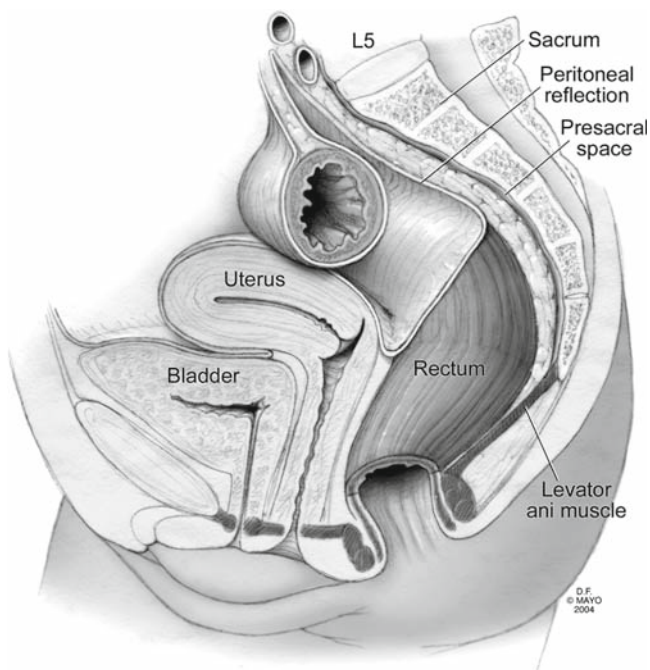


Fig. 36.1. Relationship of pelvic structures to presacral space.

function. Likewise, if the upper three sacral nerve roots are left intact on either side of the sacrum, the patient's ability to defecate spontaneously and to control anorectal contents will remain essentially intact. If, however, both S-3 nerve roots are sacrificed, the external anal sphincter will no longer contract in response to gradual balloon dilation of the rectum and this will translate clinically into variable degrees of anorectal incontinence and difficult defecation.

- If sacrectomy is to be performed, the surgeon must be familiar with the relationship between the thecal sac, sacral nerve roots, sciatic nerve, piriformis muscle, and sacrotuberous and sacrospinous ligaments (Fig. 36.2b). From a structural standpoint, the majority of the sacrum can be resected. If more than half of the S-1 vertebral body remains intact, pelvic stability will be maintained. However, preoperative radiation to the sacrum may ultimately lead to stress fractures if only S-1 remains. As such, spinopelvic stability may be augmented with fusion in select patients.

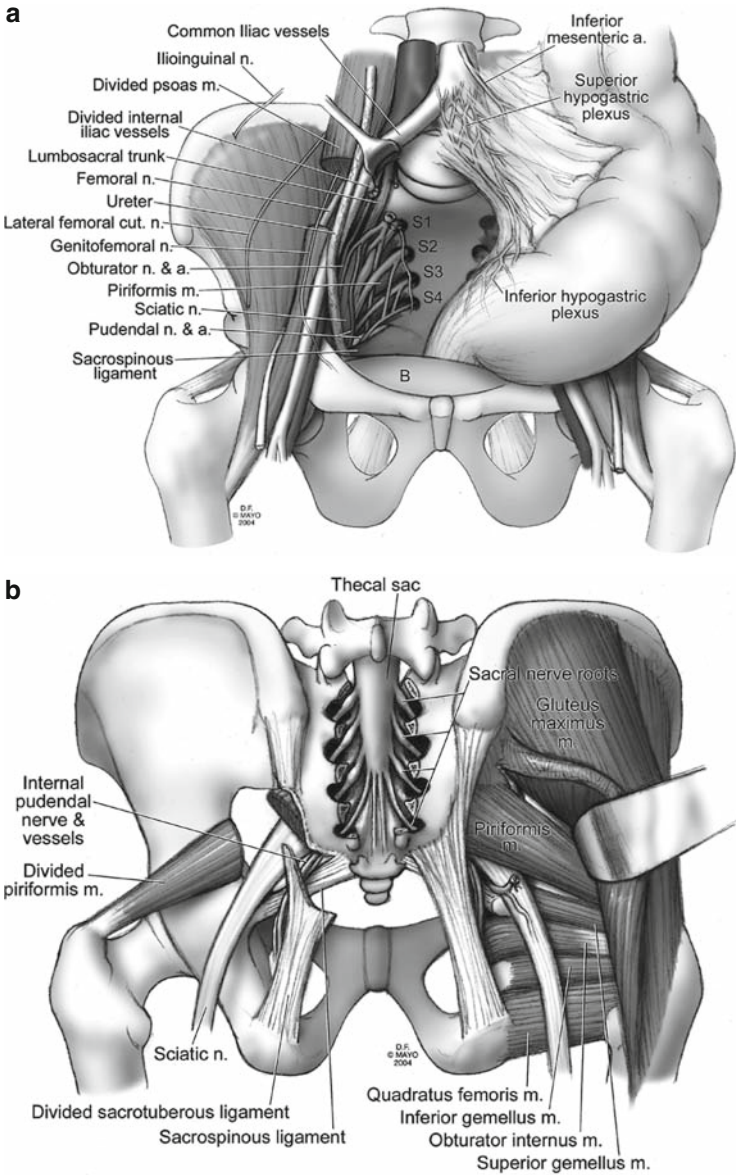


Fig. 36.2. (a) Anterior view of pelvic anatomy. (b) Posterior view of pelvic anatomy with sacral elements removed.

- Knowledge of anatomy of the thigh and lower extremity is required in complex cases requiring muscle or soft tissue flaps. It is important to discuss with patients preoperatively the potential neuromuscular and visceral losses that may occur during the operation and how this will influence their function and quality of life.

C. Classification

General Considerations

- Presacral lesions are rare. Reports from various large referral centers would indicate that their incidence may be as low as 1 in 40,000 hospital admissions (0.014%).
- Lesions found in the presacral space can be broadly classified as congenital or acquired, benign or malignant. Two-thirds of lesions are congenital and of these, two-thirds are benign and one-third are neoplastic.
- The presacral space has a complex embryologic development, and this potential space is composed primarily of connective tissue, nerves, fat, and blood vessels. Because this area contains totipotent cells that differentiate into three germ cell layers, a multitude of tumor types may be encountered.
- The classification first described by Uhlir and Johnson has been used for many years by several authors and divides tumors into the broad categories: congenital, neurogenic, osseous, and miscellaneous. The authors have modified and updated this system to subcategorize tumors into malignant and benign entities, because this greatly impacts therapeutic approaches (Table 36.1).

Table 36.1. Classification of presacral tumors.

Congenital

Benign

- Developmental cysts (teratoma, epidermoid, dermoid, mucus-secreting)
- Duplication of rectum
- Anterior sacral meningocele
- Adrenal rest tumor

(continued)

Table 36.1. (continued)

Malignant
Chordoma
Teratocarcinoma
Neurogenic
Benign
Neurofibroma
Neurilemoma (schwannoma)
Ganglioneuroma
Malignant
Neuroblastoma
Ganglioneuroblastoma
Ependymoma
Malignant peripheral nerve sheath tumors (malignant schwannoma, neurofibrosarcoma, neurogenic sarcoma)
Osseous
Benign
Giant-cell tumor
Osteoblastoma
Aneurysmal bone cyst
Malignant
Osteogenic sarcoma
Ewing's sarcoma
Myeloma
Chondrosarcoma
Miscellaneous
Benign
Lipoma
Fibroma
Leiomyoma
Hemangioma
Endothelioma
Desmoid (locally aggressive)
Malignant
Liposarcoma
Fibrosarcoma/malignant fibrous histiocytoma
Leiomyosarcoma
Hemangiopericytoma
Metastatic carcinoma
Other
Ectopic kidney
Hematoma
Abscess

Source: Modified from Uhlig and Johnson

Gross and Histologic Appearance

- *Epidermoid cysts* result from closure defects of the ectodermal tube. They are histologically composed of stratified squamous cells, do not contain skin appendages, and are typically benign.
- *Dermoid cysts* also arise from the ectoderm, but histologically they contain stratified squamous cells and skin appendages. These are also generally benign.
 - Epidermoid and dermoid cysts tend to be well circumscribed and round and have a thin outer layer.
 - Occasionally they communicate with the skin surface producing a characteristic postanal dimple.
 - They are most common in females and the infection rate may be high because they are often misdiagnosed as a perirectal abscess and incised and drained.
- *Enterogenous cysts* are lesions thought to originate from sequestration of the developing hindgut.
 - Because they originate from endodermal tissue, they can be lined with squamous, cuboidal, or columnar epithelium. Transitional epithelium may also be found.
 - These lesions tend to be multilobular with one dominant lesion and smaller satellite cysts. Similar to dermoid and epidermoid cysts, they can become infected and are more common in women.
 - These are generally benign, but case reports have described malignant transformation within rectal duplications.
- *Tailgut cysts*, which are sometimes referred to as cystic hamartomas, are also multilocular cysts.
 - These cysts are composed of squamous, columnar, or transitional epithelium that may have a morphologic appearance similar to that of the adult or fetal intestinal tract.
 - The presence of glandular or transitional epithelium will differentiate this lesion from an epidermoid or dermoid cyst.
 - Malignant transformation is rare.
- *Teratomas* are true neoplasms derived from totipotent cells and include all three germ layers.
 - They may undergo malignant transformation to squamous cell carcinoma arising from the ectodermal tissue, or rhabdomyosarcoma arising from the mesenchymal cells. Anaplastic tumors are also seen in which the tissue of origin may not be distinguishable.

- Histologically, these tumors are referred to as either “mature” or “immature” reflecting the degree of cellular differentiation.
- Teratomas are more common in females and in the pediatric age group, and are often associated with other anomalies of the vertebrae, urinary tract, or anorectum.
- In adults, malignant degeneration can occur in 40–50%. Incomplete or intralesional resection increases the likelihood of malignant degeneration.
- These also can become infected and be misdiagnosed as a perirectal abscess or fistula. Diagnosis is often delayed and these tumors may reach considerable size.
- *Sacroccygeal chordoma* is the most common malignancy in the presacral space.
 - These tumors are believed to originate from the primitive notochord which embryologically extends from the base of the occiput to the caudal limit in the embryo. They can occur anywhere along the spinal column, but have a predilection for the pheno-occipital region at the base of the skull and for the sacroccygeal region in the pelvis.
 - More than half occur in the sacrum (Fig. 36.3).

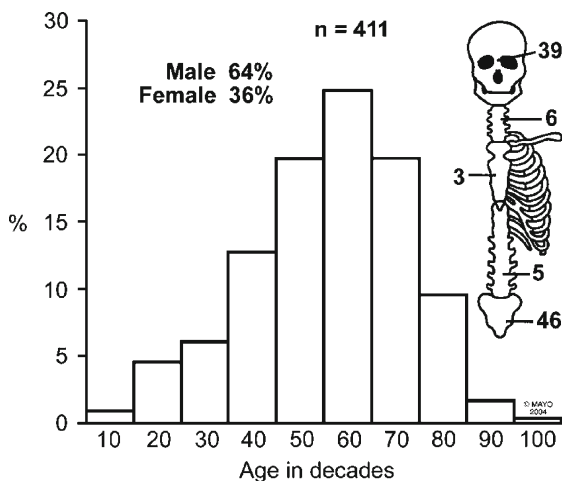


Fig. 36.3. Distribution of chordomas. (Mayo Clinic orthopedic database.)

- They predominate in men and are rarely encountered in patients younger than 30 years of age.
 - These tumors may be soft, gelatinous, or firm and may invade, distend, or destroy bone and soft tissue.
 - Hemorrhage and necrosis within tumors may lead to secondary calcification and pseudocapsule formation.
 - Common symptoms include pelvic, buttock, and lower back pain aggravated by sitting and alleviated by standing or walking.
 - Diagnosis is often delayed and these tumors may reach a considerable size.
- *Anterior sacral meningoceles* are a result of a defect in the thecal sac and may be seen in combination with presacral cysts or lipomas.
 - Typical symptoms include constipation, low back pain, and headache that is exacerbated by straining or coughing.
 - It may be associated with other congenital anomalies such as spina bifida, tethered spinal cord, uterine and vaginal duplication, or urinary tract or anal malformations.
 - Surgical management consists of ligation of the dural defect.
- *Neurogenic tumors* include neurilemmomas, ganglioneuromas, ganglioneuroblastomas, neurofibromas, neuroblastomas, ependymomas, and malignant peripheral nerve sheath tumors (neurofibrosarcoma, malignant schwannomas, neurogenic sarcomas).
 - The most common malignant neurogenic lesion in the Mayo series was neurilemmoma, which is more common in males and may occur at any age.
 - Neurogenic tumors tend to grow slowly and may reach considerable size. Differentiating between benign and malignant pathology preoperatively can be difficult, but is of paramount importance to guide operative approach.
- *Osseous tumors* include chondrosarcoma, osteosarcoma, myeloma, and Ewing's sarcoma.
 - These tumors arise from bone, cartilage, fibrous tissue, and marrow.
 - Because of relatively rapid growth, these often reach considerable size.
 - The lungs are a common site of metastasis.
 - All osseous tumors of the presacral space are associated with sacral destruction. Although benign, giant cell tumors

are locally destructive and can metastasize to the lungs (“benign metastasizing giant cell tumor”).

- *Miscellaneous lesions* in this region include metastatic deposits, inflammatory lesions related to Crohn’s disease or diverticulitis, hematomas, and anomalous pelvic ectopic kidneys.
- Overall, most presacral tumors occur in females and are cystic. Most solid tumors are chordomas and more often seen in males. Benign lesions are frequently asymptomatic and discovered incidentally during routine gynecologic examinations which may explain the greater incidence in females. By contrast, malignant tumors are more often symptomatic, but still frequently found late because of their vague symptomatology.

D. Diagnosis and Management

History and Physical Examination

- Because of their indolent course, presacral tumors are often found incidentally at the time of periodic pelvic or rectal examination.
- Symptomatic patients typically complain of vague, longstanding pain in the perineum or low back. Pain may be aggravated by sitting and improved by standing or walking. In the Mayo Clinic series, pain was more common when the tumor was malignant as compared with benign (88% vs. 39%).
- Occasionally, patients complain of longstanding perineal discharge and their symptoms may be confused with anal fistula or pilonidal disease.
- Several clues may alert the clinician to the presence of a retrorectal cystic lesion, including repeated operations for anal fistula, the inability of the examiner to uncover the primary source of infection at the level of the dentate line, a postanal dimple, or fullness and fixation of the precoccygeal area.
- Some patients may give a history of referral to a psychiatrist because of a clinician’s inability to ascertain the origin of the patient’s chronic, ill-defined pain.
- Patients with larger tumors may complain of constipation and/or rectal and urinary incontinence, and sexual dysfunction because of the sacral nerve root involvement.

- Patients should be examined carefully, focusing on the perineum, rectal examination, and assessing for a postanal dimple. In the Mayo series, 97% of presacral tumors could be palpated on rectal examination.
- Digital rectal examination will typically reveal the presence of an extrarectal mass displacing the rectum anteriorly with a smooth and intact overlying mucosa. Rectal examination is also critical in assessing the level of the uppermost portion of the lesion, degree and extent of fixation, and relationship to other pelvic organs such as the prostate.
- Rigid or flexible sigmoidoscopy can be used to assess the overlying mucosa and rule out transmural penetration of the tumor.
- A careful neurologic examination focusing on the sacral nerves and musculoskeletal reflexes is mandatory, and may also aid in the diagnosis of extensive local tumor invasion.

Diagnostic Tests

- The presence of a presacral tumor can be confirmed with plain radiographs of the sacrum, or with more sophisticated imaging modalities such as computerized tomography (CT), magnetic resonance imaging (MRI), and endorectal ultrasound (ERUS).
- Simple anterior–posterior and lateral radiographs of the sacrum identify osseous expansion, destruction, and/or calcification of soft tissue masses, but are typically not helpful in rendering a specific diagnosis. A chordoma is the most common tumor causing these findings, but sarcomas or benign, locally aggressive tumors, such as giant cell tumor, neurilemoma, and aneurysmal bone cysts, may also cause extensive bony destruction.
- The characteristic “scimitar sign” denotes the presence of an anterior sacral meningocele, a diagnosis that can be confirmed with conventional myelography or MRI with gadolinium.
- In recent years, state of the art imaging such as CT, MRI, and positron emission tomography (PET) scan has dramatically changed the way in which these tumors should be evaluated. CT and MRI complement each other and are the most important radiographic studies in evaluating a patient with a presacral lesion.
 - CT can determine whether a lesion is solid or cystic and whether adjacent structures such as the bladder, ureters,

and rectum are involved. CT is also the best study to evaluate cortical bone destruction.

- MRI is highly recommended because of its multiplanar capacity and improved soft tissue resolution that will be essential for planning specific lines of resection. Sagittal views will assist in decision making in regard to need for and level of sacrectomy. MRI is also more sensitive than CT in spinal imaging, showing associated cord anomalies such as a meningocele, nerve root, and foraminal encroachment by tumor, or thecal sac compression. MRI is superior to CT in evaluating the extent of marrow involvement in bone.
- Angiogram and venogram can be added to the MRI (MR angiogram, venogram) to delineate vascular involvement and anatomy grossly distorted by tumor mass effect. This information is helpful to the vascular, plastic, and orthopedic surgeons for operative planning.
- Gadolinium-enhanced MRI imaging before, during, and/or after neoadjuvant therapy may also show the effectiveness of this treatment in terms of volume of tumor that appears vascularized and viable.
- In patients with presacral cystic lesions thought to be the source of a chronically draining sinus, fistulogram may help clarify the diagnosis. ERUS has been used by some to characterize retrorectal tumors and their relationship to the muscularis propria of the rectum.

Preoperative Biopsy

- Historically, the role of preoperative biopsy of presacral tumors has been a controversial topic in the general surgical literature.
- This, in part, may have to do with the fact that the literature on this topic is sparse and outdated, especially when one considers the availability of modern imaging, better knowledge of tumor biology, and new opportunities for neoadjuvant therapy. Indeed, some patients will substantially benefit from preoperative chemotherapy and radiation, especially in osseous tumors such as Ewing's sarcoma, osteogenic sarcoma, and neurofibrosarcoma. Likewise, very large tumors such as pelvic desmoids can be more easily removed after reducing their size with radiation.

- The authors consider preoperative tissue diagnosis essential to the management of solid and heterogenously cystic presacral tumors.
- What is clear about preoperative biopsies of presacral tumors is that they should never be performed transrectally or transvaginally. In the presence of a cystic lesion, such an approach is likely to result in infection rendering its future complete excision more difficult and increasing the likelihood of post-operative complications and recurrence. More importantly, inadvertent transrectal needling of a meningocele may lead to disastrous sequelae such as meningitis and even subsequent death. Moreover, because the biopsy tract needs to be removed en bloc with the specimen, transrectal biopsy would mandate proctectomy in a patient whose rectum may otherwise have been spared.
- There is rarely an indication to biopsy a purely cystic presacral lesion.
- From a technical standpoint, a presacral tumor biopsy should be done by a radiologist with experience in the evaluation and management of pelvic tumors. In planning the approach for a biopsy, the surgeon should always consider the resection margins so that the needle tract can be removed en bloc with the specimen. The transperineal or parasacral approach is usually ideal and falls within the field of the pending surgical resection (Fig. 36.4a).
- Transperitoneal, transretroperitoneal, transvaginal, and transrectal biopsy should be avoided. Biopsy tracts should never traverse neurovascular planes. Normal coagulation studies are required before biopsy, because hematoma formation and/or bleeding will potentially contaminate involved areas.
- PET–CT scan can be useful to guide biopsy needles into small focal areas of high tumor density.

Role of Preoperative Neoadjuvant Therapy

- Modern protocols and the wide availability of neoadjuvant tumor irradiation and systemic chemotherapy has revolutionized the management of patients with complex malignancies. It is in large part because of these new treatment modalities before surgery that a preoperative diagnosis is of paramount importance.

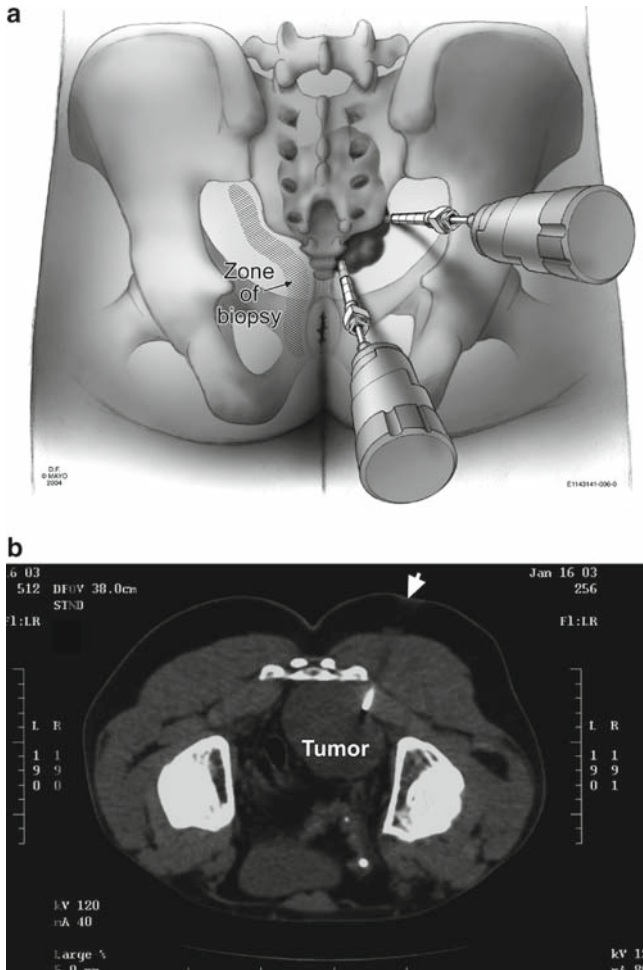


Fig. 36.4. (A) Preoperative biopsy technique using CT guidance. (B) Parasacral approach to presacral neurogenic tumor.

- Preoperative, as opposed to postoperative, irradiation can be extremely helpful in the face of large pelvic tumors. One of the significant advantages of preoperative irradiation is that it allows treatment to a smaller radiation field.

- Postoperative irradiation for a pelvic tumor would require irradiation of the entire surgical bed, previous tumor site, all contaminated surgical planes, and the sites of all skin incisions.
- Should “spillage” occur during resection of a radiosensitive tumor, this contamination may be with previously irradiated necrotic, nonviable cells.
- A third, and perhaps most important advantage of preoperative irradiation in sensitive tumors, is that decreased tumor size is often observed. A decrease in tumor size in a pelvic tumor may allow the surgeon to spare vital structures that would have had to be sacrificed in order for wide margins to be achieved without prior radiation. Additionally, a smaller tumor often means a surgery of a lesser magnitude and therefore less risk for intra-operative complications.
- Large tumors in the presacral space, especially sarcomas, are notorious for systemic metastasis. Neoadjuvant chemotherapy is the cornerstone of treatment for diagnoses such as Ewing’s sarcoma and osteogenic sarcoma.
- Micrometastatic disease must be treated in patients with diagnoses such as these preoperatively, unless the tumor has caused an immediate complication that requires emergent surgery. Furthermore, one could argue that lymphoma or Ewing’s sarcoma can be completely treated with chemoradiation, and that surgery may not be necessary at all.
- As with extremity sarcomas, there are clearly some cases in which irradiation and chemotherapy are not required. Small, low-grade malignancies without metastatic disease that can be completely excised with a histologically negative wide margin may likely be observed without adjuvant treatment. This, however, implies that any subsequent recurrence would again be amenable to excision. If a recurrence would no longer be amenable to re-resection, then most oncologic surgeons would favor adjuvant treatment to minimize the risk of this recurrence.
- Most authorities advocate irradiation, either before or after resection, of nonextremity low-grade sarcomas with “marginal” or positive margins or for any patient with an intermediate or high-grade malignancy.
- The efficacy of adjuvant chemotherapy for patients with non-extremity sarcomas has not been established firmly to date.
- As improvements in local therapy continue, fewer patients will succumb to local recurrence and more patients will succumb

to distant disease. It is in this setting that neoadjuvant chemotherapy may be of most benefit.

E. Surgical Treatment

Rationale for Aggressive Approach

- The rationale for an aggressive surgical approach for presacral tumors is based on several arguments. The lesion may already be malignant or transform into a malignant state if left in place. In patients with teratomas, especially those in the pediatric age group, the risk of malignant transformation is considerable and continues to increase dramatically if removal is delayed or incomplete. Untreated anterior sacral meningoceles may become infected and lead to meningitis, which is associated with high mortality. Cystic lesions may become infected making their excision difficult and increasing the possibility of postoperative infection and future recurrence. A presacral mass in a young woman may cause dystocia at the time of delivery. Lastly, benign and malignant tumors left untreated may grow to considerable size, making surgical resection much more complicated.
- Unfortunately, in the past, many surgeons have adopted a rather defeatist attitude toward sacrococcygeal chordomas and other tumors in this area based on a number of erroneous misconceptions.
 - Chordomas are slow-growing tumors producing vague symptoms which leads to a delay in diagnosis for months or even years. Thus, patients may seek medical treatment late in the course of their disease and the presence of a large mass in this often unfamiliar and complex anatomic area makes some surgeons reluctant to consider aggressive surgical approach for fear of serious operative and postoperative complications. This same reluctance to operate may apply to other types of lesions as well. Moreover, chordomas have all too often been considered to have a benign clinical behavior characterized by slow local growth. We now know that these tumors will metastasize and that the longer the diagnosis is delayed, the greater risk of distant spread.

- Tumors in this area have been treated inadequately in the past because of tumor violation, their large size and location, and fear of neurologic complication and/or musculoskeletal instability. Tumor violation can take place preoperatively when such tumors are biopsied transrectally, or intraoperatively when margins of resection are inadequate or tumor cells are spilled in an effort to be too conservative.
- When a surgeon is attempting to avoid injury to the rectal wall or important neurologic structures, they may inappropriately restrict excision and compromise oncologic outcome. For malignant lesions, wide margins and oncologic cure should be the primary goal of these procedures.

Role of Multidisciplinary Team

- It is of great importance that an experienced team consisting of a colorectal surgeon, orthopedic oncologic surgeon, spine surgeon, urologist, plastic surgeon, vascular surgeon, musculoskeletal radiologist, medical oncologist, radiation oncologist, and specialized anesthesiologist evaluate and surgically treat tumors that are large and extend to or destroy the hemipelvis or the upper half of the sacrum.

Surgical Approach

- Careful surgical planning is important in deciding how to approach these tumors whether it be an anterior approach (abdominal), posterior approach (perineal), or a combined abdominoperineal approach.
- CT and MRI will help define the margins of resection and the relationship of the tumor to the sacral level (Fig. 36.5).
- Small and low-lying lesions can be removed transperineally through a parasacral incision, whereas tumors extending above the S-3 level, especially if large, often require a combined anterior and posterior approach.
- For large, malignant lesions requiring extended resection, a plastic surgeon has a significant role, because adequate soft tissue coverage can often be difficult. Most often, we use the transabdominal rectus abdominus myocutaneous (TRAM) flap, which fills dead space and can cover large cutaneous defects left by the resection. Healthy, well-vascularized tissue flaps,

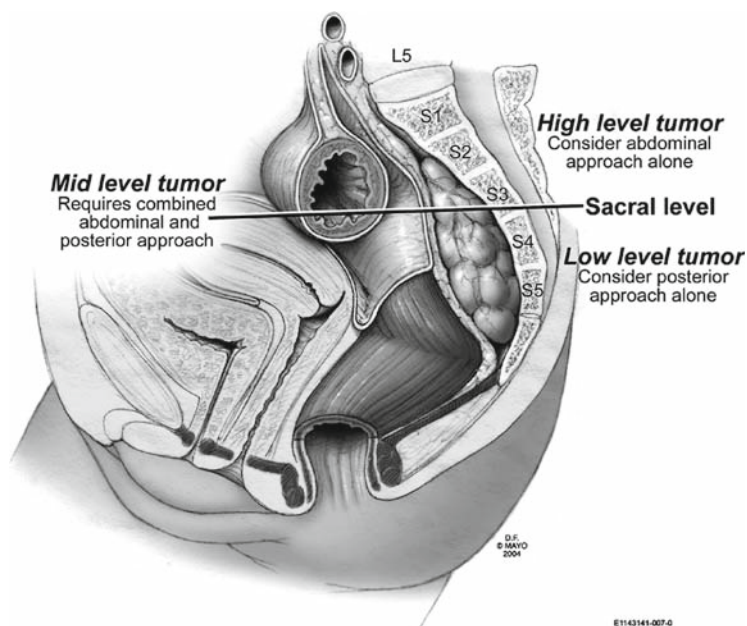


Fig. 36.5. Relationship of tumor to sacral level and proposed approach.

placed in the surgical bed, markedly decrease the incidence of wound-related complications.

Preoperative Considerations

- Optimizing patients for surgery is of extreme importance in a majority of these cases.
- Adequate nutritional repletion with total parenteral nutrition or with a feeding tube, may be necessary in patients who present severely debilitated.
- In technically complex cases, when we expect a long operative time and significant debilitation postoperatively, we consider placement of a temporary intravenacaval filter, because the risk of deep venous thrombosis and pulmonary embolus is high and postoperative anticoagulation may be contraindicated.

- A multidisciplinary team meeting preoperatively, to review films and plan surgical strategy, avoids confusion during the day of surgery.
- An operating theater capable of managing massive transfusion requirements is mandatory, as is an anesthesiologist comfortable with the physiologic management needed during the procedure.

Posterior Approach

- For low-lying tumors, the patient is placed in the prone jackknife position with the buttocks spread with tape (Fig. 36.6a). An incision is made over the lower portion of the sacrum and coccyx down to the anus taking care to avoid damage to the external sphincter. Resection of the tumor may be facilitated by transection of the anococcygeal ligament and coccyx (Fig. 36.6b).
- The lesion can then be dissected from the surrounding tissues including the rectal wall, in a plane between the retrorectal fat and the tumor mass itself.
- In the case of very small lesions, the surgeon may double-glove the left hand and, with the index finger in the anal canal and lower rectum, push the lesion outward, away from the depths of the wound (Fig. 36.6c) facilitating dissection of the lesion off the wall of the rectum without injury. If necessary, the lower sacrum or coccyx or both can be excised en bloc with the lesion to facilitate excision.

Combined Abdominal and Perineal Approach

- If the upper pole of the tumor extends clearly above the S-3 level, an anterior and posterior approach is usually indicated.
- A variety of techniques and positioning to the abdominal perineal approach have been described. If an anterior–posterior approach is necessary, the patient can be placed in a “sloppy-lateral” position to facilitate a simultaneous two-team approach (Fig. 36.7a–c).
- The authors always recommend cystoscopy and bilateral ureteral stent placement before laparotomy.
- If a malignant tumor can be safely separated from the posterior wall of the rectum without compromising a wide margin, the lesion can be dissected in a plane between its capsule and the mesorectal fat to preserve the rectum.

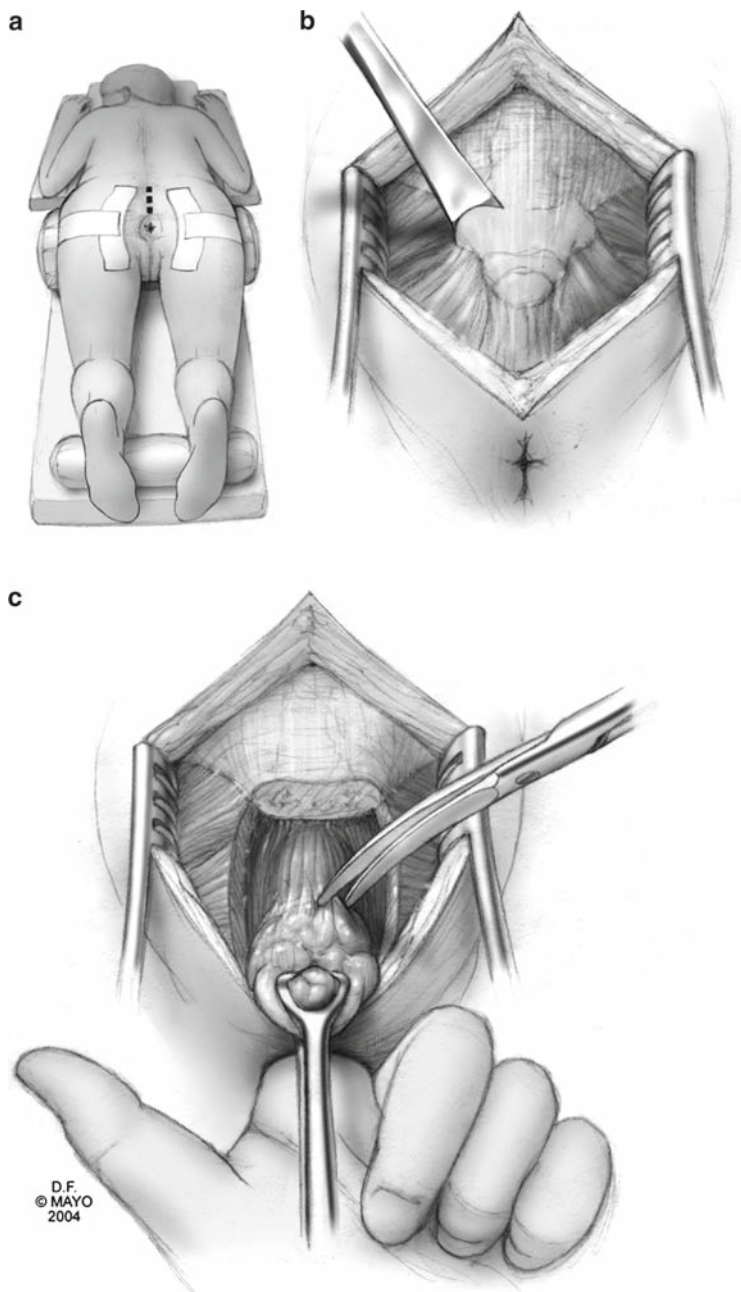


Fig. 36.6. (a) Positioning for posterior approach. (b) Coccygectomy. (c) Index finger in anal canal to “push” tumor outward facilitating dissection.

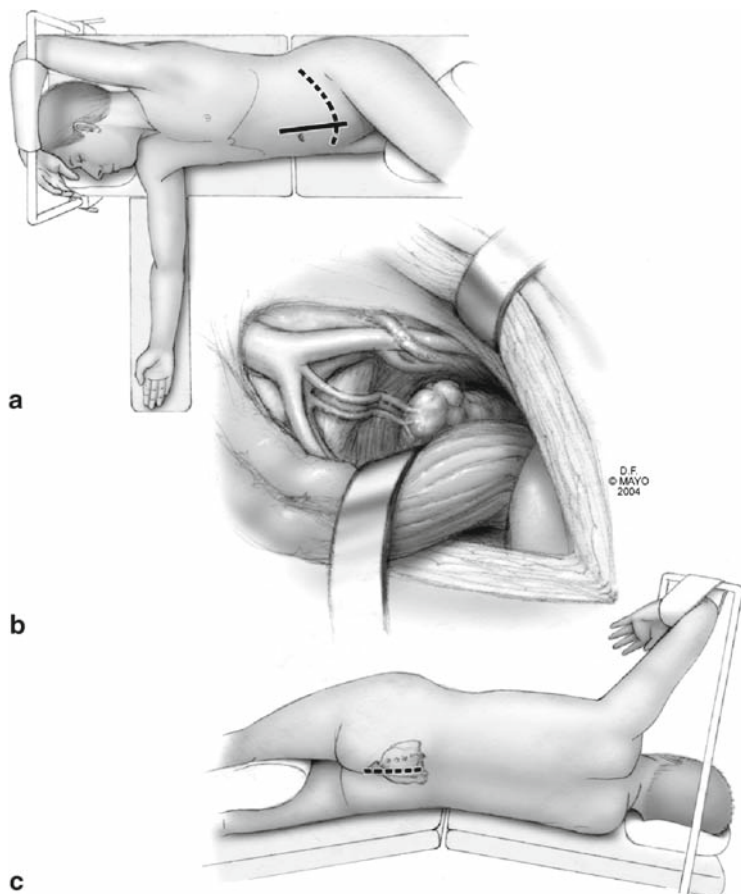


Fig. 36.7. (a) Modified lateral position for anterior exposure via a midline (*solid line*) or ilioinguinal (*dotted line*) incision. (b) Anterior exposure of vessels and tumor. (c) Posterior approach to sacrum.

- In the presence of very large tumors, blood loss during the procedure can be substantial. This may be minimized by ligating the middle and lateral sacral vessels and both internal iliac arteries and veins (Fig. 36.8). When ligating the internal iliac artery, it is best to preserve the anterior division, which gives off the inferior gluteal artery, thereby reducing the risk of perineal necrosis.

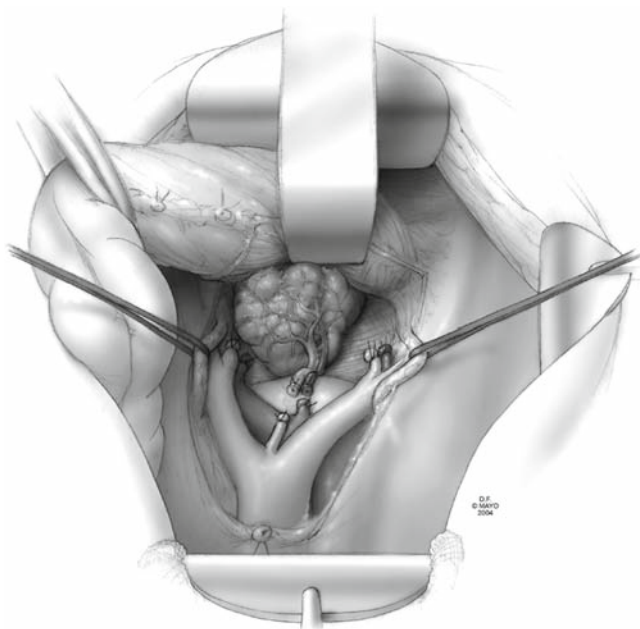


Fig. 36.8. Ligation of middle sacral and internal iliac vessel.

- A vascular surgeon can be helpful during this portion of the procedure especially in patients who have had prior irradiation or have distorted vascular anatomy.

F. Results of Treatment

Malignant Lesions

- In malignant cases, if wide margins are not achieved or if the tumor is violated, one can expect a high local recurrence rate and a poor overall outcome.
- In the literature, the prognosis for patients with chordomas has been variable, ranging from 15 to 76% at 10 years after surgical therapy.
- Isolated metastases to the lungs, ribs, spine, and long bones can sometimes be excised successfully and provide patients with symptomatic relief and a substantial prolongation of life.

Congenital Cystic Lesions

- In general, cystic lesions can be treated adequately by complete excision via a posterior approach. Large cystic lesions such as teratomas extending high into the pelvis can be excised via a combined abdominal–perineal approach.

G. Algorithm

- Based on the experience at the authors' institution, a decision-making algorithm to guide the management of presacral tumors is presented in Fig. 36.9.

H. Conclusion

- Presacral tumors are rare, the differential diagnosis is extensive, and their discovery is notoriously difficult and late. A high index of suspicion is needed to identify these patients.
- Once a benign or malignant presacral lesion is discovered and histologically diagnosed, it should be treated, even if the patient is asymptomatic.
- CT and MRI imaging can help differentiate between benign and malignant, cystic and solid and accurately define extent of adjacent organ and bony involvement to guide operative planning.
- Completely cystic lesions, in general, do not require preoperative biopsy unless malignancy is suspected. All solid tumors and heterogenous cysts should be considered for biopsy to rule out malignancy, guide neoadjuvant therapy, and plan extent of resection. Biopsies should be done transperineally or parasacrally.
- An aggressive approach, by an experienced, multidisciplinary team, that can achieve a tumor-free, en bloc resection, avoid tumor violation, restore spinopelvic stability, and minimize intraoperative and postoperative complications, should decrease the risk of local recurrence and improve survival.

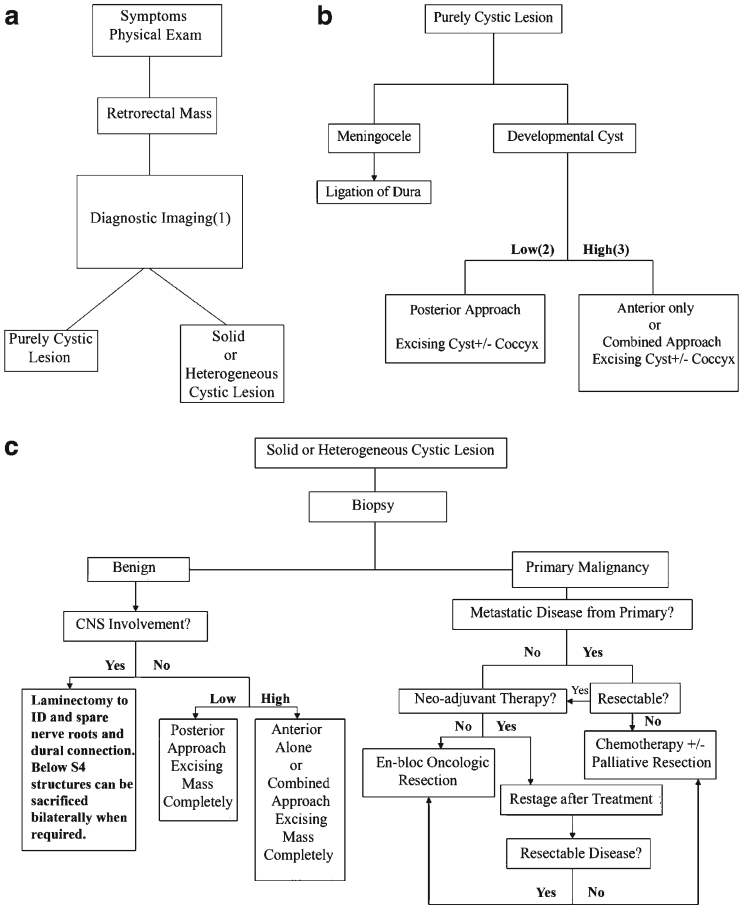


Fig. 36.9. Proposed treatment algorithm. Notes: (1) conventional radiographs of pelvis, CT scan, MRI with gadolinium, ERUS, intraluminal contrast studies of rectum, PET, myelogram; (2) lower than the third sacral vertebra; (3) higher than the third sacral vertebra.

37. Miscellaneous Neoplasms

A Carcinoids

- Carcinoid tumors originate from enterochromaffin cells, part of the diffuse endocrine system and are considered to belong in the neuroendocrine group of tumors.
- Carcinoid tumors may be located in any of a number of locations within and outside the gastrointestinal (GI) tract, may be single or multiple, may produce a wide array of biochemical products, may produce symptoms from the biochemical products or the tumor itself, and exhibit varying degrees of biochemical and aggressive behavior relative to their location.

History and Terminology

- Carcinoid tumors are histologically similar to carcinoma, but have a more benign clinical course.
- Gossett and Masson described the argentaffin-reducing properties of appendiceal carcinoids in 1914, and the tumors became known as “argentaffinomas.”
- The amine precursor uptake and decarboxylation (APUD) abilities of these tumors were recognized by Pearse in 1969, and carcinoid tumors became known as “APUDomas.” APUDomas, including carcinoid tumors, are now considered part of a group of tumors known as neuroendocrine tumors.
- Carcinoid tumors are derived from the diffuse neuroendocrine system and share some characteristics with melanomas, pheochromocytomas, medullary carcinoma of thyroid, and pancreatic endocrine tumors.

Pathology

- Silver staining has been supplanted by immunohistochemical stains for cytoplasmic proteins. Chromogranin, neuron-specific enolase, and synaptophysin are frequently used to identify a tumor as being a neuroendocrine tumor.
- Carcinoid tumors have been described to grow in one of five histologic patterns. These histologic patterns have been designated as A-D or I-IV, with the fifth pattern in each system being a combination of several patterns. These growth patterns are described in Table 37.1.

Pathophysiology

- Carcinoid tumors are known to produce at least 30 bioactive compounds. These compounds may be amines (including serotonin and histamine), proteins (a wide variety of hormones and kinins), and prostaglandins. Serotonin, an amine, is the most well-known of these compounds.

Table 37.1. Carcinoid tumor growth patterns.

Sogo and Tazawa	Martin and Potet	Pattern	Description	Frequency	Prognosis
Type A	Type I	Insular	Solid nests with peripheral palisading	Most frequent pattern	Favorable
B	II	Trabecular	Ribbon-like anastomosing pattern	Second-most frequent pattern	Favorable
C	III	Glandular	Tubular, acinar, or rosette pattern	Least frequent pattern	Poor
D	IV	Undifferentiated	No recognizable pattern	Third-most frequent pattern	Poor
Mixed	Mixed	Any combination of the above	Any combination of the above	A + C most frequent mix A + B next most frequent	Most favorable Favorable

- Serotonin is derived from tryptophan, an essential amino acid. The production of serotonin is a two-step process: hydroxylation of tryptophan to 5-hydroxytryptophan (5-HTP), followed by decarboxylation of 5-HTP to 5-hydroxytryptamine (5-HT, or serotonin). Serotonin is then stored and transported in platelets. Metabolism of serotonin occurs in the liver (monoamine oxidase) and then the kidney (aldehyde dehydrogenase) to produce 5-hydroxy-indole-acetic acid (5-HIAA) which is excreted in the urine.
- Normally, less than 1% of tryptophan is converted into serotonin. The remainder is used for synthesis of proteins, niacin (vitamin B₇), and nicotinamide (vitamin B₃). Protein malnutrition, hypoproteinemia, and pellagra (vitamin B₃ deficiency) may develop if large quantities of tryptophan are diverted to serotonin production by carcinoid tumors.

Classification

- Carcinoid tumors are grouped by their site of origin into foregut, midgut, and hindgut tumors. Foregut tumors originate in the thymus, respiratory tract, stomach, duodenum, pancreas, and ovaries. Midgut tumors originate in the jejunum, ileum, appendix, and proximal colon. Hindgut tumors originate in the distal colon or rectum.
- Godwin reported the most frequent sites of origin as the appendix, ileum, rectum, and bronchus (38%, 23%, 13%, 11.5%, respectively) in a series of 4,349 carcinoid tumors. In another large series, Modlin and Sandor reported the most frequent sites of origin as the bronchus, ileum, rectum, and appendix (32.5%, 17.6%, 10%, 7.6%, respectively) in 5,468 carcinoid tumors.

Clinical Presentation

- Carcinoid tumors may be found incidentally or may present as a result of the production of local or systemic symptoms. Local symptoms are related to the site of origin or site of metastasis, whereas systemic symptoms are related to production of bioactive compounds.

B. Local Symptoms

- Small bowel carcinoids may produce local symptoms of periodic abdominal pain, small bowel obstruction (caused by intussusception or mesenteric fibrosis and small bowel kinking), intestinal ischemia, and GI hemorrhage.
- Appendiceal carcinoids are often found incidentally at the time of appendectomy.
- Rectal carcinoids are often found incidentally at the time of colorectal cancer screening examinations. The symptoms of rectal carcinoids, when present, are related to bleeding and change in bowel habits. Liver metastases may be the initial presentation, manifested by hepatomegaly and right upper quadrant pain.

C. Systemic Symptoms and the Carcinoid Syndrome

- Systemic symptoms produced by carcinoid tumors are referred to as the carcinoid syndrome. These consist of a combination of vasomotor symptoms (flushing and blood pressure changes), diarrhea, and bronchospasm. These symptoms are brought on by release of active tumor products into the circulation. The liver is capable of metabolizing and inactivating large quantities of tumor products. Therefore, the carcinoid syndrome occurs only in the presence of liver metastases (for GI carcinoids), or a primary carcinoid tumor located outside the portal venous system.
- Episodes of symptoms of the carcinoid syndrome may be precipitated by routine daily experiences such as emotional stress, heat, alcohol consumption, or straining at stool.
- Flushing symptoms and hypotension are thought to be caused by a variety of bioactive tumor products. These include catecholamines, histamine, tachykinins, and kallikrein.
- Four different patterns of flushing have been described, and each is related to a specific site of origin. Type 1 flushing is a diffuse, erythematous rash, which may last up to 5 min, and is associated with the early stage of metastases from midgut

carcinoid tumors. Type 2 flushing is a violaceous rash with telangiectasias, which may also last up to 5 min, and is associated with the later stages of metastases from midgut carcinoid tumors. Type 3 and 4 flushing is associated with bronchial and gastric carcinoid tumors, respectively.

- The heart may be affected by carcinoid tumor products, particularly in those patients with midgut carcinoids and liver metastases. It is thought to be caused by the effects of serotonin on the heart. Specifically, serotonin has an effect on myofibroblasts resulting in fibroplasia, increased vascular tone, bronchoconstriction, and platelet aggregation. Together, these effects may cause pulmonary hypertension, tricuspid and pulmonary valve stenosis, and right ventricular hypertrophy and fibrosis. The left side of the heart is typically protected from the effects of carcinoid products by the lungs, which are capable of inactivating these substances.
- Carcinoid crisis is a life-threatening condition. It may be brought on by anesthesia, embolization or manipulation of the tumor, administration of chemotherapy, or occur spontaneously. Life-threatening manifestations of the carcinoid crisis include profound flushing and hypotension, bronchoconstriction, arrhythmias, and hyperthermia. Other manifestations include diarrhea, confusion, and stupor. The crisis may be limited or avoided by pretreatment with somatostatin and histamine blockade (both H_1 - and H_2 -receptors) before treatments known to induce a crisis.

Diagnostic Studies

Biochemical Studies

- Carcinoid tumors are often difficult to diagnose preoperatively, particularly those in the small bowel and appendix.
- The diagnosis of carcinoid tumor before surgery relies on biopsy of an accessible lesion (in the foregut, hindgut, or liver), or the identification of biochemical products from the tumor.
- The most widely accepted test currently used to diagnose the presence of a carcinoid tumor is a 24-h urine specimen analyzed for 5-HIAA (a serotonin metabolite). Urinary 5-HIAA excretion under normal circumstances is between 2 and 8 mg/24 h. Excretion exceeding these levels has shown high sensitivity and

Table 37.2. Dietary and medicinal intake affecting urinary 5-HIAA.

Foods rich in serotonin	Medicines affecting urine 5-HIAA
Bananas	Guaifenesin
Plantains	Acetaminophen
Pineapples	Salicylates
Plums	L-Dopa
Kiwi	
Walnuts	
Hickory nuts	
Pecans	
Avocados	
Tomatoes	

Table 37.3. Comparison of urine and platelet biochemical studies in carcinoid patients.

	Number	Platelet 5-HT (%)	Urine 5-HIAA (%)	Urine serotonin (%)
Foregut	14	50	29	55
Midgut	25	100	92	82
Hindgut	5	20	0	60

specificity (73% and 100%, respectively) in diagnosing carcinoid syndrome. It is important to avoid foods and medications that can produce a false-positive result by affecting urinary 5-HIAA levels. These are listed in Table 37.2.

- Carcinoid tumors vary in their ability to produce serotonin. Midgut tumors typically produce high levels of serotonin and its metabolites. Foregut tumors typically lack the ability to convert (decarboxylate) 5-HTP (5-hydroxytryptophan) into 5-HT (serotonin), resulting in low urinary levels of 5-HIAA. However, the kidney may decarboxylate sufficient 5-HTP into 5-HT, thus increasing urinary serotonin levels. Hindgut carcinoids rarely produce 5-HTP or 5-HT, and urine and blood tests are typically negative.
- Platelet serotonin levels may be more sensitive than urine or blood tests. The results of three different tests in a series of 44 patients with carcinoid tumors is shown in Table 37.3.
- Serum Chromogranin-A is a useful tumor marker for diagnosis and follow up of patients with gastrointestinal carcinoid tumors.

Imaging Studies

- Localization of primary carcinoids in the GI tract is often difficult.
- Carcinoids in the foregut and hindgut are frequently diagnosed by endoscopy and biopsy. However, ileal and appendiceal carcinoids are more common and less easily localized. These primary sites often remain unknown, despite small bowel contrast studies or computed tomographic (CT) scanning, until surgical exploration identifies the primary site.
- If these studies are positive, it is usually the mesenteric kinking and fibrosis that is evident rather than the mass itself.
- CT scans may show a characteristic stellate soft-tissue stranding in the mesentery.
- The two scintigraphic imaging techniques currently in use are somatostatin receptor scintigraphy (SRS) and positron emission tomography (PET). Both techniques rely on differential uptake of the radiotracer by the tumor relative to normal tissue. SRS relies on somatostatin receptors on the cell surface, whereas PET relies on metabolic utilization of the localizing agent.
- A recent study compared both morphologic and functional imaging modalities in localizing primary and metastatic carcinoid tumors in 17 patients. The results are summarized in Table 37.4, and suggest that the two approaches are complementary.
- F-Dopa-PET imaging is more sensitive in localizing primary tumors and lymph node involvement, whereas CT or MRI is more sensitive in identifying distant disease.

Prognosis

- The behavior and prognosis of carcinoid tumors are highly variable and are affected by multiple factors including tumor size, depth, presence and location of metastases, and primary tumor location.

Table 37.4. Morphologic and functional imaging in carcinoid tumors.

Tumor site	PET		SRS	CT/MRI
	¹⁸ F-Dopa	¹⁸ FDG		
Primary	7/8	2/8	4/8	2/8
Lymph nodes	41/47	14/47	27/47	29/47
Distant metastases	12/37	11/37	21/37	36/37

¹⁸FDG ¹⁸F-fluorodeoxyglucose; SRS somatostatin receptor scintigraphy

- Prognosis is affected by the TNM stage, as shown in Table 37.5.
- The effect of primary tumor location on prognosis (survival, likelihood of carcinoid syndrome, and additional tumors) is shown in Table 37.6.

Table 37.5. TNM staging and survival of GI carcinoid tumors.

TNM	Stage	Definition	5-year survival (%)	Comment
T	1	Submucosa	82	Survival differences related to tumor depth in absence of metastases
	2	Muscularis propria		
	3	Subserosa		
	4	Perforated or invading neighboring structure	52	
N	0	Absent	95	Survival differences related to presence and proximity of metastases
	1	Present	83	
M	0	Absent	—	
	1	Present	38	

Table 37.6. Effect of primary carcinoid location on prognosis.

Primary carcinoid location	Overall 5-year survival (%)	Incidence of metastases (%)	Carcinoid syndrome	Multi-plicity of carcinoid tumors (%)	Second primary cancer (%)
Appendix	99	<1 cm, 0; 1–1.9 cm, 11; >2 cm, 30–60	Rare	4.2	13
Small bowel	Related to metastasis (see Table 37.4)	<1 cm, 20–30; 1–2 cm, 80; LN 20 liver >2 cm, >80 LN 40–50 liver	Common	30–50	20–30
Colon	20–52	Frequent	Rare	Infrequent	25–40
Rectum	No mets – 92 LN mets – 44 Distant mets – 7	<1 cm, 3; 1–2 cm, 11; >2 cm, 74	Rare	0–3	7–32

LN lymph node

Treatment

Tumor-Directed Therapy

- The mainstay of treatment for carcinoid tumors is surgical resection.
- Difficulty arises in selecting the extent of surgery relative to the extent of disease, magnified by two considerations (1) carcinoid tumors are often located in an area where “local excision” is an option (appendix, rectum), and (2) the benefit of debulking procedures.
- The surgical decision is based on the likelihood of residual primary disease, lymph node metastases, and the benefit of debulking the tumor burden to reduce the symptoms of the carcinoid syndrome. Guidelines for extent of surgical resection are summarized in Table 37.7.
- Small bowel carcinoid tumors are frequently associated with lymph node metastases and structural abnormalities (intussusception, mesenteric fibrosis, and small bowel kinking). Lymph node metastases are common, even when the tumors are small. Lesions less than 1 cm in diameter have a 20–30% incidence of lymph node involvement. Additionally, there are often multiple small bowel lesions. Therefore, surgical management involves formal resection and wide mesenteric excision of the associated region of lymph node drainage as well as thorough exploration for additional lesions.

Table 37.7. Guidelines for extent of surgical resection.

Primary tumor	Factor	Extent of resection
Appendix	<1 cm	Appendectomy
	1–1.9 cm	Individualize, appendectomy, or right hemicolectomy
Small bowel	>2 cm	Right hemicolectomy
	Locally limited disease	Resection of primary and metastatic tumors
	Extensive disease	Resection or bypass of primary tumor
Colon		Debulking of metastases
Rectum		Colectomy
	<1 cm	Local excision
	1–1.9 cm	Individualize, local excision, or proctectomy
	>2 cm	Proctectomy

- Appendiceal carcinoids typically are frequently found during appendectomy, are less likely to have lymph node metastases (0% for lesions less than 1 cm, 11% for lesions between 1 and 1.9 cm, and 30–60% for lesions greater than 2 cm in diameter) and multicentric disease is rare. Therefore, appendectomy is adequate treatment for lesions less than 1 cm, whereas lesions greater than 2 cm are treated by formal resection (right hemicolectomy). Treatment for intermediate-size appendiceal carcinoids (1–1.9 cm) must be individualized, balancing the risk of a more extensive surgery against the risk of residual disease. Factors that suggest an increased likelihood of residual disease, and are thus used to indicate a formal right hemicolectomy, include lymphovascular invasion, involvement of the mesoappendix (by direct extension or in lymph nodes), or a positive surgical margin.
- Colonic carcinoid tumors generally behave in an aggressive manner and frequently have lymph node metastases and a poor prognosis. Therefore, they are treated with formal resection.
- Rectal carcinoid tumors are minimally aggressive lesions, and behave in a manner similar to appendiceal carcinoids. They have a similar rate of lymph node metastases and multiple lesions are uncommon. Surgical treatment also shows similarity in that local (transanal) excision is adequate for lesions less than 1 cm in diameter whereas formal proctectomy is advised for lesions larger than 2 cm in diameter. Treatment for intermediate-size rectal carcinoids (1–1.9 cm) must be individualized, balancing the risk of a more extensive surgery against the risk of residual disease. Muscular invasion is the factor that suggests an increased likelihood of residual disease, and is thus used to indicate a formal proctectomy.
- Treatment of hepatic metastases is of significant benefit, especially when metastatic disease is confined to the liver. Tumor debulking may be in the form of hepatic resection, ablative therapy (cryotherapy, radiofrequency ablation), radiolabeled octreotide, or hepatic artery embolization and chemoembolization. The expected 5-year survival rate for patients with carcinoid liver metastases is 20%. Death is often related to liver failure from local tumor progression or carcinoid heart disease.

However, several studies have demonstrated a 5-year survival rate approximating 70% when these metastases are treated with a combination of the listed techniques. Similar survival rates have been achieved with the use of liver transplantation in a small number of patients.

Systemic Therapy

- Medical treatment for patients with carcinoid tumors has two purposes: palliation of systemic symptoms of the carcinoid syndrome, and treatment of metastases. The palliation of symptoms may use medications directed at specific symptoms, or medications causing a generalized reduction in hormone production. Specific agents that may help control symptoms of the carcinoid syndrome are listed in Table 37.8. Somatostatin analogs are helpful in controlling many of the symptoms of the carcinoid syndrome by reducing synthesis and systemic release of hormone products. Octreotide is a long-acting somatostatin analog with a half-life of 90 min. In doses of 400 µg/day, octreotide improved the major symptoms of flushing and diarrhea in more than 80% of patients. Lanreotide is another somatostatin analog with a longer half-life than octreotide, and both agents are available in long-acting depot forms.
- Chemotherapy has largely been ineffective in patients with metastatic carcinoid tumor.

Table 37.8. Medical treatment of carcinoid syndrome symptoms.

Symptom	Drug category	Specific agents
Flushing	H ₂ -Blockade	Cimetidine, ranitidine, famotidine
	α ₁ -Blockade	Doxazosin, phenoxybenzamine
	Phenothiazine	Chlorpromazine
	Corticosteroid	Prednisone
Diarrhea	Serotonin blockade	Ketanserin, ondansetron, cyproheptadine, methysergide
Bronchospasm	Opiate blockade	Codeine, loperamide
	Phenothiazine	Chlorpromazine
	Bronchodilator	Salbutamol
	Corticosteroid	Prednisone

D. GI Stromal Tumors

- GI stromal cell tumors (GISTs) are mesenchymal tumors arising from the intestinal wall, omentum, or retroperitoneum that stain positive for the CD117 antigen, a marker for the KIT oncoprotein.
- Because of structural and immunohistochemical similarities between GISTs and the interstitial cells of Cajal, it is thought GISTs arise from these cells or other pluripotential mesenchymal stem cells. The interstitial cells of Cajal are located in the muscle layer of the GI tract and form a complex network that regulates intestinal motility.
- The stomach is the most common location of GISTs (45–55%) with small bowel the next most common location (25–35%). Only 10–20% of GISTs are located in the colon and rectum. The gender distribution is close to equal in all locations.
- GISTs occur throughout the colon but are most often located in the rectum.
- The most common clinical presentation is hematochezia, abdominal or rectal pain, or a mass found incidentally on physical examination or endoscopically. As might be expected, how patients present is largely related to the size of the tumor.
- Complete surgical excision, if possible, continues to be the treatment of choice. Because GISTs rarely spread to the lymphatic system, removal of the regional lymph nodes is not necessary or recommended. Wide margins are not necessary, but complete en bloc removal of the tumor and its pseudocapsule should be performed.
- The use of imatinib mesylate (Gleevec in the United States, Glivec in Europe, Novartis Pharmaceuticals) has significantly impacted the treatment of GISTs.
- In GIST tumors, abnormal activation of the KIT oncoprotein results from a mutation in the C-kit gene. This abnormal activation results in unregulated cellular proliferation. Imatinib is a selective tyrosine kinase inhibitor and acts by blocking the abnormal activation of the KIT oncoprotein.
- The incidence of local recurrence or metastatic disease after complete surgical excision is high. About 50% of patients with potentially curative resection will develop a recurrence.

E. Leiomyomas

- Leiomyomas of the colon and rectum are usually small (less than 1 cm) nodules arising from the smooth muscle of the muscularis mucosa.
- They are differentiated from GISTs by staining negative for CD117 (KIT) and positive for desmin and smooth muscle actin.
- They are almost always found incidentally on endoscopy or in surgical resections done for other pathology.
- Small incidental leiomyomas found on endoscopy are benign tumors that are adequately treated by snare polypectomy alone.

F. Squamous and Adenosquamous Carcinoma

- Squamous and adenosquamous carcinomas of the colon are thought to be variants of the same tumor. Squamous cell cancers have pure epithelial features without glandular elements; adenosquamous cancers have both epithelial and glandular features.
- Patients tend to present with advanced disease.
- The primary treatment of these tumors is surgical. Because, by definition, these tumors are located in the colon or proximal to mid rectum, a segmental resection with anastomosis should be feasible. In rectal tumors, preoperative adjuvant chemoradiation should be considered. This recommendation is based on improved control of local disease with preoperative adjuvant therapy in patients with adenocarcinoma and the good response to chemoradiation in patients with squamous cell cancer of the anus.

G. Lymphomas

- Only 6–12% of primary GI lymphomas occur in the colon. Primary colonic lymphomas represent less than 1% of large bowel malignancies. Approximately 70% involve the cecum

or ascending colon. The most common presenting symptoms are abdominal pain, palpable abdominal mass, hematochezia or melena, and weight loss.

- The majority of lymphomas in the colon and rectum are non-Hodgkin's lymphomas of B cell origin, diffuse large cell type.
- GI lymphoid tissue exists in intestinal mucosa, submucosa, and lamina propria. Low-grade B cell lymphomas arising from these specialized lymphoid tissues are referred to as MALT (mucosa-associated lymphoid tissue) tumors. MALT tumors are low-grade tumors with an indolent course and are usually located in the stomach, but cases of colonic involvement have been reported.
- MALT tumors in the colon are usually solitary lesions, but can also present as multiple polypoid lesions.
- Multiple lymphomatous polyposis is a mantle cell lymphoma that involves the GI tract. Multiple lymphomatous polyps can involve the GI tract from the stomach to the rectum, but can also involve the colon alone.
- On endoscopic examination, it can be confused with familial adenomatous polyposis or nodular lymphoid hyperplasia. The treatment is chemotherapy.
- Treatment of localized, primary colonic lymphoma is primarily surgical excision.

H. Colonic Complications of Leukemia

- Colonic complications of leukemia may be broadly divided into two categories: complications caused by leukemic invasion of the bowel and complications caused by the profound immunocompromise, as a result of the disease and its treatment.
- Leukemic infiltration of the colon is not common.
- The most common CT finding is a diffuse thickening of the bowel wall.
- Symptoms of leukemic infiltration are nonspecific, such as abdominal pain, bloating, diarrhea, and hematochezia. The treatment consists of treating the underlying leukemia. Surgery is indicated only if complications arise.
- Neutropenic enterocolitis is a serious life-threatening complication resulting from chemotherapy.

- In the report by Hogan et al., the median onset of symptoms (fever, pain, diarrhea) was 10 days after the start of chemotherapy and all patients had absolute neutrophil counts of less than $0.5 \times 10^9/\text{L}$. CT and ultrasound findings consist of thickening of the bowel wall in the ileocecal region.
- Treatment consists of bowel rest, parenteral nutrition, and broad spectrum antibiotics. Surgery should be reserved for complications such as documented evidence of bowel perforation or massive bleeding.

38. Hereditary Nonpolyposis Colon Cancer

A. Introduction

- Colorectal cancer affects 148,300 patients in the United States annually (72,600 males and 75,700 females) causing 56,600 deaths each year. Those patients who have two or more first- and/or second-degree relatives with colorectal cancer have a potentially definable inheritable disorder. Approximately 5–6% of colorectal cancers have a known germline genetic mutation. Hereditary nonpolyposis colon cancer (HNPCC) is one of the syndromes and accounts for 3% of newly diagnosed colorectal cancer cases.
- HNPCC is characterized by the early onset of colorectal cancer (mean age, 45 years), with multiple generations affected.
- These cancers tend to be proximal to the splenic flexure, poorly differentiated, and have an increased frequency of synchronous and metachronous cancers.
- There is also an excess of extracolonic cancers, including endometrial, ovarian, gastric, small bowel, hepatobiliary, and transitional cell carcinomas. Over a patient's lifetime, there is an 80% risk of cancer, with colon cancer being the most frequently diagnosed cancer.
- The syndrome is characterized by an autosomal dominant mode of inheritance.
- Germline mutations in mismatch repair (MMR) genes, which normally repair mistakes in DNA replication, are responsible for HNPCC.

B. Genetics

What Are Microsatellites?

- Microsatellites are short tandem repeating base sequences that are usually mononucleotide or dinucleotide base repeats. Most often, the repeats are found in the noncoding or intronic portion of the gene. However, microsatellites can occur anywhere within the gene.
- There are well over 200 polymorphic microsatellite loci identified. The most common sequences are repeats of adenine or thymine or the dinucleotide repeats of cytosine/adenine (CA_n) or guanine/thymine (GT_n).
- When the number of repeats in a microsatellite sequence in a cancer cell is different from the surrounding normal tissue, this is termed “microsatellite instability.”

Different Types of DNA Repair

- There are several intracellular mechanisms that repair DNA damage and maintain genomic stability and fidelity.
- “Base excision repair” (BER) repairs mutations caused by reactive oxygen species related to aerobic metabolism.
- “Nucleotide excision repair” (NER) repairs damage caused by exogenous agents such as mutagenic and carcinogenic chemicals as well as ultraviolet radiation.
- MMR genes repair single base mismatches as well as insertion/deletion loops (IDL) of up to ten nucleotides. MMR gene dysfunction is characterized by MSI and is responsible for HNPCC.
- The so-called mutator phenotype of HNPCC is characterized by an increased genome-wide mutation rate. This is in contradistinction to sporadic colon cancer or familial polyposis, which is characterized by loss of whole portions of chromosome alleles known as loss of heterozygosity (LOH).

MMR Function in Single Cells

- There are three main components of this repair system, namely, MutS, MutL, and MutH.
- MutS recognizes base mismatches and IDL. Acting as an adenosine triphosphatase (ATPase) homodimer, MutS attaches to

the abnormal DNA, undergoes a conformational change, and translocates or slides along the DNA, allowing the formation of a large DNA loop. As the DNA is being shortened into the loop, the abnormal mismatches are included in the DNA loop.

- MutL, another ATPase, again acting as a homodimer, identifies the loop segment of DNA that includes the mismatch. The loop continues to enlarge, and a DNA-methylated (DAM) GATC base sequence is encountered. The new DNA strand is recognized because it is not methylated.
- At this point, MutH, an endonuclease, is activated and a nick in the DNA strand is made. This can occur on either the 3' or 5' side of the DNA strand. Bidirectional exonucleases excise the abnormal DNA strand and DNA polymerase resynthesizes a new strand.

MMR Function in Humans

- In humans, five MutS genes have been identified (*MSH2*, *MSH3*, *MSH4*, *MSH5*, *MSH6*) and four MutL genes (*MLH1*, *PMS1*, *PMS2*, *MLH3*). No MutH gene equivalent has been discovered. In humans, MutS and MutL presumably directly activate exonucleases without the need for a MutH gene.
- Unlike single cell MMR genes that function as a homodimer, human MMR genes function as a heteroduplex (Fig. 38.1).
- *MSH2* acts as a “scout” and identifies the mismatches in the new DNA strand. It then complexes with *MSH6* to form the MutS α complex that identifies single nucleotide misrepairs.
- The most frequently mutated genes in HNPCC are *MLH1* (33%) and *MLH2* (31%) and rarely *PMS2* or *PMS1*.
- Of the mutations identified, 90% occurred in *MLH1* and *MSH2*.
- MutS has two functions – mismatch recognition and ATPase activity. Both functions are essential for repair in 7 of 8 possible single-base mismatches.
- It is generally agreed that mismatched DNA stimulates ATP hydrolysis as part of the repair mechanism, but there is disagreement as to the role this has in MMR gene function.
- In the translocation model, ATP enables MutS α or β to move like a motor protein away from the mismatch.
- The molecular switch theory proposes that this transposition from ADP to ATP in the MutS gene switches the repair complex on and off. MutS ADP has a high affinity for the misrepaired

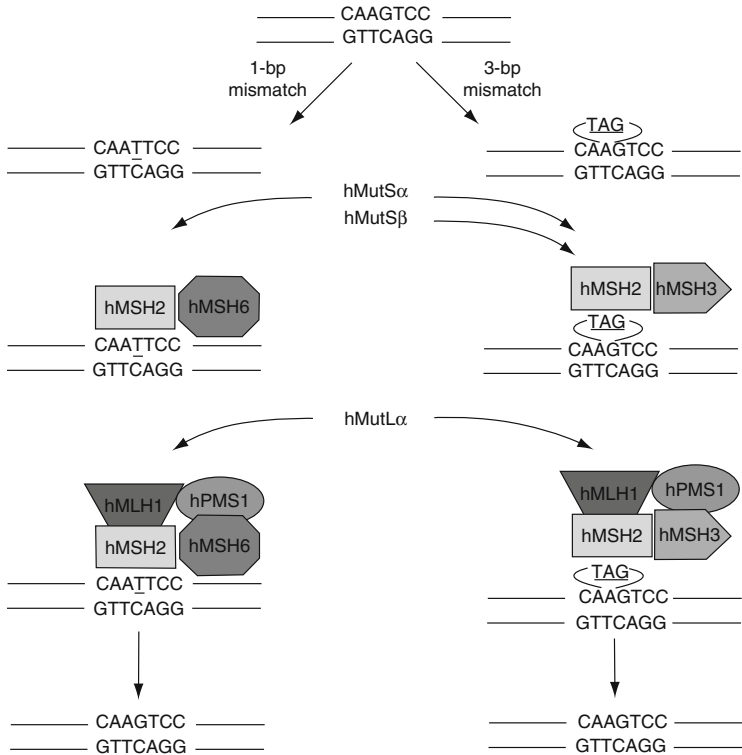


Fig. 38.1. vThe DNA MMR system can correct either single base-pair mismatches or larger loops of mismatched DNA. hMSH2 serves as the “scout” that recognizes mismatched DNA. It forms a complex with either hMSH6 or hMSH3, depending on the number of mismatched nucleotides. A second heterodimeric complex (hMLH1/ hPMSI) is then recruited to excise the mispaired nucleotides. hMUTS α = hMSH2/hMSH6; hMuTS β = hMSH2/hMSH3; hMutL α = hMLH1/ hPMS1. bp = base pair. (Reprinted with permission from Chung and Rustgi.).

- gene and then it binds to it. When this occurs, ADP is transformed to ATP and causes a conformational change in the MutS complex.
- The third theory is called “transactivation.” MutS binds both ATP and the mismatch DNA simultaneously in order to activate MMR. The ATPase in this model functions as a proofreader and binds only to heteroduplex DNA. Once the mismatch and the ATP are bound, it is believed that a signal is produced to authorize DNA repair.

Genes Implicated in HNPCC Carcinogenesis

- When MMR genes are dysfunctional, the myriad genes that have microsatellites in their coding region can become inactivated, causing acceleration of tumorigenesis.
- Transforming growth factor beta Type II receptor gene (*TGFβRII*) was found to be mutated in 70–90% of cancers with MSI. *TGFβRII* acts as a tumor suppressor gene and is a strong inhibitor of epithelial growth.
- Insulin-like growth factor II receptor gene (*IGFRII*) binds insulin-like growth factor I, thus antagonizing its growth stimulating effects.
- The *BAX* gene is another gene found to be mutated in up to 54% of MSI-H colorectal tumors. It is involved in apoptosis and is a downstream gene often activated by the P53 gene.
- *RAF* oncogenes are a family of genes that encode kinases and mediate cellular responses to growth signals.
- *BRAF* is a *RAF* gene that is common in MMR-deficient tumors and in colorectal tumors that have a normal *KRAS* gene.
- Both *BRAF* and *KRAS* mutations are found in all stages of colon cancer and in adenomas greater than 1 cm.

C. Pathologic Features

- Cancers are often mucinous or poorly differentiated with signet ring cells.
- Despite what appears to be unfavorable histology, the incidence of lymph nodes is 35% compared with 65% in sporadic colon cancer.

D. Clinical Features of HNPCC

- Affected individuals in HNPCC have an increased risk of colon cancer and other extracolonic cancers as demonstrated in Table 38.1.
- Colon cancer is the most frequently diagnosed cancer in HNPCC (80%) and endometrial cancer is the most frequent extracolonic cancer (50–60%).

Table 38.1. Lifetime risks for cancer associated with the hereditary nonpolyposis colorectal cancer syndrome.

Type of cancer	Persons with HNPCC	General population
Colorectal	80–82	5–6
Endometrial	50–60	2–3
Gastric	13	1
Ovarian	12	1–2
Small bowel	1–4	0.01
Bladder	4	1–3
Brain	4	0.6
Kidney, renal, pelvis	3	1
Biliary tract	2	0.6

Source: Reprinted with permission from Chung and Rustgi

- Colorectal cancers in HNPCC are proximal to the splenic flexure (68% in HNPCC vs. 49% of sporadic cancers), are more likely to have associated synchronous cancers (7% HNPCC vs. 1% sporadic colon cancer), and will have increased metachronous cancers at 10 years (29% HNPCC vs. 5% sporadic cancers).
- Similarly, women with HNPCC-related endometrial cancer have a 75% risk of a second cancer during a 26-year follow-up.
- The median age of onset of colon cancer is 42 years and for endometrial cancer it is 49 years.
- Despite being termed hereditary nonpolyposis colon cancer, a polyp is still the precursor lesion for a colorectal cancer.
- One cancer is prevented for every 2.8 polyps removed in HNPCC patients compared with one cancer being removed for every 41–119 polypectomies in the general population.
- It is estimated that malignant transformation occurs in 3 years in HNPCC as opposed to 10 years in sporadic colon cancer.
- Two other types of polyps – the flat adenoma and serrated adenoma – have been implicated as possible precursors of the HNPCC cancers. Flat adenomas are found proximally in up to 50% of HNPCC patients.
- These polyps are difficult to detect during colonoscopy without dye spray techniques (e.g., methylene blue). Furthermore, flat adenomas with advanced histology (high-grade dysplasia or cancer) are significantly smaller (10.75 mm) than comparable polypoid lesions (20 mm).
- Carcinomas associated with serrated adenomas have a predilection for the cecum and the rectum and are often mucinous in nature.

E. Genotype–Phenotype Relationships

- There are very few studies that evaluate phenotype–genotype correlations. One study of 35 families found the *MSH2* mutation to be associated with a late age onset of rectal cancer and more extracolonic cancers than in the *MLH1* mutation-positive group.
- The Muir–Torre syndrome is characterized by sebaceous adenomas, sebaceous carcinomas, and keratoacanthomas associated with multiple visceral tumors. Colorectal cancers are most frequently found (51%) and are often proximal to the splenic flexure (60%).
- Germline mutations in *MLH1* and *MSH2* have been identified. As expected, many of the tumors exhibit MSI.
- The visceral tumors are often low grade, and prolonged survival in the presence of metastatic disease has been reported.
- Colorectal cancers are more frequently left-sided in *MSH6* carriers. The risk of endometrial cancer is increased over *MSH2* or *MLH1* carriers (76% vs. 30%) and colon cancer is decreased (32% vs. 80%). The median age of onset is 55 years. Therefore, a distinct phenotype has emerged, characterized by a clustering of endometrial cancer, a decreased frequency of colorectal cancer, later age of onset, and MSI-L cancers.

F. Diagnosis

- The key to the diagnosis of HNPCC is a detailed family history and subsequent construction of a family pedigree.
- Amsterdam criteria (Table 38.2) were created to define clinical criteria to identify patients with a high probability of having an inheritable form of colon cancer not associated with diffuse polyposis.
- For day-to-day clinical purposes, the original definition was too restrictive because it did not account for the extracolonic malignancies associated with HNPCC, the decrease in the average family size, the late onset variants of HNPCC, and the problems with incomplete data recovery. Modifications of the Amsterdam criteria have occurred and are known as Amsterdam II and modified Amsterdam criteria (Table 38.2).

Table 38.2. Amsterdam criteria.

Amsterdam criteria

- At least three family members with colorectal cancer, one of whom is first-degree relative of the other two
- At least two generations with colorectal cancer
- At least one individual <50 years at diagnosis of colorectal cancer
- Amsterdam criteria II
- At least three family members with HNPCC-related cancer, one of whom is first-degree relative of the other two
- At least two generations with HNPCC-related cancer
- At least one individual <50 years at diagnosis of HNPCC-related cancer

Modified Amsterdam criteria

- Two first-degree relatives with colorectal cancer involving two generations
- At least one case diagnosed before 55 years *or*
- Two first-degree relatives with colorectal cancer and a third relative with endometrial cancer or another HNPCC-related cancer

Source: Modified with permission from Chung and Rustgi

Table 38.3. Modified Bethesda guidelines.

Amsterdam criteria

- Patient with two HNPCC-related tumors
- Patient with colorectal cancer with first-degree relative with HNPCC-related cancer; one of the cancers at <50 years or adenoma at <40 years
- Patient with colorectal cancer or endometrial cancer at <50 years
- Patient with right-sided, undifferentiated colorectal cancer at <50 years
- Patient with signet ring colorectal cancer at <50 years
- Patient with adenoma at <40 years

Source: Modified from Rodriguez-Bigas et al. with permission from Oxford University Press

- A National Cancer Institute workshop on HNPCC was held in 1996. Out of this meeting, a broader, less-specific set of guidelines was introduced (Table 38.3). These criteria, known as the Bethesda criteria, were formulated to increase sensitivity at the expense of specificity and focused on individual patients.
- It is important to remember that HNPCC is a clinical diagnosis and genetic testing cannot prove a family does *not* have HNPCC. Gene testing can potentially decrease the cost and morbidity of screening and surveillance, help with surgical decisions, stratify patients for chemoprevention, and help patients cope with job and family planning.

Table 38.4. Direct mutation finding (n = 70).

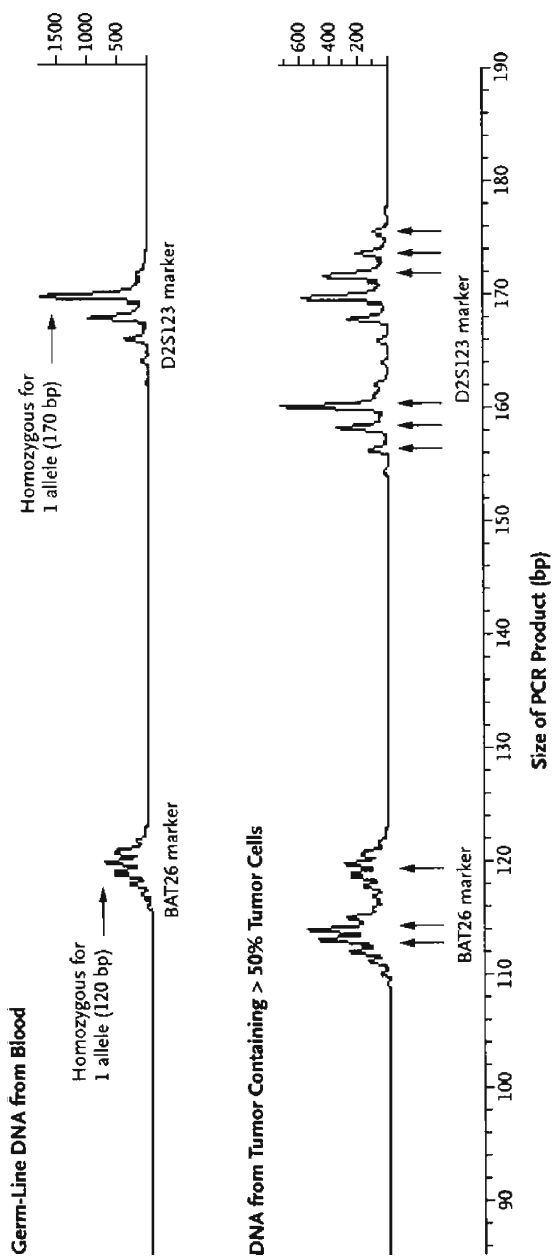
Category	Sensitivity (%)	Specificity (%)
Amsterdam [n = 28]	61	67
Amsterdam II [n = 34]	78	61
Bethesda [n = 56]	94	25
Bethesda (1–3) [n = 44]	94	49

Source: Adapted and reproduced from Syngal et al. with permission from the BMJ Publishing Group

- Table 38.4 compares the sensitivity and specificity of several of the clinical criteria for identifying a pathologic mutation.

G. Genetic Testing

- Gene sequencing of *MSH2* and *MLH1* is now commercially available. This testing may not be covered by insurance companies and the cost is approximately \$1,750.
- Interpretation of gene testing is complicated because mutations are spread diffusely throughout *MSH2* and *MLH1*.
- A data bank of known mutations is kept by the International Collaborative Group of HNPCC now known as InSiGHT.
- Only half of well-characterized HNPCC families have a mutation identified. This suggests that there are other unknown MMR genes or that current techniques are lacking in sensitivity.
- Microsatellite testing can be done on fresh tissue or paraffin blocks.
- A typical test for MSI is seen in Fig. 38.2. If none of the markers are unstable, the tumor is called microsatellite stable (MSS). When only one marker is unstable, this is termed MSI low (MSI-L), and microsatellite high (MSI-H) will have two or more markers positive. When a tumor is MSI-H, then gene sequencing of *MSH2* or *MLH1* can be performed. The cost of MSI testing is \$700.
- Immunohistochemistry is a technique using antibodies to *MSH2* and *MLH1*. This is a standard laboratory procedure to identify which MMR gene is abnormal so that only one MMR gene needs to be sequenced. If immunohistochemistry reveals that one gene is absent, this is presumptive evidence that the patient probably has HNPCC.



- MSI testing of all colorectal cancers may become standard in the future because of its potential relationship to increased survival and response to chemotherapy. This would make testing all colorectal cancers the best medical practice.
- Before genetic testing in HNPCC is done, informed consent must be obtained. Testing should begin with an affected individual (an HNPCC cancer has been diagnosed).

H. Registries

- Once a diagnosis of HNPCC is suspected, a referral to a registry for inherited colorectal cancer or to a cancer center with a high-risk clinic is important.
- A registry has a database or list of families and their members who have a high frequency of colorectal cancer.
- Personnel at the registry consist of a coordinator, oftentimes a genetic counselor, and a physician director.
- The whole focus of the registry is patient care, education of patients, families, and referring physicians, and promotion of collaborative research.
- Registry personnel provide further support for myriad problems such as family stress, health insurance difficulties, and job discrimination.

Fig. 38.2. Detection of MSI with the use of fluorescent labeling of PCR products analyzed in an automatic sequencer. Two markers are analyzed in the same track: the mononucleotide repeat marker BAT26 is shown on the *left*, and the dinucleotide marker D2S123 is shown on the *right*. The upper tracking is from germline DNA from blood. The lower tracing is from DNA extracted from a histologic section of a tumor containing more than 50% tumor cells. For marker BAT26, germline DNA shows a single peak, indicating that the patient is homozygous for this marker (*arrow*). Tumor DNA shows, in addition to the normal allele (*single arrow*), a new allele (*double arrows*) that has lost approximately five nucleotides. This constitutes microsatellite stability. For marker D2S123, germline DNA is homozygous, whereas tumor DNA shows two new alleles (*triple arrows*), one with a loss of approximately ten nucleotides (*left*) and one with a gain of two nucleotides (*right*). Thus, the tumor shows MSI with both markers. All peaks display “stutter” – that is, small amounts of material with a gain or a loss of one or a few nucleotides. This is a normal phenomenon. (Reprinted with permission from Lynch HT, De la Chapelle A. Hereditary colorectal cancer. *N Engl J Med* 2003;348:919–932. Copyright © 2003 Massachusetts Medicine Society. All rights reserved).

- A local registry can be found by accessing the Collaborative Group of the Americas on Inherited Colorectal Cancer at <http://www.cgaicc.com>.

I. Surveillance

- Because of the 80% lifetime risk of developing colorectal cancer, the American Cancer Society recommends colonoscopy every 2 years beginning at age 21, and annual colonoscopy recommended beginning at age 40.
- Because cancers in HNPCC can occur at very young ages and develop within 2 years of a negative colonoscopy, it is important to stress to patients that if they have symptoms, they should be checked regardless of their age and even if they have had a recent negative colonoscopy.
- Colonic neoplasia in individuals with HNPCC seems to develop more rapidly than in average-risk nonaffected individuals. For this reason, many, including the authors, believe that colonoscopy in these individuals should be performed annually rather than every 2 years, even in young individuals.
- Because of the high risk of endometrial cancer in women, annual transvaginal ultrasound to examine the endometrium, preferably with endometrial aspiration, is recommended beginning between ages 25 and 35 years because the increased risk for gynecologic cancer in these patients begins at age 25.
- Should a patient from an HNPCC family be diagnosed with endometrial cancer, they should undergo surveillance colonoscopy before hysterectomy in the event that colonic pathology is present and colonic resection is required at the same surgery.

J. Treatment

- The majority of patients with a diagnosis of HNPCC, based on the finding of an existing colorectal cancer or an advanced adenoma, will be offered colectomy and ileorectal anastomosis (IRA).
- The estimated risk of rectal cancer after colectomy and IRA is, however, 12% at 12 years.

- It is however *essential* that both the patient and physician recognize the need for ongoing annual colonoscopy, because the risk for a metachronous colon cancer in HNPCC is 45%. In the very young patient with a long projected life expectancy or in the patient who is not likely to be compliant with follow-up examinations, total colectomy with stapled ileal pouch anal anastomosis may be the preferred procedure, because it removes nearly all of the at-risk colorectal mucosa.
- In women undergoing colectomy, strong consideration should be given to performing a hysterectomy and bilateral salpingo-oophorectomy in the patient who has completed childbearing, because of the increased risk of both endometrial and ovarian carcinoma.

K. Prognosis

- The survival rate in HNPCC patients with colorectal cancer is better than that of patients with sporadic colorectal cancer when matched for stage and age of onset.

L. Chemoprevention

- Data exist regarding the efficacy of nonsteroidal antiinflammatory drugs (NSAIDs) in reducing the risk of colorectal cancer in the general population, such data are lacking for HNPCC.

Appendix 1: Practice Parameters for the Identification and Testing of Patients at Risk for Dominantly Inherited Colorectal Cancer

Prepared by The Standards Task Force, The American Society of Colon and Rectal Surgeons, The Collaborative Group of the Americas on Inherited Colorectal Cancer

- Take a family history. This is the first step in recognizing families possibly affected by inherited colorectal cancer.

- Document a suspicious pedigree; a family tree based on the recollection of family members is not solid enough evidence. Request medical records to confirm diagnosis.
- Identify criteria for genetic testing. FAP is easily recognized clinically when patients present with more than 100 colorectal adenomas. Fewer adenomas are needed for a diagnosis when a patient is part of an established kindred. The Amsterdam criteria are a way of clinically identifying families with hereditary nonpolyposis colorectal cancer, where an MMR gene mutation can be detected.
- Testing for MSI in tumors is a screen for families with hereditary nonpolyposis colorectal cancer where the clinical pattern of the disease is suggestive but not strong enough to fulfill Amsterdam criteria.
- Offer surveillance to families not meeting the above criteria for genetic testing. Families with more than two first-degree relatives affected with colorectal cancer, especially if one is affected at a young age (<45 years), need to be offered endoscopic surveillance even if genetic testing is not indicated.
- Adhere to all protocols for genetic testing. Institutional review board approval, informed consent, and pretest and posttest counseling are the key elements of genetic testing for inherited colorectal cancer.

Summary. It is hoped that these guidelines will assist in the recognition and management of patients affected by syndromes of inherited colorectal cancer.

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Appendix 2: Practice Parameters for the Treatment of Patients with Dominantly Inherited Colorectal Cancer (FAP and Hereditary Nonpolyposis Colorectal Cancer)

Prepared by The Standards Task Force, The American Society of Colon and Rectal Surgeons

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Section 1. Familial Adenomatous Polyposis

Guideline 1: Treatment Must Be Preceded by Thorough Counseling about the Nature of the Syndrome, Its Natural History, Its Extracolonic Manifestations, and the Need for Compliance with Recommendations for Management and Surveillance; Level of Evidence: III

Dominantly inherited colorectal cancer syndromes show a striking pattern of cancer in affected families. This is because of the high penetrance (penetrance = percent of patients with the mutation who have the disease) and often-severe expression (expression = clinical consequences of the mutation) of the mutations involved. FAP has a penetrance of close to 100%, colorectal cancer occurs at an average age of 39 years, and every affected patient is guaranteed at least one major abdominal surgery. Despite these calamitous prospects, families with FAP adapt well to their disease. Most patients are compliant with recommended treatments, take a keen interest in the syndrome, and have an active role in encouraging relatives to undergo screening. However, when a relative has a bad outcome, either because of severe disease or complications of treatment, family psychology may be affected. Noncompliance, denial, or a refusal to accept recommendations may ensue. The best way of avoiding both bad outcomes and an unfortunate response to them is to provide comprehensive, integrated counseling, support, and clinical services. These sorts of services are best provided through a department, registry, or center with personnel who have experience in managing patients and families with these syndromes.

Guideline 2: Prophylactic Colectomy or Proctocolectomy is Routine. The Timing and Type of Surgery Depend on the Severity of the Polyposis Phenotype and to a Lesser Extent on the Genotype, Age, and Clinical and Social Circumstances of the Patient; Level of Evidence: III

The recommendation for prophylactic colectomy or proctocolectomy in FAP is based on the very high rates of colorectal cancer seen in patients who are not screened. In unscreened patients, the incidence of cancer is more than 60%. Appropriate screening and timely surgery can minimize this. The risk of cancer is not uniform, however, and is related to the

severity of the colonic polyposis. Debinski and coworkers showed the rate of cancer for patients with >1,000 colonic polyps was twice that of patients with <1,000 colonic polyps. In its turn, the severity of the colorectal polyposis is often related to the site of the APC mutation in a family. The “hot spot” mutation at codon 1,309 is in an area of the gene where mutations always cause severe disease. Mutations in codons 3 and 4 are classically associated with attenuated FAP whereas mutations in the part of codon 15 that is 3' of codon 1,450 are usually associated with mild colorectal disease. Mutations in exons 5–15E have a variable colorectal phenotype, where some family members have relatively mild disease and others severe. The important aspects of surgery to consider are its timing, its type, and the technical options to be used.

Timing of Surgery

Even in patients with severe disease, cancer is rare under the age of 20. At-risk family members start screening (either genetic or with flexible sigmoidoscopy) at around puberty. If there is a positive genotype or an adenoma is seen on sigmoidoscopy, colonoscopy is recommended. The risk of cancer of any individual patient can be estimated from the size and number of the adenomas seen on colonoscopy, and surgery planned accordingly. For patients with mild disease and low cancer risk, surgery can be done in mid-teen years (15–18 years). Where there is severe disease, or if the patient is symptomatic, surgery is done as soon as convenient after diagnosis.

Type of Surgery

There are three main surgical options: colectomy and IRA, proctocolectomy with ileostomy (TPC), and proctocolectomy with ileal pouch–anal anastomosis (IPAA). For any of these options, there are choices of technique. The IPAA can be stapled, leaving 1–2 cm of anal transitional epithelium and low rectal mucosa, or it can be hand-sewn after a complete anal mucosectomy. The operation can be done conventionally (i.e., open), laparoscopically, or laparoscopically assisted. The ileostomy may be a regular end stoma or one of the varieties of continent ileostomy (K or T).

Choice of Procedure

TPC is almost never done as a first operation except when a proctocolectomy is required and there is a contraindication to a pouch–anal anastomosis (e.g., a mesenteric desmoid tumor prevents the pouch from

reaching the pelvic floor, a low rectal cancer invades the pelvic floor, or poor sphincters mean inability to control stool).

There is debate among authorities on which of the other two options should be preferred. Some recommend IPAA for all or almost all FAP patients, basing their recommendation on the risk of rectal cancer after IRA and equivalent quality of life after the two operations. Others have shown better functional outcomes after IRA and recommend it for patients with mild colorectal polyposis. However, the risk estimates of rectal cancer that are an overriding concern for the proponents of universal IPAA are based on data collected before restorative proctocolectomy was an option and may well be overestimates, especially when applied to patients with mild disease. The risk of rectal cancer after IRA is strongly related to the severity of colorectal polyposis at presentation, and IRA is a reasonable option in mildly affected patients (<20 rectal adenomas, <1,000 colonic adenomas). Retrospective data show that such patients have a very low risk of rectal cancer and include all those with attenuated FAP. Bowel function is usually good after IRA, the operation is simple, and complication rates are relatively low. Bowel function after a stapled IPAA is almost as good as with an IRA, and the anastomosis is usually safe enough to allow consideration of the option of avoiding a temporary ileostomy.

There is no argument that patients with severe rectal (>20 adenomas) or colonic (>1,000 adenomas), or those with a severely dysplastic rectal adenoma, a cancer anywhere in the large bowel, or a large (>3 cm) rectal adenoma should have a primary IPAA. A stapled IPAA is associated with a risk of anal transitional neoplasia in 30% of patients, although if serious neoplasia occurs (high-grade dysplasia or carpeting of the mucosa), the transitional zone can usually be stripped transanally and the pouch advanced to the dentate line. Even mucosectomy and hand-sewn IPAA is associated with anal neoplasia, although at a lower rate. The disadvantage of anal mucosectomy is worse function and increased complication rates. Both IRA and IPAA require lifelong surveillance of the rectum or pouch, because both are at risk of developing adenomas.

Choice of Technique

Mobilization of the colon using minimally invasive techniques such as laparoscopy or a Pfannenstiel incision is ideal for performing colectomy in children, because it minimizes the trauma of the surgery and the pain of the incisions. Its cosmetic result is appealing and it allows an early return to full activities. Whether minimally invasive techniques lower the risk of postoperative intraabdominal desmoid

tumors is unknown, but the concept is attractive. A preoperative erect abdominal X-ray will usually show the position of the flexures and indicate whether use of a Pfannenstiel incision for mobilizing the colon is feasible.

Guideline 3: Lifetime Follow-up of the Rectum (after IRA), Pouch (after IPAA), and Ileostomy (after TPC) is Required; Increasing Neoplasia in the Rectum is an Indication for Proctectomy; Level of Evidence: III

The combination of a germline APC mutation, stasis of stool, and glandular epithelium is potent at producing epithelial neoplasia. Adenomas and carcinomas have been described in the rectum, the ileostomy, and the ileal pouch itself, with the risk and severity of neoplasia increasing with time. The risk of severe neoplasia is mainly determined by the position of the mutation in the gene, as reflected by the severity of the polyposis. Severely affected patients have such a high risk of rectal cancer after IRA that subsequent proctectomy is almost routine and initial IPAA is to be preferred. Yearly endoscopic surveillance of the bowel after the index surgery for FAP is standard. Two-thirds of patients undergo spontaneous regression of rectal polyps after IRA, an effect that lasts 3–4 years. Subsequent surveillance will give a picture of the stability of the rectal mucosa. Small (<5 mm) adenomas can be watched, although random biopsies are done to exclude severe dysplasia. Increasing number and size of adenomas are indications for more frequent surveillance, and adenomas >5 mm should be removed cleanly with a snare. Repeated fulguration of rectal polyps over many years can cause dense scarring that makes cancers flat and hard to see, and rectal dissection during proctectomy can be very difficult. Chronic rectal scarring makes rectal biopsy difficult, because the forceps tend to “bounce off” the scarred mucosa. Furthermore, scarring leads to reduced rectal compliance, increased stool frequency, and a tendency to seepage and incontinence. Severe dysplasia, or villous adenomas >1 cm, are indications for proctectomy. Proctoscopy is best done with a video endoscope, because comfort is enhanced and the view is better. Excellent preparation and a good view are essential to pick up early cancers that can be flat and subtle.

Sulindac (Clinoril®; Merck & Co., Inc., West Point, PA), either by mouth or by suppository, is effective in making polyps disappear. Celecoxib reduces polyp load, as does the sulindac metabolite exisulind. However, cancers have been reported in cases where sulindac had been

effective in minimizing rectal polyps in the rectum of FAP patients who had had IRA, and these anecdotal cases make the long-term use of chemoprevention for rectal polyposis suspect. If it is used in patients who cannot tolerate rectal polypectomy, or who are unwilling or unable to have a proctectomy, close surveillance (every 6 months) with random biopsies to look for severe dysplasia is needed.

There have been at least three recent reports describing adenomas in ileal pouches, with a frequency and severity that depend on time from the initial surgery. Two prospective studies have independently calculated the rate of pouch polyposis as 42% at 7 years. There have been anecdotal reports of large adenomas and more than 100 adenomas in an ileal pouch. In general, these have been treated successfully by oral sulindac, in a dose of 150–200 mg twice daily. The full impact of pouch polyposis will not be obvious until the cadre of FAP patients with ileal reservoirs reaches a mean follow-up of 20 years. This is the time to most ileostomy cancers, and to the highest rates of rectal cancers after IRA.

Guideline 4: Use of Chemoprevention as Primary Therapy for Colorectal Polyposis is Not Proven and is Not Recommended; Level of Evidence: I–II

Sulindac, celecoxib, and exisulind are nonsteroidal antiinflammatory drugs that have been shown to reduce the number and size of colorectal adenomas in patients with FAP. Although many studies are short-term, two show effectiveness of sulindac maintained over 4 years. These studies were in patients who had undergone colectomy and IRA. A recent randomized, placebo-controlled, double-blind study of sulindac in genotype-positive, phenotype-negative FAP patients failed to show any effect of sulindac on polyp progression. Furthermore, there have been case reports of cancers occurring in patients with sulindac-mediated ablation of polyps, and the only report of a permanent, complete resolution of rectal polyposis comes from Winde and coworkers who used sulindac suppositories. The effect on polyps is dependent on continued compliance, and there are significant side effects with each medication. These medications should not be used as an alternative to surgery, except in patients with pouch polyposis or in selected patients with rectal polyposis after IRA in whom surgery is risky or unwanted by the patient. In these groups of patients, close surveillance (proctoscopy or pouchoscopy every 6 months) is indicated.

Guideline 5: Treatment of Duodenal Adenomas Depends on Adenoma Size and the Presence of Severe Dysplasia. Small Tubular Adenomas with Mild Dysplasia Can Be Kept under Surveillance, but Adenomas with Severe Dysplasia Must Be Removed; Level of Evidence: II–III

The incidence of duodenal adenomas in FAP patients is in the range of 80–90%. All FAP patients therefore undergo screening esophagogastroduodenoscopy starting at age 20 years. The risk of invasive cancer developing in a duodenal adenoma, or in the duodenal papilla, is considerably higher than that for the average population, but in absolute terms it is still low. The aim of endoscopy is not to eradicate all neoplasia but to make sure that there is no severe dysplasia. Studies of the natural history of duodenal neoplasia in FAP show that rapid progression of dysplasia is uncommon, occurring in only 11% of cases over a mean follow-up of 7 years. Prospective, randomized studies have shown that treatment with nonsteroidal anti-inflammatory drugs is ineffective in treating duodenal adenomas, although a recent report indicates that celecoxib may have some effect. If they are not medically treated, low-risk adenomas (small, tubular, low-grade dysplasia) may be biopsied and left alone. High-risk adenomas (>1 cm, villous) are treated. Adenomas with confirmed high-grade dysplasia must be removed. As endoscopic or even transduodenal excision or destruction is ineffective in the long term; duodenectomy has to be considered for duodenal adenomas with high-grade dysplasia after the diagnosis has been confirmed on review by an experienced gastrointestinal pathologist.

Guideline 6: Duodenectomy or Pancreaticoduodenectomy is Recommended for Patients with Persistent or Recurrent Severe Dysplasia in the Papilla or Duodenal Adenomas; Level of Evidence: III

A review of literature reporting treatment of advanced duodenal adenomas shows that recurrence is almost guaranteed unless the duodenum is removed. Transduodenal polypectomy or endoscopic polypectomy may be temporarily effective, but does not offer a permanent cure. The results of pancreas-preserving duodenectomy or pancreaticoduodenectomy for benign or early malignant disease are good, with low recurrence and acceptable morbidity. The outcome of surgery for established cancer is not good, with recurrence and death the usual outcome. Although the risk of duodenal/periampullary cancer is relatively low in patients with FAP,

patients with persistent high-grade dysplasia in the duodenum or papilla are a high-risk group. Careful surveillance is needed, and conservative surgery or endoscopic therapy may be tried. If the severe dysplasia returns or persists, consideration must be given to duodenectomy.

Guideline 7: Surgery for Intraabdominal Desmoid Tumors Should Be Reserved for Small, Well-defined Tumors with a Clear Margin; Abdominal Wall Desmoid Tumors Should Be Excised Whenever Possible; Level of Evidence: III

Desmoid tumors are histologically benign overgrowths of fibroaponeurotic tissue occurring rarely in the general population but in 12–17% of patients with FAP. In the general population, desmoids are usually found in limbs or limb girdles; in FAP, desmoids are usually (80%) intraabdominal and often (80%) present within 2–3 years of an abdominal surgery. Intraabdominal desmoid tumors usually involve the mesentery of the small bowel, where they are intimately involved with the mesenteric vessels. They tend to infiltrate diffusely, kink adjacent bowel loops, and may obstruct the ureters. Attempts at excision are often unsuccessful, involve removal of a variable length of small intestine, and are associated with a high morbidity and a high recurrence.

Intraabdominal desmoid tumors may affect prophylactic colorectal surgery by limiting the length of the small bowel mesentery. This will sometimes prevent an IPAA. The most common scenario in which this occurs is in patients with Gardner's variant of FAP who need proctectomy after a previous ileorectal anastomosis. Patients need to be warned about this possibility and the likelihood of ileostomy before undergoing the surgery. The second most common site for desmoids in FAP is in the abdominal wall. Abdominal wall desmoid tumors are easier to excise than intraabdominal tumors, recurrence rates are lower, and the morbidity associated with excision is less. They should be excised with a 1-cm margin. It is often necessary to use mesh to cover the defect in the abdominal wall.

Guideline 8: Intraabdominal Desmoid Tumors Involving the Small Bowel Mesentery Are Treated According to Their Rate of Growth and Their Presentation. Clinically Inert Tumors Should Be Treated with Sulindac or

Not Treated at All. Slowly Growing or Mildly Symptomatic Tumors May Be Treated with Less Toxic Regimens Such as Sulindac and Tamoxifen or Vinblastine and Methotrexate. Rapidly Growing Tumors Need Aggressive Therapy with Either Very High-dose Tamoxifen or Antisarcoma-type Chemotherapy. Radiation is an Option if Collateral Damage is Not a Big Concern; Level of Evidence: III

Intraabdominal desmoid tumors vary in their clinical behavior from aggressive, relentless growth to indolent, asymptomatic coexistence. There is no single, predictably effective way of managing intraabdominal desmoids. Evidence suggests that sulindac is partially effective but that a response to this nonsteroidal antiinflammatory agent may not be noticeable for up to 2 years. The role of high-dose antiestrogens is uncertain, with one report describing good results in aggressive desmoids with tamoxifen in a dose of 120 mg/day. Toremifene, a more potent antiestrogen than tamoxifen, has some effect on desmoid tumors but seems to work better in non-FAP desmoids than FAP. A pilot study of the antifibrosis agent pirfenidone resulted in some modest responses. Most aggressive desmoids receive chemotherapy, and there are two regimens reported. The combination of vinblastine and methotrexate has low toxicity and produces some responses. Non-FAP desmoids seem more likely to respond to this combination, although no prospective studies have been done. Antisarcoma therapy such as doxorubicin and dacarbazine is much more toxic but seems to be more effective for rapidly growing intraabdominal desmoid tumors associated with FAP. Radiation is effective in destroying tumors but its effect on the small bowel can be disastrous, causing fistulas and necrosis.

Intraabdominal desmoids that are not growing may be treated by sulindac alone. If they are growing slowly or causing symptoms, it is reasonable to add tamoxifen in a dose range of 80–120 mg/day. The dose should be gradually increased to these levels over a few weeks. If the tumor continues to grow, chemotherapy is appropriate. Really rapid growth is an indication for antisarcoma therapy, whereas a slower growth rate means vinblastine/methotrexate can be tried. A recent report of successful intestinal transplantation after resection of abdominal desmoids reinforces the extent of the surgery needed to remove them, but also offers some hope for tumors that fail to respond to anything else.

Section II: HNPCC

Guideline 1: Treatment Must Be Preceded by Thorough Counseling about the Nature of the Syndrome, Its Natural History, Its Extracolonic Manifestations, and the Need for Compliance with All Recommendations for Management and Surveillance; Level of Evidence: III

Hereditary nonpolyposis colorectal cancer is a dominantly inherited syndrome attributed to an inactivating mutation in one of the human DNA MMR genes. The syndrome is more complex than FAP because more genes are involved, penetrance is less complete, and expression is more varied. Furthermore, the clinical criteria defining HNPCC are arbitrary and not particularly accurate, and the yield of testing for germline mutations is lower than for FAP. HNPCC has a penetrance of at least 80%, and colorectal cancer occurs at a mean age of 46 years. Affected patients usually have at least one surgery and are committed to lifelong surveillance of several organs. Careful counseling is necessary to allow patients and their families to understand the implications of these complexities.

Guideline 2: When Patients with HNPCC as Defined by Genotype or Compliance with Amsterdam I Criteria Are Diagnosed with More Than One Advanced Adenoma or a Colon Cancer, They Should Be Offered the Options of Prophylactic Total Colectomy and IRA or Hemicolectomy Plus Yearly Colonoscopy. The Choice of IRA Assumes the Anal Sphincter and Rectum Function Normally; Level of Evidence: III

When patients known to be affected with HNPCC are diagnosed with advanced neoplasia, they can be offered a choice of conventional partial colectomy with surveillance of the remaining large bowel or total colectomy with rectal surveillance. Surveillance involves colonoscopy or proctoscopy (after IRA) every 1–2 years for life. There is evidence that cancers can occur in HNPCC within 2 years of a negative colonoscopy, but that cancers found on screening examinations performed with a 3-year interval can be cured. The risk of metachronous cancer after conventional treatment of an index cancer is 45% in patients with HNPCC,

high enough to make prophylactic colectomy a reasonable option. The downside of colectomy and IRA lies in its effect on bowel function and quality of life. In a study of patients having IRA for FAP, quality of life was maintained, although stool frequency increased. These patients were younger than typical HNPCC patients having surgery, but even older patients can do well after IRA provided their anal sphincters and rectums are normal. The outcome of partial colectomy and effective surveillance can be similar to that of colectomy and IRA in terms of minimizing metachronous cancers. Likely patient compliance, the anticipated quality and frequency of colonoscopy, and the relative costs and reimbursement of the two options therefore influence the choice. Even after IRA, the risk of rectal cancer is 12% in 12 years, so continuing surveillance of the rectum is mandatory.

HNPCC patients diagnosed by genotype with a normal colon are also candidates for prophylactic colectomy. If penetrance of the mutation in the family approaches 100%, this should be strongly considered. There have been two attempts to discern the relative benefits of surgery vs. surveillance using decision analysis methods. Syngal and coworkers showed that prophylactic colectomy/proctocolectomy performed at the time of diagnosis led to a greater benefit in years of life expectancy gained than surveillance, but that this benefit decreased the longer surgery was delayed. Furthermore, if prophylactic surgery is performed at the time of diagnosis of a cancer, the gain in life expectancy is only 4 days for colectomy/IRA and 6 days for proctocolectomy. The advantage of surgery is further reduced if the gain in years is discounted. When the outcome of the analysis was quality-adjusted life years (QALYs), surveillance was the most effective strategy, with a gain of 14 QALYs compared with no surveillance, 3.2 QALYs compared with prophylactic proctocolectomy at diagnosis of HNPCC, and 0.3 QALYs compared with colectomy. A similar phenomenon was seen when comparing colectomy with proctocolectomy. Use of QALYs improved the relative value of the lesser operation. In the decision analysis published by Vasen and coworkers prophylactic colectomy at age 40 conferred an increase in life expectancy over surveillance of 8–18 months. In the same scenario, Syngal et al. calculated a benefit for surgery of 9.6 months. These analyses do not take costs into account, however, and they assume a level of compliance and quality of endoscopy that may not be realistic. In the absence of a randomized comparison of surveillance and surgery, both options must be explained to the patient and individual circumstances, such as comorbidity, gastrointestinal physiology, likely compliance, and ease of colonoscopy, taken into account.

Guideline 3: Patients with HNPCC Who Have a Rectal Cancer Should Be Offered the Options of Total Proctocolectomy and IPAA or Anterior Proctosigmoidectomy, Assuming that the Sphincters Can Be Saved; Level of Evidence: III

Rectal cancer is an uncommon index cancer in patients with HNPCC. Surgical options, assuming the sphincters can be saved, are restorative proctocolectomy (with IPAA) and anterior resection. There are substantial differences in bowel function after these two procedures, but the risk of metachronous colon cancer after a primary rectal cancer is not known. The decision to preserve the proximal colon and commit to a program of intensive surveillance is therefore based on likely compliance of the patient with surveillance and the likely impact of the surgery on quality of life.

Guideline 4: Female Patients with HNPCC and Uterine Cancer in Their Family May Be Offered Prophylactic Hysterectomy Once Their Family is Complete or When Undergoing Surgery for Other Intraabdominal Conditions; Level of Evidence: III

The lifetime risk of uterine cancer in HNPCC is 42%, and although it is most common in families with hMSH6 mutations, it is also associated with hMSH2 and hMLH1 mutations. Screening for endometrial cancer in females with HNPCC has been shown in at least one study to be ineffective in detecting cancer, and so where uterine cancer is a feature in families, affected females should be offered prophylactic hysterectomy. Oophorectomy should be done at the same time, because the risk for ovarian cancer associated with HNPCC is high and in a multi-institution review of HNPCC-associated ovarian cancer, synchronous endometrial cancer was present in 21.5% of 80 patients.

Brown and coworkers have shown that an increased risk for gynecologic cancer begins by age 25 years. Although the mean age at gynecologic cancer in their series of 67 affected females (43 uterine, 24 ovarian) was 49.3 years, five gynecologic cancers were diagnosed before age 35. The timing of prophylactic hysterectomy and oophorectomy is therefore debatable. It is tempting to offer surveillance during the childbearing years and delay surgery until the patient has had a chance to have her family. Until more data are available, this is the best option. Surgery can be done at the

time of another abdominal surgery, or as a separate operation once the patient's family is complete.

Levels of evidence

Level I: Evidence from properly conducted randomized, controlled trials.

Level II: Evidence from controlled trials without randomization, or cohort or case-control studies or multiple times series, dramatic uncontrolled experiments.

Level III: Descriptive case series or opinions of expert panels.

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39. Inflammatory Bowel Disease: Diagnosis and Evaluation

A. Epidemiology

- The causes of ulcerative colitis (UC) and Crohn's disease (CD) are unknown.
- Variations in diagnostic criteria, definitions of disease, and biases resulting from surveys done in tertiary care specialty centers, make universal conclusions difficult. However, some general statements can be made using such data that relate to disease prevalence and associated risk factors (Table 39.1).
- Inflammatory bowel disease (IBD) is found most frequently in the more temperate climates of North America and Europe. Studies from those regions show prevalence rates much higher than those in Asia, South America, or Africa.
- It is generally recognized that both CD and UC have been increasing in incidence to a remarkable degree over the past 20–30 years with twofold to tenfold increases depending on population and region studied.
- CD usually occurs in the third decade of life, whereas chronic UC in the fourth decade.
- Although originally thought to be relatively rare in blacks, more recent case control studies in the United States suggest a similar incidence to whites, although Africa itself has a very low incidence of IBD.
- There is great variability in the incidence of IBD in Jews around the world, but nonetheless seems to be consistently higher than that found in the non-Jewish population in most countries studied.

Table 39.1. Epidemiologic and associated risk factors for IBD.

Epidemiology

Race/ethnicity

Whites and blacks > Hispanic, Native American, Asian

Jews > non-Jews

Geography

Northern climates > Southern

Scandinavia, North America, Europe > Asia, Africa, South America,

Japan, Spain

Sex

CD: F > M

UC: M > F

Age at greatest incidence

CD: third decade

UC: fourth decade

Residence

Urban > rural

Indoor > outdoor

Risk factors

Diet

Sugar consumption, ↑ CD

ETOH, ↓ UC

Margarine, no association

Coffee, no association

Fiber, no association

Food additives, no association

Childhood diarrheal illness ↑ IBD

Higher socioeconomic status ↑ IBD

Oral contraceptive use ↑ IBD

Cigarettes ↑ CD

↓ UC

Appendectomy ↓ UC

NSAIDs ↑ symptoms IBD

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- There is very little evidence that a specific dietary factor causes IBD although increased sugar consumption is associated with CD and alcohol intake is inversely related to chronic UC.
 - Childhood diarrheal illness, oral contraceptive and nonsteroidal antiinflammatory (NSAIDs) use are measurable risk factors for IBD, with NSAIDs reported as precipitating relapse in patients with inactive disease.
 - Smoking has been clearly shown to worsen CD, with increased risk of developing the disease de novo and increased risk of

recurrence after surgical resection. Conversely, smoking is protective for chronic UC, as is prior appendectomy.

- There is clearly a genetic predisposition to IBD. It is probably stronger in CD than UC. If an individual has IBD, there is a 10–20% risk of having another family member with IBD.
- Genetic techniques of analysis, including linkage and transmission disequilibrium testing using both sporadic and family registries of IBD patients have identified seven areas of the human genome (on chromosomes 1, 5, 6, 12, 14, 16, 19) that are significantly relevant to disease susceptibility, underscoring the complexity of the genetic predisposition to IBD. It seems that no one gene locus is responsible for disease, but that many gene products have a role in the illness.
- The strongest genetic linkage is with CD and mutations in a locus on chromosome 16 which has now been identified as being in the *NOD2/CARD15* gene. This gene is involved in innate host defense against enteric bacteria and mutations in this gene are believed to be responsible for approximately 15–30% of patients with CD.
- Its discovery represents a breakthrough in the conceptualization of disease pathogenesis in IBD. Both the epidemiology and now the molecular genetic evidence furthers the concept that IBD is the consequence of environmental exposure to a causative agent in a genetically susceptible individual.

B. Signs and Symptoms

Gastrointestinal Symptoms

Crohn's Disease

- CD can affect any portion of the gastrointestinal (GI) tract from the mouth to the anus. It is usually discontinuous, usually involving several areas of the bowel at once, with sections of normal intestine interposed. The inflammation of CD involves the entire bowel wall, from mucosa to serosa and even into adjacent structures. These features are responsible for its presenting symptomatology.
- The most common complaints of any patient with CD are abdominal pain and diarrhea, being found in more than 75%

of patients. Weight loss, fever, and bleeding are present in approximately 40–60% of patients, whereas anal symptoms of abscess and/or fistula occur in 10–20% of patients.

- CD is most frequently found in the ileocecal region, making up approximately 40% of patients. Abdominal pain usually correlates with disease in this region.
- Colonic disease is found in approximately 30% of patients and most directly correlates with symptoms of diarrhea and bleeding.
- The remaining 30% of patients have disease confined to the small bowel proximal to the terminal ileum and correlates with abdominal pain, bloating, and a sense of postprandial nausea especially if partial obstruction caused by inflammation or strictures occurs.
- Anal disease is typically associated with patients having the terminal ileal and colonic distributions of disease.
- Clinical severity of symptoms is widely variable, because CD typically has a waxing and waning course characterized by periods of disease activity interspersed with periods of remission.
- Prolonged quiescence is found in approximately 10–15% of patients. The only useful predictor of future disease activity is past clinical behavior.

Ulcerative Colitis

- The inflammation of UC characteristically starts in the rectum and extends proximally.
- Clinical symptoms relate to the extent and location of disease. Thus, rectal disease results in increased stool frequency, hematochezia, and tenesmus. Diarrhea is a frequent symptom and with tenesmus can result in incontinence, especially at night.
- Despite severe rectal inflammation, constipation with a sense of incomplete evacuation can be a complaint in 20–25% of patients, but blood and mucus are nearly always present.
- With more proximal involvement, abdominal complaints increase including left lower quadrant pain and pain associated with peristalsis or stool evacuation.
- With increasing severity and extent of disease, nausea, vomiting, and weight loss ensue.

- Weight loss is attributed both to the loss of serum proteins through the diseased mucosa and the reluctance of the patient to eat in order to avoid exacerbation of symptoms.
- The development of systemic signs of illness such as tachycardia, fever, and increasing fluid requirement bespeaks severe disease.
- High-dose steroids may disguise worsening abdominal complaints, including peritonitis in such circumstances and should not divert the clinician from recognizing the gravity of the development of such symptoms and signs.
- So-called “toxic megacolon” is a moniker that should be discarded, because severe life-threatening colitis may occur without colonic dilatation and urgent surgical intervention should be based on the triad of toxicity defined by tachycardia, fever, and increased white blood cell count.

Extraintestinal Manifestations

Musculoskeletal

- The most common non-GI complaints in IBD patients relate to the musculoskeletal system. Osteopenia and osteoporosis are very common, in part because of therapeutic steroid use, occurring in as many as 50 and 15% of IBD patients, respectively.
- One study found a 40% increased risk of bone fractures in IBD patients.
- The arthropathies associated with IBD are found in up to 30% of patients and are divided into two broad categories.
 - Peripheral arthritis usually affects multiple small joints and has little relation to GI disease activity.
 - Axial arthritis (ankylosing spondylitis) is associated with certain human leukocyte antigen subtypes (B27) and is found in approximately 5% of both CD and UC patients. Its severity usually parallels disease activity.
- Recently, anti-TNF therapies have been shown to be effective in both CD and the arthropathy of IBD.

Cutaneous

- Pyoderma gangrenosum and erythema nodosum occur in approximately 0.5–5% of patients with IBD. These, as well as oral lesions such as aphthous stomatitis and pyostomatitis

vegetans, are more frequently associated with CD than UC and usually parallel underlying GI disease activity.

Hepatobiliary

- Primary sclerosing cholangitis (PSC) has a reported incidence of approximately 3% in both CD and UC patients. It may present independently of intestinal disease activity, and colectomy in UC patients does not affect progression of liver disease. The presence of PSC in the UC patient increases the risk for malignant disease in both the colon and hepatobiliary system.
- Several studies have suggested an increased incidence of gallstones in IBD, especially CD although this is disputed. The mechanism is presumed to be attributable to an altered enterohepatic biliary circulation caused by ileal disease.

Ophthalmologic

- Iritis, uveitis, and episcleritis can affect 2–8% of UC and CD patients and are generally unrelated to disease activity. Iritis and uveitis present as blurred vision, eye pain, and photophobia and require prompt treatment to avoid scarring and even blindness.
- Episcleritis is typically less threatening and is characterized by scleral injection, burning, and tearing.

Coagulopathy

- There is an identified increased risk of deep venous thrombosis, mesenteric thrombosis, and pulmonary embolism in IBD patients that is not explained simply by increased hospitalization and surgery.
- Decreased protein S and antithrombin III levels attributed to mucosal loss and increased levels of acute phase reactants including factors V and VIII have been implicated.

C. Disease Severity Assessment

Crohn's Disease

- The CD activity index (CDAI) is the most frequently used method for quantitating disease severity in CD (Table 39.2).

Table 39.2. The CDAI.

Item	Data collected	Calculation	Weighing factor
No. of liquid stools	7-day diary	Sum of 7 days	2
Abdominal pain	0–3 scale, 7-day diary	Sum of score for each day	5
General well-being	0–4 scale, 7-day diary	Sum of score for each day	7
Symptoms ^a	At clinic visit	Sum (6 total possible)	20
Lomotil use	7-day diary	Yes = 1, No = 2	30
Abdominal mass	At clinic visit	None = 0, questionable = 2, definite = 5	10
Hematocrit (HCT)	At clinic visit	M (47 subtract patient's HCT) F (42 subtract patient's HCT)	6
Weight	At clinic visit	% below ideal weight	1

^aSymptoms include presence or absence of each of arthritis/arthralgia, iritis/uveitis, erythema nodosum/pyoderma gangrenosum/aphthous stomatitis, anal fissure/fistula/abscess, other fistula, or temperature >100°F

- It is generally accepted that a total score less than 150 points is quiescent disease, whereas more than 450 is severe, active disease.
- Relapses are defined as a score increasing to more than 150 or an increase of 100 points over baseline.
- Drawbacks of the CDAI includes a reliance on subjective complaints and requirement of patient diaries defining symptomatology.

Ulcerative Colitis

- The benchmark study evaluating the effect of cortisone on UC by Truelove et al. in 1955 also described disease activity; it is still the most frequently used clinical assessment tool for severity assessment in UC (Table 39.3).
- This index also does not take into account variability in the anatomic extent or observed severity of disease within the colon. Modern clinical studies requiring disease assessment will thus often use a variation on the Truelove and Witts classification which will include additional criteria based on colonoscopic appearance and possibly pathologic severity as well.

Table 39.3. Truelove and Witts UC activity index.

	Mild	Severe
Bowel frequency/24 h	<4	>6
Blood in stool	+	+++
Fever	Absent	>37.5
Pulse	<90	>90
Hgb	>75% nL	<75% nL
ESR	<30	>30

D. Evaluation

Radiology

- The diagnosis of IBD depends on the triad of clinical presentation, radiologic work-up, and histopathology of tissue biopsy. Thus, radiologic studies are critical in the evaluation of the patient with suspected or confirmed IBD.

Plain X-rays

- Plain abdominal radiographs can show signs of obstruction, perforation (free air), and at times thickening of the bowel or loss of haustral markings.
- Chronic colitis may result in an ahaustral, tube-like colon that can be seen with air contrast.

Contrast Radiologic Studies

- Contrast studies will more frequently be used in the patient with CD than UC because of its predisposition for small bowel involvement.
- For the colitic patient, whether caused by CD or UC, colonoscopy is usually the preferred study, frequently obviating the need for barium enema.
- Colonic contrast studies in the CD patient can show segmental disease, strictures, and fistulas. Reflux into the terminal ileum occurs in approximately 85% of patients and can reveal ileal disease more effectively than small bowel follow through because of less superposition of intestinal loops.
- When fistulas or near obstructing strictures are suspected, a water-soluble dye, such as Gastrografin is preferred. This minimizes the

complications associated with possible extravasation of the dye if a fistula or intestinal perforation is present or subsequent impaction of barium if passed proximal to a stricture.

- Not infrequently in the patient with CD, an unsuspected rectal fistula tracking to a diseased terminal ileum is found on rectal contrast study. Such a fistula can be easily missed on colonoscopy because it originates with the diseased terminal ileum and the rectum infrequently has other evidence of CD.
- The difficulty of reaching the small bowel using fiberoptic instruments results in the common use of small bowel contrast studies to assess the degree of CD involvement of the small bowel. Small bowel series can effectively show areas of stricturing and upstream dilatation but may be difficult to perform or interpret because of slow intestinal transit from strictures, overlying loops of bowel, and pain associated with compression spot views.
- Enteroclysis is preferred over simple small bowel follow through, although its need for the placement of a naso-intestinal tube makes patient cooperation and satisfaction with this study much less.
- GI contrast studies surpass computed tomography (CT) for detecting enteroenteric and enterocolic fistulas.
- Sinography or fistula-gram can be used to delineate the path or origin of fistulous disease in CD patients, whether involving the abdominal wall or perineum. Such studies can also be done via the drainage catheter after percutaneous drainage of an abscess to document intestinal communication and, again, should be done with water-soluble contrast. Such anatomic localization assists in directing subsequent surgical care (especially when fistulous disease involving the urinary tree is found) and assessing response to therapy.
- Retrograde studies through a stoma, especially an ileostomy, can provide very good evaluation for disease. The effectively foreshortened intestine allows better delineation of disease with less overlapping bowel loops and better double-contrast definition.

Computed Tomography

- CT scanning is especially useful for delineating enterovesical or colovesical fistulas and scans should be obtained before

administering intravenous contrast, as contrast originating from the bowel will be seen in the bladder defining the fistula.

- Air within the bladder without prior instrumentation is also a very sensitive sign defining the presence of a fistula.
- The great advantage of CT is its ability to look at the entire thickness of the intestine and its adjacent structures. Thus, thickened intestine, phlegmon, abscess, air in extraintestinal structures, and fistula formation are signs of CD that can be found on CT scan.
- Percutaneous drainage of abscess collections done under CT guidance can also be performed.

Magnetic Resonance Imaging

- MRI differs from CT, however, in that the intensity of T2-weighted signals from areas of disease correlate with severity of inflammation, especially after gadolinium administration. Such signal intensity in both the mesentery and bowel decreases with resolution of acute inflammation and may hold promise for monitoring the response of patients to medical therapy.
- MRI's value in defining perineal disease in the CD patient approaches, and may exceed, that achieved with examination under anesthesia.
- Intravenous injection of gadolinium highlights the fistula tract, and combined with MRI's ability to accurately define soft tissue anatomy, can result in remarkable delineation of disease.
- MRI testing is expensive, however, and is probably unnecessary in the conventional perineal CD patient because an examination under anesthesia performed by a competent surgeon is usually as accurate and can also provide simultaneous treatment.
- However, MRI is finding a role in reassessing the failed patient for unrecognized pathology and, more recently, in defining whether medical treatment with infliximab has truly healed a patient's fistulous disease.

Ultrasound

- The role of ultrasound in IBD is presently very limited.
- Intrarectal ultrasound can be used to document and map perianal fistula formation by injecting a solution of hydrogen peroxide into the external opening. The resulting bubbles are easily seen on ultrasound as they outline the path of the fistula

tract. However, such uncomfortable and operator-dependent techniques of fistula assessment have been largely replaced by MRI scanning (see above).

Nuclear Medicine

- The injection of radionuclide-labeled white cells allows subsequent scintigraphic imaging of the abdominal organs and is increasingly being used as a technique to visualize actively inflamed bowel. Most techniques use indium labeling of autologous leucocytes that are harvested from the patient, labeled, and then reinjected. Indium has the advantage of a long half-life that allows scanning at 6, 12, and 24 h with any visualized bowel activity as being abnormal.
- A fixed area of activity suggests an abscess. Newer techniques using technetium-99m-hexamethylpropyleneamine oxime (HMPAO) provide for better image quality because of their relatively selective labeling of granulocytes and also result in a lower radiation dose to the patient.
- Some studies using this tracer have shown very high sensitivity rates, but specificity is less because of its inability to differentiate between IBD and infectious causes of disease.
- The advantage of such radionuclide scanning techniques relate mostly to their ability to differentiate between inflamed vs. quiescent disease and their use will probably increase as newer labeling agents are devised.

E. Endoscopy

- Colonoscopy has strongly influenced the diagnosis and evaluation of the patient with IBD. It is the study of choice for the patient with suspected UC because it can directly visualize the entire extent of the disease process.
- It is similarly relevant for CD when involving the colon, and can also be used to intubate and evaluate the terminal ileum.
- Most significantly, colonoscopy provides biopsies, which allows a tissue diagnosis to be made by the pathologist.
- There are numerous indications for colonoscopy in the IBD patient (Table 39.4) and it has a significant role in both medical and surgical treatment.

Table 39.4. Indications for colonoscopy in IBD.

Diagnosis:	Gross appearance Tissue biopsy
Disease extent	
Disease complications:	Fistulas Stricture Bleeding
Preoperative “staging”	
Monitor response to therapy	
Stricture management:	Biopsy Dilatation
Cancer surveillance	

Table 39.5. Gross (colonoscopic) features of colitis.

	UC	CD
Early	Edema	Aphthous ulcers
	Confluent erythema	Patchy, asymmetric erythema
	Loss of vascular markings	Anal disease: Waxy skin tags Linear fissures
Intermediate	Granularity	Linear serpiginous ulcers
	Bleeding	Pseudopolyps
	Micropurulence	Anal disease: Fistulas Abscesses
Advanced/late	Ulcerations, transmural disease	Confluent ulcers
	Pseudopolyp formation	Deep “bear claw” ulcerations
	Purulence	Strictures
	Variable thinning/thickening of colon	Mucosal bridging
	Mucosal bridging	

- The gross appearance of the colon as seen on colonoscopy can frequently differentiate between CD and UC (Table 39.5).
- Although studies exist suggesting it can be safely done in the severely colitic patient, the risk of perforation caused by insufflation, biopsy, or mechanical bending of the scope is generally

acknowledged as being high and thus colonoscopy is generally avoided in the acute setting.

- The flexible sigmoidoscope is conveniently used for the evaluation of the unsedated office patient, but is limited by its 65-cm length to visualizing the colon up to approximately the splenic flexure. This can often be adequate, however, and in the case of UC, definitive. In the patient with typical presenting symptoms of bloody diarrhea and tenesmus, a flexible sigmoidoscopy with biopsies and stool culture for pathogens and ova/parasites may complete the work-up and make the diagnosis.
- There is an increasing experience with through-the-scope (TTS) pneumatic dilatation of colonic or ileocolonic strictures in CD.
 - In a prospective study of 55 patients, long-term success (mean follow-up of 34 months) with complete relief of obstructive symptoms was achieved in 62% of patients whereas 19 (38%) required operation and six (11%) suffered a perforation.
- EGD is useful in the evaluation of the differential diagnosis of upper abdominal pain or dysphagia in the IBD patient. Esophageal candidiasis brought on by immunosuppression, duodenal or gastric ulcerative disease caused by steroids or reflux disease from downstream partial obstruction all occur with increased frequency in the IBD patient and is well evaluated by EGD.

Wireless Capsule Endoscopy

- Wireless capsule endoscopy (WCE) is a recent unique development for the visualization of the small bowel. An 11 × 26 mm capsule is swallowed that transmits two video images per second to a receiver worn on the belt.
- Its role in CD is still being clarified, but criteria for its use include the recommendation of prior colonoscopy and intubation of the terminal ileum. Many studies using WCE have found CD in this most common of regions that can be easily reached by a colonoscope obviating the need for the more expensive WCE.
- In addition, a small bowel contrast series is also necessary because the size of the capsule may cause it to impact at a stricture precipitating acute bowel obstruction requiring surgery. Other problems include its limited battery life in patients with

slow transit, the inability to biopsy, and its imperfect localization of identified lesions.

CT Enterography

- The role of CT enterography is not defined but may be useful in the assessment of small bowel Crohn's disease.

F. Pathology

Ulcerative Colitis

- UC begins in the rectum and extends proximally a variable distance with the worst disease being distal and the least disease being proximal. Disease may be limited to the rectum (ulcerative proctitis), extend to only the left colon, or completely to the cecum (pancolitis).
- The terminal ileum may be inflamed in continuity with the cecum (backwash ileitis).
- Disease is in continuity and segmental or "skip" disease does not occur, although so-called "rectal sparing" or some degree of patchiness can be seen in the actively treated patient, especially when enema therapy has been given.
- The gross appearance of the inflammatory process depends on the severity and duration of the disease (Table 39.5).
- The histopathologic features of UC are listed in Table 39.6. There are no pathognomonic features of UC and in its extreme form it can resemble CD.
- Typical UC is associated with inflammation limited to the mucosa or lamina propria including relatively uniform crypt distortion and crypt abscesses. Goblet cell mucin depletion is common and the inflammatory infiltrate is usually neutrophilic, two features that distinguish it from CD where mucin depletion is uncommon and the inflammation is usually mononuclear.
- Dysplasia in longstanding UC is common but can only be interpreted in the setting of noninflamed bowel, because many of its features are common with inflammation, namely, crypt distortion, increased mitotic index, and nuclear atypia.

Table 39.6. Histology of IBD.

	UC	CD
<i>Early</i>	Crypt distortion, branching Goblet cell mucin depletion Vascular congestion (without inflammation) Mucosal inflammation	Patchy crypt distortion Minimal goblet cell mucin depletion Aphthoid ulcers
<i>Intermediate</i>	Uniform crypt abscesses Loss of mucosa with retention of crypts Lamina propria neutrophils	Focal crypt abscesses Vasculitis (20%) Noncaseating granulomas (20–60%) Mononuclear cell infiltrate
<i>Advanced/late</i>	Crypt destruction Neuronal hyperplasia uncommon Deeper submucosa inflammation Pseudo polyp, mucosal bridging Dysplasia common	Transmural inflammation Neuronal hyperplasia common Mucosal and submucosal thickening Fibrosis and strictures Dysplasia uncommon

Crohn's Disease

- The gross features of CD include its ability to affect any portion of the GI tract, its transmural inflammation, and its propensity to create fistulas and strictures, including in the perianal area. Skip lesions are common, resulting in multiple areas of bowel affected simultaneously with intervening segments of normal intestine.
- Diseased bowel may fistulize into adjacent bowel that is otherwise unaffected, a type of bystander injury that only requires surgical removal of the offending segment of intestine with primary repair of the fistula in the remaining, healthy bowel.
- Serositis is common in CD, as is fat wrapping or creeping fat, all nonspecific responses to the transmural inflammation seen.
- On the mucosal surface, the earliest changes are aphthous ulcers, which are tiny white pinpoint lesions representing mucosal ulcerations in the vicinity of enlarged lymphoid follicles. These are thought to then enlarge and coalesce into the larger, deeper, longitudinal serpiginous ulcers often found

in CD. These will have a deep, fissuring appearance and will extend ever deeper into the bowel wall, infrequently perforating freely, but instead recruiting an inflammatory response from adjacent organs that tend to wall off the inflamed bowel and that can then lead to fistulization.

- Healing is associated with granulation tissue and stricture formation, features not usually found in UC.
- The classic noncaseating granuloma is found in 20–60% of patient biopsies and is composed of epithelioid and giant cells of the Langhans type.

Indeterminate Colitis

- Approximately 10–15% of colitis patients will have either clinical or pathologic features that do not allow a clear diagnosis of either CD or UC to be definitively made. This is often attributable to rapidly deteriorating, fulminant colitis, where even UC can have transmural or irregular mucosal involvement.
- Frequently, the correct diagnosis involves the judgment of an experienced clinician who considers not only the histopathology, but also the clinical characteristics of the patient, the history of disease progression, and even more subtle data such as serum antineutrophil cytoplasmic antibody (ANCA) and ASCA testing (see Serum Tests for IBD).
- More than half of such indeterminate cases can usually be resolved with such consideration of the entire clinical picture. This is especially important in the patient who is a candidate for pelvic pouch reconstruction, where the results of such surgery are significantly worse in the misdiagnosed Crohn's diseased patient.

Serum Tests for IBD

- Serum tests for IBD can be divided into several categories: acute phase reactants, nutritional parameters, and inflammatory markers. The prototypic acute phase reactant is the ESR, which is frequently used, especially in CD despite its imperfect correlation with disease activity. It is a necessary component to determine the CDAI (see section above). Some have suggested ESR correlates better with colitis, either CD or UC, than small bowel CD.

- Nutritional parameters are often used to assess the consequence of acute and subacute disease in IBD. Albumin, prealbumin, and iron studies (transferrin, serum iron) are reflective of the combined effects of decreased food intake (to minimize symptoms), compromised absorption (from inflammation or surgical shortening of the bowel), and increased losses (from loss of proteins and blood from mucosal ulceration).
- B12 is often decreased in CD patients with ileal disease or after surgical resection.
- Perinuclear ANCA (pANCA) is an autoantibody found in the serum of approximately 50–70% of UC patients but only 20–30% of CD patients. It does not correlate with disease activity, but is thought to indicate a more aggressive disease type, because of its association with patients who are relatively resistant to medical management and also with patients who frequently suffer pouchitis after ileal pouch anal anastomosis.
- Another serum antibody, that to a common yeast, *Saccharomyces cerevisiae* (ASCA), has been shown to be present in 50–70% of CD patients but only 10–15% of UC patients.
- Three mutations affecting the NOD2/CARD15 gene on the short arm of chromosome 16 have been identified as being associated with CD. The NOD2/CARD15 gene codes for an intracellular protein that has high binding affinity for bacterial peptidoglycan and may have a role in innate immunoresponsiveness to enteric bacteria. Mutations in this gene are found in approximately 10–30% of CD patients vs. 8–15% of healthy controls. The relative risk of developing CD if mutations are carried in both copies of this gene is 10–40 times that of the general population.

Evaluation of the Acute IBD Patient

- There is no one good test for IBD, so the clinical judgment, experience, and acumen of the physician is key in patient management.
- A basic outline of evaluation of the acutely presenting IBD patient is found in Table 39.7.
- It is important to remember that the patient with a known diagnosis of IBD will frequently still require such a basic work-up whenever their disease flares. This is in part attributable to the recognition that these patients are at significant risk for

Table 39.7. Evaluation of the IBD patient.

	Test	Purpose
Serum labs	CBC	r/o anemia, leukocytosis
	Electrolytes, renal function	r/o electrolyte disturbance 2° diarrhea, dehydration
	ESR or CRP	≠↑ in systemic disease
	LFTs, albumin	r/o PSC, nutritional compromise
Stool studies	C. diff.	r/o infectious causes
	O&P	r/o infectious causes
	Pathogens	r/o infectious causes
X-rays	Plain abdominal X-rays	r/o free air, toxic colitis, stones, obstruction
	SBFT/enteroclysis	For small bowel disease
	Barium/Gastrografin enema	For fistulas, strictures, distribution of disease
	CT scan	For abscess, obstruction, fistulas, adjacent organ involvement
Endoscopy	Flexible/rigid scope	For biopsy to r/o CMV, granulomas, pseudomembranes
	Colonoscopy	For biopsy, visualize extent and severity of disease

LFTs liver function tests; *O&P* ova and parasites; *C. Diff* *Clostridium difficile* toxin; *SBFT* small bowel follow through; *CMV* cytomegalovirus

the development of a superimposed secondary diagnosis not infrequently related to iatrogenic causes. These might include pseudomembranous or cytomegalovirus colitis, stress- or steroid-induced gastric ulceration, fungal sepsis, or neutropenia.

- In addition, a known IBD patient presenting with worsening symptoms may now have progression of disease or the development of a directly related complication, such as an intraabdominal abscess, bowel obstruction, toxic colitis, or colovesical fistula.

40. Medical Management of Inflammatory Bowel Disease

A. Introduction

- Recent advances in our knowledge of the immunopathogenesis of IBD have also opened an exciting new door to biologic therapy.
- Pharmacotherapy remains the cornerstone of IBD management, with most patients requiring lifelong therapy because of the chronicity of the disease and its typical onset before 30 years of age.
- The aims of therapy are to control symptoms, improve quality of life, and minimize short- and long-term complications of both the disease and its therapy.
- An important principle in the medical therapy of IBD is that there are two phases to treatment: inducing symptomatic remission of active disease and maintaining this remission for the long term.
- Establishing the anatomic extent and clinical severity of disease is essential to guiding the therapeutic approach. Other important considerations include patient response to previous or current treatment, presence of complications, and side effects of the pharmacologic agents.
- Tailoring treatment according to the patient's unique needs and preferences has an important role in enhancing treatment adherence, which is crucial to an optimal long-term outcome.

B. Medical Management of Crohn's Disease

Induction Therapy for Crohn's Disease

Mild–Moderate Crohn's Disease

- Patients with mild–moderate Crohn's disease are generally ambulatory and tolerate liquid and solid intake.
- These patients typically do not have severe abdominal tenderness, inflammatory masses, bowel obstruction, weight loss of >10%, and are not manifesting signs of systemic toxicity [e.g., fever (>37.5°C), tachycardia (>90/min), anemia (<75%) of normal value, an increased erythrocyte sedimentation rate (ESR) (>30 mm/h)].
- Aminosalicylates and antibiotics are the mainstay of therapy for mild–moderate Crohn's disease, although the topically acting steroid, budesonide, is increasingly being used as a drug of choice for mild–moderate disease, with minimal side effects.
- Sulfasalazine, also known as mesalamine, has minimal efficacy in Crohn's disease of the small bowel. Its use is also limited by more side effects at higher doses secondary to the systemic absorption of sulfapyridine.
 - Sulfasalazine also impairs folate absorption and patients receiving sulfasalazine should receive daily folic acid (1 mg/day) supplements.
- Because of these limitations with sulfasalazine, newer formulations of 5-ASA or mesalamine were developed that minimized side effects and utilized varying drug delivery systems to deliver the active drug intact to the mucosa of the small bowel and colon.
 - Delayed-release formulations of mesalamine include Asacol® that releases 5-ASA in the terminal ileum and cecum at pH 7.
 - Pentasa® (a sustained-release formulation of mesalamine microgranules enclosed within a semipermeable membrane of ethylcellulose) is designed for controlled release throughout the small and large intestine, beginning in the duodenum.
 - Newer azo-bonded formulations designed for release in the colon include the 5-ASA dimer, olsalazine (Dipentum®), and balsalazide (Colazal®).

- Antibiotics are an alternative first-line therapy in mild–moderate Crohn’s disease, and seem to work better in patients with colonic rather than small bowel disease.
 - Metronidazole, when compared with sulfasalazine in a crossover trial, had initial similar efficacy, although more patients who failed sulfasalazine therapy responded when “crossed over” to metronidazole than vice versa. Side effects to metronidazole include a metallic taste, and most importantly peripheral neuropathy that can be irreversible, when administered long term in doses of > 1 g/day.
 - A more effective and possibly better-tolerated alternative to metronidazole is ciprofloxacin in doses of 1 g daily. Trials using this dose show it to be equally efficacious to mesalamine, 4 g/day, with approximately 50% of the patients entering clinical remission.
- Controlled-release oral budesonide is the only Food and Drug Administration (FDA)-approved agent for treating mild–moderate Crohn’s disease involving the ileum or right colon.
 - Budesonide is a more potent glucocorticoid than prednisolone, but has a hepatic first-pass metabolism of 90% such that only 10% reaches the systemic circulation; thus, steroid side effects are greatly minimized.
 - In a recent metaanalysis of trials comparing budesonide to conventional corticosteroids, budesonide was slightly less effective than prednisone, but was associated with significantly fewer steroid side effects.
- Regardless of the treatment strategy chosen, response to therapy should be evaluated after several weeks; 8–16 weeks of therapy may be needed for maximal benefits. Patients achieving remission should be considered for maintenance treatment; treatment failures should be offered an alternative first-line therapy or considered for treatment options offered to patients with moderate–severe Crohn’s disease.

Moderate–Severe Crohn’s Disease

- Patients with moderate–severe Crohn’s disease have either failed therapy for mild–moderate disease, or have significant systemic toxicity symptoms including fever, weight loss of > 10%, abdominal pain and tenderness, nausea and vomiting without bowel obstruction, or significant anemia.

- The treatment options for these patients include corticosteroids (prednisone or budesonide), infliximab, and at a relatively early stage, immunomodulator therapy with either thiopurines or methotrexate.
- Antibiotics may also be used for moderate–severe disease, but only for infectious complications such as abscesses, fistulae, or when used in conjunction with surgical drainage procedures.
- In patients for whom steroids are either ineffective or contraindicated, infusions of infliximab can provide an alternative therapy.
- Corticosteroids are the mainstay of therapy in moderate–severe Crohn’s disease and clinical trials with prednisone at doses of 40–60 mg daily for 8–12 weeks have achieved remission in 50–70% of patients.
 - In clinical practice, prednisone is usually initiated at 40 mg daily and is continued at this dose until remission has been achieved—usually within 7–28 days. Subsequently, prednisone is tapered by 5–10 mg weekly until patients are on 20 mg, and then by 2.5–5 mg weekly from 20 mg until it is discontinued.
 - Corticosteroids are neither safe nor effective as maintenance therapy and therefore, once steroids are initiated, maintenance strategies must be simultaneously devised.
 - In patients with moderately severe ileal or ileocolonic Crohn’s disease, budesonide 9 mg daily is an effective first-line alternative to prednisone. Treatment failures are usually switched to a conventional corticosteroid.
 - More than 50% of patients with moderate–severe Crohn’s disease who are initially treated with steroids will become steroid dependent or steroid resistant, and may require therapy with an immunomodulator. Patients who smoke and those with colonic disease are particularly at risk; adjunctive treatment strategies usually are needed.
- In recent years, steroid-dependent or refractory patients have been treated with the thiopurines—azathioprine (AZA) (2–2.5 mg/kg daily) or 6-mercaptopurine (6-MP) (1–1.5 mg/kg daily), although dose-response studies for these agents have not been performed.
 - The use of thiopurines in moderate–severe active Crohn’s disease is limited by their slow onset of action –

3–4 months; however, their addition to steroid therapy has been shown to increase remission rates and to allow steroid-sparing.

- Patients on thiopurines require regular complete blood counts to monitor for leukopenia; these should be performed every 1–2 weeks initially, and then every 3 months once doses are stabilized. Despite previous concerns, there is no increased risk of lymphoproliferative disorders with the thiopurines and they are considered safe during pregnancy.
- Parenteral methotrexate, in a dose of 25 mg weekly either subcutaneously or intramuscularly, is an alternative steroid-sparing agent for patients with moderate–severe Crohn’s disease.
 - Parenteral methotrexate has been shown to induce remissions and to be steroid sparing.
 - Nausea and asymptomatic mild increases of liver function tests are the most frequently encountered side effects; more serious side effects such as leukopenia and hypersensitivity pneumonitis are seen only rarely.
- Infliximab is a chimeric monoclonal antibody to tumor necrosis factor, and is indicated for the induction and maintenance of moderate–severe Crohn’s disease patients who are not responding to corticosteroids and immunomodulators.
 - Infliximab is also effective at reducing the number of draining fistulae in patients with fistulizing Crohn’s disease.
 - Emerging indications for infliximab include maintenance therapy for luminal and fistulizing disease, steroid-sparing in steroid-dependent patients, early use in hospitalized patients when rapid amelioration of symptoms is desired, and to curtail some of the extraintestinal manifestations of Crohn’s disease.
 - Concurrent immunomodulator therapy with AZA, 6-MP, or methotrexate may also improve outcome by reducing the formation of antibodies to infliximab or reducing the incidence of acute infusion reactions or delayed hypersensitivity reactions; most evidence to support this hypothesis is only anecdotal.
 - Given the risk of reactivation of latent tuberculosis, all patients should be screened for tuberculosis with tuberculin skin testing (and chest X-ray if skin testing is positive) before initiating therapy with infliximab.

- Adalimumab, a subcutaneously injected, human monoclonal antibody, may also be used for moderate-to-severe Crohn's disease.

Severe–Fulminant Crohn's Disease

- Patients with severe or fulminant Crohn's disease have ongoing symptoms despite oral steroids or infliximab given as an outpatient and present with high fever, cachexia, persistent vomiting, or may have evidence of an intestinal obstruction or an abscess.
 - These patients almost always require hospital admission and resuscitation with intravenous fluids.
 - Patients with clinical signs of a bowel obstruction or an abscess require an urgent surgical consultation, and intravenous antibiotics should be administered immediately, especially if sepsis is suspected.
 - If sepsis can be excluded, then high-dose intravenous steroids should be started at doses equivalent to 40–60 mg of prednisone by either divided doses or continuous infusion. If patients do not respond to steroids within 5–7 days, alternative therapies such as infliximab, cyclosporine (CSA), or tacrolimus can be considered.
 - Responders to parenteral steroids or CSA are then transitioned to an equivalent oral dose, whereas those failing medical treatments require surgery.

Management of Perianal Crohn's Disease

- Perianal complications of Crohn's disease include ischiorectal abscesses and perianal fistulae, and often require surgical intervention. Abscesses require surgical drainage. Symptomatic fistulae often require medical therapy including antibiotics, immunomodulators, or infliximab, combined with seton placement.
- Asymptomatic, nondraining fistulae can be safely observed without treatment once coexisting sepsis has been excluded.
- Metronidazole in doses of 10–20 mg/kg is effective in reducing or stopping fistula drainage, although it seems that continuous therapy is needed to avoid recurrence, and side effects may be troublesome, especially peripheral neuropathy.
- In such cases, ciprofloxacin 500 mg per os twice a day is a reasonable alternative, or the two antibiotics can be given as combination therapy.

- The next line of treatment for perianal disease should be with an immunosuppressant agent such as AZA, 6-MP, CSA, or tacrolimus.
- Steroids have no role in perianal Crohn's disease.
- In a placebo-controlled trial, patients who had previously not responded to antibiotics, steroids, or immunomodulators were given 5 mg/kg infliximab at 0, 2, and 6 weeks. Of these patients, 68% had a positive clinical response defined as a reduction by half the number of draining fistulae, and 55% had cessation of draining of all fistulae. The average duration of closure of fistulae was 12 weeks, although maintenance therapy to prevent recurrent drainage or abscess has been demonstrated to be efficacious in the same manner as for luminal disease.
- Patients receiving infliximab for perianal fistulae may benefit from temporary setons to ensure that recurrent abscess formation is prevented.

Maintenance Therapy for Crohn's Disease

- Whereas corticosteroid therapy is successful in inducing remission in the majority of patients, it has no role as maintenance therapy in Crohn's disease, and carries the risk of steroid dependence.
- The thiopurines – AZA (2–2.5 mg/kg) and 6-MP (1–1.5 mg/kg) – have been proven to be steroid sparing and to maintain medically induced remission.
- Patients on either the thiopurines or methotrexate require regular monitoring of blood counts and liver enzymes; hence, only reliably compliant patients should be chosen for these therapies.
- The evidence base for maintenance infliximab therapy is rapidly expanding.

Postoperative Prophylaxis for Crohn's Disease

- Postoperative disease recurrence at 1 year after first resection for Crohn's disease is seen endoscopically in 60–80% of patients and clinically in 10–20%, with smoking being the strongest predictive factor for recurrence.
- Luminal factors also seem to be responsible for disease recurrence, as fecal diversion prevents recurrence, only for it to recur once continuity is reestablished.

- Aminosalicylates and metronidazole have both been proven to reduce postoperative recurrence in certain subgroups of patients, particularly those with isolated ileal disease.
- At present, there are no consistent recommendations regarding medical therapy after surgical resection for Crohn's disease.
- Many patients with longstanding strictures have a good postoperative prognosis, whereas patients with rapid progression of perforating complications and smokers have a worse prognosis.
- All patients should be advised to stop smoking.

C. Medical Management of UC

Induction Therapy for UC

- The primary goal of therapy is to induce clinical remission and promote mucosal healing. Clinical remission is achieved when the inflammatory symptoms of diarrhea, bleeding, passage of mucopus, tenesmus, and urgency resolve, and with patients' renewed ability to distinguish gas from feces.
- In endoscopic remission, there is regeneration of an intact mucosa with a visible submucosal vascular pattern, without ulceration, significant friability, or granularity.
- Pseudopolyps, mucosal bridging, and areas of "atrophic mucosa" with distorted vasculature represent previous episodes of severe inflammation.
- Clinical remission usually precedes endoscopic healing, which usually precedes histologic remission.
- Therapies for inducing remission are based on the anatomic extent of disease and clinical severity. Proctitis and distal colitis refer to inflammation limited to below the splenic flexure, and thus amenable to the reach of topical and oral therapy.
- In extensive disease, the inflammation extends proximal to the splenic flexure and requires systemic medication.
- Supplementary topical therapy is often beneficial to treat prominent rectal symptoms of urgency or tenesmus.
- Disease severity is classified as mild, moderate, severe, or fulminant.

- Patients with mild disease have less than four stools daily, with or without blood, no systemic signs of toxicity, and a normal ESR.
- Moderate disease is characterized by features of both mild and severe disease.
- Severe disease is characterized by more than six bloody stools per day, abdominal tenderness with signs of systemic toxicity including fever ($>37.5^{\circ}\text{C}$), tachycardia ($>90/\text{min}$), anemia ($<75\%$ of normal value), and an increased ESR ($>30\text{ mm/h}$).
- Fulminant colitis is manifested by more than ten bloody stools per day, anemia requiring transfusion, signs of systemic toxicity, abdominal distension, and tenderness.
- For patients with mild–moderate UC, oral and/or topical mesalamine is the mainstay of therapy, whereas topical corticosteroids may be useful in those with distal disease.
- Oral corticosteroids are reserved for those with moderate–severe disease and for those who did not respond to optimized doses of oral 5-ASA and topical therapies.
- Patients with severe colitis or those refractory to maximal oral and topical doses of corticosteroids and 5-ASA should be treated with intravenous corticosteroids.
- Failure to show significant improvement with intravenous corticosteroids is an indication for intravenous CSA, infliximab or a curative colectomy.

Mild–Moderate Proctitis

- Patients with proctitis have disease limited to the rectum, allowing effective topical therapy with suppositories. Mesalamine suppositories 1–1.5 g/day (Canasa[®]) either nightly or in divided doses are highly effective for proctitis up to 20 cm, and superior to oral 5-ASA therapy and to topical corticosteroids.
- In patients not responding to rectal mesalamine alone, combination therapy with a topical corticosteroid (foam or enema) is better than either therapy alone.
- Systemic corticosteroids are rarely required in patients with ulcerative proctitis and should only be reserved for patients with severe or refractory disease.

Mild–Moderate Distal Colitis

- Topical 5-ASA is the treatment of choice for patients with distal colitis and achieves higher response rates than topical corticosteroids or oral 5-ASA therapy.
- Remission rates increase with the duration of therapy (63–72% after 4 weeks) and are independent of dose; there are no apparent advantages of giving doses greater than 1 g/day.
- Generally, mesalamine suppositories are easier to retain because of their smaller volume and more viscous state.
- Alternatively, combination therapy of mesalamine enemas at night and morning topical corticosteroids [e.g., hydrocortisone foam: 80 mg per application (Cortifoam®), or enema 100 mg/60 mL (Cortenema®)] may be considered, which is superior to either therapy alone.
- The systemic bioavailability of rectally administered hydrocortisone approaches 80% because of low first-pass hepatic inactivation, and absorption tends to increase as colonic inflammation is reduced. Therefore, steroid-related side effects may begin to manifest after 2–4 weeks of treatment.
- Newer formulations of corticosteroids, such as budesonide, are another therapeutic option to treat mild–moderate distal colitis. Their high first-pass hepatic metabolism markedly reduces systemic bioavailability, endogenous cortisol suppression, and thus reduces the potential for steroid-induced side effects.
- For patients with mild–moderate colitis who are not responding to topical mesalamine (with or without topical corticosteroid), oral mesalamine may be added as combination therapy and is superior to either oral or topical therapies alone.

Mild–Moderate Extensive UC

- Oral sulfasalazine or one of the newer 5-ASA formulations is the treatment of choice.
- The development of sulfa-free 5-ASA delivery forms have enabled clinicians to deliver larger amounts of the active moiety without the dose-limiting systemic toxicity.
- Clinical improvement or remission can be achieved in as many as 84% of patients with Asacol® (2.4–4.8 g/day), Salofalk®, Claversal®, Mesasal® (1.5–3 g/day), Pentasa® (2–4 g/day), olsalazine (1–3 g/day), and balsalazide (6.75 g/day).

- Patients with mild–moderate extensive UC not responding to optimal doses of oral mesalamine (with or without topical mesalamine) and those with more severe but nontoxic systemic symptoms will require the addition of oral corticosteroids.

Severe UC

- Patients with severe colitis that is refractory to maximal oral treatment with prednisone, 5-ASA, and topical medications should be hospitalized for further management. Initial patient evaluation should include blood tests for hematology, a metabolic panel, and total cholesterol level. An infectious process should be ruled out by stool analysis for ova, parasites, and *Clostridium difficile* toxin, fecal culture and sensitivity, and a rectal biopsy for cytomegalovirus. Indiscriminate use of nonsteroidal antiinflammatory drugs (NSAIDs), anticholinergic agents, and antimotility (e.g., loperamide, diphenoxylate) should be avoided because of the potential of worsening colitis or inducing toxic megacolon.
- The mainstay of treatment for severe colitis is parenteral corticosteroids in daily doses equivalent to 300 mg hydrocortisone or 48 mg methylprednisolone.
- Bowel rest and total parenteral nutrition (TPN) alone have minimal benefit as primary therapy for acute severe UC. Nutritional support should be provided for severely malnourished patients with the recognition that enteral nutrition has the benefit of fewer complications compared with TPN.
- The routine use of antibiotics has been shown to have no primary, therapeutic benefit in the treatment of severe UC; however, most experienced centers administer broad-spectrum antibiotics to patients with fulminant or anticipated transmural disease.
- Patients with signs of transmural and fulminant colitis (fever, leukocytosis, abdominal tenderness, “thumbprinting” on abdominal radiograph) who are at risk of toxic megacolon and perforation should be placed on bowel rest and started on broad-spectrum antibiotics.
- Abdominal radiograph should be done to assess for colonic dilation and to look for free air. Narcotics and anticholinergics, which may worsen colonic atony and dilation, must be avoided. Because the failure rate of medical therapy in hospitalized severe UC patients approaches 40%, they should also be followed closely by an experienced surgeon.

- Patients failing to respond to 7 days of intravenous corticosteroids are unlikely to benefit from prolonging this treatment and should either be considered for intravenous CSA or referred for surgery.
- Patients with toxic megacolon are managed as above. In addition, the gastrointestinal tract should be decompressed with the insertion of a nasogastric tube.
 - These patients should be monitored closely in the intensive care unit for any signs of deterioration.
 - Serial abdominal radiographs are usually reviewed every 12 h and electrolyte abnormalities, such as hypokalemia that may aggravate colonic dysmotility, are treated aggressively.
 - Medical therapy may avoid the need for surgery in up to two-thirds of patient cases.
 - Failure to improve within 72 h is an indication for surgery; any clinical, laboratory, or radiologic deterioration on medical therapy mandates an immediate colectomy.
- Intravenous CSA is an effective “rescue” therapy for severe steroid-refractory UC and acts as a bridge to maintenance therapy with the slower-acting thiopurines, AZA or 6-MP.
- Clinical improvement is generally seen within 4–5 days of initiating CSA treatment. Patients who have not demonstrated a significant improvement within 7 days of intravenous CSA therapy, or whose condition deteriorates during CSA therapy, are candidates for surgery.
- Most recently, infliximab has been used in patients with refractory or steroid-resistant UC.

Maintenance Therapy for UC

- The second goal of therapy in UC is to sustain the symptomatic improvement of a clinical remission. Clinical remission is achieved when the following inflammatory symptoms resolve: diarrhea, bleeding, passage of mucopus, tenesmus, and urgency. Endoscopic remission implies maintenance of an intact mucosa without ulceration, friability, or granularity and histologic remission presumes the absence of neutrophils in the epithelial crypts.
- Aminosalicylates are the primary maintenance therapy to prevent relapse of remitted UC.

- AZA and 6-MP are useful steroid-sparing agents for steroid-dependent patients and for maintaining remission in those patients not adequately sustained by 5-ASA alone.
- Patients experiencing their first episode of proctitis that has responded promptly to topical treatment may not need maintenance medication as long-term remission may persist.

5-ASA–Induced Remission of UC

- Remission can be maintained with oral and/or topical 5-ASA formulations alone after induction therapy for mild–moderate UC.
- Once remission is attained, topical 5-ASA is the most effective maintenance therapy to prevent relapse of distal disease. Mesalamine suppositories (1–1.5 g/day) and enemas (1–4 g daily) are effective for patients with proctitis and distal colitis, respectively.
- Oral maintenance therapy for distal colitis is less effective than topical; however, most patients still prefer an oral aminosalicylate for its convenience, and transitioning to an oral maintenance regimen can be attempted.
- An oral aminosalicylate is the primary maintenance therapy for extensive colitis.

Steroid-Induced Remission in UC

- Corticosteroids (oral or topical) are ineffective maintenance agents and should be tapered and weaned off once remission has been achieved.
- 5-ASA remains the primary maintenance therapy after a steroid-induced remission, but will usually require higher doses equivalent to 2.4–4.8 g of mesalamine daily.
- Because chronic long-term use of corticosteroids is unacceptable, patients should be considered for long-term immunosuppressive drug therapy with the thiopurines or a curative colectomy.

CSA-Induced Remission in UC

- Steroid-refractory patients achieving remission with intravenous CSA are transitioned to oral CSA.

Refractory UC Disease

- Uncontrolled series have demonstrated the value of AZA and 6-MP in achieving remission in these steroid refractory, chronically active UC patients.
- It is anticipated that infliximab will become an alternative option for this subgroup of patients who do not tolerate or respond to AZA or 6-MP.
- Colectomy may be the final option in these patients.

41. Surgical Management of Ulcerative Colitis

A. Indications for Surgery

- The overall incidence of colectomy in a UC patient ranges from 23 to 45%. This risk is higher in patients with pancolitis than in patients with left-sided disease.
- Indications for colectomy include an acute flare unresponsive to medical measures, development of a life-threatening complication (e.g., toxic colitis, perforation, or hemorrhage), medical intractability, risk of malignancy, disabling extracolonic disease, and growth retardation in children.
- Encouraging results have been reported with the use of cyclosporine in acute colitis yet long-term effectiveness of this particular treatment modality remains undefined. However, there is no reported increase in the incidence of perioperative complications after subtotal colectomy in patients treated before surgery with cyclosporine.
- Infliximab has recently been used for ulcerative colitis.
- Medical intractability is the most common indication for operation and may seem difficult to define.
- It is important to recognize that medical intractability is a problem the patient identifies in conjunction with the physician.
- Patients with longstanding UC have an increased risk for the development of colorectal cancer. The risk of cancer is relatively low for the first 10 years after disease onset but then begins to increase at a rate of 1–2% per year.
- Most surgeons contend that during a surveillance biopsy program, identification of high-grade dysplasia by an experienced pathologist is an indication for colectomy.

- Patients with low-grade dysplasia should also be offered colectomy, although nonoperative management of these patients has been suggested by some because the natural history of low-grade dysplasia has not been well established.
- Elective colectomy may be indicated for some categories of severe extraintestinal manifestations of the disease. Persistent or recurrent monoarticular arthritis, uveitis, or iritis all respond favorably to colectomy. However, primary sclerosing cholangitis, ankylosing spondylitis, and sacroiliitis are not improved by colectomy. The response of pyoderma gangrenosum to colectomy is unpredictable.
- Growth retardation is a common feature in children with UC. Contrary to popular belief, steroid therapy cannot be entirely blamed for delayed growth. Inadequate protein intake and excess loss in the colon are also contributory. A rapid growth spurt is often observed after definitive surgery.

B. Emergency Versus Elective Procedures

- Operative management of UC largely depends on whether the surgery is elective or emergent. Under elective conditions, the four available surgical options are: (1) total proctocolectomy and Brooke ileostomy, (2) total proctocolectomy and continent ileostomy, (3) abdominal colectomy with ileorectal anastomosis (IRA), and (4) ileal pouch-anal anastomosis (IPAA).
- Total proctocolectomy and Brooke ileostomy has been traditionally regarded as the optimal surgical approach and remains the operation with which alternative procedures should be compared.
 - Although quality-of-life studies have demonstrated excellent results, the loss of fecal continence and its attendant physical and psychologic sequelae continue to be significant drawbacks of the procedure.
 - In addition, problems with nonhealing of the perineal wound, and the high incidence of small bowel obstruction and ileostomy revision, are not to be minimized.
- Total proctocolectomy and continent ileostomy couples the benefit of complete large bowel excision with a reduction in some of the untoward aspects of an ileostomy, because no

external appliance is needed and the stoma can be placed in a less conspicuous position on the abdominal wall.

- Because of increased surgical experience and improved surgical techniques, continent pouch morbidity has decreased since its initial clinical description.
 - Nonetheless, troublesome complications leading to incontinence continue to plague the postoperative course of a substantial number of patients.
- There are many attractive features of colectomy and IRA. The procedure avoids the perineal complications of total proctocolectomy, the risk of sexual dysfunction is minimal, is technically easy to perform, may provide perfect control of feces and flatus, and is well accepted by most patients.
 - However, unlike the three other surgical options, ileorec-tostomy does not achieve total excision of colorectal mucosa. Many surgeons have not used this operation for UC, arguing that more than 25% of patients will require subsequent rectal excision for persistent proctitis, a small percentage of patients will develop cancer in the rectal remnant, and only half of the patients have satisfactory long-term functional results.
 - Although we concur that this operation should not be advised in most UC patients, IRA does have a role in certain clinical situations. For example, an elderly patient with a long history of UC who develops a transverse colon cancer may be well served with an IRA in lieu of total proctocolectomy.
 - Decisions must be made on an individualized basis, taking into account the compliance of the rectum and the integrity of the sphincter mechanism.
- IPAA has the attractive features of complete excision of the colorectal mucosa, avoidance of a permanent intestinal stoma, continence via a normal route of defecation, and no prospect for a troublesome nonhealing perineal wound.
 - Although the operation is associated with minimal mortality, the morbidity of this complex procedure is relatively high, and problems such as small bowel obstruction and pouchitis continue to be a cause for concern.
- Under emergent conditions, surgical alternatives are limited.
 - If the patient is septic, the diseased or perforated bowel should be removed.

- If the colon is bleeding, the colon should be removed. Traditionally, it has been taught that the rectum should also be removed. However, with the sphincter-saving alternatives that are currently available, careful preoperative proctoscopic evaluation to exclude a rectal etiology for the bleeding and a subsequent abdominal colectomy with end ileostomy can be safely performed. A subsequent procedure can then restore intestinal continuity.
- Similarly, with toxic colitis, it is seldom necessary to perform a proctectomy at the time of colectomy. In general, concerns over healing of the perineal wound in these frequently malnourished patients who are taking high-dose steroids should deter surgeons from doing proctectomy in the emergent setting.
- There is a trend to avoid subjecting patients to multiple surgical procedures and to perform a definitive procedure at the time of emergent surgery. Although an IPAA can be successfully performed in patients undergoing surgery for emergent complications, the authors believe this generally is not a safe approach.
 - Patients with UC receiving high-dose steroids (more than 40 mg/day) have a significantly greater risk of developing pouch-related complications after colectomy than patients with UC receiving 1–40 mg/day and patients with UC who are not receiving corticosteroids.
- Salvage of the patient should be the primary concern. Abdominal colectomy is safe in these very ill, nutritionally depleted patients and the procedure does not preclude any of the other surgical alternatives in the future. Additionally, the patient is able to live with an ileostomy and assess its impact on his or her life, thus allowing for an informed decision regarding subsequent continence-restoring surgery.

C. Brooke Ileostomy

- The preoperative period should include effective patient education. A patient must be fully informed of the effects of an ileostomy on his or her quality of life. An ileostomy visitor, preferably age and sex matched and who has completely recovered from surgery, is invaluable during this period.

- It is also essential, when possible, to select the stoma site preoperatively with the help of an enterostomal therapist.

Postoperative Complications

- Delayed healing of the perineal wound is not uncommon and can be quite problematic. Failure of the wound to close should prompt investigation to exclude the presence of retained mucosa, foreign material, or Crohn's disease (CD).
- Sexual complications of proctocolectomy in men are much less common than in patients having a radical resection for cancer, yet permanent impotence or retrograde ejaculation can occur.
- Almost 30% of women complain of dyspareunia after this operation, presumably as a result of perineal scarring.
- Intestinal obstruction is a troublesome complication that can be managed conservatively in most patients. Gentle irrigation of the stoma is an important therapeutic maneuver.
- Although problems from the ileostomy have diminished markedly with the use of modern appliances and the Brooke modification, skin irritation, stomal stenosis, prolapse, and herniation remain significant causes of postoperative morbidity. Treatment of these problems can be as simple as reeducating a patient about the proper maintenance of the ileostomy. However, up to one-third of these patients ultimately require operative revision.
- More than 90% of patients are happy with their current lifestyle. However, significant problems do remain.
- Current indications for the procedure include elderly patients, individuals with distal rectal cancer, patients with severely compromised anal function, and patients who choose this operation after appropriate education.

D. Continent Ileostomy

- A continent ileostomy is usually reserved for patients who have failed Brooke ileostomy or those who are candidates for an IPAA but cannot have a pouch because of rectal cancer, perianal fistulas, poor anal sphincter function, or occupations that may preclude frequent visits to the toilet.

- Preoperatively, a search for CD using barium examination of the stomach and small intestine is important. Suspicion of CD contraindicates construction of a continent ileostomy, because the risk of recurrent disease in the pouch is increased; this could necessitate resection of 45 cm of valuable small bowel and diminish the patients ability to maintain nutrition.
- Obesity and age over 40 years are associated with an increased risk of pouch dysfunction and represent relative contraindications to the continent ileostomy.
- The period before surgery must also include an open discussion with the patient, stressing that although continence is likely, major complications often occur. These setbacks generally must be corrected surgically, sometimes leading to pouch excision and creation of a standard Brooke ileostomy.

Postoperative Complications

- Postoperative complications that occur with sufficient frequency are nipple valve slippage, pouchitis, intestinal obstruction, and fistula.
- Nipple valve slippage remains the most common complication after continent ileostomy, occurring in almost 30% of patients. Although nonoperative approaches have been attempted to correct this problem, surgical correction is virtually inevitable.
- Pouchitis is recognized in 25% of patients, making this the second most common postoperative complication after continent ileostomy.
- Patient satisfaction with a continent ileostomy is excellent. Most patients note a marked improvement in their lifestyle, and almost all patients work and participate in social and recreational activities without restriction.

E. Ileorectal Anastomosis

- Currently, IRA is mainly considered in patients with indeterminate colitis (IC), in high-risk or older patients who are not good candidates for IPAA, or if there is mild rectal disease in which rectal compliance remains adequate.

- The use of the operation may also be indicated in the teenager or young adult to rapidly regain good health, avoid a stoma, and return to school or work quickly.
- Functional results depend on the level of the anastomosis as well as the state of the rectum.
- Contraindications to IRA include a very diseased and noncompliant rectum, dysplasia or nonmetastatic cancer, perianal disease, and a severely compromised anal sphincter.

Postoperative Complications

- The overall complication rate is much lower than that of an IPAA.
- Although the frequency of defecation after IRA is variable, most patients pass between two and four semiliquid stools a day. Nocturnal defecation is quite common, but true incontinence is rare.
- The main concerns surrounding IRA for UC are the long-term issues regarding cancer risk in the retained rectum and the incidence of persistent rectal inflammation.
- The overall risk of cancer developing in the rectum after IRA approximates 6%, but this depends on the duration of follow-up. Few of these cancers develop less than 10 years after operation, with most cancers appearing 15–20 years after operation.
- Cancer in the rectum after IRA produces few symptoms and early lesions are not always easily identified at sigmoidoscopy.
- Patients being offered IRA must realize the need for semianual sigmoidoscopy with multiple biopsies to detect dysplasia, polyps, or invasive cancer.
- The rectal stump may be the site of recurrent or persistent inflammation in 20–45% of patients. Clinical features include severe diarrhea, tenesmus, bleeding, and urgency.
- Rectal excision is needed in those cases that do not respond to topical or systemic therapies. About one-quarter of patients require proctectomy after IRA for severe proctitis.
- The only clinical factor that predicts a successful outcome is the degree of inflammation in the rectum preoperatively, minimal proctitis being associated with an excellent prognosis.
- A great advantage of the IRA is that should a failure occur, other options remain. Conversion from an IRA to an IPAA may

be required when there is a poor functional outcome because of poor rectal compliance, persistent and disabling proctitis, and with development of an upper rectal cancer. If conversion to IPAA is required, it can be performed safely, although poorer bowel function may be expected. However, quality of life is similar before and after conversion in these patients.

F. Ileal Pouch–Anal Anastomosis

- The most attractive of the continence-preserving alternatives is the IPAA, which consists of near total proctocolectomy, creation of an ileal reservoir, and preservation of the anal sphincter complex.
- In an attempt to improve functional outcome, some surgeons preserve the anal transition zone and perform a stapled anastomosis between the ileal pouch and the anal canal immediately cephalad to the dentate line (“double-stapled” technique).
- Use of this procedure in patients with poor sphincter function or fecal incontinence must be carefully individualized.
- Ileostomy output can be quite high, because the stoma is more proximal than a traditional Brooke ileostomy. Patients should be encouraged to keep themselves well hydrated. In some instances, antidiarrheal medication is prescribed.
- Patients are usually discharged after 7–10 days in the hospital and return 6–12 weeks later to have the temporary ileostomy closed.
- Before closure, however, the pouch is thoroughly investigated. Digital rectal examination is used to assess anal sphincter tone and detect anastomotic strictures or defects. The pouch is examined endoscopically to ensure that the suture lines are healed, and a contrast study is performed to detect pouch leaks, fistulas, and sinus tracts.
- Sphincter strengthening exercises should be encouraged in the period leading up to ileostomy closure, because they seem to improve functional results.

Postoperative Complications

- Performing an ileoanal anastomosis is safe, with reported mortality rates ranging from 0 to 1%. In distinct contrast to mortality, however, morbidity after IPAA remains considerable.

- Small bowel obstruction occurs in 20% of patients and results from adhesion formation to the large number of raw surfaces after colectomy and from kinking at the ileostomy site. Most of the obstructive episodes occur in the immediate period after either procedure.
- Although the incidence has decreased with increasing surgical experience, pelvic sepsis still occurs in 5% of patients after IPAA.
 - Pelvic sepsis may present in the immediate postoperative period or it may be delayed, manifesting as abscess formation (usually presacral) or a perineal fistula.
 - The symptoms suggestive of early pelvic sepsis are fever, anal pain, tenesmus, and discharge of pus or secondary hemorrhage through the anus.
 - Diagnosis is confirmed using computed tomography or magnetic resonance imaging which demonstrates the presence of an abscess or of edematous tissues.
 - Because patients who develop sepsis in the early postoperative period have a higher likelihood of subsequent pouch failure, an aggressive therapeutic approach should be adopted in these patients.
 - Although most patients respond to intravenous antibiotics within 24–36 h, patients with ongoing sepsis and an organized abscess should undergo early operative endo-anal or imaging-guided percutaneous drainage.
- The reported incidence of ileoanal anastomotic stricture has varied between 5 and 38%.
 - The etiology is usually anastomotic tension that also predisposes to infection from leakage.
 - An apparent stricture may be noted when digital examination is performed for the first time after the operation. These asymptomatic, weblike strictures can be easily disrupted by gentle passage of the finger.
 - More fibrotic strictures can usually be fractured digitally but occasionally the insertion of graded dilators under anesthesia is necessary.
 - Operative management usually requires repeated dilations yet reasonable function can be expected in more than 50% of patients.
- Anastomotic separation is seen in approximately 10% of patients. If this complication is recognized during preileostomy closure

contrast studies or as a defect on digital examination, ileostomy closure should be delayed until complete clinical and radiographic evidence of healing.

- The reported incidence of pouch-vaginal fistula ranges from 3 to 16%.
 - The patient complains of a vaginal discharge and clinical examination usually demonstrates the fistula.
 - Occasionally, it is only detected by radiologic contrast enema (pouchogram).
 - It is important to exclude a pouch-vaginal fistula by careful operative examination of the vagina as well as the anal canal before closing the defunctioning ileostomy.
 - The fistula may present before ileostomy closure or after stoma closure.
 - The internal opening is usually located at the ileoanal anastomosis, but less often it may arise at the dentate line, perhaps as a form of cryptoglandular sepsis.
 - Causative factors may include injury to the vagina or rectovaginal septum during the rectal dissection or anastomotic dehiscence with pelvic sepsis. The latter is probably the major predisposing factor because pelvic sepsis rates are significantly higher in patients with pouch-vaginal fistula than in those without.
 - CD has been reported to be more common in patients with pouch-vaginal fistula, yet is difficult to prove in the majority of cases.
 - Management depends on the severity of symptoms. When these are minimal and acceptable to the patient, no action or the placement of a seton may be all that is necessary. In those with a clinically significant degree of incontinence, a diverting ileostomy should be established if not already present. On defunctioning, sepsis is drained with or without placement of a seton suture and, once it has settled, repair is indicated. Simple defunctioning alone does not often lead to fistula closure.
 - Medical therapy is generally not indicated in managing these fistulas, although one recent series showed efficacy of infliximab.
 - Surgical options are divided into abdominal and local procedures. The former includes abdominal revision with advancement of the ileoanal anastomosis, and the latter

fistulectomy with or without sphincter repair, endoanal advancement flap repair, and endovaginal or transvaginal repair.

- The most frequent long-term complication after IPAA for UC is a nonspecific inflammation of the ileal pouch commonly known as pouchitis.
 - The presence of extraintestinal manifestations of UC before colectomy, especially primary sclerosing cholangitis, has been associated with the development of pouchitis.
 - The etiology of this nonspecific inflammation is unclear but, as with the continent ileostomy, may be attributable to an overgrowth of anaerobic bacteria.
 - Presenting symptoms include abdominal cramps, fever, pelvic pain, and sudden increase in stool frequency.
 - Treatment of pelvic reservoir pouchitis relies primarily on the use of antibiotics such as metronidazole and ciprofloxacin.
 - Patients with chronic pouchitis should be suspected of having CD. Uncommonly, an ileostomy with or without pouch excision is required for severe refractory pouchitis.
- The number of bowel movements after successful ileoanal pouch procedures averages six per 24 h.
- Major incontinence is very unusual, although minor incontinence to mucus or stool, particularly at night, is observed in approximately 30% of patients.
- Although continence is clearly altered after pelvic pouch surgery, quality of life is extremely well preserved. To obtain these results, however, approximately half of these patients regularly take a bulking agent or antidiarrheal medication to help regulate their bowels.
- Total failure, defined as removal of the pouch, occurs in only 5–8% of cases and is usually caused by pelvic sepsis, undiagnosed CD, or an unacceptable functional outcome.
- Quality-of-life studies have disclosed that more than 95% of patients are satisfied with their pouch and would not go back to an ileostomy.
- Two large studies have shown decreased postoperative fertility. The severe decrease in postoperative fertility was attributed to probable tubal occlusion from adhesions, a phenomenon observed in another study.

- A second report from the same group on a different patient cohort found normal fecundity before UC diagnosis and from UC diagnosis to colectomy. However, fecundity decreased 80% after IPAA.
- The optimal method of delivery remains controversial.
 - Cesarean delivery decreases the risk of incontinence resulting from damage to the anal sphincters and yet is associated with complications inherent to abdominal surgery, including injury to the pelvic pouch and adhesion formation.
 - Vaginal delivery may damage the pudendal nerve and the anal sphincter mechanism, but it reduces the problems associated with abdominal surgery and recovery is more rapid.

Controversies

- In approximately 10% of colitis patients, there are inadequate diagnostic criteria to make a definite distinction between UC and CD, especially in the setting of fulminant colitis. These patients are labeled as having IC.
 - Several major clinical concerns remain regarding performance of IPAA for IC, including a higher rate of perineal complications, development of CD, and eventual pouch loss.
 - Other investigators, however, have demonstrated acceptable outcomes of this procedure in IC.
 - Until the reasons underlying these discrepant data are uncovered, patients with IC should be counseled that undergoing IPAA may predispose them to a higher incidence of pouch-related complications.
 - Although preoperative clinical factors that can predict those IC patients at risk for developing pouch complications or CD after IPAA have yet to be identified, a recent prospective study suggests that IC patients who express specific inflammatory bowel disease serologic markers before surgery have a significantly higher incidence of chronic pouchitis and CD after IPAA than IC patients who have a serologically negative profile.
- Another debated issue is whether IPAA should be offered to elderly patients.

- Two reasons to avoid these procedures in older patients relate to the higher incidence of anal sphincter dysfunction with increasing age and the morbidity of reoperations in these potentially medically more compromised patients.
 - Many groups have demonstrated that IPAA in the elderly patient is safe and feasible. It seems that chronologic age should not itself be used as an exclusion criterion.
- Another controversy relates to the use of the IPAA in UC patients who have an established colorectal cancer.
 - The presence of distant metastatic disease is generally a contraindication to IPAA. These unfortunate patients should be managed with segmental colectomy or abdominal colectomy with IRA to facilitate early discharge and allow them to spend the rest of their lives relatively free of complications.
 - Patients with middle and low rectal tumors, in accordance with basic principles of cancer surgery, may not be eligible for this procedure. Radiation therapy, if indicated, should be performed preoperatively; a pelvic pouch should not be subjected to radiation because of a high incidence of pouch loss.
 - UC patients with cecal cancers represent another unique subgroup of patients. The sacrifice of a long segment of adjacent distal ileum with its mesenteric vessels may limit positioning of the reservoir into the pelvis.
- Studies examining the use of the ileoanal pouch in patients with locally invasive cancers of the colon and upper rectum have been conflicting. In one series, UC patients with a carcinoma had postoperative complications and functional results identical to UC patients without cancer. Metastatic disease developed in a small number of patients. In contrast, another study revealed that almost 20% of UC patients with cancer who had an IPAA died of metastatic disease. Because both of these patients had T3 cancers at surgery, it is unclear that their course was adversely influenced by performing IPAA.
 - This conservative management approach is advocated by some groups. UC patients with a T3 cancer initially undergo an abdominal colectomy with ileostomy. An observation period of at least 12 months is recommended to ensure that no recurrent disease develops. Another

reason to postpone IPAA in these patients is to allow adjuvant chemoradiation therapy to proceed unhindered without any added morbidity from a pouch-anal anastomosis and a relatively proximal ileostomy.

- Some authors believe that the entire rectal mucosa does not need to be removed. They favor leaving 1–2 cm of distal mucosa behind, transecting the rectum just above the puborectalis muscle and stapling the pouch to the rectal remnant. The potential advantages of the double-stapled approach include technical ease because it avoids a mucosectomy and the perineal phase of the operation, less tension on the anastomotic line, and improved functional results because sphincter injury is minimized and the anal transition zone with its abundant supply of sensory nerve endings is preserved.
- However, surgeons who oppose this operative approach contend that residual diseased mucosa is at risk of malignancy. There have been nine reports of cancer developing after IPAA, eight in patients who underwent the procedure for dysplasia or colorectal cancer. Two of these cases occurred in the preserved mucosa within the anal transition zone.
- In addition, the potential for continuing colitis in this residual mucosa is another concern. Rauh and coworkers have described a “short-strip pouchitis” that manifests as inflammation at the pouch anal anastomosis thought secondary to residual colitic mucosa.
- In an effort to resolve these issues, three prospective, randomized trials have demonstrated no significant differences in perioperative complications or functional results in those patients where a mucosectomy was done versus those patients where the distal rectal mucosa was preserved.
- Another controversial technical issue is the shape and size of the reservoir.
- At present, most centers perform a J-pouch because it is easier and faster to construct. An S-pouch can provide additional length (2–4 cm) compared with the J-pouch and can be useful in minimizing anastomotic tension. However, the 2-cm exit conduit of the S-pouch may lengthen over time and obstructive defecation may develop.
- A controversy that merits discussion relates to the routine use of a diverting loop ileostomy.

- Proponents of routine fecal diversion contend that post-operative septic complications are minimized. Loop ileostomy also obviates the problem of immediate severe diarrhea through an edematous ileal pouch and a sphincter that has been damaged surgically by mucosectomy or double-stapling.
- However, many surgeons believe that the loop ileostomy is counterproductive. Notwithstanding the additional operation and increased hospitalization associated with its closure, the morbidity of ileostomy closure is not insignificant, because small bowel obstruction and anastomosis leaks can occur.
- It should be stressed that problems associated with the ileostomy or its closure such as dehydration, anastomotic leak, or bowel obstruction are easily managed with medical or surgical means.
- The development of a pouch-specific complication in those patients without an ileostomy is a particularly morbid event requiring repeat laparotomy and fecal diversion in a septic patient.
- It is clear that although associated with more skin irritation and stomal nursing care, a loop ileostomy is preferred over an end ileostomy for temporary fecal diversion after IPAA because of the ease of loop stoma closure.

42. Surgery for Crohn's Disease

A. Introduction

- Crohn's disease is a chronic, unremitting, incurable, inflammatory disorder that can affect the entire intestinal tract.
- The presenting symptoms and signs, medical and operative options, and outcome likely depend on the disease genotype and phenotype.
- Specifically, the surgical procedures typically utilized in the operative management of Crohn's disease include nonresectional techniques such as internal bypass, fecal diversion, and strictureplasty as well as resectional procedures with or without concomitant anastomoses.

B. Etiology and Incidence

- The cause of Crohn's disease is unclear but recent investigations continue to provide insight into the etiology and pathogenesis through a complex interplay between conditioning factors and effector mechanisms. The conditioning factors include genetic influences and triggering events that create a permissive host, whereas the effector mechanisms mediate tissue damage through dysregulation of the intestinal immune and nonimmune functions.
- Patients afflicted with symptomatic disease are likely genetically susceptible because abnormalities in seven loci on chromosomes 16q, 12, 6p, 14q, 5q, 19, and 1p have been identified in selected populations.
- Initiating or triggering events such as environmental factors and microbial agents also probably contribute to disease sus-

ceptibility as evidenced by reports that describe the effects of tobacco usage and fecal flora on disease activity. In addition, abnormalities in immune cellular function, nonimmune cell activity, protein expression, and cellular apoptosis hint as to the role of the dysregulated effector mechanisms in the pathogenesis of Crohn's disease.

- The prevalence of Crohn's disease in the United States is approximately seven cases per 100,000 persons, and the incidence has steadily increased over the past five decades.
- The male-to-female ratio of the disease is 1.1–1.8:1 and the disease has a bimodal age distribution with the first peak occurring between the ages of 15–30 years and the second between 60 and 80 years; most persons experience the onset of disease symptoms before 30 years of age.
- A twofold to fourfold increase in the prevalence has been found among the Jewish population in the United States, Europe, and South Africa compared with other ethnic groups.

C. Disease Classification

Vienna Classification

- Prospectively designed simple phenotypic classification system based on objective and reproducible clinical variables that include age at diagnosis, anatomic location, and disease behavior.
- The age at diagnosis is stratified into patients <40 years and those ≥40 years.
- The anatomic location is classified as terminal ileum, colon, ileocolon, and upper gastrointestinal disease.
 - Terminal ileal disease is defined as disease limited to the lower third of the small bowel with or without cecal involvement.
 - Colon disease is any colonic involvement between the cecum and rectum without small bowel or upper gastrointestinal disease.
 - Ileocolon disease is disease of the terminal ileum with colonic involvement noted between the cecum and rectum.
 - And, upper gastrointestinal disease is defined as any disease location proximal to the terminal ileum regardless of involvement in other areas.

- The disease behavior is grouped as nonstricturing nonpenetrating (inflammatory), stricturing, and penetrating. Subsequent application of the Vienna Classification to clinical practice has demonstrated that the Crohn's disease phenotype markedly changes for a given patient over time with 15% of patients experiencing a change in anatomic location and 80% of individuals with inflammatory disease ultimately demonstrating a stricturing or penetrating behavior.
- Recent advances in determining the genetic linkages associated with Crohn's disease will likely lead to a revised Crohn's disease classification system that combines genotype and phenotype characteristics.

D. Operative Indications

Toxic Colitis

- Toxic colitis is a potentially fatal complication of Crohn's disease, particularly if accompanied by megacolon.
- The definition includes a disease flare accompanied by two of the following criteria: hypoalbuminemia (<3.0 g/dL), leukocytosis ($>10.5 \times 10^9$ cells/L), tachycardia (>100 beats/min), temperature increase ($>38.6^\circ\text{C}$).
- The initial management is directed at reversing physiologic deficits with intravenous hydration, correction of electrolyte imbalances, and blood product transfusions.
- Free perforation, increasing colonic dilatation, massive hemorrhage, peritonitis, and septic shock are indications for emergent operation after the patient has been adequately resuscitated. In the absence of these features, medical therapy is initiated with high dosages of intravenous corticosteroids, immunomodulators, and/or biologic agents. Broad-spectrum antibiotics directed against intestinal flora are prescribed to minimize the risk of sepsis secondary to transmural inflammation or microperforation.
- Any worsening of the clinical course over the ensuing 24–72 h mandates urgent laparotomy.
- The principal operative options in patients with toxic colitis complicating Crohn's disease include subtotal colectomy with

end ileostomy, total proctocolectomy with end ileostomy, and loop ileostomy with decompressive blowhole colostomy. Of these alternatives, subtotal colectomy with end ileostomy is the most widely practiced procedure.

Hemorrhage

- The principal management of disease-related hemorrhage is determined by the severity and persistence of bleeding as well as the risk for recurrence. Localization of the bleeding site is essential regardless of the planned therapy.
- Laparotomy and resection with or without anastomosis are required if the patient's hemodynamic state cannot be sustained, bleeding persists despite six units of transfused blood, hemorrhage recurs, or another indication for surgery exists.

Perforation

- Free perforation of the small bowel is also unusual and typically occurs at or just proximal to a strictured site.
- The most appropriate treatment is resection of the involved bowel with immediate or delayed anastomosis.
- Perforation of the colon in patients with Crohn's disease is also rare and typically requires subtotal colectomy for optimal management because these cases often occur in the setting of severe colitis or steroid usage.

Neoplasia

- Persons with Crohn's disease are at increased risk for developing cancer compared with the general population.
- In a population-based study from Canada, these patients had an increased relative risk of developing carcinoma of the small intestine [17.4; 95% confidence interval (CI), 4.16–72.9] as well as malignancies of the liver and biliary tract (5.22; 95% CI, 0.96–28.5), and males were at a particular risk for lymphoma (3.63; 95% CI, 1.53–8.62). Their patients with Crohn's disease were also at increased risk for the development of colon cancer (2.64; 95% CI, 1.69–4.12) and the risk was similar to that seen in persons with ulcerative colitis (2.75; 95% CI, 1.91–3.97).

Growth Retardation

- Abnormal linear growth secondary to delayed skeletal maturation is frequently encountered in children and adolescents with Crohn's disease.
- Surgical resection is often accompanied by growth response and associated psychologic benefit.

Extraintestinal Manifestations

- Operative management of the intestinal disease can provide beneficial control of the extraintestinal manifestation. Conversely, abnormalities affecting the hepatic, vascular, hematologic, pulmonary, cardiac, or neurologic systems behave independent of the intestinal disease.

Failed Medical Therapy

- When all appropriate medical therapy has failed, operative intervention is warranted.
- The continuation of ineffective medical management risks the development of further disease complications that may detrimentally impact surgical outcome.

E. Operative Considerations

- Some fundamental observations that must be considered when operating for Crohn's disease are as follows:
 - Crohn's disease is incurable.
 - Intestinal complications are the most common operative indication.
 - Operative options are influenced by myriad factors.
 - Asymptomatic disease generally does not require surgery.
 - Nondiseased bowel can be involved by inflammatory adhesions or internal fistulas.
 - Mesenteric division can be difficult.
 - Resection margins should be conservative (2 cm).
- Crohn's disease is a chronic inflammatory disorder that cannot be cured by medical therapy or operative intervention. Accord-

ingly, treatment focuses on safely alleviating disease symptoms and restoring quality of life while attempting to maintain continuity of the intestinal tract.

F. Operative Options

Internal Bypass

- Continuity bypass is sometimes the preferred method of managing symptomatic gastroduodenal Crohn's disease that is refractory to medical treatment where resection would entail extensive reconstruction of the upper intestinal tract or pancreaticobiliary system.

Fecal Diversion

- Fecal diversion can be permanent or temporary.
- Many of the stomas created to permanently bypass unresected disease fail to control symptoms secondary to the out-of-circuit bowel, and resection is ultimately warranted.

Strictureplasty

- The situations for which strictureplasty is considered are as follows:
 - Diffuse involvement of the small bowel with multiple strictures
 - Stricture(s) in a patient who has undergone previous major resection(s) of small bowel (>100 cm)
 - Rapid recurrence of Crohn's disease manifested as obstruction
 - Stricture in a patient with short bowel syndrome
 - Nonphlegmonous fibrotic stricture
- The contraindications to strictureplasty are as follows:
 - Free or contained perforation of the small bowel
 - Phlegmonous inflammation, internal fistula, or external fistula involving the affected site
 - Multiple strictures within a short segment
 - Stricture in close proximity to a site chosen for resection
 - Hypoalbuminemia (<2.0 g/dL)

Resection

- The basic principles of resection should be followed whether an open or laparoscopic approach is used, and include mobilization of both diseased intestine as well as sufficient nondiseased bowel to facilitate the subsequent creation of a tension-free anastomosis or construction of an ostomy.
- A laparoscopic approach can be used for a variety of resectional procedures and is typically associated with longer procedure times, but shorter lengths of stay and briefer periods of recovery.
- After the diseased bowel has been resected, the surgeon must decide whether to create an end stoma, an anastomosis, or a diverted anastomosis. In general, an end stoma is desirable in patients who are critically ill, demonstrate fecal peritonitis, or have coagulopathy. An anastomosis can be safely created in most other instances assuming a few general principles are respected that include the following:
 - Adequate blood supply must be assured
 - Tension or torsion are unacceptable
 - Luminal size needs to be equivalent
 - The mesenteric defect may be closed

G. Specific Anatomic Locations

Terminal Ileum

- Terminal ileal disease is defined as disease limited to the lower third of the small bowel with or without cecal involvement.
- Approximately 20% of patients with Crohn's disease will express this phenotype, and usually present with symptoms suggestive of inflammation or obstruction.
- In the majority of cases, resection with construction of an ileal-ascending colon anastomosis is feasible and desirable.

Colon

- Colon disease is any colonic involvement between the cecum and rectum without small bowel or upper gastrointestinal disease.

- Nearly 40% of patients have this disease distribution, and often complain of inflammatory disease symptoms including abdominal cramping, bloody diarrhea, and urgency.
- Persons presenting with segmental disease are best treated with segmental resection to protect against dehydration and electrolyte imbalances associated with loss of the large intestine's physiologic role.
- Crohn's disease of the transverse, descending, and sigmoid colons presents a situation in which segmental resection and colocolic or colorectal anastomosis is most frequently used.
- In younger patients and those without prior small bowel resection, the diseased segment and uninvolved proximal colon are resected and an ileosigmoid or ileorectal anastomosis is constructed.
- Patients with extensive colonic involvement, relative rectal sparing, and adequate fecal continence without active anoperineal sepsis or compromised rectal compliance are candidates for colectomy with ileoproctostomy.
- Patients with proctocolitis that warrants operative treatment usually require a total proctocolectomy with creation of an end ileostomy, especially those persons with colitis whose proctitis, sphincter dysfunction, or anoperineal sepsis is too severe for rectal preservation and ileoproctostomy.

Ileocolon

- Ileocolon disease is disease of the terminal ileum with colonic involvement noted distal to the cecum and proximal to the rectum.
- This disease phenotype occurs as often as terminal ileal disease, and the operative approach to these patients is similar to that already outlined for individuals with terminal ileal or colon disease.

Upper Gastrointestinal

- Upper gastrointestinal disease is defined as any disease location proximal to the terminal ileum regardless of involvement in other areas, and represents the phenotype that is often the most difficult to manage because of its predilection for extensive disease and predominantly stricturing or penetrating behavior.

- Small bowel disease proximal to the terminal ileum is often typified by several stenotic segments separated from one another by noninvolved bowel.
- The prognosis for Crohn's disease diffusely involving the small bowel is significantly worse than that of localized disease.
- The operative options in a symptomatic patient with diffuse jejunoileitis include internal intestinal bypass, strictureplasty, and resection.
- An operation that consists of multiple strictureplasties is the procedure of choice using the previously discussed techniques to safely conserve small bowel and relieve symptoms secondary to luminal stenosis.
- Gastroduodenal Crohn's disease is relatively rare, and the most common presenting complaints are upper abdominal pain and symptoms of duodenal obstruction.
- For duodenal disease, medical therapy is the mainstay of treatment for inflammatory and penetrating disease, whereas strictures present a different challenge.
- Recently, success with duodenal strictureplasty has been reported by several centers, and the technique seems to be the procedure of choice if the affected bowel is sufficiently supple and devoid of associated sepsis.

Anoperineum

- Crohn's disease will affect the anus or perineum in as many as 61–80% of patients, and typically occurs with or following the onset of disease in other anatomic locations.
- Involvement of this area can manifest itself as a fissure, skin tag or hemorrhoid, cavitating ulcer, abscess or fistula, anovaginal fistula, anorectal stricture, or carcinoma.
- The evaluation of anoperineal Crohn's disease should include a regional examination as well as investigations to determine the extent and activity of disease located elsewhere through varied imaging and endoscopic studies. The regional examination may be significantly enhanced by assessment with fistulography, endoanal ultrasonography, magnetic resonance imaging, or examination under anesthesia.
- The first priority of therapy is to drain any associated sepsis through the insertion of drainage catheters with or without placement of noncutting setons. The second priority focuses

on stabilizing the infectious component using antibiotic therapy such as metronidazole or ciprofloxacin. In addition, attempts at medical management of the disease process are initiated with immunomodulators and biologic agents; 5-aminosalicylic acid compounds and steroids provide little benefit. The third priority is optimization of quality of life through continued medical therapy or operative intervention used individually or in combination.

- Asymptomatic fissures, skin tags, or hemorrhoids are best ignored because surgical treatment may escalate the disease to a point in which proctectomy is eventually required.
- The operative management of a perineal abscess or anoperineal fistula is predicated upon the patient's baseline continence, complexity of the fistula, amount of sphincter encompassed by the fistula, and severity of rectal involvement.
- The clinical scenario best suited for fistulotomy is the continent patient with a simple, low-lying, posterior fistula without associated rectal disease.
- Alternatively, a chronic indwelling noncutting seton can be used in this setting. These setons are more ideally suited for chronic drainage of a fistula complicated by rectal inflammation, with proctectomy required in 0–33% of patients reported in series composed of at least 20 patients.
- Most clinicians use medical therapy in combination with operative treatment.

H. Special Circumstances

Enteroparietal Abscess

- An enteroparietal abscess is likely best treated by initial external drainage using a computed tomography (CT)-guided catheter if the cavity is accessible or, otherwise, by surgical drainage.

Interloop Abscess

- Interloop abscesses, which are considerably smaller than the enteroparietal form, are often occult or subtle in presentation and are usually identified only at the time of resection when separating loops of matted bowel.

Intramesenteric Abscess

- Intramesenteric abscesses arise from penetrating disease eroding into the mesentery of the small bowel, colon, or rectum.
- Resection of the bowel with a cuff of mesentery carries a particular risk for vascular injury or secondary hemorrhage. Instead, the abscess is identified by intraoperative needle aspiration, and the purulent fluid is drained back into the small bowel.
- An exclusion bypass of the involved bowel is then performed by creating proximal and distal mucus fistulas, and constructing an enteroenterostomy above and below the diseased segment to restore bowel continuity. The excluded segment is then resected 6 months later.

Retroperitoneal and Psoas Abscess

- Abscesses arising in this anatomic location may be large and well-circumscribed or poorly localized with the infectious process extending deep to the psoas fascia in both caudad and cephalad directions.
- CT-guided drainage is usually first used followed by elective resection of the diseased segment.

Enterocutaneous Fistula

- Enterocutaneous fistulas can develop before any surgical therapy, during the immediate postoperative period, or several weeks after an operation.
- Medical therapy is then usually initiated with operative management warranted for significantly symptomatic fistulas that are unlikely to heal or fail to heal with medical treatment.
- In a patient with a complex fistula requiring a prolonged operation with extensive enterolysis, multiple anastomoses, enterotomy closures, or strictureplasties, a diverting stoma proximal to all procedure sites is often prudent to allow healing before restoration of the normal fecal flow.
- The management of a fistula developing during the early postoperative period depends on the timing of the presentation and other variables. If the operation was relatively straightforward and the fistula presents in the first 7–10 postoperative days,

re-laparotomy, resection, or fistula repair, and probable proximal fecal diversion is warranted. Beyond that time interval or after a difficult operation, re-laparotomy may be associated with more harm than benefit because of formidable adhesions and the risk of iatrogenic bowel injury.

Enteroenteric Fistulas

- Enteroenteric fistulas are the most common type of internal fistula arising in people with Crohn's disease, and they have been reported to occur in 33% of patients whereas external fistulas affect 15% of people. Isolated enteroenteric fistulas usually cause few symptoms unless obstructive or septic complications dominate the clinical presentation.
- Nearly 40% of patients with internal fistulas initially managed by nonoperative methods will require surgery within 1 year, mainly because of disease intractability.
- One year after an initial resection, 60–80% of patients possess endoscopic recurrence, 10–20% experience clinical relapse, and 5% demonstrate operative recurrence.
- Although disease behavior may impact the likelihood of recurrence, tobacco usage has been almost uniformly linked to recurrence. Specifically, smoking is an independent risk factor for symptomatic, endoscopic, and operative recurrence.
- Despite the symptomatic recurrence rate, it is important to recall that segmental colonic resection delays the need for permanent ileostomy and partially conserves a portion of the large intestine's functional absorbing surface.
- Various forms of medical therapy have been trialed to prevent the likelihood of recurrent Crohn's disease after operative management, but no clear prophylactic drug regime has emerged.

43. Less-Common Benign Disorders of the Colon and Rectum

A. Ischemic Colitis

- Vascular disorders of the midgut and hindgut are extremely morbid conditions. This is because these diseases often afflict elderly individuals with various coexisting morbidities and limited physiologic reserve. This is compounded by the fact that these disorders are often diagnosed late, only after full-thickness intestinal injury has occurred, with perforation or gangrene.
- Major postoperative complications remain excessive and both early and late mortality rates continue to be significant.
- Ischemic colitis is the most common form of ischemic injury to the gastrointestinal (GI) tract.
- It is paramount that the surgeon involved in the care of ischemia and hemorrhage of the colon and rectum has a thorough understanding of the anatomy of the large bowel.
- Ischemic injury to the colon is now recognized to manifest distinct clinical subtypes, ranging in severity from transient segmental colopathy to fulminant gangrenous colitis.
- Etiologies including shock, autoimmune disease, coagulopathies, long-distance running, illicit drug use, and medication-induced colonic ischemia have been reported, in patients both young and old.
- Ischemic colitis is often recognized as a specific entity characterized by sudden abdominal pain and diarrhea. A spectrum of disease exists, ranging from transient mucosal injury that spontaneously resolves to transmural disease with full-thickness gangrene. An intermediate form also exists in which, after resolution of symptoms, stricture formation occurs.

- An increased awareness and suspicion that ischemic colitis is present should initiate prompt diagnostic endoscopy.
- Colonoscopy is responsible for the increasing awareness of colon ischemia and remains the procedure of choice to document its presence or absence and identify or exclude other colonic pathology.
- Two distinct forms of ischemic colitis have been repeatedly described throughout the last 40 years. The spontaneous, usually self-limiting form of ischemic colitis contrasts drastically with the often catastrophic, more fulminant form. Despite the widely divergent outcomes, the initial presentations of the two forms may be identical and are not predictive of the patient's clinical course.
- Ischemic colitis is generally viewed as a nonocclusive form of intestinal ischemia.
- Clinical risk factors are important to consider when evaluating a patient for ischemic colitis. Cardiovascular disease and hypertension are common, prevalent, preexisting medical conditions among our group of patients, and many of these patients are taking vasoactive medications, which may have limited the flow to the ischemic segments or have blunted the colon's ability to compensate for low blood flow.
- Additionally, many have renal failure.
- Nongangrenous ischemic colitis should be managed conservatively, because resolution is often self-limiting.
- Even strictures can be managed without operation because obstruction is rarely complete and endoscopy can differentiate benign from malignant strictures.
- Adequate hydration initially is important to maintain tissue perfusion. Systemic antibiotic therapy is given with monitoring of white blood cell count and hematocrit. There is no role for systemic anticoagulation.
- Abdominal pain, acidosis, and clinical deterioration all suggest impending infarction.
- At surgery, all ischemic colon needs to be resected. Primary anastomosis should be avoided.
- Colonic ischemia affecting younger people is being recognized more frequently where identifiable causes include collagen vascular disease, hematologic disorders, long-distance running, and cocaine abuse.

B. Collagen Vascular-Associated Colitis

- The collagen vascular diseases represent a collection of conditions that are believed to be the result of pathologic alterations in the immune system.
- They may occur in any organ and may be associated with GI manifestations. Often these entities affect the blood supply to the colon and rectum and may produce ischemic changes and a colitis.
- Deposition of immune complexes in blood vessel walls resulting in either ischemia or thrombosis is the most widely accepted pathogenic mechanism.

Polyarteritis Nodosa

- PAN is a systemic necrotizing vasculitis of small- and medium-sized arteries often with visceral involvement. Lesions are segmental and tend to involve bifurcations and branches of arteries.
- In the United States, the incidence is about 3–5 per 100,000 population per year. Men are affected more frequently than women and the age of onset is 40–60 years.
- Patients typically present with nonspecific signs and symptoms such as fever, weakness, headache, abdominal pain, weight loss, and malaise.
- PAN affects multiple systems including renal, musculoskeletal, nervous, GI, integument, cardiac, and genitourinary. The GI tract involvement is similarly nonspecific and presenting signs and symptoms include abdominal pain, nausea, and vomiting, bleeding, bowel infarction, and perforation, as well as cholecystitis, or hepatic/ pancreatic infarction.
- PAN carries a high mortality rate when untreated. Nearly half of patients die within the first 3 months of onset. When immunosuppressive agents are combined with corticosteroids, the 5-year survival rate may increase to greater than 80%.
- GI involvement of PAN is often a poor prognostic factor.
- Patients often have an abnormal visceral arteriogram with both saccular and fusiform aneurysms of the mesenteric vessels.
- Abdominal symptoms are often manifested as pain where organ damage caused by ischemia and hemorrhage may occur.

GI hemorrhage, bowel perforation, and bowel infarction are often the underlying pathology.

- Surgical intervention is required for acute surgical conditions as a consequence of PAN or CSS. Bowel resection with avoidance of an intestinal anastomosis should be performed.

Cryoglobulinemia

- Cryoglobulins are immunoglobulins that undergo reversible precipitation at low temperatures.
- Cryoglobulinemia may be associated with a particular disease such as autoimmune disease, lymphoproliferative disorder, infectious diseases, or it may be idiopathic form termed essential cryoglobulinemia.
- Cryoglobulinemia may complicate chronic hepatitis infection, and many immune diseases including inflammatory bowel disease.
- The GI manifestations are rare and may result in ischemia or infarction secondary to a mesenteric vasculitis.

Henoch-Schönlein Purpura

- Henoch-Schönlein purpura is a distinct systemic vasculitis characterized by the tissue deposition of immunoglobulin A containing immune complexes.
- The clinical symptoms include abdominal manifestations, arthralgias or arthritis, palpable purpura, glomerulonephritis, and colicky abdominal pain.
- Although the disease is frequently seen in children, adults of any age may be affected. Abdominal symptoms are usually the result of vasculitis in which symptoms include abdominal pain, nausea, and vomiting, and GI bleeding may occur in up to 40% of patients. Intramural hematomas, intussusception, infarction, and perforation of the gut may be a sequelae of this disease.

Behçet's Syndrome

- Behçet's syndrome is a chronic relapsing inflammatory, multi-system disorder characterized by widespread vasculitis of large and small arterial and venous vessels.

- It is most prevalent around the Mediterranean and Japan. When it appears, it affects young men and runs an aggressive course.
- In Europe and North America, it mainly affects women.
- The etiology of the disease is unknown, but most authors believe it arises from a genetic predisposition with a triggering event such as streptococcal infection that leads to alteration in immune function.
- The GI tract is affected in 15–65% of cases, and when involved carries a poor prognosis.
- Mesenteric ischemia and infarction are a result of large vessel disease and ulceration is a sequelae of small vessel disease involving the mucosa. The ileocecal region is the most frequently involved segment.
- Behçet's disease and inflammatory bowel disease share many of the extraintestinal manifestations involving the eye, mouth, liver, and joints. Behçet's disease behaves similarly to Crohn's disease with anorectal ulceration and rectovaginal fistula.
- Endoscopic and radiographic evaluation of the small and large bowel will reveal deep ulcers, pseudopolyps, and mucositis.
- Surgery is often encouraged early in treatment before fatal complications occur. Wide surgical margins are preferred and intestinal anastomoses discouraged because anastomotic leaks, reperforation, and fistulization are common.

Systemic Lupus Erythematosus

- SLE is a chronic multisystem inflammatory disease that can affect any and every organ system of the body, and follows a relapsing and remitting form. It is an autoimmune disorder involving microvascular inflammation and the generation of autoantibodies.
- Although the specific cause of SLE is unknown, multiple factors are associated (genetic, hormonal, environmental) with this disease.
- Disturbances within the immune system result in the formation of immune complexes in the microvasculature leading to complement activation and inflammation.
- Antinuclear antibodies are present in the serum of virtually all patients with SLE and antibodies to native DNA are highly specific for the diagnosis of SLE.

- GI symptoms are common in patients with active SLE. Nausea and dyspepsia are frequent complications. Abdominal pain may be related directly to active lupus.
- One of the most devastating complications of lupus is GI vasculitis and carries a 50% mortality rate.
- Common sequelae include ulceration, hemorrhage, perforation, and infarction. The diagnosis of small or large bowel vasculitis is frequently difficult to make because arteriography rarely demonstrates small vessel disease and computed tomography (CT), endoscopy, and small bowel series may also be unrevealing. The diagnosis is often made from surgical specimens after an acute surgical emergency.
- Medical treatment of abdominal lupus vasculitis often involves corticosteroids and cyclophosphamide.

Scleroderma

- Scleroderma is a multisystem, multistage disorder of small arteries, microvessels, and connective tissue.
- The disease occurs in all races but affects women three to four times more often than men. Initial symptoms occur in the 20s to 40s.
- Systemic manifestations may include skin involvement, Raynaud's disease, polyarthritis, and lung, heart, kidney, and thyroid problems.
- In the GI tract, the disease may affect the esophagus, stomach, or small or large bowel. The GI symptoms may precede the diagnosis by several years, and are often the most difficult to treat.
- Overproduction of collagen, increased humoral immunity, and abnormal cellular immune function all contribute to the development of scleroderma in other organs.
- More importantly, the changes seen in the blood vessels in scleroderma have a role in the development of the clinical manifestations of the disease. The esophagus is the GI organ that is most frequently involved and more than 50% of patients diagnosed with scleroderma have esophageal manifestations.
- In the small bowel and the stomach, chronic intestinal pseudoobstruction, bacterial overgrowth, and malnutrition are the main consequences. These patients often require prokinetic agents which can be used to enhance gut motility. Antibiotic therapy

is the treatment for bacterial overgrowth. Somatostatin is used for severe diarrhea.

- Scleroderma may also affect the large bowel and colonic motility. Clinically, patients may have severe constipation and may have fecal impaction, rectal prolapse, megacolon, and diverticula.
- Anorectal dysfunction frequently occurs with scleroderma and is similar to that of the esophageal dysmotility.
- The treatment of constipation may prove difficult, and after conventional treatment fails, daily balanced electrolyte solutions containing polyethylene glycol may be required.
- Prokinetics are often tried, but results are disappointing.

Polymyositis

- Polymyositis is an inflammatory muscle disease of unknown etiology. It is characterized by weakness, high levels of striated muscle enzymes, and electromyographic or biopsy evidence of an inflammatory myopathy.
- This all is a result of immune-mediated muscle inflammation and vascular damage. The immune system is primed to act against previously unrecognized muscle antigens.
- It is a disease of adults and common among blacks.
- Symmetric proximal muscle pain and weakness, dysphagia, arthralgias, joint pain, and, when accompanied by a rash over the face, chest and hands, it is referred to as dermatomyositis.
- Serum creatine kinase is the most sensitive and specific laboratory study with levels 5–50 times that of normal.
- Treatment includes systemic steroids and immunosuppressive agents.
- Overall, the 5-year mortality rate is 20%.

C. Microscopic Colitis

- Microscopic colitis encompasses two subtypes: lymphocytic colitis and collagenous colitis.
- From a clinical perspective, disease manifestations and treatment are alike. These entities are separated by their histologic features.

- Pardi estimates that microscopic colitis accounts for about 10% of cases of chronic diarrhea referred to major centers for study.
- Collagenous colitis occurs more often in women (studies exceed 80%) whereas there seems to be no gender differential in lymphocytic colitis.
- Both entities principally afflict patients over the age of 60 but cases have been demonstrated in all age groups including pediatrics.
- Bo-Linn and associates were able to demonstrate that watery diarrhea was secondary to marked depression of colonic absorption.
- Crampy abdominal pain and weight loss are the major clinical complaints from patients. Stool frequency ranges from 3 to 20 per day. Despite this, dehydration is unusual as are fever, vomiting, and GI bleeding.
- The diagnosis is most commonly made by colonoscopic biopsies. Lymphocytic colitis tends to occur uniformly throughout the colon and rectum but collagenous colitis is often patchy, therefore requiring frequent colon biopsies at intervals throughout.
- The histologic criteria for lymphocytic colitis requires more than 10 lymphocytes per 100 epithelial cells in the colon. Normal colons will have less than five lymphocytes per 100 cells.
- The excess deposition of collagen in collagenous colitis occurs in the subepithelial layer of the bowel.
- Studies demonstrating a high prevalence of arthritis (82%) and autoantibodies (50%) suggest the possibility of an autoimmune disorder.
- Treatment options are empiric and are directed at symptom management, management of the inflammatory process, and the potential role of disordered immunoregulation in the pathogenesis of this disease.
- Initially, dietary modifications can be tried, eliminating caffeine, dairy, alcohol, and artificial sweeteners. Nonsteroidal antiinflammatory drugs (NSAIDs) should be discontinued. Loperamide and diphenoxylate/atropine are generally effective at symptom resolution. Bismuth subsalicylate has been demonstrated over an 8-week course to be safe and efficacious in disease management when dosed at 524 mg four times daily.
- Surgical options include ileostomy for diversion or colectomy, with or without restoration of continence. Surgery, as a treatment

option, requires failure or intolerance to the medical options available and symptoms severe enough to warrant such aggressive intervention.

D. Eosinophilic Colitis

- This rare condition is characterized by eosinophilic infiltration of the involved tissues and increased eosinophil counts in peripheral blood. Eosinophilic colitis is usually encountered in the gastric antrum and proximal small bowel.
- Differential diagnosis includes tuberculosis, Crohn's disease, parasite infestations, allergic enteropathies, and collagen vascular disorders. Colonoscopic biopsies should differentiate eosinophilic colitis from these other grossly similar appearing conditions.
- Therapy for symptomatic patients consists of steroids. Spontaneous remissions have been documented. Surgery has a role for management of complications, such as intussusception, obstruction, or hemorrhage and in cases in which diagnostic dilemmas require more tissue.

E. Fungal Colitis

- Clinical settings in which this diagnosis must be considered include human immunodeficiency virus (HIV) infections, immunocompromised states such as splenectomy, chronic liver disease, and steroid therapy as well as in chronically ill patients being treated with broad-spectrum antibiotics.
- The major pathogens in this category include *Candida* spp., *Histoplasma capsulatum*, and *Cryptococcus neoformans*.
- *Candida* colitis is the more common of these entities found predominantly in patients in the intensive care unit. Usually, the infection is systemic involving septicemia, the pulmonary tract, the urinary tract, and the GI tract.
- Colonic involvement may be diffuse and thus results in diarrhea, fever, and abdominal pain.
- Stool cultures or endoscopic biopsies are diagnostic when typical spores, yeast, or pseudomycelia are demonstrated.

- Medical treatment is first-line therapy in the absence of peritonitis. This consists of oral nystatin 500,000–1,000,000 units four times daily or in sicker patients, ketoconazole 200–400 mg daily.
- Surgical intervention may be required in the face of free perforation or clinical findings of peritonitis. Despite aggressive surgical intervention, mortality is very high because of the severity of the associated conditions.

F. Histoplasmosis

- *H. capsulatum* is found endemically throughout the Midwestern United States. Although principally a pathogen of the reticuloendothelial system, it can cause systemic infection in the immunocompromised host. Pulmonic disease is most common but ileocolitis does occur.
- Endoscopic examination can be confusing because the lesions may appear to resemble adenocarcinoma. Skip areas, pseudopolyps, ulcerations, and plaque-like lesions may be present but biopsies will reveal intracellular budding yeasts within the mucosa when this organism is present. Serologic tests and fungal cultures may also confirm the diagnosis.

G. Cryptococcus

- Cryptococcosis usually affects the central nervous system. *C. neoformans* is acquired via inhalation of soil contaminated with this encapsulated yeast. Isolated GI infection is rare but does occur in immunocompromised patients.
- A high index of suspicion must be maintained when patients present with symptoms of colitis and a concomitant history of immune suppressive therapy or infection with HIV.
- Diagnosis is confirmed by biopsy of infected mucosa demonstrating encapsulated budding yeasts or via culture of stool.
- Ketoconazole is effective in less severely ill patients but amphotericin B is standard therapy in severely ill or immunocompromised patients.

H. Bacterial Colitis

- Because bacterial pathogens can produce clinical syndromes, which may mimic other conditions in which surgery is more likely a therapeutic consideration, colorectal surgeons must have a basic understanding of the organisms that cause enterocolitis as well as diagnostic and therapeutic options (see Table 43.1).
- Bacterial pathogens cause disease within the GI tract in several ways: mucosal adherence leading to secretory diarrhea, toxin production, and mucosal invasion.
- The very young and the elderly are at greater risk of serious sequelae as are immunocompromised hosts.
- The majority of infections worldwide occur in developing countries where water contamination, poor food preservation techniques, and fecal contamination of food supplies is more likely.
- For the most part, watery diarrhea syndrome requires supportive measures such as fluid and electrolyte replacement.
- Dysenteric syndromes characterized by bloody diarrhea, fever, and abdominal pain generally necessitate identification of the organism so that appropriate antibiotic therapy can be initiated (see Table 43.2).
- The goals of treatment are to decrease the period of bacterial shedding in the stools and to improve the patient's clinical condition, thus lessening the likelihood of invasive complications of infection.

Table 43.1. Clinical pathologic characteristics of bacterial colitis.

Sign	Organisms capable of producing syndrome
Watery diarrhea	<i>E. coli</i>
	<i>Salmonella</i>
	<i>Shigella</i>
Dysentery	<i>E. coli</i>
	<i>Salmonella</i>
	<i>Shigella</i>
	<i>Yersinia</i>
	<i>Campylobacter</i>
Enteric fever or syndrome	<i>Salmonella spp.</i>
	<i>Yersinia</i>
	<i>Campylobacter</i>

Table 43.2. Antibiotic therapy for bacterial colitis (adults).

Pathogen	Illness	Treatment
<i>E. coli</i>	Traveler's diarrhea	TMP/SMX 1 double strength tab b.i.d. $\times$ 3–5 days <i>or</i> ciprofloxacin 500 mg p.o. b.i.d. $\times$ 3–5 days
<i>Salmonella</i>	Bacteremia, sepsis, immunocompromised host, dysentery	Ceftriaxone 1 g IV <i>or</i> IM q 12 h $\times$ 2 weeks <i>or</i> cefoperazone 30 mg/kg q 12 h $\times$ 2 weeks <i>or</i> chloramphenicol IV 75 mg/kg/d in four divided doses $\times$ 2 weeks <i>or</i> ciprofloxacin 500 mg IV <i>or</i> p.o. q 12 h $\times$ 2 weeks <i>or</i> ampicillin 100 mg/kg/d IV <i>or</i> IM q 6 h $\times$ 14 days
<i>Shigella</i>	Dysentery	TMP/SMX double-strength tablets (DS), one b.i.d. p.o. $\times$ 5 days <i>or</i> norfloxacin 400 mg tablets p.o. b.i.d. $\times$ 5 d <i>or</i> ciprofloxacin 500 mg p.o. b.i.d. $\times$ 5 days
<i>Yersinia</i>	Sepsis, severe abdominal pain with mesenteric adenitis	Gentamicin 7.5 mg/kg/d administered IV q 8 h for 7–10 days <i>or</i> TMP/SMX DS b.i.d. for 5 days <i>or</i> chloramphenicol IV 75 mg/kg/d given q 6 h for 7–10 days
<i>Campylobacter</i>	Dysentery <i>or</i> sepsis	Ciprofloxacin 500 mg p.o. t.i.d. $\times$ 5 days <i>or</i> azithromycin 500 mg q d $\times$ 3 days <i>or</i> gentamicin <i>or</i> chloramphenicol as for Yersinia, if severe
<i>Tuberculosis</i>	Enterocolitis	Isoniazid 300 mg p.o. q d and rifampin 600 mg p.o. q d for 4–6 months
<i>Aeromonas</i>	Dysentery, enteric fever syndrome, immunocompromised patient	TMP/SMX DS p.o. b.i.d. $\times$ 7–10 days <i>or</i> doxycycline 100 mg p.o. b.i.d. <i>or</i> chloramphenicol IV 75 mg/kg/d given q 6 h for 7–10 days
<i>Brucellosis</i>	Colitis	Doxycycline 100 mg p.o. b.i.d. for 3–6 weeks and streptomycin 1 g IM q 12–24 h for 14 days
<i>Actinomycosis</i>	Abdominal pain, mass, fever	Penicillin G 12–18 million units/d given q 4–6 h for 2–6 weeks

b.i.d., twice a day; p.o., per os; q, every; IV, intravenously

I. *Escherichia coli*

- Enteropathic *E. coli* is primarily a problem causing outbreaks of severe diarrhea in nurseries.
 - Diarrhea is caused by the bacteria adhering to the mucosa of the enterocytes and the production of a cytotoxin causing mucosal damage.
 - Infection is primarily within the small bowel.
 - The clinical syndrome may consist of watery diarrhea, vomiting, and fever.
 - The process is generally self-limiting and so therapy is supportive.
 - Trimethoprim–sulfamethoxazole (TMP/SMX) is effective and is recommended in complicated cases.
- Enterotoxigenic *E. coli* is ubiquitous in developing nations and is the major organism causing traveler's diarrhea.
 - Thirty to fifty percent of travelers from industrialized nations spending 3 weeks or more in developing nations will experience this infection.
 - The toxin produced does not damage the mucosa but causes a secretory diarrhea.
 - Infection is self-limiting but may cause cramping and low-grade fevers.
 - Treatment is supportive. For travelers wishing to avoid becoming ill with this pathogen, prophylaxis with bismuth subsalicylate, 2 tablets four times daily during periods of exposure is helpful. Unfortunately, salicylate intoxication is a concern in children and thus not recommended in this group.
- Enteroinvasive *E. coli* produces a syndrome much like *Shigella*. Mucosal invasion of enterocytes by this strain produces the illness but is usually self-limited. Treatment is supportive unless dysentery develops. Should this occur, TMP/SMX is indicated.
- Enterohemorrhagic *E. coli* can cause serious dysenteric problems related to production of a cytotoxin.
 - It has occurred in the United States in outbreaks associated with undercooked hamburger meat.
 - Cramps, low-grade fever, and watery diarrhea progress to a more severe bloody diarrhea.

- Treatment remains supportive because no effective anti-microbial therapy is known.
- The clinical presentation may mimic inflammatory bowel disease or ischemic colitis.
- A hemolytic uremic syndrome or thrombocytopenia may complicate the recovery phase, especially in patients at either age extreme.

J. Shigella

- *Shigella* is the prototypical pathogen causing a dysenteric syndrome based on the ability of this gram-negative rod to produce toxins permitting epithelial cell penetration and destruction.
 - Malnourished and immunocompromised hosts are most at risk for the debilitating complications of infection.
 - Onset of infection follows fecal–oral transmission of a small number of inocula.
 - Sexual transmission does occur but most cases originate from overcrowded housing and daycare facilities.
 - Watery diarrhea, fever, fatigue, and malaise herald the onset of colitis.
 - Gross bleeding and mucus denotes dysentery and requires the more virulent properties usually associated with *S. dysenteriae* and least likely with *S. sonnei* as found in the United States.
 - Bowel obstruction and toxic megacolon are most frequently seen in *S. dysenteriae* infections in underdeveloped nations.
 - Although stool volume is low, making dehydration unusual, the colonic inflammatory process leads to spasm and tenesmus (10–100 bowel movements per day).
 - Diagnosis is best made by stool cultures for enteric pathogens.
 - Endoscopic examination reveals a friable, edematous, erythematous mucosa with focal ulcerations and bleeding. The most often affected area is the rectosigmoid but the more severe the infection, the more proximal the changes progress.

- Since infections with *S. sonnei* in the United States tend not to cause the dysenteric syndrome, supportive care is generally all that is necessary. Avoidance of antimotility agents is critical because their use exacerbates symptoms and predisposes to toxic megacolon.
- In the immunocompromised host or with the development of dysentery, TMP/SMX, ciprofloxacin, and ampicillin are usually effective at shortening the duration and severity of illness.
- Treatment should continue until stool cultures convert to no growth of the organism.

K. Salmonella

- A gram-negative bacilli, *Salmonella* causes predominantly two clinical conditions.
 - The first is typhoid fever caused by *S. typhi* and *S. paratyphi*, endemic in third world countries. The organism is ingested and is susceptible to destruction by normal gastric acidity, pancreatic enzymes, and enteric secretions. Where these barriers to infection are altered either by postsurgical changes or acid-blocking medications, infection is more likely. Incubation periods range from 5 to 21 days with the onset of remitting fevers, headache, abdominal pains, and diarrhea. Hyperplasia of the reticuloendothelial systems can cause marked swelling in the ileocecal area. Hemorrhage, obstruction, and perforation may occur requiring emergent surgical intervention with resection and proximal diversion necessary.
 - The second and by far more common condition in the United States is non-typhoidal salmonellosis. *S. enteritidis* is usually responsible for causing a self-limited gastroenteritis in the warmer months of the year. Contaminated food products lead to nausea, vomiting, and abdominal pain. Most patients experience watery diarrhea but dysenteric symptoms may develop, especially in the immunocompromised host. Infection is primarily small bowel but can progress to a colitis. Stool cultures, rectal swabs, or colonoscopic biopsies will assist in diagnosis.

For severe infections in patients who are immune suppressed, have foreign body implants, hemolytic anemia, or pregnant, antibiotic therapy with ampicillin or TMP/SMX should be given as first-line therapy. In the majority of affected patients in the United States, supportive care will suffice.

L. *Campylobacter*

- This gram-negative rod is the most frequently identified cause of acute diarrheal illness in United States and industrialized nations. *C. jejuni* is the most common.
- Outbreaks generally occur during warm weather and are most frequently traced to poor handling or preparation of chicken products.
- The organism can produce a spectrum of disease from watery diarrhea to dysentery depending on the strain's ability to produce enterotoxin, cytotoxin, or to cause mucosal invasion.
- The terminal ileum and cecum are most frequently involved.
- Most cases present with fever, abdominal pain, diarrhea, nausea, and malaise. Symptoms are generally self-limited resolving within 1 week but may linger up to 3 weeks.
- Endoscopic findings range from segmental colonic ulcerations to a diffuse colitis. Disease limited to the ileocecal region may mimic Crohn's disease.
- Diagnosis requires stool cultures because clinically the disease mimics *Salmonella* and *Shigella*.
- Treatment with erythromycin or ciprofloxacin should be reserved for severely ill patients or any of those affected having an immunocompromised state, i.e., HIV, the very young, or the very old. Otherwise, treatment is supportive.
- Surgical intervention may be necessary to rule out appendicitis, or less frequently, to treat complications such as megacolon, hemorrhage, or perforation.

M. *Yersinia*

- *Yersinia* is a gram-negative coccobacillus capable of producing gastroenteritis commonly in Europe and North America.

Y. enterocolitica and *Y. pseudotuberculosis* are most frequently associated with clinical disease, the latter being the more severe. Poor food handling and contaminated water are usually associated with outbreaks in the United States.

- Of significant import to surgeons is that 40% of cases present in a manner very similar to acute appendicitis. The organism invades Peyer's patches causing swelling in the terminal ileum, enlarged mesenteric nodes, localized pain, and watery diarrhea. At surgery, the appendix will appear normal.
- In severe cases, polyarthritis, erythema nodosum, and Reiter's syndrome may suggest the possibility of Crohn's ileocolitis.
- Colonoscopic evaluation may demonstrate erythema, aphthous ulcerations, and swelling of lymphoid tissue.
- Specific fecal culture techniques enhance identification, and serology is available, but both are time consuming.
- Treatment of uncomplicated cases with antibiotics has not demonstrated clinical improvement except in the immunocompromised host or in the more complicated infection, i.e., enteric-like fever or mesenteric adenitis. In these more serious conditions, tetracycline, ciprofloxacin, TMP/SMX, or aminoglycoside are effective.

N. Tuberculosis

- Within the United States, tuberculosis occurs primarily in immunosuppressed populations (especially associated with HIV), among immigrants from underdeveloped nations, among the urban poor, and impoverished Native Americans.
- Tuberculous enterocolitis is generally contracted via consumption of unpasteurized milk or from swallowing sputum infected from pulmonary tuberculosis.
- Distal small bowel and cecal infections are noted and present with abdominal pain, weight loss, and fever. From exposure to illness, clinical illness can be delayed for up to a year.
- Ulcers of varying depth, fistulas, and stenosis may result from the infectious process. Physical findings include generalized wasting and up to 50% of patients have a palpable mass in the right lower quadrant.

- Barium enema and/or CT may suggest the diagnosis but features can mimic inflammatory disease or malignancy.
- Tuberculous pericolic adenitis may produce extrinsic compression and can lead to partial or complete obstruction. Tuberculous peritonitis can present as a surgical emergency mimicking acute appendicitis. Colonoscopic biopsy or fine-needle aspiration have permitted detection of acid-fast bacilli or caseating granulomas without the delay of awaiting culture reports. Diagnostic laparoscopy demonstrated tuberculous peritonitis with 95% accuracy in one series.
- Stool cultures for viable tuberculosis organisms rarely demonstrate growth but is more likely in active cases of pulmonary tuberculosis. Serology tests have been developed and demonstrate sensitivity for intestinal tuberculosis of more than 80%.
- Treatment is usually medical with multi-drug regimens. Isoniazid and rifampin are first-line treatment but pyrazinamide and streptomycin or ethambutol may be added until sensitivity in the immunocompromised host can be established.
- In more established cases, obstruction of the bowel secondary to sclerosing lesions or fistulous disease may require surgical intervention. It is still recommended that a medical trial be attempted because many patients will improve and resolve without surgery.

O. *Neisseria gonorrhea*

- As a cause of proctitis, oroanal spread or anal-receptive sexual practices account for the majority of infections in the United States.
- Sexually transmitted diseases (STDs) are frequently encountered as co-infections with other STDs such as HIV, syphilis, and chlamydia.
- A mucopurulent discharge is the most common finding (71% in one study).
- Cultures require a stool-free cotton swab of the rectal discharge which must be promptly plated on Thayer Martin media. A positive smear for gram-negative diplococci should be followed up with appropriate cultures.

- Treatment is best with a single dose of ceftriaxone intramuscularly. Alternatively, a single dose of oral cefixime, ciprofloxacin, or ofloxacin is effective. Cure rates approach 97%.

P. Syphilis

- *Treponema pallidum* infection of the anorectum is primarily a disease of anal-receptive males and females.
- Symptoms are usually minimal and frequently, when present, may be attributed to trauma from the sexual behavior or from mixed co-infections with other STDs. Chancres do occur but may be mistaken for idiopathic anal ulcers, cryptitis, or fissure disease.
- Mucus, bleeding, and tenesmus may occur. In long-standing infections, a mass may be noted.
- Endoscopy may demonstrate ulcers but the mass may appear to represent carcinoma. Biopsies, of course, will fail to demonstrate tumor cells. Darkfield examination of the discharge reveals *T. pallidum* organisms that are quite motile. Immunofluorescent stains are highly sensitive to detect this organism.
- Once diagnosed, parenteral penicillin G provides effective therapy.
- Missed primary infections may result in secondary- and tertiary-stage disease with the attendant long-term sequelae. Condyloma lata in the perianal area is evidence of secondary syphilis.

Q. Aeromonas

- Colitis caused by *Aeromonas* species seems primarily related to host immunity, i.e., HIV status, immunocompromised adults, children under the age of two, and in generally debilitated patients.
- Most infections in the United States are secondary to drinking untreated water.

- Adults tend to have a more protracted, less severe diarrheal illness whereas children are more prone to an acute, fulminating illness. The latter are more likely to be complicated by hemolytic uremic syndrome, sepsis, and peritonitis.
- In septic patients, mortality as high as 75% has been reported.
- *Aeromonas colitis* or severe associated illness should be treated with antibiotics. Quinolones are effective as are TMP/SMX, tetracycline, and chloramphenicol.
- Endoscopic findings are nonspecific showing erythema (patchy or continuous), superficial ulcerations, exudates, and friable mucosa. Fortunately, in most patients, infections are mild and self-limited requiring no treatment.

R. Brucellosis

- *Brucellosis melitensis* is a bacterium that may contaminate unpasteurized goat milk or cheese predominantly in underdeveloped nations. Rare in the United States, it can produce a nonspecific colitis.
- Single-agent therapy has an unacceptably high relapse rate so that currently, doxycycline 100 mg orally twice daily for 3–6 weeks and streptomycin 1 g intramuscularly (IM) every 12–24 h for 14 days is preferred.

S. Actinomycosis

- *Actinomyces israelii* is an anaerobic gram-positive bacterium normally found in the mouth, lungs, and GI tract of humans. Infection can be oro-cervical, pulmonary, or ileocolic.
- The lesions may fistulize to the abdominal wall where the characteristic sulfur granules within the discharge may be noted. Unfortunately, the enterocolic mass often suggests an obstructing neoplasm and so this diagnosis is usually made postoperatively.
- Pus or fistula drainage generally will demonstrate the classic microscopic appearance of *A. israelii* on Gram's stain.

- Treatment of ileocolic actinomycosis is resection. Concomitant treatment with high-dose penicillin G, 12–18 million units/day for 2–6 weeks is recommended. Oral penicillin, tetracycline, or erythromycin are usually continued for several weeks after any apparent cure.

T. Miscellaneous Colitis

Diversion Colitis

- Diversion colitis is a term used to describe the clinical entity of nonspecific inflammation of excluded colonic and rectal mucosa. Its importance lies in the difficulty to differentiate it from other colorectal inflammatory states when endoscopically evaluating the excluded segment of bowel.
- The etiology of diversion colitis is thought to be a deficiency of short-chain fatty acids which are the nutrients to the colonic mucosa. This is supported by the fact that daily instillation of short-chain fatty acids results in improved endoscopic appearance of the diverted segment.
- Often this entity is asymptomatic, but when symptoms occur, rectal bleeding is the prominent symptom. Other symptoms include tenesmus, mucous discharge, and abdominal pain.
- Endoscopy may reveal mucous plugs, contact irritation, erythema, and ulcerations.
- Asymptomatic disease requires no pharmacologic treatment. Patients whom diversion is permanent and are symptomatic, twice daily irrigation of short-chain fatty acids is recommended for 2–4 weeks. Other treatments include 5-aminosalicylic acid (5-ASA) enemas and steroid enemas.
- Periodic examination of the diverted segment for neoplasia is warranted. Diversion colitis completely resolves once intestinal continuity is reestablished.

Neutropenic Enterocolitis

- Neutropenic enterocolitis is a potentially fatal condition that is now a commonly recognized complication of chemotherapy for neoplastic disease. However, this disease has been seen

in patients who have undergone transplantation, and aplastic anemia.

- The process has a predilection for the terminal ileum and cecum, but any segment of the bowel can be involved.
- Common presenting symptoms are abdominal pain, fever, diarrhea, abdominal distention, nausea, vomiting, and diarrhea with or without blood. A tip-off is coexisting neutropenia in the appropriate patient population.
- CT seems to be the most accurate method of diagnosis which reveals a thickened and inflamed terminal ileum and cecum.
- The management of these patients remains challenging. Bowel rest, intravenous fluids, broad spectrum of antibiotics with parenteral nutrition are the cornerstones of treatment.
- Surgery is reserved for perforation or peritonitis, or lack of systematic improvement despite conservative measures after a defined time period.

Disinfectant Colitis

- Commercially available endoscope disinfecting solutions readily cause colonic damage if allowed to contact the mucosa. These endoscopic cleaning solutions, often either hydrogen peroxide or glutaraldehyde, may produce a controversial lesion referred to as pseudolipomatosis.
- Furthermore, endoscopists may note the appearance of plaque-like lesions that resemble pseudomembranes upon withdrawal of the scope in an area that was previously noted to be normal in appearance.
- Clinically, in patients suspected of having developed disinfectant colitis, 24–48 h after the procedure, abdominal cramping, bloody diarrhea, fever, and leukocytosis may develop. This entity remains self-limited although no long-term outcome is currently available.
- Efforts to prevent this include diligent rinsing and forced air drying. Automatic disinfecting machines should be routinely serviced and volume adjustments in the rinse cycle maintained.

Corrosive Colitis

- Glutaraldehyde and formalin are two potential corrosives used in a wide spectrum of medical care that may be responsible for corrosive colitis.

- As with disinfectant colitis, these patients develop a self-limiting spectrum of symptoms such as abdominal pain, mucous diarrhea, and rectal bleeding within 48 h of exposure to the corrosive agent.
- Treatment remains supportive with intravenous fluids as needed.

NSAID and Salicylate-Induced Colitis

- NSAIDs may produce colonic mucosal injury. These drugs are also associated with the reactivation of quiescent inflammatory bowel disease, colonic stricture formation, and perforation and hemorrhage.
- Presenting symptoms are often diarrhea, rectal bleeding, and abdominal pain, along with a history of NSAID usage.
- Endoscopic findings range from patchy erythema and granularity to severe extensive mucosal ulcers. Often the clinical and endoscopic features are indistinguishable from idiopathic colitis.
- Treatment involves discontinuing NSAID and salicylate use as well as administering 5-ASA and steroid medications. At times, inpatient therapy is required. Relapse is not uncommon and chronic colitis may require surgery.

Toxic Epidermal Necrolysis

- TEN, also known as Stevens-Johnson syndrome, is a severe mucocutaneous exfoliative disease with an uncertain pathogenesis and a high mortality rate. The primary manifestation is the appearance of an erythematous confluent eruption that rapidly evolves into exfoliation of the skin at the dermal–epidermal junction, resulting in large sheets of necrotic dermis.
- This process seems to be immune-complex mediated and represents an idiosyncratic reaction to a drug or chemical agent.
- Sepsis, GI hemorrhage, leukopenia, fluid and electrolyte imbalance, and renal insufficiency are the major complications that contribute to the high mortality rate.
- The colonoscopic appearance may resemble severe ulcerative or pseudomembranous colitis; however, biopsies show extensive necrosis and lymphocytic infiltration without crypt abscesses or neutrophils. The mucosal sloughing of the bowel may result in melena or intestinal perforation.

U. Viral Colitis

CMV Colitis

- CMV is the most common viral cause of diarrhea and a frequent cause of diarrhea in patients with multiple negative stool test results. It is an affliction that typically occurs late in the course of HIV infection when CD4 counts plummet. Infection is most common in the colon, but concomitant disease may occur in the proximal gut.
- Symptoms of these infections include fever, weight loss, abdominal pain, and diarrhea with or without blood. Patients may complain of fever and weight loss without diarrhea.
- As the disease progresses, frank ulceration, toxic megacolon, and perforation may occur.
- Findings on endoscopy include patchy erythema, with or without ulcerations ranging from small to shallow that may be wide and deep. Because these processes are diffuse, biopsies should be obtained from multiple sites to facilitate diagnosis.
- Histopathologic examination of biopsy tissue will reveal the characteristic changes of these infections. The inclusions may be very atypical in appearance or few in number. They may also be present in tissue that macroscopically appears normal.
- In the end, the diagnosis rests primarily on demonstrating viral cytopathic effect in tissue specimens.
- Treatment includes supportive care and antiviral agents. Agents of choice for CMV are 9-(1,3 dihydroxy-2-propoxymethyl) guanine (DHPG, ganciclovir) and phosphonoformate (Foscarnet) and for herpes simplex virus, acyclovir.
- Surgical therapy is required for complications such as bleeding and perforation. Because of the nature of the disease and the immunocompromised state of the patient, subtotal colectomy with ileostomy is advised. Mortality is high and often attributed to sepsis as a result of underlying opportunistic infection.

Herpes Simplex Colitis

- Herpes simplex virus, when involved in the GI tract, usually manifests itself as a proctitis. This remains a disease frequently afflicting homosexual males as well as those with AIDS.

- It usually presents with anorectal pain, discharge, tenesmus, and rectal bleeding as well as difficulty urinating, and sacral paresthesias.
- The diagnosis is established by history, sigmoidoscopic demonstration of an acute proctitis, and isolation of the virus by culture.
- Oral acyclovir has been demonstrated to be effective in alleviating symptoms.
- Relapses are common, especially in sexually active homosexuals.

V. Parasitic Colitis

Amebiasis

- Amebiasis is the second leading cause of death from human parasitic disease worldwide. The causative protozoan parasite, *Entameba histolytica*, is a potent pathogen.
- Infection usually begins with the ingestion of cysts in food or water that have been contaminated by human species. *E. histolytica* trophozoites invade the intestinal mucosa causing amebic colitis.
- In some cases, amebas breach the mucosal barrier and travel through the portal circulation causing amebic abscesses.
- Symptomatic patients present with bloody diarrhea and abdominal pain and tenderness. The onset is often gradual with patients reporting several weeks of symptoms. The diarrhea may be profuse without blood; also, rectal bleeding without diarrhea may be an uncommon presentation.
- Occasionally, individuals develop fulminant amebic colitis with widespread abdominal pain, fever, and peritonitis.
- Amebomas, which are localized inflammatory annular masses, may develop in the cecum or ascending colon, and can cause obstructive symptoms and mimic carcinoma.
- The diagnosis rests on the demonstration of *E. histolytica* in the stool or colonic mucosa of patients with diarrhea.
- The cornerstone of treatment for amebiasis is nitroimidazole derivatives such as metronidazole. Amebic colitis is treated by

metronidazole followed by a luminal agent such as paromomycin, iodoquinol, or diloxanide to eradicate colonization.

Balantidiasis

- *Balantidium coli* is the largest and least common protozoal pathogen of humans and is the only ciliate that produces important human disease. It is most frequently found in tropical and subtropical regions.
- Communities that are in close association with pigs have an increased prevalence of disease because of the high rate of carriage of this organism by these animals. *B. coli* infection is spread to humans by ingestion of cysts spread by contaminated water and food.
- The trophozoite invades the distal ileal and colonic mucosa and produces intense mucosal inflammation and ulceration.
- If allowed to progress, it can develop into fatal fulminant colitis with peritonitis and colonic perforation.
- The diagnosis is made by identification of trophozoites excreted in the stool or from the margin of ulcers seen in the rectum.
- The most frequently used treatment is tetracycline 500 mg four times daily for 10 days.

Cryptosporidiosis

- *Cryptosporidium* colonizes both the small and large intestine and is commonly found in developing countries. It is now closely associated with immunocompromised patients, particularly associated with AIDS.
- The organism may be transmitted by a variety of routes, including fecal–oral, hand to mouth, contaminated foods and water, and by pets.
- In immunocompromised individuals, the disease is more severe and can be fatal.
- The diagnosis is made by identification of oocysts on fecal smears or in large intestinal mucosal biopsies.
- Treatment remains challenging and spiramycin and paromomycin have been moderately effective.

Giardiasis

- Giardiasis is a disease caused by the protozoan *Giardia lamblia*. It is a worldwide condition with the vast majority of patients being asymptomatic.
- It is common in hikers and bikers who drink from mountain lakes, adults who care for children who are in diapers, and there is an increased incidence in male homosexuals.
- Infection results from ingestion of the cyst and produces diarrhea, the most common complaint in the symptomatic patient. Malabsorption may also be manifested.
- The diagnosis is made by identification of trophozoites in the stool or by a *Giardia* ELISA.
- The drug of choice for the treatment of *Giardia* is metronidazole or other nitroimidazole compounds that are better tolerated.

Trypanosomiasis

- *Trypanosoma cruzi* is the organism responsible for Chagas' disease or trypanosomiasis.
- It occurs primarily in Central America and is spread to humans by the bite of the blood-sucking vector Reduviid bug which carries the parasite. The local irritation from the bite results in scratching and subsequent inoculation of the organism into the circulation.
- Trypomastigotes convert to amastigotes and enter the bloodstream to infect and destroy muscle and nerve cells leading to motility disorders of the intestinal tract and congestive heart failure.
- Clinically, esophageal and colorectal symptoms develop with the latter manifesting as severe constipation with abdominal pain and distention.
- Once the chronic form develops and tissue damage occurs, surgery is offered. Indications for surgery are megacolon, severe constipation, and chronic fecal impaction.
- Although various operations have been proposed, either the Duhamel retrorectal abdominotransanal pull through, or if the lower rectum is not involved, extended left hemicolectomy with colorectal anastomosis, may be used.

Ascariasis

- Ascariasis is caused by the large round worm *Ascaris lumbricoides*. It is endemic in tropical and subtropical areas and it is estimated that more than one-fifth of the world's population is affected.
- Infection occurs from ingestion of the eggs in contaminated food or water. After migrating from the small intestine into the portal venous system, they pass through the liver into the lungs where they are coughed up and swallowed.
- Intestinal ascariasis produces crampy abdominal pain, but with a large worm load, intestinal obstruction can occur.
- The diagnosis is made by finding eggs in the stool. Small bowel series may demonstrate worms in the distal ileum.
- A variety of drugs including pyrantel pamoate, mebendazole, and levamisole have been recommended.
- Surgery is required for unremitting intestinal obstruction, and if perforation has not occurred, manipulation of the worms through the ileocecal valve will prevent migration of worms through an intestinal anastomosis.

Schistosomiasis

- Five species of schistosome are known to produce disease in human intestine. Human infection occurs after penetration of the skin or mucous membranes by cercariae, the infective form of the parasite which is liberated into fresh water by the intermediate snail host.
- Symptoms are referable either to the skin or the viscus involved with the disease. If migration through the bowel occurs, patients will develop severe lower abdominal pain, rectal bleeding, diarrhea, and passage of mucus.
- The diagnosis is made by the identification of the ova in fresh stool specimens.
- Treatment depends on which species is involved. Patients with longstanding schistosomal colitis are at risk for carcinoma, but this applies primarily to *S. japonicum*. Cirrhosis with portal hypertension may produce massive hemorrhage from varices requiring portal decompression.

Strongyloidiasis

- *Strongyloides stercoralis* is one of the major nematodes that infects humans. It is a soil-dwelling organism endemic to the rural southeastern United States and Appalachia that infects the upper small intestine of humans and rarely the colon.
- Patients present with diarrhea, weight loss, and a microcytic anemia.
- The diagnosis can be made by stool aspirates during colonoscopy demonstrating *S. stercoralis* larvae on wet mount examination.
- Treatment is with oral thiabendazole 25 mg/kg by mouth twice daily for 3 months.

Trichuriasis

- *Trichuris trichiura* (whipworm) is found worldwide in both developed and developing countries. Human infection begins after ingestion of ova. Larvae are released into the small intestine and most frequently the cecum and the terminal ileum are colonized.
- In symptomatic individuals, diarrhea with blood and mucus occurs often associated with abdominal pain and tenesmus. Chronic infection can result in iron deficiency.
- Stool examination for the barrel-shaped eggs of *T. trichiura* confirms the diagnosis.
- Mebendazole is the treatment of choice in a dose of 100 mg twice daily for 3 days.

Anisakiasis

- Anisakiasis is a disease caused by human infection by the *Anisakis* larvae, a murine nematode found in raw or undercooked fish. With the increased popularity of eating sushi and raw fish in the United States, infection with *Anisakis* is expected to increase.
- Most human infections have been reported from Japan and the Netherlands and involve the stomach.
- If the larvae have invaded the intestine or the stomach wall, diagnosis and cure occur with endoscopic or surgical removal if evidence of obstruction or perforation are found.

Tapeworm

- A number of adult tapeworms parasitize the intestinal tract of humans. Infection is acquired through the ingestion of the infected flesh of the intermediate host that is raw or inadequately cooked.
- The diagnosis of tapeworms is made by finding the ova in the feces. *Diphyllobothrium latum* is the fish tapeworm that results from the ingestion of raw fish.
- The worm produces vitamin B₁₂ deficiency and fatigue.
- *Taenia solium* is the pork tapeworm acquired by eating inadequately cooked pork.
- *T. saginata* are the organisms responsible for beef tapeworm.
- The clinical symptoms of all tapeworms are variable and include abdominal discomfort, nausea, vomiting, cutaneous sensitivity, headache, and malaise.
- Many infections are asymptomatic. Treatment of all tapeworms is with either niclosamide or praziquantel.

W. AIDS Diarrhea

- AIDS can result in life-threatening opportunistic infections of the GI tract, of which many present with diarrhea.
- The etiology of diarrhea in the HIV-positive patient is multifactorial. There are various colitides, distinct ulcerative infections, and a number of malignancies that may occur. HIV infection can affect the entire GI tract and the hepatobiliary system.
- Diarrhea, weight loss, swallowing disturbances, and abdominal pain as the major gastroenterologic disorders in AIDS. GI manifestations range in severity from the inconvenience and discomfort of oral and perianal infections through to life-threatening diarrhea caused by intestinal cryptosporidiosis.
- In the evaluation of the HIV patient with diarrhea, one must be aware that there remains a wide range of infectious pathogens: viral (CMV, herpes simplex), bacterial (*M. avium-intracellulare*) and parasitic (*Cryptosporidium*, *Isospora belli*).
- The most important goal of evaluating diarrhea in HIV infection is to identify a treatable cause with the minimal amount of diagnostic testing. Evaluation of patients with diarrhea includes three stool samples and colonoscopy with biopsy.

- A comprehensive investigation will reveal an etiologic agent in 90% of patients. If stool evaluation and flexible endoscopy are nondiagnostic, there is some rationale for a limited trial of empiric antibiotics.
- Treatment of pathogen-negative diarrhea consists of volume resuscitation and somatostatin analogs.
- The differential diagnosis of diarrhea in AIDS includes protozoa, viruses, bacteria, fungi, gut neoplasms, and pancreatic insufficiency. In all patients, at least three stool specimens for fecal leukocytes, ova and parasites, acid fast bacteria, *Clostridium difficile* toxin, bacteria and fat stain should be obtained.
- Surgery is reserved for acute abdominal emergencies and carries a substantial risk of mortality.

HIV Colitis

- Diarrhea is the most frequent and often most morbid GI manifestations of HIV and AIDS. However, the role of HIV as a diarrheal pathogen remains controversial. Several investigators have identified HIV within the gut tissue in up to 40% of patients with AIDS. Despite the ability of HIV virus to infect colon cell lines, its ability to produce an HIV colitis remains controversial.

X. Radiation-Induced Bowel Injury

- Radiation injury to the bowel is biphasic; there is an acute injury demonstrable during administration of radiation therapy (RT) and a delayed, chronic injury that may be encountered months to years after completion of treatment.
- Both total radiation dose and rate of administration of that dose are important factors in the incidence of bowel complications. Between 1 and 5% of patients receiving 4,500 cGy are expected to experience radiation-induced complications over a 5-year period. The complication rate increases to 25–50% when 6,500 cGy are administered. The rectum tolerates 5,500 cGy but at 8,000 cGy, 25–50% of patients will experience chronic complications. Higher doses administered over shorter times result in more acute injury. However, the absence of symptomatic

acute-phase injury does not correlate with diminished chronic sequela.

- Risk factors within the population being treated with RT have been reported and they principally relate to factors that compound the effects of ionizing radiation or increase the likelihood that higher doses of radiation will be delivered to the bowel. Examples of the former include conditions predisposing to intestinal ischemia, i.e., cigarette smoking, hypertension, diabetes mellitus, vasculitides, or arteriosclerotic processes. Examples of the latter include processes that fix the intestine within the field of radiation maximizing exposure, i.e., previous abdominopelvic surgery causing adhesions and inflammatory intraabdominal processes causing immobility of the bowel. For this reason, the terminal ileum is most frequently injured by RT because of fixation within the pelvis secondary to adhesions.
- In the absence of adhesions, the rectum and rectosigmoid are most frequently injured because of their normal fixation anatomically within the pelvis.
- Currently, the most common indications for RT in the United States is cervical cancer, endometrial cancer, prostate cancer, and anorectal malignancies.
- Techniques to minimize tissue-volume exposure to administered RT include multiplanar delivery systems, patient positioning and blocking to remove other organs from the target area, and filling the bladder to displace other tissues from the pelvis.
- The acute effects of radiation on the intestines occurs during the administration of RT. It generally takes several weeks for the injury to become manifest. Concomitant administration of chemotherapy, especially common in the presurgical phase of treatment with rectal cancer, increases the tissue's susceptibility to the therapeutic properties of RT. Likewise, acute-phase radiation toxicity/enteritis is more likely to be noted.
- The acute injury is primarily mucosal with disruption of the rapidly dividing and growing cells at the base of the crypts. This leads to flattening of the villi and resultant diminution of absorptive and resorptive functions of the affected intestine. Mucositis, cramps, and diarrhea are the typical problems noted.

- Antimotility agents and, where applicable, antiinflammatory agents generally ameliorate symptoms. Sucralfate, mesalamine, or hydrocortisone enemas have been reported to be efficacious in the acute injury setting.
- Cessation of radiation or, at least, delaying the ongoing course generally permits most patients to resolve the acute toxicity.
- For the most part, preoperative radiation permits excision of the targeted tissues, excepting the distal portion of the rectum or anus being used when anastomosis (sphincter preservation) is possible. Nonirradiated proximal bowel is essential in maintaining acceptably low anastomotic leak rates when reconstruction is performed. When coloanal anastomosis is constructed in an irradiated field, many experienced surgeons elect to divert the fecal stream proximally to permit distal healing before restoration of continence, thus minimizing the deleterious effect of pelvic sepsis and anastomotic leakage.
- Chronic radiation injury is characterized by progressive, obliterative arteritis, as well as submucosal and transmural fibrosis. The endothelial thickening results in arterial and arteriolar thrombosis leading to ischemia. Submucosal collagen deposition leads to impaired tissue oxygenation, especially in the face of obliterative arterial disease.
- These pathologic changes cause the long-term problems associated with radiation such as obstruction, perforation, fistulization, and hemorrhage.
- Evaluation of complications may necessitate GI contrast studies with barium, CT, magnetic resonance imaging, endoscopy, and fistulography. Detailed assessment is mandatory when surgical intervention is considered to optimize operative planning and to have adequate specialized help intraoperatively if the need exists.
- Treatments for the complications of chronic radiation enteritis are directed toward symptom relief. Bleeding from ischemic mucosa with telangiectatic vessels can be managed in one of several ways. Nd:YAG and argon lasers have proven effective in ablating bleeding vascular lesions within reach of an endoscope. Argon is preferred because its energy is specifically absorbed by hemoglobin and so minimizes tissue damage to the already ischemic bowel.

- A recent Cochrane Review comparing nonsurgical options for managing chronic radiation proctitis found sucralfate together with metronidazole effective in a small number of patients.
- Where bleeding occurs within the rectum, it is usually associated with radiation treatment of the cervix or prostate. Topical application of 4% formalin to these distal bleeding injuries has proven successful whether done in the office setting or the operating room, depending on the time entailed and amount of tissue needing treatment. More recently, GI bleeding secondary to chronic radiation injury has been shown to respond well to hyperbaric oxygen therapy.
- Fistulizing complications are best managed as conservatively as possible. When the severity of symptoms warrants consideration of surgery, the type of surgery will depend on how proximal in the GI tract the problem is and the organ to which the fistula connects.
 - At laparotomy, as little adhesiolysis as possible should be performed because the already ischemic bowel tends to perforate (micro or macro) frequently necessitating more surgery.
 - When possible, fistulizing tissue is best resected back to normal-appearing margins.
 - When the amount of bowel is too excessive to permit resection, proximal diversion or bypass can be considered. Bypass is frequently avoided because diseased tissue is left behind, blind-loops create more symptoms, and bypass anastomosis still leaks at higher than normal rates.
 - Enteric fistulas involving the genitourinary tract can be handled in the same manner with resection generally preferred where feasible.
 - Frequently, within the pelvis, fecal diversion proximally proves safe and effective palliation in an otherwise high-risk situation.
 - In the case of radiation-induced intestinal stenosis or obstruction, the same surgical considerations and options apply. Where feasible, resection and anastomosis of normal-appearing bowel are preferred. In the event of radiation-induced ischemic necrosis of the bowel, resection of necrotic tissue with diversion may be lifesaving.

- The most important determinant of operative morbidity and mortality was the location of the radiation injury itself. Small bowel radiation injury in one series had a 38% mortality whereas colonic injury had a 15% mortality rate.
- When long segments of small bowel have chronic radiation enteritis, malabsorptive problems arise. Because the malabsorption is secondary to tissue ischemia and subsequent fibrosis, treatment or resection will not restore this function. Patients with this chronic complication therefore require parenteral nutrition to sustain life and are subject to the metabolic complications of long-term parenteral alimentation.
- Unless the clinical presentation of radiation injury to the bowel is emergent, a careful clinical assessment of the patient is vitally important to identify comorbid conditions. Patient nutrition, hydration, and sepsis need to be addressed and corrected wherever possible. Radiologic and endoscopic assessments need to be completed before finalizing a treatment plan. Therapeutic interventions should be considered beginning with the least invasive means first. Chronic radiation injury cannot be reversed because of the secondary ischemic changes. Therefore, goals for treatment should optimize quality of life while minimizing the morbidity and mortality of therapeutic intervention.

Y. *C. difficile* Colitis

- *C. difficile* infection, an important source of colitis particularly in hospitalized patients, presents from either an asymptomatic infection to severe pseudomembranous colitis with bowel perforation and death.
- The majority of cases are seen after antibiotic usage. The remaining cases include patients receiving chemotherapy, patients with inflammatory bowel disease, and those with a variety of other medical problems.
- Almost all antibiotics have been associated with *C. difficile* infection. The most frequently implicated classes of drugs are the cephalosporins, ampicillin/amoxicillin, and clindamycin. Neither the antibiotic dosage nor the length of administration

has been found to correlate with the development of *C. difficile* infection. The majority of infections occur 5–7 days into the course of antibiotics, but it may present weeks after cessation of the antimicrobials.

- Diarrhea is the most common symptom and is found in 90–95% of cases.
 - Patients with mild disease may present with diarrhea alone, or associated with a low-grade fever and abdominal pain. These patients may also have mild abdominal tenderness and an otherwise unremarkable abdominal examination.
 - A small percentage of patients develop fulminant colitis with high fever and severe abdominal pain.
 - Diarrhea may be absent in patients with severe disease and progress to toxic megacolon. Hypotension, oliguria, and other manifestations of septic shock may also be found in these severely ill patients.
- The laboratory diagnosis of *C. difficile* depends on the detection of the *C. difficile* toxins in the patient's stool.
- Patients suspected of having *C. difficile* infection can be evaluated endoscopically. The mucosal findings vary with the severity of the disease. In those with mild or moderate disease, endoscopy most often reveals normal mucosa or nonspecific inflammatory changes. In the great majority of those with severe disease, examination demonstrates the classic pseudomembranes which are round, punctate yellow or whitish lesions.
- Although the finding of pseudomembranes suggests the diagnosis of pseudomembranous colitis, biopsy of these lesions is recommended to definitively establish the diagnosis.
- When *C. difficile* infection occurs in patients receiving antibiotics, the offending antibiotic should be immediately discontinued if possible. In patients with mild disease, no other specific treatment is necessary.
- Most physicians will begin empiric antimicrobial therapy if there is a strong clinical evidence of colitis.
- Three orally administered antimicrobials have been shown to be effective against *C. difficile* infection: vancomycin, metronidazole, and bacitracin. Vancomycin used to be the drug of choice. In most patients, a significant improvement will occur within 2–5 days of treatment. Vancomycin is costly and

distasteful. Metronidazole is generally well tolerated and is much less expensive than vancomycin. Metronidazole, unlike vancomycin, is absorbed rapidly from the GI tract and consequently fecal concentrations are low. Despite this, metronidazole has been shown to be highly effective and is given in a dosage of 250 mg orally four times a day for 10 days.

- In patients unable to take antimicrobials orally, intravenous metronidazole seems to be the most effective.
- Surgery may be necessary for patients in whom a perforation is suspected or those with toxic megacolon. When surgery is necessary, subtotal colectomy with ileostomy or fecal diversion via end ileostomy and mucous fistula are the most frequently performed procedures.
- Recurrent infection is as responsive to antimicrobial treatment as are primary infections. Unfortunately, up to one-third of patients who relapse once will have further recurrences.
- Surgery for fulminant colitis still commands a poor prognosis.

44. Intestinal Stomas

A. Introduction

- An ostomy is a surgically created opening between a hollow organ and the body surface or between any two hollow organs.
- The word *stoma* comes from the Greek word for mouth and is used interchangeably with ostomy.
- An ostomy is further named by the organ involved. An ileostomy is an opening from the ileum to the skin, a colostomy is from the colon.
- The majority of ostomies today are created as a temporary measure, either as an end ostomy in the acute setting with later planned takedown and anastomosis, or as a proximal loop diversion to protect a low pelvic or high risk anastomosis.

B. Indications for an Ostomy

- An ostomy is created when an anastomosis is not possible for technical reasons or risk of failure, when there is nothing distally to attach to such as after an abdominoperineal resection of the rectum, or for proximal diversion (Table 44.1).
- Ostomies may be *temporary* or *permanent*.
 - Temporary stomas divert the fecal stream away from an area of concern such as a high-risk anastomosis, located in a radiated field, low in the rectum, or after an injury.
 - Permanent ostomies are required when the anorectum has been removed (abdominoperineal resection) in cancer or Crohn's disease. A permanent ostomy may also be an option in patients with severe fecal incontinence or complications of trauma or radiation such as a rectourethral fistula.

Table 44.1. Indications for an ostomy.

Cancer
Diverticular disease
Inflammatory bowel disease – ulcerative colitis, Crohn’s disease
Radiation enteritis
Complex perirectal, rectovaginal, or rectourethral fistulas
Trauma
Obstruction
Perforation
Motility and functional disorders including ideopathic megarectum and megacolon
Infections – necrotizing fasciitis, Fournier’s gangrene
Congenital disorders – imperforate anus, Hirschsprung’s disease necrotizing enterocolitis, intestinal atresias

- Creation of an ostomy is a traumatic event for most patients, both physically and mentally. Whenever possible, a detailed discussion of the proposed procedure, consequences, and alternatives should be undertaken. A trained enterostomal therapy nurse (ET) or wound ostomy care nurse (WOCN) should meet with the patient both before and after the surgery. When available, a *United Ostomy Association Visitor* should be called to meet with the patient, either before (if the surgery is elective) or after the surgery.

C. Stoma Physiology

- The physiologic changes that occur in patients with ostomies are primarily related to the loss of continence and reduced colonic absorptive surface area. These affect fluid and electrolyte balance and lifestyle but generally have little effect on nutrition. However, once more than 50 cm of terminal ileum has been removed or taken out of continuity, nutritional consequences are likely.

Output

- Ostomy output is directly related to the location of the opening in the bowel. Distal left or sigmoid colostomies normally produce formed stools that are of similar consistency to that of

the anorectum. The more proximal the colostomy, the less surface area is available for water and electrolyte absorption and so the more liquid the stools. Right-sided colostomies not only produce a high volume but also have the additional disadvantage of a malodorous output because of the effects of colonic bacteria.

- Initially after creation the output from an ileostomy tends to be fairly watery and green or bilious in color. Within a few days to a week of resumption of a regular diet, the material becomes thicker and more yellow-brown, although a greenish tinge often remains.
 - The typical consistency is of watery porridge or apple-sauce. It is affected by diet, fluid intake, medications, and ongoing problems such as Crohn's disease or adhesions.
 - If a substantial amount of small bowel has been removed, the output is looser and the patient is more prone to dehydration.
 - It is not uncommon for some food to come through in a recognizable state. Foods notable for this include corn, other vegetables, and nuts. Some pills may also not be broken down in the small bowel, decreasing the bioavailability of these medications.
 - Most ileostomates notice little odor from the output; however, certain foods, such as eggs and fish, may produce an offensive smell.

Volume

- In the healthy control subject, about 1,000–2,000 mL of fluid passes through the ileocecal valve daily. This is reduced by 80–90% to 100–200 mL in normal stool as it passes through the colon. Unless the patient has diarrhea, left-sided colostomy output is similar to the feces that would be passed transanally, and there is little loss of total body fluid or sodium.
- Although postoperative ileostomy output may be high, it eventually settles down to a regular volume. "Ileostomy dysfunction," although a general sounding term, refers to increased ileostomy output attributed to partial obstruction caused by inflammation and stenosis.
- The average output of an established ileostomy (in contrast to a newly created ileostomy) is about 200–700 mL with a median of

about 500 mL per day. Total bowel rest results in a decrease in output by at least half and may be as low as 50–100 mL per day.

- The volume of ileostomy output varies fairly widely among patients but only mildly from day to day in a single individual. Although the average output is about 500 mL per day, a healthy, functioning ileostomy may produce up to 1,000–1,500 mL in a day especially in the early postoperative period. Outputs above this level usually cause dehydration. Large amounts of fluid intake usually do not alter the output volume very much because most of it is absorbed and excreted through the kidneys.
- Ileostomates may generally eat a regular diet without restrictions. Decreased fluid intake slows the output and thickens it, whereas fatty food and large amounts of liquid increase transit and the fluidity of the effluent.

Transit

- An ileostomy discharges frequently and output is not eliminated by the timing of meals or rest. Yet, in most patients, the output increases with meals and certain foods.
- Although the data are limited, it seems that small bowel transit times decrease after ileostomy, possibly related to mucosal hypertrophy and adaptation.
- Ileostomy output and dehydration may be decreased by prolonging the transit time to allow for more absorption. Codeine, loperimide, and Lomotil have all been shown to have this effect.

Fluid and Electrolyte Balance

- The average ileostomy puts out about 500 mL of water and 60 mmoles of sodium per day. This is 2–3 times higher than found in normal fecal output. Consequently, the ileostomate must compensate by increasing intake or conserving other losses.
- Urinary volume is relatively decreased in patients with ileostomies by as much as 40%, whereas renal sodium losses may be decreased by 55%. Yet, despite the efforts of the kidneys to maintain balance, total body water and sodium reductions may be a chronic condition in ileostomy patients.

- The chronic dehydration and loss of fluid and electrolytes make ileostomy patients prone to dehydration. Rehydration is best accomplished with fairly large amounts of normal saline. There is an inverse relationship between absorption of nutrients and electrolytes and transit time.

Flora

- The normal terminal ileum harbors few organisms in the healthy individual.
- After creation of an ileostomy, the distal ileum is rapidly colonized with a variety of bacteria. The microflora of an individual is fairly stable over time whereas there is great variability among individuals.
- Staphylococci, streptococci, and fungi are increased whereas *Bacteroides fragilis* is rarely found in ileostomy effluent.
- The major variations in the flora of effluent from ileostomies, transverse colostomies, and feces per anum are in the relative numbers of anaerobes with log differences increasing from proximal to distal.

Nutrition

- The colon has little role in the maintenance of normal nutrition, working primarily to absorb fluid and to store feces so that the frequency of bowel evacuation may be limited. Thus, removal of the colon alone has little effect on nutrition.
- Loss of more than a few feet of the terminal ileum may result in loss of bile acids and poor absorption of fat and fat-soluble vitamins.
- Specifically, vitamin B₁₂, necessary for normal hemoglobin synthesis, may not be adequately absorbed in patients with terminal ileal loss or significant Crohn's disease. This results in pernicious or macrocytic anemia, and these patients may require monthly administration of vitamin B₁₂ (intramuscular or nasal).
- Kidney stones may be a consequence of chronic dehydration and acid urine. Adding sodium bicarbonate to the diet as well as increasing fluid intake may help to prevent uric acid stone formation.

D. Preoperative Considerations

Access, Adherence, Activity, Attire

- Preoperative patient preparation is essential and patients should be counseled and marked. In many institutions this is done by an enterostomal therapist.
- Factors to consider in relation to stoma placement include: occupation, clothing styles (including belt line), flexibility and range of motion, abdominal wall contour when sitting and standing, and physical limitations or disabilities. Other factors include prior abdominal incisions, bony prominences, and abdominal girth.
- Although in most elective settings, the stoma therapist will provide preoperative marking, it is imperative for any abdominal surgeon to have this skill as well because at times a stoma therapist may not be available.
- Standard ostomy sites lie to either side of the midline overlying the rectus muscle and are the preferred location for stoma placement (Fig. 44.1). In the supine position, a site is marked 5 cm away from prior incisions, bony prominences, the umbilicus, and the patient's belt line. This is usually located just lateral and inferior or in some cases superior to the umbilicus.

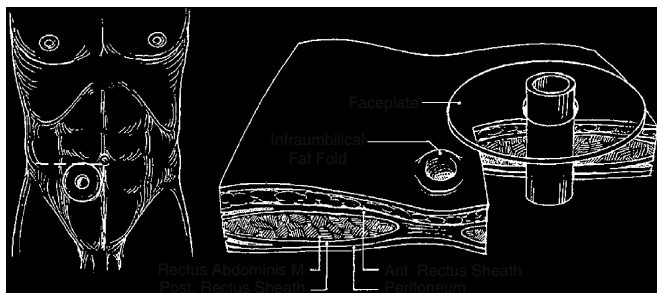


Fig. 44.1. Stomal placement. The site is selected to bring the stoma through the rectus abdominis muscle. (From Beck DE. Intestinal stomas. In: Beck D, ed. Handbook of Colorectal Surgery. 2nd ed. Copyright 2003 by Taylor & Francis Group LLC (B). Reproduced with permission of Taylor & Francis Group LLC (B) in the format Textbook via Copyright Clearance Center).

- With the patient sitting and standing, the site is checked to ensure skin folds or crevices do not interfere with appliance fitting. In obese individuals, the stoma must not be hidden below a large abdominal pannus or stoma care will be very difficult. In this circumstance, a supraumbilical stoma is often more functional.
- Once proper placement is ascertained, the spot is marked with indelible ink. In complex cases, a stoma appliance can be fixed to the proposed site and worn for 24 h to test placement.

E. End Ostomies

- Most left colon colostomies are placed in the left lower quadrant of the abdominal wall, exiting through the rectus sheath. Most distal ileostomies are placed in the right lower quadrant. Occasionally, a higher or more lateral site may be chosen depending on body habitus, other scars, clothing, mesentery and bowel length, and surgical considerations.
- The surgeon should not hesitate to make a large fascial incision because a late hernia is preferable to early ischemic necrosis or retraction.

Maturation

- The maturation technique of an ileostomy or a colostomy differs because of the nature of the effluent and the size of the lumen.
- Because of the more formed nature of the stool, colostomies may be flatter, although a small amount of protrusion is beneficial for appliance placement and adherence.
- In general, the stoma is *matured primarily* by everting the end and sewing it to the skin edge as the last phase of the operation.

Mucous Fistula

- The term mucous fistula refers to the distal end of the divided bowel that has been brought through the skin and matured as a stoma.

- Typically, when the bowel is completely transected, with or without resection of a segment, the proximal end may be made into an end stoma, e.g., ileostomy or colostomy. This is the functioning stoma through which the bowel contents empty. The other, or distal, end may be closed as in a Hartmann's procedure or may be brought to the surface and matured. The distal matured end is referred to as a mucous fistula because it is an opening that occasionally produces mucous.
- The advantage of a mucous fistula is primarily that the distal portion of the bowel may be decompressed through this opening. This is important when an obstruction remains in the distal bowel such as an unresectable tumor. Closure of the distal end might result in a closed loop which, when filled with mucous, secretions, and bacteria, could rupture and result in peritonitis.
- A mucous fistula may also be used to access the distal bowel for purposes of observation, irrigation for washout, or for therapy. It is also a simple matter to find the distal limb when operating to close the ostomy.
- The obvious disadvantage of a mucous fistula is the second stoma site on the patient's abdominal wall. Although a mucous fistula does not produce a large amount of material, small amounts of mucous do emanate from time to time.

F. Diverting Stomas

Indications

- Whether a colostomy or ileostomy, diverting stomas are nearly always created for a single purpose: to prevent fecal content from reaching a distal segment of the large bowel, either because of fear of leak (distal or difficult anastomosis) or to treat a leak (trauma, perforation, or anastomotic disruption).
- Table 44.2 lists the common current indications for diverting ileostomies, colostomies, and end-loop stomas. These include protection of distal anastomoses, predominately ileal pouch-anal or coloanal anastomoses, complicated diverticulitis, treatment of anastomotic leaks and pelvic sepsis, large bowel obstruction, trauma, and fecal incontinence.

Table 44.2. Indications for diverting stomas.

Protection of distal anastomosis
Treatment of anastomotic leak
Large bowel obstruction
Trauma
Diverticular disease
Cryptoglandular sepsis
Radiation complications
Fecal incontinence
Fulminant colitis

- When deciding which stoma to create, the surgeon must thoughtfully consider the following principles:
 - Will the stoma achieve its primary purpose? Will it protect the anastomosis or treat the anastomotic leak?
 - Can a stoma be safely created? Can that segment of bowel reach an appropriate site on the abdominal wall and be matured successfully?
 - How will life with this stoma be, particularly if subsequent stoma takedown does not take place?
 - Will stoma choice affect subsequent stoma takedown? Loop stomas and end-loop stomas avoid the necessity of laparotomy for takedown versus the Hartmann procedure.
 - Will stoma choice limit future reconstructive options? Sigmoid colostomy may make a subsequent coloanal anastomosis more difficult versus loop ileostomy.
- In both urgent and elective situations, these factors should be considered before initiating the surgical procedure. The patient can then be marked for potential stoma sites and counseled appropriately before surgery begins.
- Although loop ostomies are usually meant to be temporary, a significant number are never closed. Because the patient must live with the loop stoma for at least several months, and sometimes for the remainder of his or her life, careful attention to ostomy construction remains very important.

Loop Ileostomy Versus Transverse Loop Colostomy

- When treating pelvic infection from a colonic source or particularly when choosing elective diversion for protection of

low pelvic anastomosis, transverse loop colostomy and loop ileostomy are the major options. In nearly all situations, loop ileostomy is the superior choice. Transverse loop colostomy, except in rare circumstances, should be a procedure of historic significance only.

- Loop transverse colostomies have a much larger lumen, rarely stay everted, often prolapse or retract, are usually placed in the epigastrium (a very inconvenient location), and are quite malodorous.
- Considering the available data, loop ileostomy should be the procedure of choice for proximal diversion of left-sided anastomoses (Table 44.3). The ileostomy is smaller, may be located in the right lower quadrant rather than the right upper quadrant as for a loop transverse colostomy, is less odorous, and easier to pouch and manage. Closure of the ileostomy is also an easier operation with fewer complications.

Loop Ostomy Closure

- The time interval between creation of the ostomy and closure will vary depending on the initiating disorder and the condition of the patient. It is best to wait until any inflammatory process has had adequate time to settle and for adhesions to soften. The patient should also be in as good condition as possible.
- Most temporary ostomies are closed in 1.5–3 months. A 6-week interval is the usual minimal period because adhesions tend to be severe before this.

Table 44.3. Comparison of complications in a randomized trial of transverse loop colostomy and loop ileostomy.

	Transverse colostomy	Loop ileostomy
	(%)	(%)
Prolapse	10	5
Skin problems	50	26
Leakage	31	18
Odor	53	6
Infection at takedown	30	0

Results of Stoma Closure

- Overall complication rates of 15–30% are consistently reported, although there are a few studies that report a wide range from 2.4 to 57%.
- The most common complications of loop ostomy closure are wound infection (9–34%), bowel obstruction (0–10%), fecal fistula (0–5%), and leak (0–3%). Anastomotic strictures (0–1%) and intraperitoneal abscess (0–1%) after closure are fairly rare.
- Long-term consequences such as incisional hernias and small bowel obstructions are not uncommon with rates increasing over time from 2 to 10% or more for both.
- Risk factors that increase the complication rates of ostomy closure include diabetes, advanced age, type of ostomy being closed (end loop), increased operative time, and higher blood loss. The most significant factors in several studies were steroid dependence and hypoalbuminemia. A combination of factors, such as a high ASA score, diabetes, and renal, cardiac, or pulmonary disease also portend a more difficult course.
- Stapled and sewn anastomosis methods are of equal efficacy for colostomy closure.
- In a randomized trial, Hull et al. from the Cleveland Clinic found that stapled and hand-sewn closures were equivalent in terms of complications, resumption of intestinal function, and length of stay. The only difference was that the stapled procedure was slightly faster. Others have also found these two techniques to be equivalent.
- The timing of ostomy closure has been a hotly debated topic for years. Some believe that early closure, even during the original hospital stay, will reduce costs and speed recovery. Others believe that early closure will abrogate the benefits of the diversion and result in higher complication rates.
- Most surgeons recommend a 1.5-to 3-month interval.
- It is generally believed today that loop ileostomies have a lower complication rate than loop colostomies.
- Closure of a Hartmann's procedure is a major operation with all of the risks of any resection and anastomosis in a reoperative setting. In this setting, most authors have also found that delaying the closure for 3 months is beneficial.
- Recently, several small reports of successful laparoscopic closures of Hartmann's procedures have appeared. This seems

to be a reasonable approach; however, there should be a low threshold for conversion to an open procedure.

G. Minimally Invasive Stomas

- Minimally invasive stomas can be created through three different approaches: (1) trephine stomas (those created with all exposure through the stoma site itself), (2) endoscopically assisted stoma creation, and (3) laparoscopically assisted stoma creation. Each offers its specific advantages and disadvantages as do traditional techniques for stoma creation. None of these techniques change the indications for, or proper siting of, a stoma. These less-invasive techniques should be used only when stoma creation is indicated and a properly sited stoma can be safely created.

Laparoscopic-Assisted Stomas

- End and loop colostomies as well as end-loop ileostomies can be created with laparoscopic assistance. Laparoscopy does not change the indications for stoma construction. Additionally, the techniques for stoma maturation are identical to those for open stomas.
- In many cases of laparoscopic-assisted ileostomy, laparoscopy is only necessary to facilitate the proper selection and identification of an appropriate ileal segment as well as ensure maturation of the proximal limb.
- As in laparoscopic-assisted ileostomy, if the sigmoid colon is redundant and has minimal retroperitoneal attachments, then proper identification and orientation of the sigmoid colon are all that are required. This technique mirrors that described for laparoscopic-assisted ileostomy. If, however, the sigmoid colon is short and relatively fixed, then additional laparoscopic dissection will be required.
- Minimally invasively created ileostomies and colostomies are generally safe and well tolerated. They avoid the need for a major laparotomy and patients resume regular diet and activities fairly quickly in most cases. They have been shown to be safe and are now often the procedure of choice when a

diverting ostomy is needed and no other abdominal procedure is necessary.

H. Technical Tips for Difficult Stomas

- Stomas should be well vascularized, approximated without tension, formed from healthy bowel, and constructed with attention to technical detail. In addition, the stoma should be placed properly, through a trephine of correct size, and created from an intestinal segment appropriate to accomplish the stoma's purpose whether temporary or permanent.

Appliances Systems

- Appliances are available for colostomies, ileostomies and urostomies. Most are disposable and available in one- or two-piece systems.
- The basic appliance has an adhesive faceplate with a central opening and a collection piece or "bag."
- Most of the two-piece systems are connected by a Tupperware-style plastic ring. The central opening is sized to fit the stoma with a small 2- to 3-mm margin so that it is not too tight and does not erode into the mucosa.
- The ET/WOCN can assist patients and physicians in product selection.

Ostomy Management

- The most common problems encountered in the care of ostomy patients are attributed to stoma location and construction. Ostomy appliances should be changed when the stoma is least likely to function, usually before meals in the morning.
- Left-sided colostomy patients are candidates to learn the process of colostomy irrigation. Colostomy irrigation is essentially a method of performing an enema through the colostomy to stimulate evacuation and avoid further drainage for a time. The goal of irrigation is not to actually wash the colon out but to stimulate motility and evacuation. This allows more freedom of activity for the patient with little worry of bowel action.

Many ostomates may be trained to irrigation once every 1–3 days and a significant number are fairly dry in between.

I. Outcome and QOL

- Long-term survival is primarily related to the underlying disease process, and many patients with a permanent ostomy live a long life.
- Recent studies have shown that patients with a well-constructed and managed ostomy often enjoy a very good QOL, and that a stoma may actually be preferable to a poorly functioning anorectum with incontinence, pruritus, odor.
- In addition, colostomy patients seem to function better than ileostomy patients. This is probably attributable to the less-frequent and more-formed output of the colostomy.
- QOL improves markedly after surgery in all patients with inflammatory bowel disease and seems to improve over time in most patients. Patients undergoing colostomy for cancer continue to worry about the risk of cancer recurrence and are less concerned about the consequences of the stoma.
- Several studies have highlighted the importance of preoperative and postoperative counseling by an ET/WOCN. All patients improved their QOL after stomatherapy and this intervention seems to be most important during the first 3–6 months after surgery.

45. Stoma Complications

A. Introduction

- The rate of stoma-specific complications in the literature varies quite widely, ranging from 10 to 70% depending on the methodology of the study, the length of follow-up, and the definition of a “complication.”
- For example, virtually all ostomates will have at least transient episodes of minor peristomal irritation and skin irritation is the most frequently reported stoma complication.
- Stoma-related complications may be classified as those that are metabolic or best managed by medical intervention and those that have a purely structural etiology and are best managed by surgical intervention.
- Among the medical complications, the most common early complications are peristomal skin irritation, leakage, high output, and ischemia. The most frequently reported late complications include dehydration and nephrolithiasis, cholelithiasis in ileostomy patients, bleeding in patients with liver disease, and of course also in those with recurrence of the disease for which a stoma was created, such as Crohn’s disease.

B. Incidence

- The stomal type with the highest risk of complications was loop ileostomy with a rate of almost 75%. The only other stoma location to have a complication rate exceeding 50% was descending end colostomy with 65%.
- The intestinal stoma with the lowest risk was an end colostomy of the transverse colon.

C. Skin Problems

Skin Irritation/Leakage

- Skin irritation is very common among patients with a stoma. The problem is seen more often in patients with an ileostomy because of the liquid, high alkaline, active enzymatic caustic effluent.
- Although a minor degree of skin irritation on occasion is probably inevitable, most significant cases of skin irritation are potentially preventable.
 - Preoperative marking by an enterostomal therapist (ET) can help assure proper siting and a secure fit. Appropriate location and careful appliance fitting minimizes the noxious, irritating effect that can be associated with leakage on unprotected peristomal skin.
 - Patients also need to be monitored for allergic reactions to the components of the appliance.
 - An adequate spigot with a close-fitting faceplate prevents exposure of the peristomal skin to the ileostomy effluent.
 - However, even the best-fitting appliances around the best-made stoma will leak if frequent emptying of the appliance is not practiced and pooling of effluent around the base of the stoma occurs.
- Particular attention must be given to older patients who may have limitations in eyesight or dexterity.
- Patients with a high-output stoma are at particular risk for skin irritation and ulceration if they do not have an appropriately fitted appliance.
- Obesity has been frequently reported to be associated with an increased risk of skin irritation, which is likely attributable to technical problems with stoma construction.

In obese patients, strong consideration should be given to placing the stoma in the upper abdomen where there is typically much less creasing of the abdominal wall, subcutaneous fat, and the patient can see it much more readily.

- The patient should be instructed to avoid creams or ointments that may interfere with the adherence of their appliance.
- In the postoperative period, a stoma will tend to become less edematous and the abdomen becomes less distended. As such, it is quite common to need to “downsize” the appliance at the first postoperative visit to minimize exposed skin.

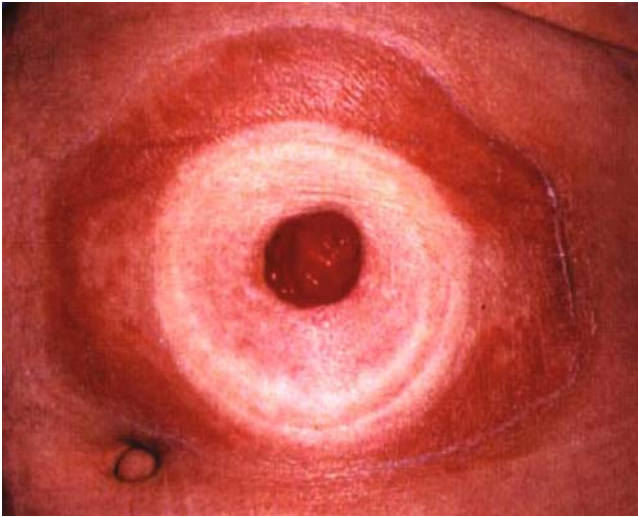


Fig. 45.1. Allergic skin reaction.

- Even with the help of an excellent ET, specific skin infections may occur.
- Fungal overgrowth is evident when there is a bright red rash around the stoma with associated satellite lesions. This is typically easily treated by dusting the peristomal skin with an appropriate antifungal powder.
- If the dermatitis conforms precisely to the outline of the stoma appliance, then an allergic reaction to the wafer or other component of the appliance is likely the culprit (Fig. 45.1).

High-Output Stomas

- A high-output state is typically described in association with an ileostomy, rather than a colostomy. Marked diarrhea and dehydration occur in 5–20% of ileostomy patients, with the greatest risk occurring in the early postoperative period.
- An ileostomy usually functions by the third or fourth postoperative day. The output typically peaks on the fourth postoperative day, with outputs of 3.2 L or more reported.
- Because the ostomy effluent is rich in sodium, hyponatremia can be a problem.

- The particular window of vulnerability for dehydration seems to be between the third and eighth postoperative day.
- Patients with an ileostomy, particularly those who have had concomitant small bowel resection, remain at risk to become dehydrated.
 - Most often, this is easily managed by oral rehydration with one of the commonly available sports drinks.
 - However, patients who have lost considerable absorptive surface because of previous bowel resection and/or those with recurrent/residual active Crohn's disease are at particular risk.
 - In addition to the loss of absorptive surface area, ileal resection also removes the fat or complex carbohydrate stimulation of the so-called "ileal brake" which slows gastric emptying and small bowel transit.
 - Fluid and electrolyte maintenance in these patients may require a period of parenteral hydration and nutrition.
 - Elements of the diet can augment output and potentially troublesome foods should be avoided in marginal cases. These might include foods high in sugar, salt, or fat.
- Ileostomy diarrhea may be treated in its milder forms with fiber supplements or cholestyramine which can thicken secretions, but not change water content.
- Often opiates may be required to slow intestinal transit.
- In refractory cases, somatostatin analog has been used with some success. Somatostatin reduces salt and water excretion and slows gastrointestinal tract motility. However, its clinical usage has met with variable results.

Nephrolithiasis

- A related problem in patients with an ileostomy is the development of urinary stones. The obligatory loss of fecal water, sodium, and bicarbonate reduces urinary pH and volume.
- Approximately 4% of the general population develops urinary stones; the incidence in patients with an ileostomy is approximately twice that.
- Uric acid stones comprise less than 10% of the calculi in the general population; they comprise 60% of stones in ileostomy patients.

Bowel Obstruction

- As many as 23% of patients with an ileostomy have been reported to develop bowel obstruction. Adhesions are probably the most common cause, but small bowel volvulus or internal hernia may also be the cause.
- Many patients with an ileostomy will develop signs and symptoms of bowel obstruction because of the accumulation of poorly masticated or digested food (e.g., popcorn, peanuts, fresh fruits, meat, and vegetables). A careful history may reveal dietary indiscretions.
 - The possibility of a food bolus obstruction should be considered in any patient with an ileostomy who has radiologic evidence of a distal obstruction.
 - A well-lubricated finger can be gently inserted into the stoma to feel for impacted material. A red rubber catheter is inserted gently into the ostomy and saline irrigation initiated. If suspicious concretions begin to pass into the stoma, the irrigations may be carefully repeated until the obstruction is relieved.
 - A water-soluble contrast enema through the obstructed stoma may also be both diagnostic and therapeutic by dislodging the bolus.

Ischemia

- Stomal ischemia is more serious and often related to tension on the mesentery or excessive mesenteric division, particularly in obese patients.
 - A stoma of questionable viability may be examined by insertion of a glass test tube, rigid or flexible endoscope into the stoma. If the stoma is viable at fascial level, then the patient may be carefully observed. However, if there is question about the viability of the stoma at fascial level, immediate laparotomy and stoma revision is required.
 - Early ischemia is seen in 1–10% of colostomies and 1–5% of ileostomies.
 - Efforts should be made at construction of the original stoma to, assure good blood flow in and out to the skin. It seldom takes as long to do this as it does to manage an ischemic or necrotic stoma.

Late Hemorrhage

- Late stomal bleeding may be caused by direct trauma, but heavy bleeding is, especially from an ileostomy, caused by portal hypertension and the development of stoma varices. Many therapies have been described for this, but none subjected to rigorous clinical trials. Correction of coagulopathy and direct pressure are important first steps.
- The placement of a transjugular intrahepatic portosystemic shunt (TIPS) is a nonoperative alternative that should be considered. Other options include stomal detachment or relocation or hepatic transplant.

Surgical Complications

- Surgical complications of intestinal stoma formation can broadly be divided into those that occur early, those that occur long (late) after their construction, and those that occur at stoma closure.
 - Early complications of stoma construction include necrosis, retraction, skin irritation, small bowel obstruction, surgical wound infection, and sepsis.
 - Late complications are dominated by prolapse (Fig. 45.2), peristomal hernia, skin irritation, and fecal fistula.



Fig. 45.2. Stomal prolapse.

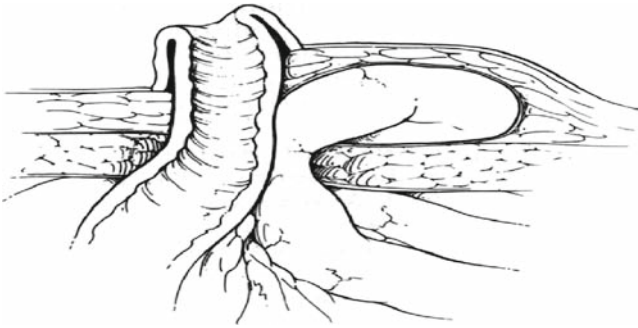


Fig. 45.3. Peristomal hernia.

- Closure-related complications include surgical wound infection, fecal fistula, anastomotic dehiscence, small bowel obstruction, and incisional (peristomal) hernia (Fig. 45.3).
- The prevention and management of each of these complications are best assessed in randomized, controlled clinical trials.
 - The most common study design has been randomization of patients to receive either temporary loop colostomy or loop ileostomy, then following these patients for various complications.
 - These analyses show that the only significant difference between the two stoma types was an increased risk of stoma prolapse associated with loop colostomy.

Stoma Closure

- The risk of anastomotic obstruction was significantly less in the metaanalysis in patients having stapled closures as opposed to hand-sewn (Table 45.1).

Parastomal Hernia

- Opinion concerning the treatment of prolapse, hernia, retraction, or necrosis is anecdotal and not evidence based.

Table 45.1. Metaanalysis of similar studies; odds ratios, 95% confidence intervals, and *P* value for heterogeneity.

Comparison groups	Stomal		Fecal fistula		Retraction	Sepsis	Small bowel obstruction	Surgical wound infection	Time to flatus	Skin irritation
	Prolapse	hernia								
Loop ileostomy and loop colostomy	10.72	0.68	1.79	0.39	0.39	0.97	1.04	1.89	1.23	1.35
	2.79–41.22	0.09–5.16	0.36–8.9	0.07–2.27	0.07–2.27	0.17–5.48	0.34–3.17	0.72–4.94	0.32–4.81	0.59–3.09
Stapled and sewn ileostomy closure	0.78	0.28	0.9	0.40	0.40	0.40	0.64	0.66	0.72	0.27
							0.23			
							0.06–0.87			
							0.51			
Stoma wrap in an adhesion barrier			1.64				1.26			
			0.94–6.09				0.40–3.9			
			0.73				0.84			

- Incidence of hernia is described to occur in anywhere from 0 to 48.1% of individuals.
- The risk of recurrence is high so it seems best to be conservative in undertaking operative repair, limiting surgery only to highly symptomatic patients.
- There are studies that have examined whether or not a stoma should be within the rectus muscle to prevent hernia. Most authors found that it made no difference, but the studies had limitations.
- The options available for repair of parastomal hernia include direct local tissue repair, resiting of the intestinal stoma with closure of the primary aperture, and the application of mesh around the stoma at various levels within the abdominal wall.
- Three techniques, colon fascia repair, mesh, and relocation in a small series were assessed in a nonrandomized trial. Surgical wound infection was more common when mesh repair was used and recurrent hernia much more common when there was just direct fascial repair around the stoma.
- The best operation to perform in individuals having significant complications is closure of the stoma and restoration of intestinal continuity. This should be done whenever possible.

46. Incontinence

A. Introduction

- Fecal incontinence is the inability to control feces and to expel it at a proper place and at a proper time.
- Many factors contribute to the ability to control feces.
 - The consistency of the feces is important. Firm stool can be controlled much easier than liquid stool.
 - Peristalsis in the rectosigmoid has a role in keeping the rectum empty, for most of the time. This special antiperistaltic movement in the original rectosigmoid explains why patients with low anterior resection often have urgency and difficulties controlling their stool because they miss this mechanism.
 - The rectal capacity is important to store feces for some time. A nondistending rectum gives frequency and urgency and leads to loss of stool when there is no toilet available.
 - The pelvic floor muscles help to form a barrier when they are contracted and help during defecation to open the anus.
 - The internal anal sphincter is consistently contracted and gives a watertight closure of the anal canal with the help of the hemorrhoidal tissue that fills the opening of the anal canal.
 - The sensibility of rectum and anus gives awareness of stool in the distal rectum and activates the contraction of the external sphincter as additional help for the internal sphincter.
 - The central nervous system has to be intact to govern the sensoric input and the motor output.

- When something goes wrong in one of these factors, it is dependent on the quality of the other factors whether this leads to incontinence.
- Fecal incontinence forms an enormous economic problem for society. In younger people it often means loss of jobs and dependency on social welfare.

B. Symptoms

- Incontinence is a socially devastating disorder, which affects at least 2.2% of community-dwelling adults and 45% of nursing home residents.
- Fecal incontinence is the most common reason to place patients in a nursing home.
- Because of the social stigma surrounding the loss of bowel control, the complaint is often not directly voiced. The patients become so embarrassed that they do not seek medical advice but rather become confined to their homes and are afraid to visit family and friends.
- Many suffer from social isolation and loss of self-esteem.
- Flatus, involuntary passage of gas, is often the first, sometimes the only, symptom. Increasing degrees of severity involve loss of liquid stools followed by loss of solid feces.
- Partial incontinence may be defined as uncontrolled passage of gas and/or liquids and complete incontinence as the uncontrolled passage of solid feces.
- Soiling is a bothersome disorder characterized by continuous or intermittent liquid anal discharge. It should be differentiated from discharge due to fistulae, proctitis, and prolapse.
 - Patients complain about stains in their underwear. They often wear sanitary napkins or tissues.
 - The discharge causes inflammation of the perineal skin with excoriation, perianal discomfort, burning sensation, and itching.
 - It usually indicates the presence of an impaired internal sphincter function or a solid fecal mass in the rectum.
- Pseudoincontinence and encopresis are the involuntary loss of formed, semiformed, or liquid stool associated with functional constipation in a child.
 - Pseudoincontinence is caused by anatomic disorders such as a mega sigmoid or anal stenosis whereas no anatomic abnormalities are found in encopresis.

- The most common cause of encopresis is functional fecal retention defined by a history of more than 12 weeks of passage of less than two large-diameter bowel movements per week, retentive posturing, and accompanying symptoms such as fecal soiling.
- Sometimes it is associated with enuresis and urinary tract infection.
- The persistent fecal incontinence frequently brings ridicule and shame to the affected child.
- An assessment of bowel habit is essential. Is there diarrhea, and how often?
 - Irritable bowel syndrome should be excluded. It is a common functional bowel disorder characterized by intermittent abdominal pain and changes in defecation pattern in the absence of other medical conditions with similar presentations.
 - Physical findings and currently available diagnostic tests lack sufficient specificity for clinical use.
 - The diagnosis is based on characteristic clinical findings and the exclusion of other disorders. Episodes of diarrhea and constipation alternate. Incontinence often occurs as a consequence of diarrhea.
- Urgency refers to patients with a need to defecate immediately. It can lead to incontinence when facilities are absent. It is seen in patients with impaired rectal compliance as in proctitis or after low anterior resection, or with impaired sphincter function.
 - Details of frequency, stool consistency, and frequency of defecation should be evaluated.
 - The severity of incontinence can be described by numerical scores using one of the many incontinence-scoring lists. The most popular are the Vaisey and the Wexner index. They give not only a value for the loss of gas, liquid, and solid stool, but also for the impact on daily life.
- The best evaluation is a combination of severity index, special quality of life questionnaires (FIQOL) developed by the American Society of Colon and Rectal Surgeons and patient diaries.
 - Is there passage of stool without the patient being aware of it or is he/she aware but unable to control it?

- Is there a regular use of laxatives or other medications that promote diarrhea or constipation (fecal impaction)?
- A sexual history should be obtained. Anoreceptive sex may lead to internal sphincter dilatation and soiling.
- A careful obstetric history should be taken noting multiparity, forceps assistance, difficult childbirth, episiotomy, and perineal tears.
- Specific inquiry should be made concerning perineal trauma and anorectal surgery. Previous prolapse surgery, urinary incontinence, and the presence of prolapse should be noted because they often occur in pelvic floor denervation.
- A history of neurologic disorders is essential. The presence of central nervous system disorders, peripheral neuropathy, low back injury, and diabetes mellitus should be established.
- Is the patient immobilized or bedridden?
- A history of large or small bowel resection, pelvic irradiation, or inflammatory bowel disease should be recorded.

C. Causes of Incontinence

Congenital

- Patients with low forms of anorectal agenesis have little impairment in continence after early surgery whereas patients with high defects affecting the pelvic floor, the rectum, and urogenital tract, are usually incontinent.
- The anal canal may be absent. Most patients have different degrees of development of the pelvic muscle structures and consequently different degrees of rectal proprioception.
- There may be rectal communication with the urinary tract or vagina.
- Control of defecation after surgical correction of high and intermediate types of congenital anorectal malformations is difficult. Most adults with high anorectal malformations who have undergone abdominoperineal or direct perineal repair have severely defective fecal continence and poor quality of life.

- The posterior sagittal approach has led to a better understanding of the internal anatomy of these defects, and a more rational way to manage the patients. Voluntary bowel movements are achieved in 75% with occasional soiling in 40%.
- Fecal incontinence is common in patients with spinal cord lesions such as spina bifida and meningocele. Constipation is another major stigma. The congenital defects in the lumbosacral spine disturb the sensory and motor nerves supplying the skin and pelvic floor muscle.

Pelvic Floor Denervation

- Intense and recurrent straining, as in difficult childbirth and constipation may lead to stretch-induced injury of the pelvic floor innervation, especially the pudendal nerves. Irreversible injury occurs when nerves are stretched as little as 12%.
- Manometric and electromyographic features have been found in normal elderly women and men suggesting a normal age-related denervation with a compensatory reinnervation of the pelvic floor muscle.
- Although increased pudendal nerve terminal motor latency may indicate that neuropathy is present, normal pudendal nerve terminal motor latency does not exclude weakness of the pelvic floor.

Obstetric

- There are two ways by which vaginal delivery may damage the pelvic floor and anal sphincters.
- The first one is direct mechanical tear of the anal sphincters, a serious complication of childbirth. The incidence of obstetric tears varies from 0.6 to 9%.
 - Defects of the external anal sphincter have traditionally been diagnosed by palpation and electromyography but anal endosonography enables clear imaging of both the internal and external sphincter muscles.
 - Factors that affect the risk for developing obstetric tears are use of forceps, mediolateral episiotomy, and primiparity.
- The other mechanism is pelvic floor denervation resulting from compression or traction injury to the pudendal nerves during vaginal delivery, particularly when it is prolonged or requires forceps assistance.

- Birth weight also correlates. Assessment of pudendal nerve function is important in women with postpartum fecal incontinence because it can influence treatment options.

Iatrogenic

- Fecal incontinence is a frequently neglected but rather common complication of anorectal surgery.
 - The incidence increases to 30–50% after partial internal sphincterotomy and fistulotomy with soiling being the most common complaint occurring in 35–45%.
 - Local sphincter lesions and intraanal scarring (keyhole deformity) are not the sole explanation for the high incidence of incontinence because it also occurs after non-muscle-cutting anorectal surgery such as anal stretch, hemorrhoidectomy, and transanal advancement flaps.
 - The internal anal sphincter is easily damaged with an anal retractor used to gain access to the anal canal and lower rectum. This excessive dilatation of the anal canal results in a serious damage of the internal sphincter resulting in a decrease of resting pressure. The Park's anal retractor is especially notorious for this.
- Low anterior resection compromises anorectal function. Postoperative continence is even poorer after radiochemotherapy.
 - Anal sphincter function is preserved but neorectal capacity, maximum tolerable volume, and rectal compliance are reduced resulting in an increased stool frequency, and episodes of incontinence and soiling.
 - Colonic pouch construction has gained increasing popularity in reconstruction after low anterior resection because it offers superior long-term function compared with low straight or side-to-end colorectal anastomosis.

Traumatic

- Fecal incontinence caused by non-obstetric trauma is uncommon.
- Causes include military or traffic accidents complicated by pelvic fractures, spine injuries or perineal lacerations, insertion of foreign bodies in the rectum, and sexual abuse.
- There is often extensive destruction of the sphincter complex and pelvic floor complicated by pelvic nerve injury.

- Immediate recognition is vital to a successful outcome and may obviate the need for a diverting stoma.
- Evaluation must include a search for involvement of other structures and an evaluation of the anal sphincters.
- Foreign bodies most often do not cause significant anorectal injuries.
- Superficial injuries may be left open or sutured closed.
- Anal intercourse is associated with reduced resting pressure in the anal canal and an increased risk of anal incontinence.

Radiation

- More than three-quarters of patients receiving pelvic radiotherapy experience acute anorectal symptoms and up to one-fifth experience late-phase radiation proctitis. Many of these symptoms are self-limiting, and mucosal complications may often be treated by nonsurgical methods such as topical formalin application, endoscopic argon plasma coagulation, and hyperbaric oxygen therapy.
- Approximately 5% develop other chronic complications, such as fistula, stricture, and disabling fecal incontinence.
- Causes of radiation-induced incontinence are proctosigmoiditis, small bowel injury, fistula formation, reduced rectal capacity, diminished internal and external sphincter function, and rectal mucosal sensitivity.
- These are the results of progressive changes in the connective tissues and vasculature resulting in fibrosis, ulceration, stricture, and occasionally fistula formation.
- Conservative treatment options are of limited value. Surgery may be considered if symptoms are severe, provided sphincter function is adequate and recurrent disease is excluded.
- When the condition becomes intolerable, colostomy is the last resort.

D. Physical Examination

- Routine abdominal examination should be performed. The presence of scars should be noted.
- Neurologic assessment should be done when there is suspicion of neurologic disorders.

- At first, the physician should explain to the patient what to expect during the examination in an effort to allay embarrassment and anxieties.
- Observation should be made of whether the patient wears a pad or whether there are signs of fecal soiling on the underwear.
- The kneeling prone-jackknife position gives the best exposure. Inspection of the perineum may reveal perineal soiling, excoriation, a patulous anus, an ectropion, a keyhole deformity, or other anal deformities.
 - The physician should inspect for evidence of scars from previous operations or trauma, fistulas, hemorrhoids, or prolapse.
 - The perineum should also be inspected while the patient is bearing down to observe for mucosal or complete rectal prolapse. Perineal descent is present when the perineum balloons during straining. It is a physical sign of weakness of the pelvic floor and is often seen in the descending perineum syndrome and pelvic floor denervation.
 - The most prevalent abnormality of descending perineum syndrome on testing is perineal descent >4 cm.
- Digital rectal examination should assess the degree of anal resting tone, a function of the internal sphincter.
- Normally the anal canal is closed snugly around the examining finger. Decreased tone may be noted if there is a rectal prolapse, a history of previous anorectal surgery, or repeated anal intercourse.
- The increase of anal tone during squeezing, a function of the external sphincter, should also be noted.
- Simple lateral retraction of the buttocks or downward pulling of the puborectalis are other methods to reveal a patulous anus.
- Digital examination of the vagina should be performed to check for vaginal prolapse, rectoceles, cystoceles, or enteroceles.
- An impaired sphincter tone during bearing down is found in incontinence and descending perineum syndrome.
- The sphincter complex and perineal body can be assessed by bidigital anovaginal examination (the thumb in the vagina and the index finger in the anorectum). An empty and destroyed anterior perineal body is suggestive for an obstetric sphincter lesion.
- The puborectalis muscle can be palpated bilaterally and posteriorly as a prominent sling passing around the rectum thus creating

the anorectal angle that is normally 90°. During bearing down, the dorsal transverse bar should flatten out as a sign of pelvic floor relaxation. Paradoxical contraction suggests anismus.

- Inserting the index finger into the rectum and pushing the anterior wall forward and downward into the vagina can demonstrate a rectocele. Impacted feces can be felt in the lower rectum.
- The “o’clock” position requires a known patient position; recording in an anatomic manner (anterior, posterior, right, left) is a better alternative.

E. Anal Manometry

- Anorectal manometry includes a number of specific tests that are helpful in the diagnostic assessment of patients with fecal incontinence. It includes resting anal pressure, anal squeeze pressure, the rectoanal inhibitory reflex, compliance of the rectum in response to balloon distension, and sensory thresholds in response to balloon distension.
- The interpretation of these diagnostic tests is complicated by the fact that patients are able to compensate for deficits in specific physiologic mechanisms maintaining continence and defecation by using other biologic and behavioral mechanisms.
- Resting pressure represents internal sphincter function whereas squeeze pressure reflects external sphincter function.
- Anal pressures in normal individuals have a large range and vary with sex and age: patients with low values may be continent whereas high pressures do not guarantee continence.
- Squeeze pressures are higher in men than in women.
- Older patients exhibit lower pressures but a significant age-related difference cannot be demonstrated.
- Resting and squeeze pressures are lower in incontinent patients than in normals. It does not correlate with the severity of incontinence and neither does it predict postoperative results.
- Patients with soiling often have normal squeeze pressures but lowered resting pressures.
- Anal manometry may be useful in fecal incontinence to exclude impaired sphincter function as the cause of incontinence and to assess the effects of operative procedures on sphincter functions.

F. Defecography

- Defecography is the radiologic visualization of the act of defecation.
- It provides a picture of the successive phases of defecation and gives an impression of pelvic floor activity during these actions. Changes in the rectal configuration and the anorectal angle become visible and the degree of evacuation can be studied.
- It can demonstrate abnormalities that were unsuspected on clinical examination.
- The value of defecography in fecal incontinence is to demonstrate the presence of internal rectal intussusception in patients with perineal symptoms or the solitary rectal ulcer syndrome.

G. Endosonography

- Endosonography is a diagnostic tool to investigate the anal sphincters.
- Atrophy, scar tissue, and also defects in the sphincters can be seen. These endosonograms make it possible to find old ruptures even when there is no marking in the anal skin.
- Sometimes it is difficult to visualize defects in the perineum of a woman. In these cases, additional vaginal endosonography can be helpful.

H. Magnetic Resonance Imaging

- Magnetic resonance imaging (MRI) of the pelvic region is an excellent way to visualize the anal canal, lower rectum, and the surrounding tissue of prostate, bladder, and uterus.
 - The MRI can be performed with an endo-coil in the anus and with surface phased array coil.
 - The endo-coil has the advantage that the sphincters are better visualized but in an unnatural way.
 - An MRI without an endo-coil but with a phased array coil gives a view of the natural contracted sphincter.
 - Both methods reveal lesions as well as atrophy of parts of the sphincters.

I. Pudendal Nerve Latency Time

- Pudendal nerve latency time offers the opportunity to evaluate nerve damage to the pelvic floor. It measures the time from an electrical stimulus of the pudendal nerve to the onset of the electrical response in the muscles of the pelvic floor.
- An easy, painless way of performing this test is with the use of the finger electrode. This electrode is mounted on a glove and contains an electrode at the end of the finger that can be placed intrarectally on the pudendal nerve.
- A prolonged latency is taken as evidence of neuropathy.

J. Sensation Test

- The sensitivity of the rectum is studied with inflation of an intrarectal balloon.
- A high threshold of the minimal volume sensed in the rectum is abnormal (usually >20 mL).

K. Endoscopy

- Endoscopy has a limited value for investigation of fecal incontinence. It can exclude some diseases that give diarrhea and mucus production (proctitis, colitis, solitary rectal ulcer, villous adenoma, etc).

L. Treatment

Conservative Treatment

- Nonsurgical treatment is the initial approach to the incontinent patient. It aims at improving continence, quality of life, psychologic well-being, and anal sphincter function.
- Diarrhea is the most common aggravating factor for fecal incontinence. Its cause should be evaluated.

- Perineal pads are efficient and acceptable for minor incontinence only.
- The aim of pharmacologic treatment of fecal incontinence is to try to achieve passage of one or two well-formed stools a day. It can be tried with simple constipating agents such as loperamide diphenoxylate, codeine phosphate, or bile acid binders. Many of these suppress the propulsive activity of the small bowel and colon. Bulking agents may improve the consistency of a liquid stool.
- Laxative abuse should be stopped.
- Successful treatment of encopresis, overflow incontinence, or pseudo-incontinence requires a combination of parent and child education, behavioral intervention, medical therapy, and long-term compliance with the treatment regimen. After complete evacuation of the impacted rectum, reaccumulation of stool should be prevented by appropriate use of laxatives and well-balanced diets including fibers and fluids followed by gradual weaning of the laxative regimen and instituting toilet training such as regular attempts to defecate and habit training.
- Surgical treatment can be considered for an anatomic defect in pseudo-incontinence such as resection of a megasigmoid.
- Dietary advice may help some patients. Patients with the pattern of soiling may be successfully treated with stool bulking agents (e.g., psyllium or bran).
- An empty rectum is the best prevention of involuntary loss of stool. Glycerine or bisacodyl suppositories and phosphate enemas may be helpful.
- Daily colonic irrigation is a suitable alternative. Retrograde colonic irrigation can be performed by influx of lukewarm water from a water bag or from a pump. The antegrade continence enema (Malone) procedure has improved the lives of many patients who struggle with intractable forms of constipation or incontinence.
- The non-refluxing, catheterizable appendicocostomy provides the opportunity to treat previously therapy-resistant patients to administer large-volume enemas through a right lower quadrant stoma to flush the colon every other day. It works well in patients with incontinence secondary to spinal cord disorders.

- Even patients with soiling seem to benefit from colonic irrigation. It reduces or eliminates soiling in approximately 78% of children with myelomeningocele.

Biofeedback Treatment

- Biofeedback is the use of technology to give the patient better information about specific physiologic activities that are under the control of the nervous system but not clearly or accurately perceived by the patient. The rationale underlying biofeedback assumes that the physiologic activity that is monitored is causally related to a clinical problem and that alteration of that activity can lead to resolution of the problem.
- Biofeedback is a time-consuming and labor-intensive, but harmless and inexpensive, treatment for fecal incontinence, which benefits approximately 75% of patients but cures only about 50%.
- It may be most appropriate when there is neurologic injury (i.e., partial denervation), but it has been reported to also benefit incontinent patients with minor structural defects.
- Fecal incontinence is one of the few indications for which biofeedback is considered to be clinically effective.
- Rectal sensation seems to be a critically important determinant in achieving success with biofeedback.
- It is not helpful in patients with profound denervation of the pelvic floor or absence of innervation. Patients with decreased rectal capacity as in proctectomy or proctitis do not respond.

Balloon Training

- Increasing volumes of water in a rectal balloon can be of help to bring down the threshold of first urge. It is a tool to improve the sensibility of the rectum.

Electrostimulation

- Electrostimulation as a treatment for fecal incontinence is widely used among physicians and physiotherapists. It is claimed to improve muscle function and to decrease the susceptibility of the muscle to fatigue. Data to support this claim, however, are lacking.

- Electrostimulation is not a clinically effective treatment of anal incontinence.

Operative Treatment

Anal Encirclement Procedures

- The complication rate is high and a variety of complications have been described such as fecal impaction, infection, wire migration, and perineal discomfort.
- An indication for this procedure does not exist anymore. Instead, a colostomy should be considered.

Anterior Sphincteroplasty

- Patients with incontinence secondary to an obstetric or iatrogenic anterior defect are best suited for surgical correction of fecal incontinence.
- Poor result after adequate sphincter repair is attributed to coexistent pelvic floor denervation. Primary sphincter repair is inadequate in most women with obstetric ruptures after vaginal delivery because most have residual sphincter defects and about 50% still experience incontinence.
- Good functional results are usually obtained in 50–80% but seem to deteriorate with time. Continence is rarely perfect and many have residual symptoms.
- The most important factor in the return to normal sphincter function is an increase in squeeze pressure.
- Repair of laterally and posteriorly placed injuries is less successful.

Injection Therapy

- Transsphincteric injection of silicone biomaterial can provide a marked improvement in fecal incontinence related to a weak or disrupted internal anal sphincter. This is associated with improved sphincter function and quality of life.

Postanal Repair

- Postanal repair was originally described by Parks as a method to improve fecal incontinence by restoring the anorectal angle and lengthen the anal canal.

- The principal indication is denervation damage of the pelvic floor.
- The initial results are good; continence for solid stool is restored in 40–50%. Long-term benefits, however, are only reported by 30–40% of patients; 30% are not improved at all.
- Despite the low success rate, due to the absence of any mortality, and the low morbidity, it has a place in the management of fecal incontinence because there are few alternatives.
- Posterior reconstruction may be replaced by sacral nerve stimulation.

Sacral Nerve Stimulation

- The method is very attractive because it offers the opportunity to test the stimulation before the decision for a permanent implant is made.
- When there is an improvement in continence, an implant may follow in which a permanent electrode is fixed to the sacrum and connected to an implantable stimulator.
- The best indication for sacral nerve stimulation is fecal incontinence in patients with intact anal sphincters or for patients who had an unsuccessful anal repair in the past.
- It seems to work well in patients with neurogenic incontinence.

Dynamic Graciloplasty

- Patients with a completely destroyed anal sphincter or a large gap between both ends of the sphincters cannot be helped anymore with anal repair. For these patients, dynamic graciloplasty may be a good solution.
- Anatomically, this muscle is probably the best replacement of the destroyed sphincter, but it is intrinsically the worst muscle for sphincter function because of its composition of a minority of type one fibers (long acting, slow twitch) and a majority of type two fibers (short acting, fast twitch). This makes the gracilis a fatigable muscle that only conscientiously contracts by will.
- With chronic low-frequency stimulation, the gracilis can change its fiber composition and become a nonfatigable muscle that contracts on demand of the stimulator.
- The electrical stimulation is given by an implanted stimulator through an intramuscular electrode that is placed very close to

the gracilis nerve. The muscle remains contracted but the anal canal can be opened by switching off the stimulator with the help of a handheld programmer.

- The results are dependent on the experience of the surgeon and the success rate varies between 40 and 80%.

Artificial Bowel Sphincter

- An alternative for dynamic graciloplasty is in some cases the artificial bowel sphincter. Instead of autologous muscle, the anus is now encircled with an implantable fluid-filled, silicone elastomer cuff.
- This cuff is connected by tubings with a control pump and a pressure-regulating balloon. The inflated cuff compresses the anus all the time. By using the control pump situated in the labia or scrotum, the fluid is manually pumped from the cuff toward the balloon. The empty cuff allows passage of stool.
- Erosion from the cuff through the anus and the vagina is a common complication. Infection is also a major concern.

Colostomy

- When conservative and operative treatment has failed to create an acceptable level of continence, the patient is in fact left with a perineal colostomy. An abdominal colostomy may then be offered to the patient as a last alternative but it should be performed only after thorough counseling.
- Because mucus production in the excluded rectosigmoid will persist and mucus retention is impossible because of the impaired sphincter function, a continuous drainage of brown-grayish, foul-smelling mucus will occur, wetting and staining the underwear and eroding the perineal skin.
- Rectosigmoid resection leaving a rectal stump of 3–4 cm should therefore be added to the procedure. Resection does not completely eliminate mucus secretion but normally reduces it to an acceptable level.

Perioperative Management

- Perioperative antibiotic prophylaxis is advisable for all interventions for incontinence and mandatory in the operations with implant of foreign material.

- Postoperative administration of laxatives is of help in the prevention of passage of firm stool in the first postoperative days. Perioperative protection with a diverting colostomy is usually not necessary.

M. Conclusion

Fecal incontinence is no longer an untreatable disease. In almost all cases, it is possible to help patients with conservative management, operations, or with combinations (Table 46.1).

Table 46.1. Algorithm for treatment of fecal incontinence.

Consistency	Cause	First choice	Second choice	Third choice
Diarrhea	Inflammatory	Antiinflammatory drugs	Constipating drugs	Colostomy
Pseudodiarrhea	Encopresis	Laxatives	Lavage	Colostomy
Solid	Pelvic floor	Biofeedback	SNS	Colostomy
	Sphincter intact	SNS	Lavage	Colostomy
	Sphincter rupture	Anal repair	SNS/DGP/ABS	Colostomy
	Anal atresia	Lavage	ABS/DGP	Colostomy
	Rectal prolapse	Rectopexy	Perineal resection	Colostomy
Soiling	Keyhole defect	Lavage	PTQ implant	

SNS sacral nerve stimulation; *DGP* dynamic graciloplasty; *ABS* artificial bowel sphincter; *PTQ* implant silicone particles

47. Rectal Prolapse

A. Introduction

- Prolapse, in general, is defined as: “A falling down of an organ or part... from its normal position.” Rectal prolapse is a “falling down” of the rectum so that it is outside the body.
- Its appearance is that of an erythematous, proboscis-like object and is a true intussusception of the rectum through the sphincters.
- It is associated with fecal incontinence, and in women, is associated with other pelvic floor abnormalities.
- More recently, with the benefit of cinedefecography, Broden and Snellman proposed that prolapse is actually a circumferential intussusception of the rectum. It is this theory that most investigators subscribe to.
- The majority of patients afflicted with rectal prolapse have a long history of constipation and straining.
- The disorder is more common in women, especially in older age groups. Affected men tend to be younger (20–40 years of age) and usually have a predisposing disorder (e.g., congenital anal atresia).
- A vast number of different procedures have been described to manage the disorder serving as testimony to the uncertain etiology of the disease and the resultant disagreement about optimal surgical therapy (Table 47.1).
- Patient factors that influence the choice of operation are: age, sex, medical condition, extent of prolapse, bowel function, and status of fecal continence.
- Procedure-related factors that influence the choice of operation include: extent of procedure, potential morbidity, recurrence rate, impact on fecal continence and bowel habit, familiarity and ease of technique.

Table 47.1. Operations described for rectal prolapse.

Transabdominal procedures**Repair of the pelvic floor**

Abdominal repair of levator diastasis

Abdominoperineal levator repair

Suspension-fixation

Sigmoidopexy (Pemberton-Stalker)

Presacral rectopexy

Lateral strip rectopexy (Orr-Loygue)

Anterior sling rectopexy (Ripstein)

Posterior sling rectopexy (Wells)

Puborectal sling (Nigro)

Resection procedures

Proctopexy with sigmoid resection

Anterior resection

Perineal procedures

Perineal rectosigmoidectomy (Altemeier)

Rectal mucosal sleeve resection (Delorme)

Perineal suspension-fixation (Wyatt)

Anal encirclement (Thiersch + modification)

B. Patient Evaluation

- Constipation and straining, fecal incontinence, and erratic bowel habits typify the symptoms associated with prolapse.
- Spontaneous prolapse is obvious on inspection. Some patients may require straining to produce the prolapse, and the straining patient is best examined in the squatting or sitting position. The patient can be examined while he or she is on the toilet by having the patient lean forward or using a long rod to which a mirror is attached placed between the patient's legs to view the prolapse.
- Full-thickness prolapse is distinguished by its concentric rings and grooves as opposed to the radially oriented grooves associated with mucosal prolapse (Fig. 47.1).
- A digital rectal examination is important to detect concomitant anal pathology and to assess resting tone and squeeze pressure of the anal sphincters and function of the puborectalis muscle.
- Colonoscopy or flexible sigmoidoscopy with barium enema should be performed to rule out associated mucosal abnormalities.

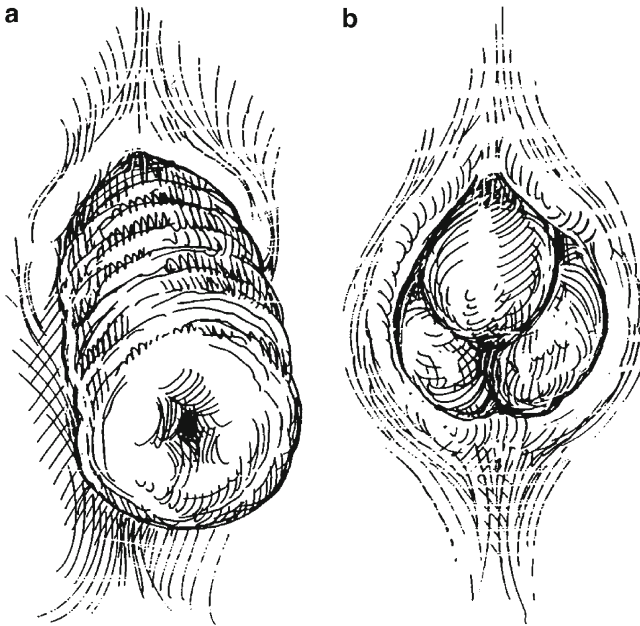


Fig. 47.1. Mucosal versus full-thickness prolapse. (From Beck and Whitlow. Copyright 2003 by Taylor & Francis Group LLC (B). Reproduced with permission of Taylor & Francis Group LLC (B) in the format Textbook via Copyright Clearance Center). (a) Circumferential full-thickness prolapse; concentric mucosal folds (b). Radial folds seen with hemorrhoidal prolapse.

- Defecography is usually not necessary in the evaluation of full-thickness prolapse but it is an essential part of the evaluation of internal procidentia (rectoanal intussusception).
- Anal manometry can help assess sphincter function; longstanding prolapse typically damages the internal anal sphincter and may cause poor resting pressures.
- Anal electromyography and pudendal nerve terminal motor latency are generally not clinically helpful unless there is a history of severe straining.
- Colonic transit times should be done in patients with a coexisting history of severe constipation so that the correct operation can be chosen.

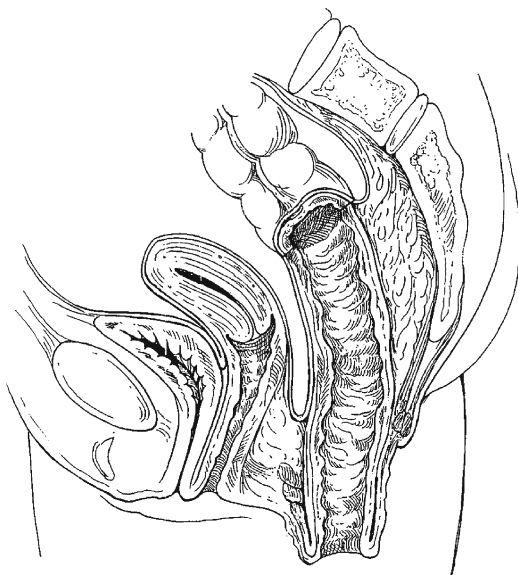


Fig. 47.2. Sagittal view of full-thickness rectal prolapse. (From Beck and Whitlow. Copyright 2003 by Taylor & Francis Group LLC (B). Reproduced with permission of Taylor & Francis Group LLC (B) in the format Textbook via Copyright Clearance Center).

C. Surgical Procedures

- The surgeon must decide between a perineal operation and an abdominal procedure. Men are at risk for sexual dysfunction with an abdominal approach, therefore this option is chosen cautiously.
- The most common abdominal operations are resection with or without rectopexy or rectopexy alone.
- The perineal procedures are perineal rectosigmoidectomy (Altemeier) or mucosal sleeve resection (Delorme).
- Elderly, high-risk patients are best treated by perineal procedures which can be performed under a regional anesthetic, or even a local anesthetic with intravenous sedation.
- Healthy adults with normal bowel habits may undergo either rectopexy $\pm$ sigmoidectomy or perineal rectosigmoidectomy $\pm$ levatorplasty.

- Constipated patients should undergo resection and rectopexy.
- Incontinent patients should undergo either abdominal rectopexy or perineal rectosigmoidectomy levatorplasty.
- Recurrent prolapse mandates knowledge of the prior repair because that information will dictate future options; the prior dissection may limit the available alternatives because of blood supply divided.

Perineal Procedures

Perineal Rectosigmoidectomy

- Perineal rectosigmoidectomy was popularized by Altemeier and his name is the eponym attached to the procedure (Fig. 47.3).
- Reported results of the perineal rectosigmoidectomy are summarized in Table 47.2. Mortality has been low and morbidity ranges from 5 to 24%.
- Recurrence rates range from 0 to 10% in series with a follow-up of 6 months to 5 years. Recurrence rates are higher for series with longer follow-up.
- Improvement in incontinence has been reported in the majority of patients in whom levatorplasty is performed.

Delorme Procedure

- It is ideally suited to those patients with full-thickness prolapse limited to partial circumference (e.g., anterior wall) or less-extensive prolapse.
- The Delorme's procedure for treating rectal prolapse differs from the perineal rectosigmoidectomy (Altemeier) in that only the mucosa and submucosa are excised from the prolapsed segment (Fig. 47.4).
- Results of Delorme's procedure are summarized in Table 47.3.
- Reported operative mortality rates from a series of patients treated by Delorme's procedure range from 0 to 2.5%.
- Morbidity reported at 0–32% includes hemorrhage, anastomotic dehiscence, stricture, diarrhea, and urinary retention.
- Recurrence rates (7–22% at 1–13 years postoperatively) are higher than with a perineal rectosigmoidectomy. Incontinence is improved in 40–50% of patients.

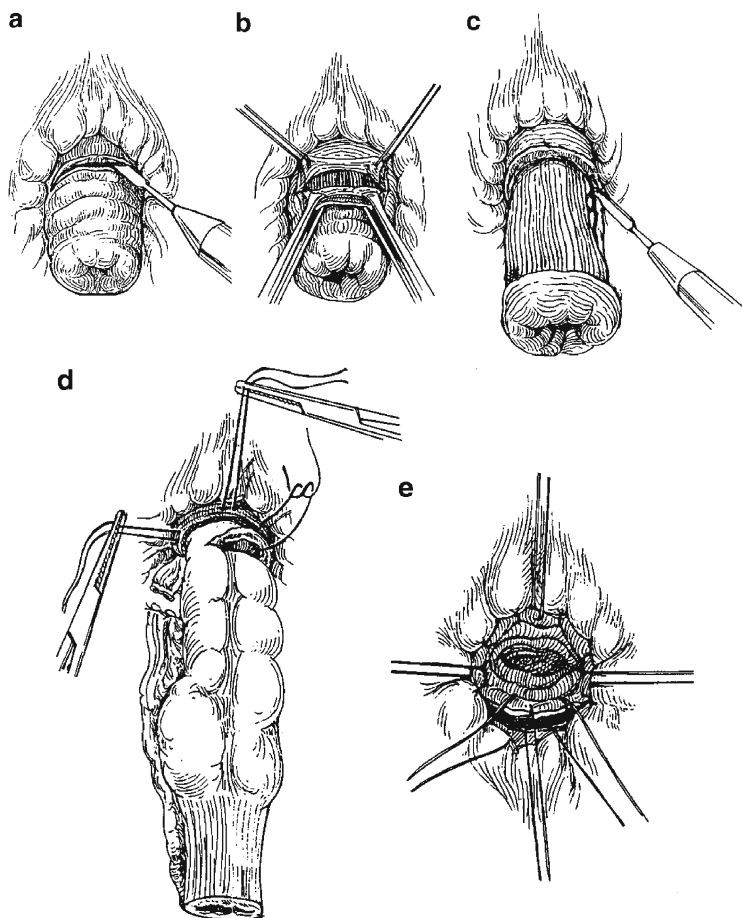


Fig. 47.3. Perineal rectosigmoidectomy. (a, b) Incision of rectal wall. (c) Division of vessel adjacent to bowel wall. (d) The prolapsed segment is amputated. Stay sutures previously placed in distal edge of outer cylinder are placed in cut edge of inner cylinder. (e) Anastomosis of distal aspect of remaining colon to the short rectal stump. (From Beck and Whitlow. Copyright 2003 by Taylor & Francis Group LLC (B). Reproduced with permission of Taylor & Francis Group LLC (B) in the format Textbook via Copyright Clearance Center).

Thiersch Procedure

- Anal encirclement was first described by Thiersch in 1891. He placed a silver wire subcutaneously around the anus with the patient under local anesthesia. The mechanism of this procedure

Table 47.2 . Results of perineal rectosigmoidectomy.

Authors	Number of patients	Recurrence (%)	Mortality (%)	Morbidity (%)
Altmeier et al.	106	3	00	24
Friedman et al.	027	50	00	12
Gopal et al.	18	6	06	17
Finlay and Aitchison	17	6	06	18
Williams et al.	114	11	00	12
Johansen et al.	20	0	05	05
Kim et al.	183	16	00	14
Azimuddin et al.	36	16	—	—
Zbar et al.	80	4	—	—

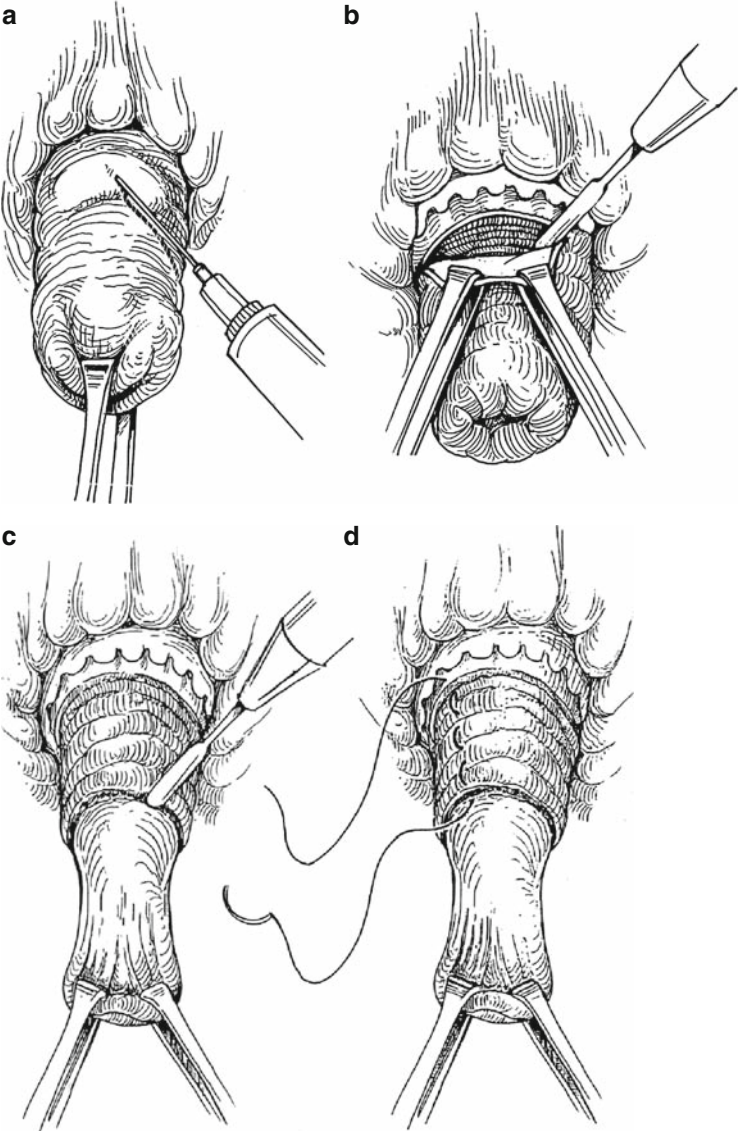
was to mechanically supplement or replace the anal sphincter and stimulate a foreign body reaction in the perianal area (Fig. 47.5).

- Complications of this procedure include breakage of the suture or wire, fecal impaction, sepsis, and erosion into the skin or anal canal.
- The Thiersch operation does not correct the prolapse but narrows the anus enough that the prolapse is confined to the rectum, accomplishing this goal in 54–100% of cases.
- Because of its failure to correct prolapse and the morbidity of this procedure, it is reserved for the most seriously ill patients who are unable to undergo one of the previously described perineal procedures. Results of the Thiersch procedure are summarized in Table 47.4.

Abdominal Procedures

Abdominal Rectopexy and Sigmoid Colectomy

- The operation consists of four essential components:
 - Complete mobilization of the rectum down to the levator musculature, leaving the lateral stalks intact
 - Elevation of the rectum cephalad with suture fixation of the lateral rectal stalks to the presacral fascia just below the sacral promontory
 - Suture of the endopelvic fascia anteriorly to obliterate the cul-de-sac
 - Sigmoid colectomy with anastomosis
- The modern components of the operation are essentially the same with the exception that most surgeons no longer obliterate the cul-de-sac (Fig. 47.6).



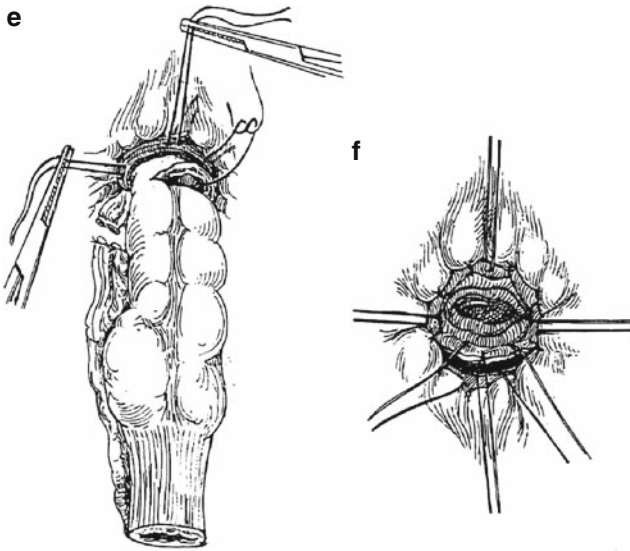


Fig. 47.4. Delorme's procedure. (a) Subcutaneous infiltration of dilute epinephrine solution. (b) Circumferential mucosal incision. (c) Dissection of mucosa off muscular layer. (d) Plicating stitch approximating cut edge of mucosa, muscular wall, and mucosa just proximal to dentate line. (e) Plicating stitch tied. (f) Completed anastomosis. (From Beck and Whitlow. Copyright 2003 by Taylor & Francis Group LLC (B). Reproduced with permission of Taylor & Francis Group LLC (B) in the format Textbook via Copyright Clearance Center).

Table 47.3. Results of Delorme's procedure.

Authors	Number of patients	Recurrence (%)
Uhlig and Sullivan	44	7
Monson et al.	27	7
Senapati et al.	32	13
Oliver et al.	41	22
Tobin and Scott	43	26
Graf et al.	14	21

- Results with abdominal rectopexy and sigmoidectomy are summarized in Table 47.5.

Abdominal Rectopexy

- Typically, this operation has been used in patients who do not have associated constipation with prolapse.

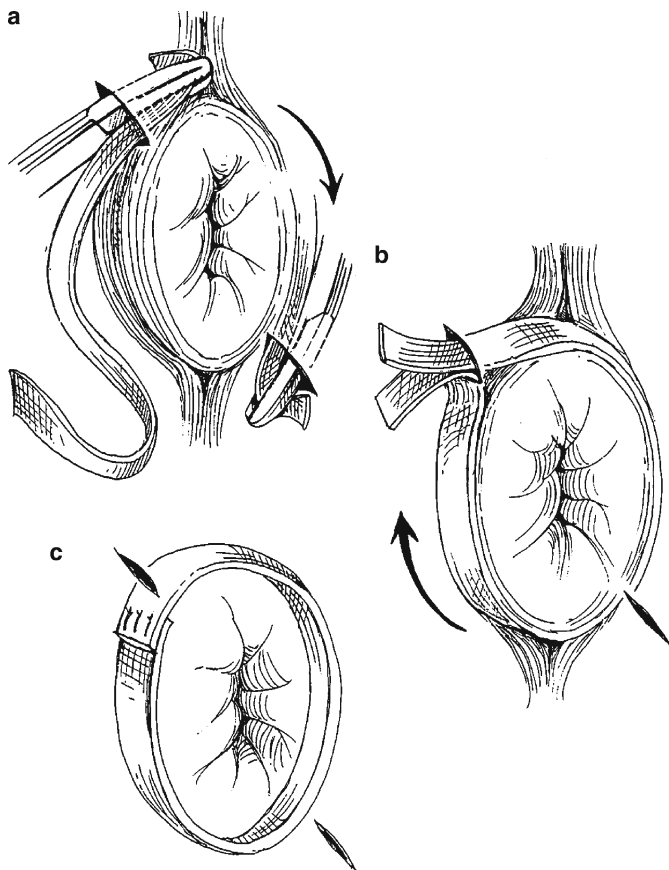


Fig. 47.5. Anal encirclement (Thiersch). (a) Lateral incisions with prosthetic mesh tunneled around the anus. (b) Mesh completely encircling the anal opening. (c) Completed anal encirclement procedure. (From Beck and Whitlow. Copyright 2003 by Taylor & Francis Group LLC (B). Reproduced with permission of Taylor & Francis Group LLC (B) in the format Textbook via Copyright Clearance Center).

Table 47.4. Results of Thiersch procedure.

Authors	Number of patients	Recurrence (%)	Mortality (%)	Morbidity (%)
Jackaman et al.	52	33	—	—
Labow et al.	9	0	—	0
Hunt et al.	41	44	—	37
Poole et al.	15	33	—	33
Vongsangnak et al.	25	39	—	59
Earnshaw and Hopkinson	21	33	—	—
Khanduja et al.	16	0	—	25

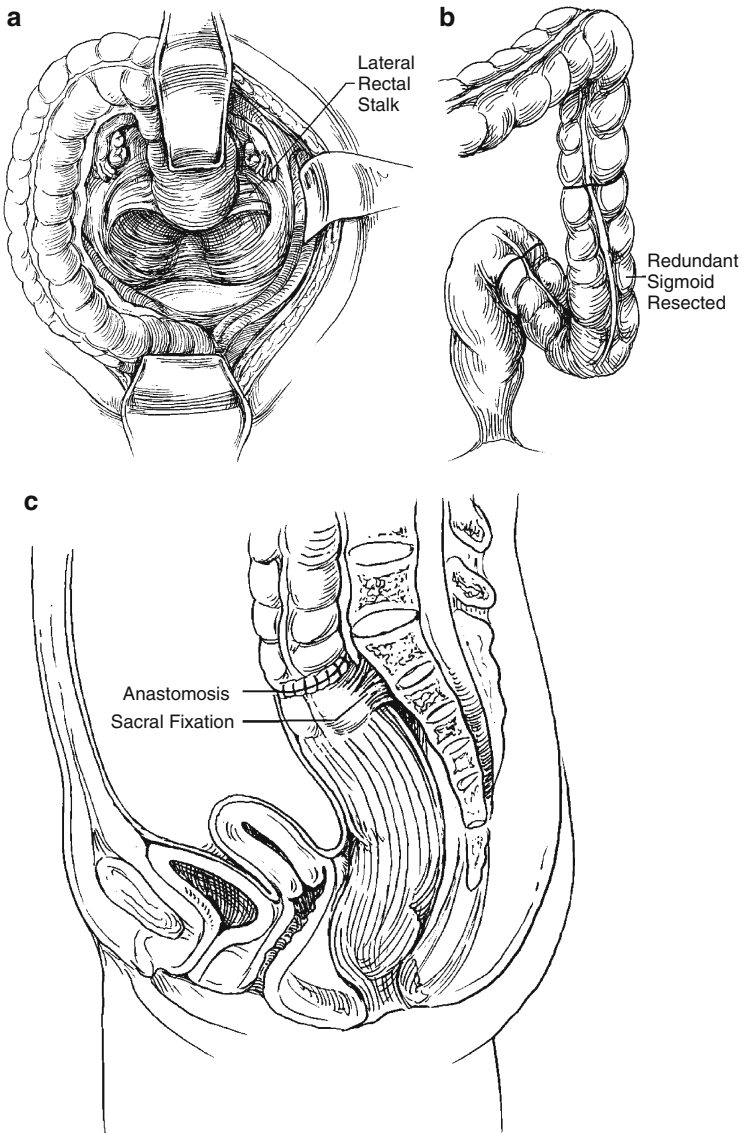


Fig. 47.6. Abdominal rectopexy and sigmoidectomy. (a) Rectum is fully mobilized in the posterior avascular plane. (b) Redundant sigmoid colon is resected. (c) Anastomosis is completed and rectopexy sutures are placed.

Table 47.5. Results of abdominal rectopexy and sigmoid colectomy.

Authors	Number of patients	Recurrence (%)	Mortality (%)	Morbidity (%)
Watts et al.	102	1.9	00	04
Husa et al.	48	09	02.1	00
Sayfan et al.	13	00	00	23
McKee et al.	09	00	00	00
Luukkonen et al.	15	00	06.7	20
Canfrere et al.	17	00	00	—
Huber et al.	39	00	00	7.1

Table 47.6. Results of abdominal rectopexy.

Authors	Number of patients	Recurrence (%)	Mortality (%)
Loygue et al.	140	3.6	01.4
Blatchford et al.	42	02	00

- The rectum is mobilized down to the levator floor preserving the lateral ligaments. The lateral rectal stalks are then sutured to the presacral fascia just below the sacral promontory, using a nonabsorbable suture, such as Prolene. Results are summarized in Table 47.6.

Ripstein Procedure

- It is currently seldom used, probably because of the success of alternate therapies and because this particular operation requires the use of prosthetic material, placed around the rectum.
- The rectum is mobilized posteriorly down to the coccyx. A 5-cm piece of prosthetic mesh (Marlex or Prolene) is sutured to the presacral fascia, 5 cm below the sacral promontory in the midline. The rectum is retracted cephalad and the lateral edges of the sling are wrapped around the rectum and sutured to it (Fig. 47.7).
- Results are summarized in Table 47.7.

Ivalon Sponge

- The Ivalon (polyvinyl alcohol) sponge wrap operation, first described in 1959 by Wells, is currently the most popular operation for rectal prolapse in the United Kingdom (Fig. 47.8).

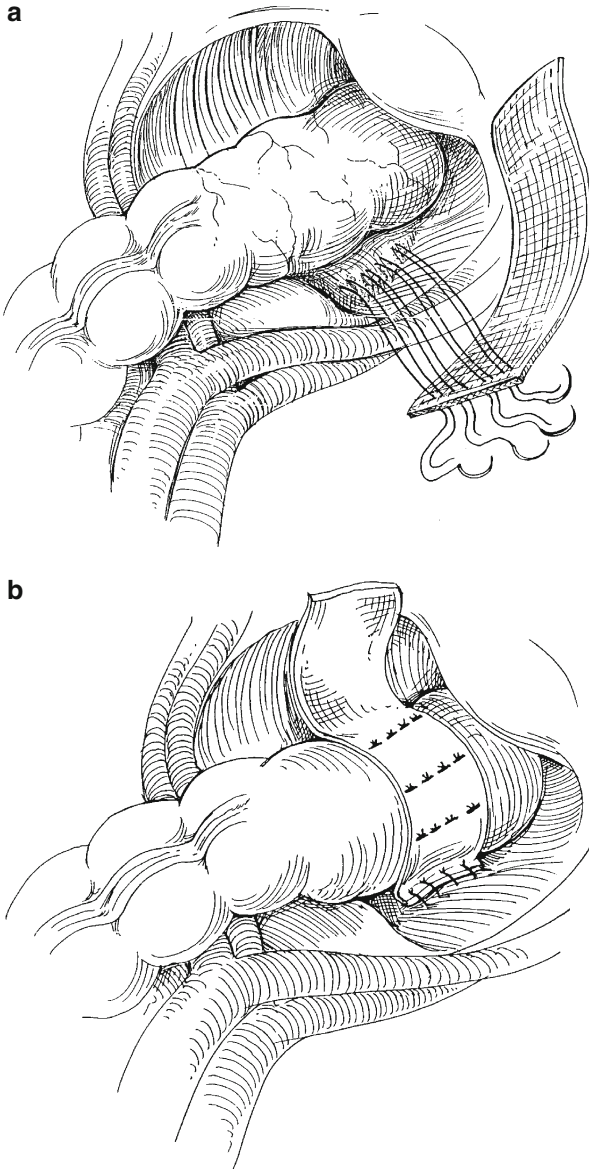


Fig. 47.7. Mesh rectopexy (Ripstein). (a) Posterior fixation of sling on one side. (b) Sling brought anteriorly around mobilized rectum. (c) Sling fixed posteriorly on the opposite side. (d) Sagittal view of the completed rectopexy. (From Beck and Whitlow. Copyright 2003 by Taylor & Francis Group LLC (B). Reproduced with permission of Taylor & Francis Group LLC (B) in the format Textbook via Copyright Clearance Center).

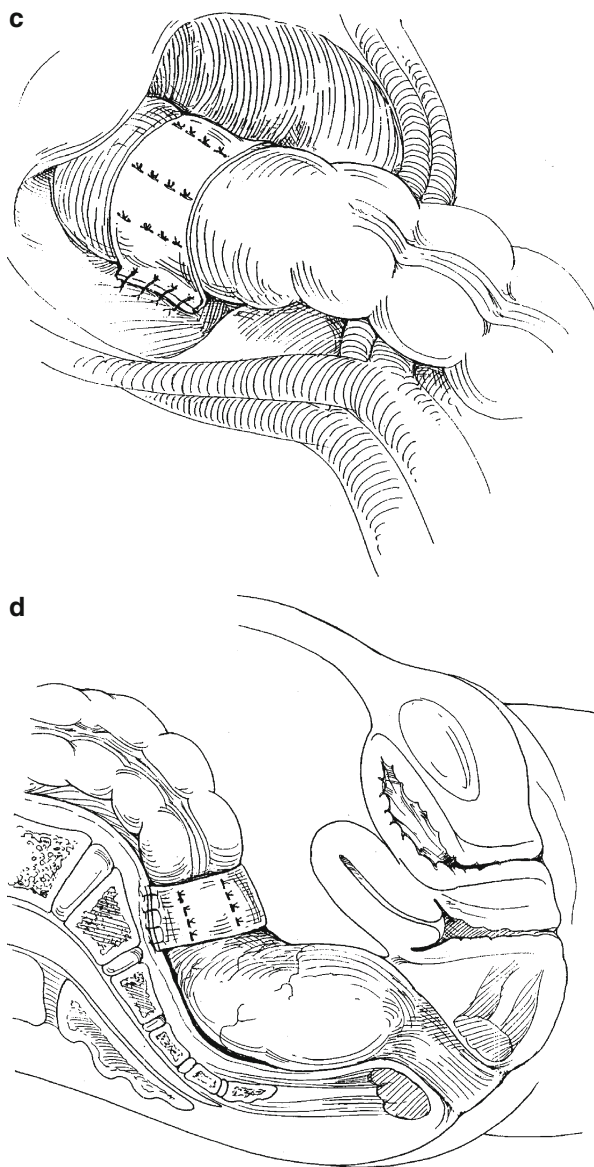


Fig. 47.7. (continued)

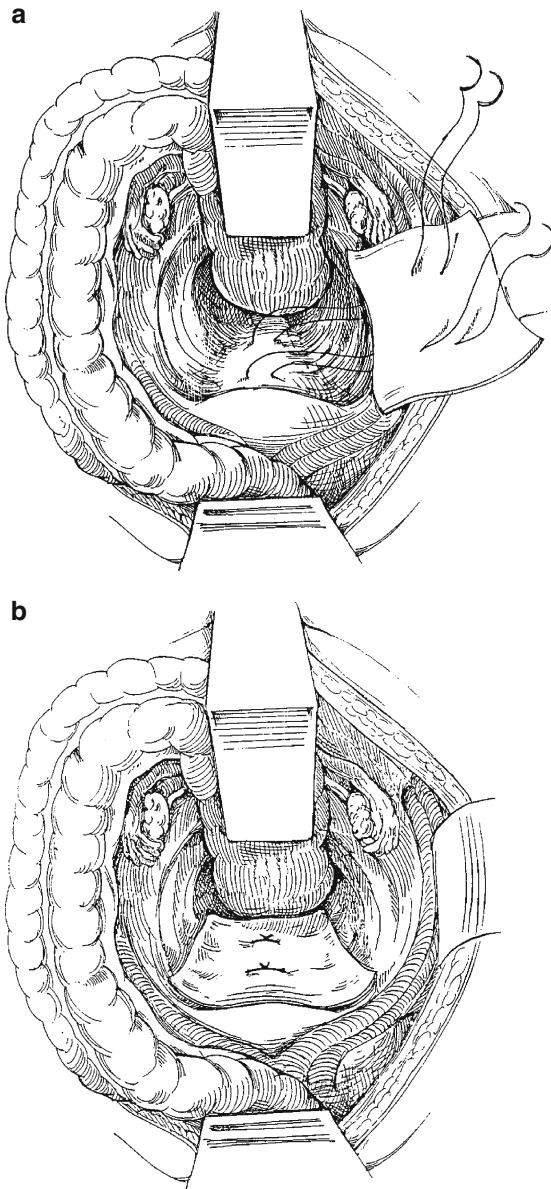


Fig. 47.8. Ivalon (polyvinyl alcohol) sponge rectopexy (Wells). (a) Polyvinyl sponge being fixed to the sacrum. (b) Sponge in place before fixation to the

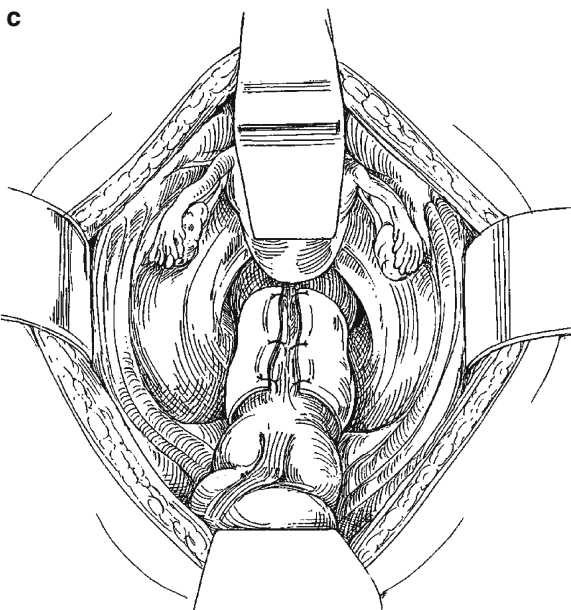


Fig. 47.8 (continued) rectum. (c) Incomplete encirclement of the rectum anteriorly with the sponge sutured in place. (From Beck and Whitlow. Copyright 2003 by Taylor & Francis Group LLC (B). Reproduced with permission of Taylor & Francis Group LLC (B) in the format Textbook via Copyright Clearance Center).

Table 47.7. Results of Ripstein procedure.

Authors	Number of patients	Recurrence (%)	Mortality (%)	Morbidity (%)
Ripstein and Lanter	289	00	00.3	—
Gordon and Hoexter	1,111	02.3	—	16.6
Eisenstadt et al.	30	00	00	13.3
Tjandra et al.	134	08	00.6	21
Winde et al.	35	00	00	28

- In the United States, surgeons have used prolene or Marlex mesh instead of a polyvinyl alcohol sponge to perform a posterior wrap. Results of posterior wraps are summarized in Table 47.8.

Table 47.8. Results of Ivalon sponge operation.

Authors	Number of patients	Recurrence (%)	Mortality (%)	Morbidity (%)
Sayfan et al.	16	00	00	12.5
Luukkonen et al.	15	00	00	13.3
Novell et al.	31	3	00	19

Laparoscopic Rectopexy

- Laparoscopic approaches to the management of full-thickness rectal prolapse, including rectopexy alone, or in combination with sigmoid colectomy have been reported to have comparable success rates and morbidity to open surgery, with the added benefit of shorter hospital stays. These laparoscopic approaches likely represent the future direction of definitive operative management.

Recurrent Prolapse

- Depending on the specific initial therapy selected, recurrent full-thickness rectal prolapse can occur in more than 50% of patients, although most recent reports place recurrent prolapse after resection with rectopexy to be less than 10%.
- Typically, perineal operations for prolapse have a higher risk of recurrence compared with abdominal approaches.
- When full-thickness rectal prolapse recurs, it is important to reevaluate the patient for both constipation and other pelvic floor abnormalities in order to tailor the management to address those issues. Therefore, patients with recurrent prolapse will require evaluation in the anorectal physiology laboratory with manometry and defecography.
- Patient comorbid conditions will also have an important role in treatment selection, as was likely the case in selecting the initial operation.
- A major consideration in determining the best surgical option to treat the recurrent prolapse is the residual blood supply of the remaining large bowel. Any patient who has undergone a prior rectal or sigmoid resection with anastomosis requires very careful evaluation before undergoing a secondary procedure.

- In such patients, the obvious risk to a secondary resection is ischemia to the segment of large intestine between two anastomoses.
- Recurrent full-thickness rectal prolapse can be successfully managed using the same operative options applied to initial disease.
- Reports in the literature place successful treatment of recurrence at between 85 and 100%.
- There is no specific algorithm available that can be applied to select the best operation for treating recurrence, except that many reports suggest treating young patients using an abdominal approach and elderly patients using a perineal approach.
- The treating surgeon is left to make an individualized recommendation from the options that are summarized in Table 47.9.
- The bowel dysfunction associated with prolapse, including constipation and diarrhea, is largely unimproved after correction of the recurrence.
- If the patient has undergone an initial perineal rectosigmoidectomy, then a repeat perineal rectosigmoidectomy or abdominal rectopexy can be safely performed. However, in such cases, abdominal rectopexy with sigmoid colectomy should be avoided because of the risk of ischemia to the retained rectal segment.
- For those patients who have undergone prior abdominal rectopexy but who now have recurrent prolapse, a redo abdominal rectopexy is an acceptable approach.

Solitary Rectal Ulcer Syndrome and Colitis Cystica Profunda

- Solitary rectal ulcer syndrome (SRUS) and colitis cystica profunda (CCP) are uncommon conditions frequently associated

Table 47.9. Management options for recurrent rectal prolapse.

Initial operation	Options for management of recurrence
Perineal rectosigmoidectomy	Redo perineal rectosigmoidectomy Abdominal rectopexy (avoid resection)
Abdominal rectopexy	Redo abdominal rectopexy ($\pm$ sigmoid colectomy) Perineal rectosigmoidectomy
Abdominal rectopexy + Resection	Redo abdominal rectopexy ($\pm$ re-resection) Avoid perineal rectosigmoidectomy

with rectal prolapse. SRUS is a clinical condition characterized by rectal bleeding, copious mucous discharge, anorectal pain, and difficult evacuation.

- Despite its name, patients with this condition can have single, multiple, or no rectal ulcers.
- When present, the ulcers usually occur on the anterior rectal wall just above the anorectal ring. Less frequently, they may occur from just above to 15 cm above the dentate line.
- Ulcers usually appear as shallow with a “punched out” gray-white base surrounded by hyperemia.
- *Cystica profunda* is a benign condition characterized by mucin-filled cysts located deep to the muscularis mucosae.
- When these lesions are found in the colon or rectum they are called CCP and appear as nodules or masses on the anterior rectal wall.
- Patients can be asymptomatic (with the lesions identified on screening endoscopy) or complain of rectal bleeding, mucous discharge, or anorectal discomfort. Most will admit to difficulty with bowel movements.
- CCP is a pathologic diagnosis whose most important aspect is to differentiate it from colorectal adenocarcinoma. This prevents unnecessary radical operations.
- CCP and SRUS are closely related diagnoses and some authors consider them interchangeable.
- The etiology of these conditions remains unclear, but a common feature is chronic inflammation and/or trauma. The inflammation may result from inflammatory bowel disease, resolving ischemia, or trauma associated with internal intussusception or prolapse of the rectum, direct digital trauma, or the forces associated with evacuating a hard stool.
- In symptomatic patients, an endoscopic evaluation of the distal colon and rectum will reveal the lesions described above.
- Defecography documents intussusception in 45–80% of patients.
- The differential diagnosis of both CCP and SRUS includes: polyps, endometriosis, inflammatory granulomas, infectious disorders, drug-induced colitides, and mucus-producing adenocarcinoma.
- Differentiation among these entities is possible with an adequate biopsy.

- CCP is characterized pathologically by mucous cysts lined by normal columnar epithelium located deep to the muscularis mucosae.
- Treatment is directed at reducing symptoms or preventing some of the proposed etiologic mechanisms.
 - Conservative therapy (high fiber diet and modifying bowel movements to avoid straining) will reduce symptoms in most patients and should be tried first.
 - Patients without rectal intussusception should be offered biofeedback to retrain their bowel function.
 - Pharmacologic therapy has had limited success, but is reasonable to try before embarking on surgery.
 - If symptoms persist, a localized resection may be considered in selected patients. Those suitable for localized resection should be significantly symptomatic, be good surgical risks, and have localized, accessible areas of disease.
 - Patients with prolapse are considered for surgical treatment [abdominal rectopexy, segmental resection and rectal fixation, perineal proctectomy (Altmeier), or a mucosal proctectomy (Delorme)]. Those without prolapse may be offered excision which varies from a transanal excision to a major resection with coloanal pullthrough.

48. Constipation and Irritable Bowel Syndrome

A. Introduction

- To facilitate research into and treatment of constipation and other functional bowel disorders, a multinational panel of experts was convened in Rome, Italy. The Rome criteria for the diagnosis of constipation requires two or more of the following for at least 3 months:
 - Straining more than 25% of the time
 - Hard stools more than 25% of the time
 - Incomplete evacuation more than 25% of the time
 - Two or fewer bowel movements per week
- Four million people in the United States complain of frequent constipation, a prevalence rate of 2%.
- Complaints of constipation are two to three times more common in women than men and complaints increase with increasing age.
- The incidence of constipation is also higher in nonwhites than whites, in people from a lower socioeconomic and educational status, and in the southern United States.

B. Etiology

- Constipation can be secondary to a long list of conditions and medications (see Table 48.1).
- Diet affects the size, consistency, and frequency of bowel movements. Dietary intake of fiber is highly correlated with stool bulk.

Table 48.1 Factors associated with constipation.

Lifestyle

Inadequate fluid intake
 Inadequate fiber intake
 Inactivity
 Laxative abuse

Medications

Anticholinergics
 Antidepressants
 Calcium channel blocker anti-HTN
 Iron
 Opiates

Medical illness

Neurologic
 Spinal cord dysfunction/damage
 Parkinson's disease
 Multiple sclerosis

Endocrine/metabolic dysfunction

Diabetes mellitus
 Hypothyroidism
 Electrolyte abnormalities
 Uremia
 Hypercalcemia
 Porphyria

Psychological

Depression
 Anorexia
 Psychiatric illness
 Sexual abuse

Colonic structure/function

Cancer
 Crohn's disease
 Irradiation
 Endometriosis
 Hirschsprung's disease
 Chagas' disease

Pelvic floor abnormality

Nonrelaxing puborectalis
 Anal stenosis
 Rectocele/enterocele

- Because colonic distension triggers peristalsis, bulkier stools are a stronger and more efficient stimulus for colonic propulsion than smaller stools.

- Hypothyroidism and diabetes, lupus and scleroderma, neurologic illness, immobilization, and psychiatric disease are but a few of a long list of medical maladies associated with increased rates of constipation and should be considered as a source of constipation during evaluation.
- Mechanisms of dysfunction include alteration in motor function of the gut and autonomic neuropathy as seen in hypothyroidism and diabetes mellitus, respectively.
- Hirschsprung's disease and Chagas' disease alter the function of the colon through damage to the enteric nervous system. Connective tissue disorders alter the functionality of intestinal smooth muscle.
- Colonic stricture secondary to carcinoma, inflammatory bowel disease, radiation, or endometriosis can cause colonic obstruction.
- Medications for the management of common disorders such as hypertension promote the development of constipation. Opiate and anticholinergic use, as well as laxative abuse, is associated with constipation.

C. Evaluation

- The evaluation of the patient complaining of constipation begins with a detailed history.
 - Specific details of the patient's complaints - stool size, frequency, consistency, ease and efficacy of evacuation - should be noted.
 - Also important to note are the age at onset of symptoms, diet and exercise details, medical history, surgical history, and medication.
 - Query into psychiatric illness and sexual and physical abuse must be performed, because they are associated with defecation difficulties.
 - Symptoms of pelvic floor dysfunction involving the urinary tract should be ascertained.
 - A patient diary of dietary intake, defecation frequency, stool consistency, and any associated symptoms can be very helpful to both the patient and the medical provider.
- Physical examination will likely be unremarkable.
 - Abdominal distension or the presence of a mass may be noted.

- Rectal examination should involve a clinical evaluation of resting tone and the ability to voluntarily contract and relax the anal sphincter.
 - Evaluation for pelvic floor dysfunction such as perineal descent with straining, the presence of a rectocele or cystocele, and the volume and consistency of stool in the rectal vault should be noted.
- The evaluation of the patient with symptoms of constipation that do not respond to a trial of diet and medical therapy begins with the elimination of a structural bowel obstruction via colonoscopy or barium enema. Once obstruction has been eliminated as the cause of constipation symptoms, colonic transit time should then be assessed.
- Specifically, slow-transit constipation (colonic inertia) and pelvic floor outlet obstruction are entities that may be better treated with surgery and biofeedback, respectively.
- Colonic transit time can be estimated via marker studies or through scintigraphy.
- The most widely available technique for determining colonic transit uses radiopaque markers and radiographs of the abdomen.
- To obtain a global assessment of whether or not patients have slow-transit constipation, the technique requires the patient to refrain from all enemas, laxatives, and most medications for 2 days before the ingestion of 24 radiopaque markers. The patient is required to ingest 30 g of fiber daily during the test and must continue to refrain from taking medication and laxatives. An abdominal radiograph is obtained on the fifth day. The distribution and the number of markers present in the colon are noted. Eighty percent of normal patients will have passed all the markers by 5 days. If the markers are found to have accumulated in the rectum, outlet obstruction is suggested. If the markers remain scattered throughout the colon and more than 20% of the markers remain in the colon after the fifth day after ingestion, colonic inertia can be diagnosed. Alternate techniques involve obtaining radiographs on day 3 and 5, days 1, 3, and 5 or daily for 5 days.
- The mean colon transit time through the entire colon in men has been shown to be 31 h in males and 39 h in women.
- Patients with normal transit constipation will have a colon transit time that is in the normal range (<65 h in 95% of men, <75 h in 95% of women).

- Scintigraphic evaluation of colonic transit has been described, and although not as widely available, is useful in the assessment of transit in the colon and proximal gut.
- Outlet obstruction suggested on a marker study can be further characterized through defecography. Defecography facilitates visualization of the mechanism of defecation. Nonrelaxing puborectalis or a large rectocele can both be identified on a defecogram.
- Anal manometry reveals the absence of the rectoanal inhibitory reflex and therefore suggests the presence of Hirschsprung's disease.
- Balloon expulsion testing performed during manometry can add to the reliability of the diagnosis of pelvic floor outlet obstruction caused by nonrelaxation of the puborectalis muscle.
- Anal electromyography is performed in conjunction with manometry. The recruitment of puborectalis muscle fibers during defecation simulation indicates the entity of nonrelaxing puborectalis outlet obstruction.
- Assessment of upper gastrointestinal motility is appropriate in patients who are demonstrated to have slow-transit constipation. Patients with generalized motility disturbances and colonic inertia have less favorable results after surgical intervention than patients with colonic inertia alone.

D. Medical Treatment of Constipation

- It is sage advice to help the patient understand that a daily bowel movement is not requisite to good health. All providers should strive to decrease patient anxiety over the act of defecation.
- Simple measures that can influence the passage of colonic content are increasing physical activity and fluid intake. Exercise, even gentle walking, can facilitate the elimination of stool.
- Medications that promote constipation should be eliminated or substituted with alternatives that are less constipating.
- Bulk-forming agents are a first-line therapy in the prevention and treatment of constipation. Bulk-forming agents facilitate an increase in the size of the stool bolus as well as make the stool softer. Bulking agents facilitate these changes by delivering a mass of nondigestible substrate to the colon and, because of their hydrophilic nature, facilitate the absorption and retention of fluid. Bulk laxatives are derived from the nondigestible components of plants or are synthetic methylcellulose derivatives.

- Common bulk agents are psyllium (Metamucil, Konsyl), methylcellulose (Citrucel), calcium polycarbophil (FiberCon), and Gum (Benefiber). Side effects of fiber therapy include bloating and flatulence.
- A dietary intake of 20–30 g of nonstarch polysaccharide is generally recommended to minimize symptoms of constipation.
- Osmotic laxatives are a class of medications that promote the accumulation of large volumes of fluid in the colon lumen through the delivery of osmotically active molecules into the small and large bowel.
 - Sorbitol and lactulose are examples of sugar-based osmotic agents.
 - Osmotic laxatives can also be based on nonabsorbable ions, frequently derived from magnesium or phosphate. Examples are magnesium hydroxide (milk of magnesia) or sodium phosphate (Fleets Phospho-soda). Caution must be exercised in patients with renal insufficiency because hypermagnesemia or nephroliathiasis can result.
 - Polyethylene glycol-based products are used in many bowel-cleansing regimes. Over the counter preparations are currently available for chronic use in managing constipation.
- Colonic irritants are a class of agents that diminish constipation through stimulation of colonic motility.
 - Anthracene derivatives include senna and cascara and are found in Senokot and Peri-Colace.
 - Bisacodyl is another irritant and can be found in the agent Dulcolax.
 - Long-term use of laxatives has not been objectively shown to lead to poor colon function.
- Mineral oil and docusate sodium (Colace) are laxatives that act through the manipulation of the composition of stool. Mineral oil coats the stool bolus, preventing fluid absorption from it. Docusate sodium lowers the surface tension at the stool water interface, allowing greater penetration of the stool with fluid.
- Enemas and suppositories are also used to stimulate a bowel movement. Strategies include promotion of defecation through distension (saline enema), rectal irritation (soapsuds, bisacodyl), or physical softening of the stool (glycerine).

E. Colonic Inertia

- Colonic inertia, also called slow-transit constipation, represents a severe functional disturbance of colonic motility, which results in significant disability to the patient.
- Patients with colonic inertia, similar to patients with normal transit constipation and patients with outlet obstruction, exhibit infrequent defecation and may experience abdominal pain, bloating, nausea, difficulty with and incomplete evacuation of stool.
- Only a very small percentage of patients with constipation actually have colonic inertia.
- Precise evaluation of colonic motility and pelvic floor function is critical in the identification of patients that truly exhibit colonic inertia and have the highest probability to benefit from surgical intervention.
- The diagnosis of colonic inertia requires the documentation of abnormal colonic transit ($>20\%$ of ingested markers present and scattered throughout the colon on day 5 of colonic transit time testing).
- Total abdominal colectomy (TAC) is appropriate for documented colonic inertia.
- Despite consistently increasing stool frequency, TAC to treat colonic inertia does not guarantee a successful functional outcome. Furthermore, even extensive preoperative work-up does not ensure patient satisfaction.
- Persistent or recurrent constipation, progression to small bowel inertia, and fecal incontinence may occur after TAC with ileorectal anastomosis and must be explained to the patient.
- Historically, patients having segmental colectomy have had poor results.
- Proctocolectomy with ileoanal pouch reconstruction has been described as a salvage operation for selected patients with recurrent constipation after subtotal colectomy with ileorectal anastomosis for slow-transit constipation.
- A difficult subgroup of patients with slow-transit constipation to treat is those with concomitant pelvic floor dysfunction.
 - Bernini et al. from the University of Minnesota evaluated 16 patients who had a combination of colonic inertia and nonrelaxing pelvic floor as diagnosed by transit marker

study, electromyography, and defecography. All patients completed preoperative biofeedback training and could demonstrate relaxation of the pelvic floor musculature.

- Despite biofeedback training, difficult evacuation persisted. Postoperatively, 43% of patients had complete resolution of symptoms of constipation or difficult evacuation. Eighteen percent complained of diarrhea and incontinence of liquid stools. Six of the 16 patients complained of incomplete evacuation.
- The authors concluded that subtotal colectomy could improve some symptoms in patients with colonic inertia and nonrelaxing pelvic floor, however, incomplete evacuation persisted in a significant number of patients. Almost half were dissatisfied with their surgery.

F. Irritable Bowel Syndrome

- Irritable bowel syndrome (IBS) is a disorder in which patients have abdominal discomfort and altered bowel habits that defy explanation by identifiable organic pathology.
- There are no specific tests to identify this disorder. Rather, it is a diagnosis of exclusion, and remains a clinical diagnosis.
- The Rome criteria for a clinical diagnosis of IBS are listed in Table 48.2. In essence, patients must have chronic symptoms that include abdominal pain relieved by defecation and or associated with a change in the consistency or frequency of stools.

Table 48.2. Rome criteria for IBS.

Abdominal pain or discomfort characterized by the following

Relieved by defecation

Associated with a change in stool frequency

Associated with a change in stool consistency

Two or more of the following characteristics at least 25% of the time

Altered stool frequency

Altered stool form

Altered stool passage

Mucorrhea

Abdominal bloating or subjective distension

These symptoms are variably associated with mucorrhea and/or abdominal bloating.

- Population-based studies in Western countries report an overall prevalence of IBS of 10–20%.
- In Western countries, women are 2–3 times more likely to develop IBS than men.
- The prevalence seems to be lower in the elderly.
- It has been recognized for many years that there are a variety of disorders associated with a clinical diagnosis of IBS. These include nonulcer dyspepsia, fibromyalgia, chronic fatigue syndrome, dysmenorrhea, urinary tract symptoms, and psychiatric disorders.
- Patients who undergo physician evaluation for IBS tend to have increased scores for depression, anxiety, somatization, and neuroticism on standardized tests, although no specific pattern of personality traits in patients has been identified.
- Patients with IBS who present for evaluation are at least twice as likely to meet criteria for psychiatric disorders as patients with organic disease. The most frequent of these disorders are depression and generalized anxiety.
- It has been estimated that only 10% of patients with IBS symptoms consult a physician for evaluation or treatment of their symptoms.
- The current theories regarding the pathophysiology of IBS are of a complex interaction between altered gut motility and or visceral hyperalgesia and neuropsychopathology.
- Studies suggest an underlying generalized hyperresponsiveness of smooth muscle in patients with IBS.
- Visceral hyperalgesia seems to be another component of this disorder. Studies measuring the perception of gut distension using various techniques have demonstrated abnormally low sensitivity in both the small and large bowel. It seems that patients with a diagnosis of IBS have both an increased awareness of gut distension, and experience such distension as painful at lower volumes and pressures as normal subjects.
- In summary, patients with IBS have been demonstrated to have abnormal gut motility, visceral hyperalgesia, and neuropsychologic abnormalities. In a particular patient, any of these factors may predominate, but all may be involved and they are not mutually exclusive. An understanding of these abnormalities has led to the emergence of new possibilities in the pharmaceutical treatment of this syndrome.

- The altered stool habits reported by patients with IBS can be constipation, diarrhea, or alternating constipation and diarrhea. Constipation can be described as hard and/or infrequent stools, or painful defecation requiring laxative use. Diarrhea is usually described as small volume, frequent, urgent, and watery stool. Diarrhea when present is often postprandial in nature. Usually patients have either constipation or diarrhea alone, however, alternation between each can be present.
- Abdominal pain is usually perceived as diffuse, and is most common in the lower abdomen, especially on the left.
- Pain may be precipitated by meals and is often relieved by defecation.
- Patients often report increasing bloating and gas through the daytime hours, which may or may not be associated with objective evidence.
- Overall symptoms may be worse in times of stress.
- Although there are emerging novel medications for IBS that may prove useful, much current medical therapy depends heavily on reassurance.
- Fiber supplementation may improve symptoms of either constipation or diarrhea, although studies are inconclusive because of a strong placebo effect.
- Many physicians believe that polycarbophil-based bulking agents may be tolerated better than psyllium-based compounds because of an exacerbation of bloating symptoms in some patients with the latter.
- Similarly, ingesting more water, avoiding caffeine and legumes are all reasonable patient advice.
- As noted above, treatment strategies are symptom directed. Currently available and widely used pharmacologic agents for patients with diarrhea-predominant IBS include anticholinergic medications, nonabsorbable synthetic opioids, and tricyclic antidepressants.
 - Anticholinergics inhibit intestinal smooth muscle depolarization at the muscarinic receptor. These include dicyclomine hydrochloride (Bentyl) and hyoscyamine sulfate (Levsin).
 - Diphenoxylate hydrochloride with atropine (Lomotil) or loperamide (Imodium) inhibit intestinal motility and prolong transit through the gut. They also reduce visceral

nociception via afferent pathway inhibition. They improve stool frequency, urgency, and consistency.

- Tricyclic antidepressants such as amitriptyline (Elavil) and imipramine (Tofranil) have also been evaluated in off-label use in very low doses for a visceral analgesic effect. Either medication increases orocecal transit time, reduces abdominal pain, mucorrhea, and stool frequency. These results are at subtherapeutic doses for the treatment of depression.
- For patients with constipation-predominant IBS who do not respond to fiber supplementation (20 g/day) or do not tolerate it, osmotic laxatives such as milk of magnesia, sorbitol, or polyethylene glycol may be tried.
- A novel pharmacologic agent that is currently available is the serotonin (5-HT₄) agonist, Tegaserod. Tegaserod is a partial 5-HT₄ agonist and accelerates transit in the small bowel and colon. It has been demonstrated to be useful in improving constipation and improving global IBS symptoms in women with constipation-predominant IBS.
- An adjunctive therapy to medication is psychological treatment. This is appropriate when there is evidence that stress or psychological factors are contributing to an exacerbation of symptoms, or patients have failed to respond to medical treatment. A clear explanation of the rationale for such treatment is important in patient acceptance of such therapy.

49. Pelvic Floor Disorders

A. Rectoceles

- A common clinical definition of rectocele is abnormal rectovaginal anatomy that allows the rectum to be in direct contact with the vaginal serosa without an intervening layer.
- Usually, rectoceles are diagnosed when rectovaginal support abnormalities are observed during physical examination. There may be protrusion of the posterior vaginal wall beyond the hymen with or without strain effort.
- The differential diagnosis for this physical finding includes other abnormalities of vaginal attachment, usually the vaginal apex (with or without the uterus).
- Differences in physical examination techniques affect the degree of prolapse that is detected. The side-lying or prone jackknife examination that is favored by many colon and rectal surgeons is sufficient to detect some forms of prolapse; however, the standing straining vaginal examination provides the best opportunity to determine the full extent of anatomic abnormalities.
- Another important differential diagnosis includes abnormalities in perineal support, including severe atrophy or denervation of the levator muscles.
- Some specialists use fluoroscopy as an aid to physical diagnosis.
- It is clear, however, that the finding of “rectocele” in asymptomatic women during fluoroscopic examination should not prompt surgical repair.
- The promptness and completeness of defecation are probably more important than the maximum excursion of the anterior rectal wall.

- Isolated rectoceles are distinctly uncommon and virtually always occur in the presence of a significant defecation disorder.
- The symptoms of rectocele are believed to be stool trapping, difficult defecation, and vaginal protrusion of the posterior vaginal wall. Rectoceles are not painful and reports of pain should prompt the physician to seek other diagnoses.
- It is widely appreciated that many women with relatively large “rectoceles” have no symptoms attributable to this finding. They are able to conduct all pelvic functions without difficulty, including sexual function, and bowel storage and emptying.
- Other women with minimal abnormalities on physical examination may report great bother from difficult defecation and stool trapping.
- In the absence of severe symptoms or findings, the recommended primary intervention is generally attention to optimize stool consistency.
- Biofeedback to establish pelvic floor outlet relaxation during defecation may be helpful.
- Honest surgeons will recognize that surgery has significant limitations in relief of certain forms of defecation disorders, but is reasonably effective at normalizing anatomy.
- Preoperative testing should include age and risk-appropriate cancer screening (e.g. colonoscopy).
- Defecography may be helpful in documenting failure of the puborectalis muscle to relax during attempted defecation and to establish the presence or absence of internal intussusception as a cause of outlet obstruction of the rectum.
- There are only two randomized surgical trials. Both of these studies report that the transvaginal approach is superior to the transanal route.
- Unsuccessful rectocele repair can occur when either anatomy or symptoms are not corrected.
- One very troubling postoperative complication can be dyspareunia, which in some women can completely preclude sexual activity and destroy intimacy.
- A combined gynecologic-colorectal-urologic approach is sometimes needed to address the combination of issues.
- Continued attention to underlying disorders, such as severe constipation, is necessary to preserve optimal rectocele repair.

B. Pelvic Pain Syndromes

Epidemiology

- The prevalence of chronic pelvic pain in the female population is estimated to be 3.8%.
- Although pelvic pain is more common in women, it is certainly not confined to the female gender. In a United States survey of functional gastrointestinal disorders, the prevalence of functional anorectal pain was 11.1% of the male and 12.1% of the female respondents to the survey.
- The role of the specialist in the care of these patients is to eliminate intrinsic disorders of the genitourinary and gastrointestinal organs in the pelvis and, if none are found, to treat the pain.
- The more common pain syndromes are described below. An algorithm for the management of these patients is depicted in Fig. 49.1.

Levator Syndrome

- The term coccygodynia has been applied to this symptom complex in the early descriptions. It has also been referred to as piriformis syndrome, puborectalis syndrome, diaphragma pelvis spastica, and pelvic tension myalgia. Grant et al., in one of the largest modern series of cases, described it as pain, pressure, or discomfort in the region of the rectum, sacrum, and coccyx that may be associated with pain in the gluteal region and thighs.
- The prevalence of this symptom complex in the general population is approximately 6%. It is more common in women.
- The Committee on Functional Anal/Rectal Disorders at a conference to develop diagnostic criteria for Functional Gastrointestinal Disease (Rome II) described the pain of levator syndrome as a vague, dull ache or pressure sensation high in the rectum, often worse with sitting or lying down, that lasts for hours to days.
- These diagnoses should be entertained only after the presence of alternative diseases are excluded with careful physical examination, endoscopy, and ancillary studies such as defecography, ultrasound, computed tomography, or magnetic resonance imaging (MRI).

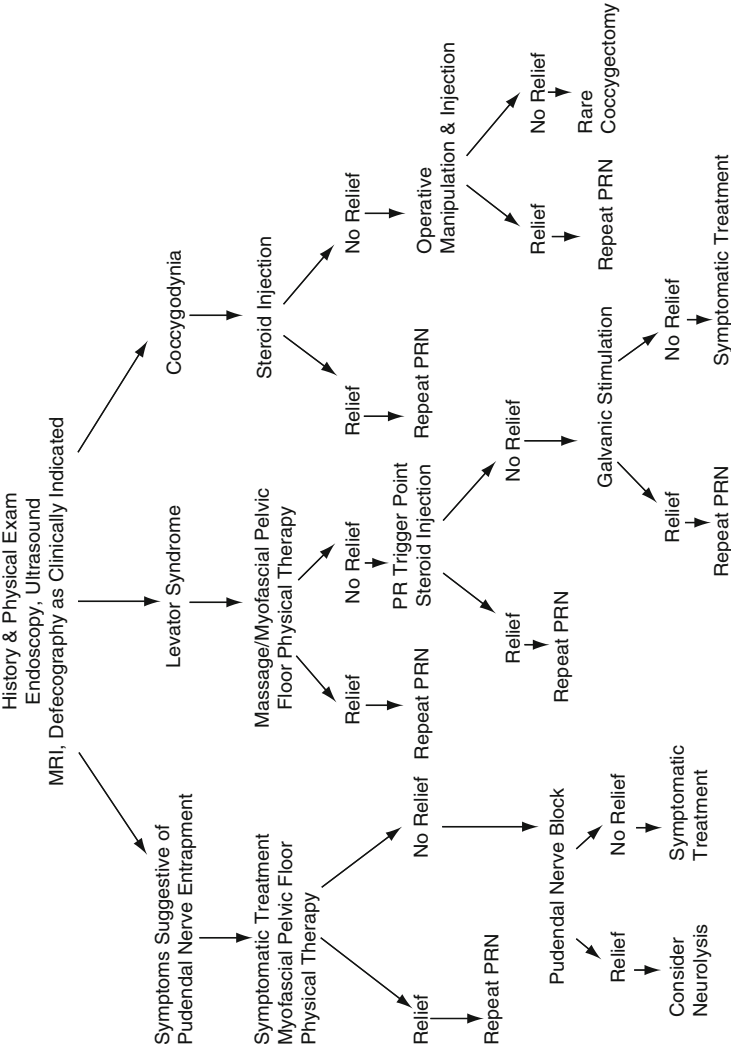


Fig. 49.1. Algorithm for management of chronic anorectal pain.

- The utility of electromyography, anal manometry, and pudendal nerve studies has not been established. No consistent abnormalities in any of these tests have been demonstrated in the majority of patients.
- A wide variety of treatments have been described.
 - Grant et al. used two to three massages 2–3 weeks apart, combined with heat and diazepam, and had good results in 68% of the patients and moderate improvement in 19%.
 - Kang et al. described a series of 104 patients in which transanal injection of triamcinolone rendered 37% of patients pain free.
 - Biofeedback has been used with some success.
 - Electrical sacral nerve stimulation, which has been used for voiding disorders and fecal incontinence, has also successfully reduced the severity of pain in patients who were broadly characterized as having chronic pelvic pain.
 - Anxiety and depression have been associated with chronic pelvic pain syndrome and these conditions should be considered in the comprehensive approach to the management of these patients with pelvic pain.

Coccygodynia

- Coccygodynia, although may be part and parcel of the whole group of pelvic floor musculoskeletal problems, is distinguished by the distinct pain evoked with pressure or manipulation of the coccyx.
- Although coccygectomy was popular at one time, in recent times, it has generally been regarded as ill conceived by most surgeons.

Proctalgia Fugax

- Proctalgia fugax, as the name implies, is a fleeting pain in the area of the rectum lasting no more than a minute or two.
- Presumably, it is secondary to spasm of the rectum itself or muscular components of the pelvic floor.
- The role of the physician in these cases is mainly to assure the patient that this is not a symptom of any serious disorder.
- The use of perianal nifedipine in the same doses and method as for anal fissure and hypertrophic internal anal sphincter may be of benefit. There are no randomized trials to document improvement.

Pudendal Neuralgia

- Pudendal neuralgia is a symptom complex, which is manifest by chronic pelvic/perineal pain in the distribution of one or both pudendal nerves. It may be manifest as vulvodynia, orchalgia, proctalgia, or prostatodynia.
- The pain patterns overlap with those of levator syndrome, coccydynia, and urethral syndrome.
- It is attributable to compression or entrapment of the pudendal nerve and often is positional in nature.
- This diagnosis should be entertained if there is a history of trauma, either a distinct episode or chronic perineal trauma such as seen in cyclists or rowers.
- The two documented sites of pudendal nerve entrapment are between the sacrotuberous and sacrospinous ligament and in the pudendal (Alcock's) canal.
- The diagnosis of pudendal neuralgia is supported by reproduction of the pain with pressure on the ischial spine although this is not a constant finding.
- Pudendal nerve latency is often prolonged when it is tested.
- Nerve block under computed tomography or ultrasound guidance has been used to sort out those patients who would likely benefit from neurolysis.

50. Laparoscopy

A. Learning Curve

- A coordinated team consisting of a surgeon, an assistant, and often a camera person is required.
- It is estimated that with conventional laparoscopic techniques and instruments that the learning curve for laparoscopic colectomy is at least 20 cases and more likely 50 cases.
- A difficulty with the broad application of laparoscopic colectomy is the number of colon resections performed by most general surgeons.
- Either the learning curve will need to be shortened, as some have suggested by the use of hand-assisted laparoscopic (HAL) techniques, or we will need to limit the performance of laparoscopic colectomy to surgeons who perform a greater number of colon resections per year.

B. Conversions

- The rates of conversion are inconsistent in the literature, with reports as low as 0% to as high as 48%. Most series report the need to convert in 10–25% of cases.
- Several patient- and disease-related factors such as obesity, prior abdominal surgery, acuity of inflammation (i.e., abscess and fistula formation), tumor bulk or contiguous involvement, and disease location, may also affect the rate of conversion.
- More recent studies of laparoscopic surgery involving enteric fistulae suggest a conversion rate of 25–35%.
- The presence of a fistula or small abscess is not a contraindication to a minimally invasive approach, but should alert the

surgeon to consider a variation in operative approach if obstacles cannot be overcome.

- Conversion from a laparoscopic to conventional resection should not be viewed as a failure of the laparoscopist.
- More crucial than the rate of conversion is the time spent before conversion.
- Earlier reports suggested a poorer outcome for patients who required conversion; however, more recent studies, including a recent presentation of the COST trial results, suggest that if conversion is made early the outcome of converted cases is similarly matched with patients undergoing conventional surgery.
- The goal is to perform a preemptive conversion once it is determined the case cannot be completed laparoscopically, rather than a reactive conversion to a complication that occurred because of adverse conditions that the surgeon could have avoided.

C. Outcomes

- In comparison to conventional colectomy, the proposed benefits of laparoscopic colectomy include a reduction in postoperative ileus, less postoperative pain and concomitant reduction in the need for analgesics, an earlier tolerance of diet, a shortened hospital stay, a quicker resumption of normal activities, improved cosmetic results, and possibly preservation of immune function.
- This is offset by a prolongation in operative time, the cost of laparoscopic equipment, and the learning curve of these technically challenging procedures.
- Few studies, with the exception of the larger prospective, randomized studies, leave the “converted” cases in the laparoscopic group as part of the “intention to treat” laparoscopic group. This clearly introduces selection bias.

D. Operative Time

- With the exception of a few reports, nearly all studies demonstrated a prolonged operative time associated with a laparoscopic procedure.
- In prospective, randomized trials, the procedure was approximately 40–60 min longer in the laparoscopic groups.

E. Return of Bowel Activity and Resumption of Diet

- Nearly all of the historical and prospective studies comparing open and laparoscopic colectomy have shown a statistically significant reduction in the time to passage of flatus and stool. Most series demonstrate a 1- to 2-day advantage for the laparoscopic group.

F. Postoperative Pain and Recovery of Pulmonary Function

- Three of the early prospective, randomized trials have evaluated pain postoperatively and all three have found a reduction in narcotic requirements in patients undergoing laparoscopic colectomy.
- Whether subject to bias, the results of comparative studies suggest a quicker recovery of pulmonary function and reduction in postoperative pain in patients subjected to laparoscopic colectomy.

G. Length of Stay

- The quicker resolution of ileus, earlier resumption of diet, and reduced postoperative pain have resulted in a shortened length of stay for patients after laparoscopic resection when compared with traditional procedures.
- Although psychological conditioning of the patient cannot be helped and likely has a desirable effect, the benefits of minimally invasive procedures on the overall length of stay cannot be discounted. The benefit, however, is more likely a 1- to 2-day advantage only.

H. Quality of Life and Return to Work

- In the COST study, quality of life was evaluated by three complementary viewpoints: patient self-reported symptoms, patient self-reported functional status, and a third more objective

measurement scale of compliance to treatment referred to as Q-TWIST (quality-adjusted time without symptoms of disease and toxicity of treatment).

- In every category, however, the results of patients who had a laparoscopically completed procedure were improved compared with conventionally performed procedures and in laparoscopic patients who required a conversion to open surgery. However, this did not achieve significance.
- In a nonrandomized comparison, patients undergoing laparoscopic procedure returned to full activities and to work sooner than matched patients undergoing conventional resection [mean, 4.2 vs. 10.5 weeks, 3.8 vs. 7.5 weeks, respectively ($P < 0.01$ for all)].

I. Hospital Costs

- One of the proposed disadvantages of laparoscopy is the higher operative costs related to longer operative times and increased expenditure in disposable equipment. Whether the total cost of the hospitalization (operative and hospital costs) is higher after laparoscopic colectomy is debatable.
- Clearly, if operative times and equipment expenditure are minimized, the overall cost of a laparoscopic resection should not exceed a conventional approach.

J. Crohn's Disease

- Crohn's disease of the terminal ileum seems an ideal model for the application of a minimally invasive approach.
- The resection and anastomosis are generally performed extracorporeally.
- Patients with Crohn's are typically young and are interested in undertaking a procedure that minimizes incisional scarring. Additionally, because many of these patients will require reoperation over their lifetime, a minimally invasive approach is appealing.

- Early reports of laparoscopic ileocolic resection showed it to be feasible and safe, but were typically small nonrandomized uncontrolled studies. More recent studies (Table 50.1) have a larger experience in which to draw more meaningful conclusions.
- Most series report the rate of conversion from 10 to 20% with the mix of complex cases (abscess, fistula, or reoperative surgery) ranging from 40 to 50%.
- As expected, the outcomes after laparoscopically assisted ileocolic resection for Crohn's disease mirror those seen in other studies of laparoscopic colectomy for benign and malignant disease. In comparative studies (Table 50.1), laparoscopic ileocolic resection is associated with a quicker return of bowel function and an earlier tolerance of oral diet.
- The quicker resolution of ileus, earlier resumption of diet, and reduced postoperative pain has resulted in a shortened length of stay for patients after laparoscopic resection when compared with traditional procedures.
- With the loss of tactile sensation, one of the remaining concerns of performing laparoscopic surgery in the patient with terminal ileal Crohn's is missing an isolated proximal lesion.
- Laparoscopic ileocolic resection does not seem to offer any advantage over conventional resection with regard to symptomatic recurrence, but it also did not lead to a higher rate of recurrence or discovery of a missed lesion.

K. Ulcerative Colitis

- There are no prospective, randomized studies of laparoscopic proctocolectomy for ulcerative colitis. The only results available for analysis are prospective and retrospective case control studies and noncomparative reports (Table 50.2).
- The majority of reports have shown that laparoscopic total colectomy and laparoscopic proctocolectomy with and without ileoanal pouch construction are technically feasible and share the same advantages of minimally invasive surgery as segmental colonic resection.

Table 50.1. Recent studies of laparoscopic resection for Crohn’s disease: ileocolic resection.

Author	Year	Number of patients		OP time (min)		LOS (days)		Morbidity (%)		Comment
		LAP	CON	LAP	CON	LAP	CON	LAP	CON	
Bauer et al.	1996	25	14	–	–	6.5	8.5	–	–	High conversion if mass and fistula
Wu et al.	1997	46	70	144	202	4.5	7.9	10	21	52% complex or redo cases
Dunker et al.	1998	11	11	–	–	5.5	9.9	9	9	Improved cosmesis
Wong et al.	1999	55		150		6.0		5		46% complex cases
Canin-Endres et al.	1999	70		183		4.2		14		41 with fistulae, 1 conversion
Alabaz et al.	2000	26	48	150	90	7.0	9.6	–	–	Favorable results
Bemelman et al.	2000	30	48	138	104	5.7	10.2	15	10	Different hospitals for each group
Young-Fadok et al.	2001	33	33	147	124	4.0	7.0	–	–	Laparoscopy less expensive
Schmidt et al.	2001	46		207		5.7				Safe and effective, high conversion rate
Milsom et al.	2001	31	29	140	85	5.0	6.0	16	28	Prospective, randomized trial
Evans et al.	2002	84		145		5.6		11		Results improve with experience
Dupree et al.	2002	21	24	75	98	3.0	5.0	14	16	Laparoscopy less expensive
Shore et al.	2003	20	20	145	133	4.3	8.2	–	–	Laparoscopy less expensive
Benoist et al.	2003	24	32	179	198	7.7	8.0	20	10	Similar operative times, 17% converted
Bergamaschi et al.	2003	39	53	185	105	5.6	11.2	9	10	Long-term obstruction less, 11% versus 35%

OP operative; *LOS* length of stay; *LAP* laparoscopic; *CON* conventional

Table 50.2. Recent studies of laparoscopic colectomy for ulcerative colitis.

Author	Year	Number of patients	Comment
Meijerink et al.	1999	10	Feasible, seven for acute colitis
Marcello et al.	2000	13	Restorative proctocolectomy, favorable results
Seshadri et al.	2001	37	25% morbidity
Hamel et al.	2001	21	Compared with ileocolic resection, similar morbidity and LOS
Marcello et al.	2001	16	For acute colitis, comparative study, favorable results
Brown et al.	2001	25	Longer op time in LAP group
Dunker et al.	2001	35	Better cosmesis
Ky et al.	2002	32	Single-stage procedure, good results
Bell and Seymour	2002	18	Total colectomy for acute colitis, seems safe
Rivadeneira et al.	2004	23	Hand-assisted procedure reduced operative time
Kienle et al.	2003	59	Large study, laparoscopic colon mobilization only
Nakajima et al.	2004	16	Hand-assisted technique, favorable results

IPAA ileal pouch–anal anastomosis; *EBL* estimated blood loss; *LOS* length of stay

- These procedures, however, are still not recommended for the patient with toxic colitis.
- It seems that hand-assisted restorative proctocolectomy can be accomplished without detriment to bowel function, length of stay, or patient outcome.
- The use of HAL for ulcerative colitis patients requiring surgery is likely another venue that may shorten operative time while maintaining the benefits of a minimally invasive approach.

L. Diverticulitis

- Laparoscopic sigmoid resection remains the leading indication for minimally invasive colon resection for benign disease.
- There are now a large number of studies evaluating laparoscopic surgery for diverticulitis (Table 50.3).
- Most series report an operative time of 2–3 h with a conversion rate of 10–20% for most larger series.

Table 50.3. Case-control studies pertaining to laparoscopic resection for diverticulitis.

Study	Year	Number of patients		Mortality (%)		Morbidity (%)		Convert	OR time (min) ^a		Resume diet (d) ^a		Flatus/BM (d) ^a		LOS (days) ^a		Total costs ^a	
		CON	LAP	CON	LAP	CON	LAP		CON	LAP	CON	LAP	CON	LAP	CON	LAP	CON	LAP
Diverticulitis																		
Liberman et al.	1996	14	14	0	0	14	14	0	182	192	6.1	2.9 ^b	NA	NA	9.2	6.3 ^b	P	11,500
																	13,400	
Bruce et al.	1996	17	25	0	0	23	16	12	115	397 ^b	5.7	3.2 ^b	NA	NA	6.8	4.2 ^b	\$ 7,068	10,230 ^b
Kohler et al.	1998	34	27	0	0	61	15	7	121	165 ^b	5.8	4.1 ^b	5.3	3.7 ^b	14.3	7.9 ^b	DM	7,185 ^b
																	8,975	
Senagore et al.	2002	71	61	0	1.6	30	8 ^b	7	101	107	NA	NA	NA	6.8	3.1 ^b	\$ 4,321	3,458 ^b	
Dwivedi et al.	2002	88	66	0	0	24	18	20	143	212 ^b	4.9	2.9 ^b	NA	NA	8.8	4.8 ^b	\$ 13,953 ^b	
																	14,863	
Lawrence et al.	2003	215	56	1.6	1	27	9 ^b	7	140	170 ^b	NA	NA	NA	NA	9.1	4.1 ^b	\$ 17,414 ^b	
																	25,700	
Gonzalez et al. ^c	2004	80	95	4	1	31	19 ^b	NA	156	170	NA	3.7	2.8	12	7 ^b	NA		

OR operating room; BM bowel movement; LOS length of stay; CON conventional surgery; LAP laparoscopic surgery; NA not available; P pounds; DM Deutsch marks

^aMedian or mean values listed

^bStatistically significant difference

^cResults of non-converted laparoscopic cases given

- Nearly all comparative studies of laparoscopic to open sigmoid resection demonstrate a benefit to the laparoscopic approach including a shorter duration of ileus, shortened length of stay, but as in other studies, with a prolonged operative time.
- Early reports suggested a higher overall cost associated with a laparoscopic approach for diverticular resection; however, more recent studies (Table 50.4) have demonstrated a cost saving with the laparoscopic approach.
- It should be noted that these are generally the elective uncomplicated cases with fewer patients presenting with abscess or fistula formation.
- Less-experienced surgeons should consider an early conversion of complicated diverticular resection or potentially an alteration in the approach to a hand-assisted technique in which the difficult pelvic dissection can be guided by the hand laparoscopically or by conventional means through the open wound.

M. Rectal Prolapse

- There are many studies that have evaluated not only laparoscopic fixation procedures but also the combination of sigmoid resection and rectopexy for the treatment of rectal prolapse (Table 50.4).
- The magnified view into the pelvis with the laparoscope provides unparalleled visualization into the pelvic floor and the relative laxity of the rectal fixation to the presacral area is beneficial to performance of a laparoscopic procedure. This likely is the reason for the relatively low rate of conversion (<10%) for a laparoscopic rectopexy or resection and rectopexy in comparison to other laparoscopic colorectal procedures.
- In addition to case series results, there have been several non-randomized comparative studies of laparoscopic versus conventional rectopexy and resection rectopexy. These studies showed a longer operative time of 45–60 min with the laparoscopic procedures but with a shortened length of stay of 2–3 days.
- One of the major issues when discussing surgery for rectal prolapse is the rate of recurrent prolapse. For an abdominal approach, the risk of recurrence should be less than 5–10% over 5 years.

Table 50.4. Recent results of laparoscopy for rectal prolapse.

Study	Year	Number of patients	Follow-up		Operative time			Recurrence (%)	Comment
			(months)	Procedure	(min)	LR/ LRR	LOS (days)		
Poen et al.	1996	12	19	LR	195		10	0	Improved continence
Himpens et al.	1999	37	6–48	LR	130		7	0	3% conversion
Bruch et al.	1999	57	30	LR/LRR	227/257		15	0	Constipation improved in 76%
Boccasanta et al.	1999	10						0	Compared with open – longer op time, lower cost, shorter LOS
Xynos et al.	1999	10	NS	LRR	130		4.7	NS	Compared with open – longer op time, shorter LOS
Kessler et al.	1999	32	33	LR/LRR	150		5	FT 6.2	10% developed bowel obstruction
Heah et al.	2000	25	26	LR	96		7	0	16% conversion
Kellokumpu et al.	2000	34	24	LR/LRR	150/255		5	7	Constipation improved in 70%
Benoist et al.	2001	48	20–47	LR/LRR	–		–	MP 8	Suture rectopexy preferred to mesh
Solomon et al.	2002	20	24	LR	153		3.9	0	Prospective, randomized study
Kairaluoma et al.	2003	53	12	LR/LRR	127/210		5	6	Compared with open – longer op time, shorter LOS
D’Hoore et al.	2004	42	61	LR	NS		NS	FT 4.8	Constipation improved in 84%
Lechaux et al.	2005	48	36	LR/LRR	193		4–7	MP 4.2	Constipation worsened in 23%
Ashari et al.	2005	117	62	LRR	110–180		5	FT 2.5; MP 18	Large study with long-term follow-up

RR resection rectopexy; *PFR* pelvic floor repair; *AR* anterior resection; *FRM* full rectal mobilization without fixation; *LARR* laparoscopic resection rectopexy; *LAR* laparoscopic rectopexy; *FT* full thickness; *MP* mucosal prolapse; *NS* not specified

- Unfortunately, the majority of reports on laparoscopic surgery for rectal prolapse have limited follow-up (less than 3 years). The reported rate of recurrence ranges from 0 to 6% in these studies (Table 50.4).

N. Colorectal Cancer

Background

- In 2004 the results of the large multicenter COST study group with almost 900 patients randomized either to the open or the laparoscopic arm of the study, found no differences in overall survival or disease-free survival.
- The results of these recent trials (Table 50.5) have demonstrated that similar oncologic resections can be achieved by experienced surgeons performing laparoscopic colorectal resections.

O. Laparoscopic Resection of Colon and Rectal Cancer

General Considerations

- After detection of a colon or rectal cancer, routine evaluation incorporates preoperative staging, assessment of resectability, and determination of the patient's operative risk.
- There are several factors to consider, primarily in terms of gauging the difficulty of the procedure and the likelihood of being able to perform it laparoscopically.
 - The site of the tumor is important, because right and sigmoid colectomy are generally less technically demanding than, for example, low anterior resection.
 - Documented extensive adhesions may preclude a minimally invasive approach, although laparoscopic resection is frequently possible in patients who have had prior abdominal operations.
 - Obesity, and particularly the distribution of abdominal fat, may preclude laparoscopic resection, especially in

Table 50.5. Prospective, randomized trials comparing laparoscopic and conventional surgery for colorectal cancer.

	Lacy et al. 2002	COST 2004	CLASICC 2005
Baseline characteristics	LAP versus OPEN	LAP versus OPEN	LAP versus OPEN
No. assigned	111:108	435:437	526:268
No. completed (dead or no data)	105:101	435:428	452:231
Age	68:71	70:69	74:37
Gender (F)	55:58	49%:51%	69:69
Previous surgery	40:47	43%:46%	44%:46%
Operative findings			
Procedure			
Right	49:49	54%:54%	24%:24%
Left	4:1	7%:7%	7%:9%
Sigmoid	52:46	38%:38%	13%:12%
AR/LAR	3:9		37%:36%/12%:13%
Other	3:3		4%:3%
TNM stage			
0		5%:8%	Not given
I	27:18	35%:26%	
II	42:48	31%:34%	
III	37:36	26%:28%	
IV	5:6	4%:2%	
No. lymph nodes	11.1:11.1	12:12	12:13.5
Conversion	12 (11%):N/A	21%:N/A	29%:N/A
OR time (min)	142:118 ^a	150:95 ^a	180:135 (anesthesia time)
Incision length (cm)		6:18 ^a	10:22
Short-term outcomes			
Oral intake (h)	54:85 ^a		6:6
(d)			6:6
Hospital stay (d)	5.2:7.9 ^a	5:6 ^a	9:11
30-d mortality		<1%:1%	4%:5%
Postoperative complications	12:31 ^a	19%:19%	33%:32%
		Colon	Rectum
Wound infection	8:18	5%:5%	13%:12%
Pneumonia	0:0	7%:4%	10%:4%
Ileus	3:9		
Leak	0:2	2%:0%	10%:7%
Duration of oral analgesics (d)		1:2 ^a V	

(continued)

Table 50.5 (continued)

Duration of parenteral analgesics (d)		3:4 ^a
Cancer outcomes		
Tumor recurrence	18:28	76:84
Distant	7:9	
Locoregional	7:14	
Peritoneal seedling	3:5	
Port site	1:0	2:1
5-y overall survival ^b	82%:74%	79%:78%
I	85%:94%	84%:94%
II	75%:77%	78%:81%
III	72%:45%	60%:63%
5-y disease-free survival ^b		78%:80%
I	90%:88%	92%:96%
II	80%:76%	82%:88%
III	70%:45%	62%:60%
Cancer-related survival ^b	91%:79% ^a	
I	100%:99%	
II	88%:85%	
III	84%:50% ^a	

^aStatistically significant difference.^bExtrapolated from graphs in manuscript.

the case of a rectal cancer in an obese male patient with a narrow pelvis.

Tumor Localization

- The entire colon and rectum should be evaluated to eliminate synchronous lesions. This is usually achieved with colonoscopy, but this has limitations in terms of localization, particularly if a minimally invasive approach is being considered. Colonoscopy is most accurate for localization of a tumor in the rectum and cecum only.
- A laparoscopic approach requires accurate localization of the tumor to a specific segment of the colon, because even a known cancer may not be visualized from the serosal aspect of the bowel during laparoscopy.

- A variety of other options is available to localize a lesion including preoperative colonoscopic marking with ink tattoo or metallic clips, barium enema, or intraoperative endoscopy.
- Preoperative endoscopic tattooing is a common method of tumor localization. India ink is a nonabsorbable marker that has been reported in more than 600 cases for tumor localization since 1975. The ink is injected into the submucosa in three or four quadrants around the lesion, or 2 cm distal to the lesion if the tumor is in the distal colon and distal margins are potentially an issue (typically 0.5 cc per site).

Preoperative Staging

- In patients with colorectal cancer, the liver should be thoroughly evaluated using computed tomography (CT) with intravenous contrast, ultrasound, or magnetic resonance imaging. Because of limitation in tactile sensation associated with laparoscopy, these studies should be performed preoperatively.
- Alternatively, intraoperative laparoscopic ultrasonography offers the ability to fully evaluate the liver at the time of colorectal resection.

Preparation For Operation

- Despite lack of clear evidence of benefit from metaanalysis and randomized, controlled trials, a mechanical bowel preparation is frequently used in North America. Aside from the aesthetic aspects, an empty colon facilitates manipulation of the bowel with laparoscopic instruments.

Operative Issues

Operative Techniques: Colon

- Oncologic principles must not be compromised by a laparoscopic resection for colon cancer. Guidelines for colon cancer surgery outline recommendations for proximal and distal resection margins (based on the area supplied by the named feeding arterial vessel); mesenteric lymphadenectomy containing a minimum of 12 lymph nodes; and ligation of the primary feeding vessel at its base.

- Inability to achieve these aims laparoscopically should prompt conversion to an open procedure.

Operative Techniques: Rectum

- Similar guidelines exist for oncologically appropriate open rectal cancer surgery, with levels of evidence and grades of recommendation. These include a distal margin of 1–2 cm, removal of the blood supply and lymphatics up to the origin of the superior rectal artery (or inferior mesenteric artery if indicated), and appropriate mesorectal excision with radial clearance.
- Prospective and retrospective case series indicate that laparoscopic rectal resection is possible in selected patients.
- Multiple factors affect feasibility of an oncologically adequate laparoscopic resection for rectal cancer: tumor factors such as bulkiness, proximal or distal location; and patient factors, e.g., width of the pelvis, obesity, presence of a bulky uterus, and obscuration of tissue planes by prior radiation. Inability to perform an appropriate resection should prompt conversion.

Contiguous Organ Attachment

- En bloc resection is recommended for locally advanced adherent colorectal tumors.
- If a T4 lesion is discovered intraoperatively, conversion is indicated unless the surgeon is capable of performing en bloc resection.

Prevention of Wound Implants

- Current consensus is that wound implants should be kept at a rate less than 1% by correct oncologic technique and experience.
- Tumor growth may be proportional to insufflation pressure.
- Carbon dioxide is associated with increased tumor implantation and growth, but is clinically the safest and most widely used gas.
- The most important developments in the issue of wound implants are experience and the refinement of laparoscopic techniques and equipment that permit a true oncologic resection to be performed.

P. Training and Credentialing in Laparoscopic Colorectal Surgery

- In terms of technical complexity, laparoscopic colon and especially rectal operations are considered toward the higher end of the spectrum.
- Early studies estimated the learning curve for laparoscopic colectomy to be 20–50 cases.

Q. Hand-Assisted Laparoscopy

- HAL colectomy has been advocated as an alternative to straight laparoscopic techniques.
- The development of new sleeveless hand-assist devices provides for hand exchanges without the loss of pneumoperitoneum, allowing surgeons to perform the procedures without disruption.
- By returning the hand back to the abdomen, one of the potential advantages of a HAL colectomy is that surgeons with less laparoscopic skills may be able to perform these complex procedures more easily.

51. Pediatric: Hirschsprung's, Anorectal Malformations, and Other Conditions

A. Hirschsprung's, Disease

- Hirschsprung's, disease (congenital megacolon) is an anomaly characterized by functional partial colonic obstruction caused by the absence of ganglion cells.
- It occurs in approximately 1 in 5,000 births. Boys are more frequently affected than girls and it is more common in Caucasians than in other races.
- A deletion in the long arm of chromosome 10 has been found.
- The functional disturbances in this condition are attributed to the absence of ganglion cells from the Auerbach's, myenteric plexus (located between the circular and longitudinal layers of smooth muscle of the intestine), the Henle's, plexus (located in the submucosa), and the Meissner's, plexus (in the superficial submucosa).
- The absence of these cells probably produces uncoordinated contractions of the affected colon. This is translated into a lack of relaxation of the colon that results in partial colonic obstruction.
- The length of the aganglionic colonic segment varies. In the most common type, the aganglionic segment includes the rectum and most of the sigmoid colon. Nearly 80% of all patients have this type.
- In approximately 10% of the patients, the aganglionosis extends to the area of the splenic flexure or the upper descending colon. Total colonic aganglionosis occurs in another 8–10% of the patients.
- In the so-called "ultrashort" aganglionosis, the ganglion cells supposedly are lacking only a few centimeters above the pectinate line of the rectum.

- The clinical manifestations are those of a partial colonic obstruction.
- In addition, these patients have a poorly characterized immunologic mucosal defect that may explain why they suffer from an inflammatory process called enterocolitis, which is the main cause of death.
- Additionally, fecal stasis seems to promote the proliferation of abnormal colonic flora (*Clostridium difficile*) as well as production of endotoxins that contribute to the aggravation of the clinical condition.
- The patient usually becomes symptomatic during the first 24–48 h of life. Delayed passage of meconium (more than 24 h), abdominal distention, and vomiting are the most common symptoms.
- A rectal examination may produce explosive passage of liquid bowel movements and gas, which dramatically improves the baby's condition.
- This clinical improvement only lasts for a few hours, after which the symptoms recur. If the colon is not decompressed, the infant usually suffers from sepsis, hypovolemia, and endotoxic shock.
- Cecal perforation may occur. About 25–30% of these babies die when unrecognized or not treated.
- Patients who do survive unrecognized and without treatment, ultimately develop the classic clinical picture initially described for this condition. They have severe constipation, a huge megacolon, and an enormously distended abdomen. This clinical situation is extremely rare nowadays in developed countries.
- Occasionally, these patients are misdiagnosed as having idiopathic chronic constipation. In the latter condition, the patients are not seriously ill, and it is very common for them to have overflow pseudoincontinence (encopresis). A rectal examination discloses a rectum full of fecal matter.
- On the contrary, patients with Hirschsprung's disease usually have malnutrition, lack of normal development, an empty aganglionic narrow rectum, and they do not have soiling.
- An abdominal film shows massive dilatation of small bowel and colon. It is almost impossible to differentiate colon from the small bowel, in a plain abdominal film during the newborn period.
- A contrast enema is used in most institutions to clarify the diagnosis. The catheter should be introduced only a few centimeters into the rectum in order to be able to visualize the nondilated aganglionic segment of the rectosigmoid, followed by a transitional zone and then a proximal dilatation.

- The definitive diagnosis is based on both the histologic absence of ganglion cells, and the presence of hypertrophic nerves in a rectal biopsy. These can be taken as full-thickness rectal biopsies under direct vision. More recently, a suction biopsy has gained wide acceptance. The specimen, however, must include mucosa and submucosa.
- An important diagnostic alternative is the determination of acetylcholinesterase activity in the mucosa and submucosa.

Medical Management

- Colonic decompression and irrigation with saline solution is the most valuable tool for the emergency management of newborn babies. This maneuver may dramatically improve a very ill neonate. Irrigations should not be confused with enemas.
- Patients with Hirschsprung's disease are, by definition, incapable of expelling this fluid and, therefore, enemas are contraindicated.
- A colonic irrigation, however, promotes the expelling of the rectocolonic contents through the lumen of a large rubber tube, which is cleared with small amounts of saline solution.
- Rectocolonic irrigations may save the baby's life, but are not the ideal long-term form of treatment.
- Once the histologic diagnosis has been established, the baby must remain with nothing by mouth, and the irrigations must continue in preparation for the surgical treatment.

Surgical Treatment

- The basis of the surgical treatment consists of the resection of the aganglionic segment and pullthrough of a normoganglionic segment to be anastomosed to the rectum, immediately above the pectinate line.
- More recently, the treatment most often used consists of a neonatal primary procedure without a protective colostomy.
- However, approaches may vary from country to country as may the surgeon's experience. In addition, a primary procedure, without a protective colostomy, requires the presence of an experienced clinical pathologist, familiar with the interpretation of frozen sections.
- The abdominal portion of all of these operations can be laparoscopically undertaken. This method has recently been advocated by a number of pediatric surgeons.

- A feared but fortunately preventable sequela is fecal incontinence. This incontinence is likely related to injury to the continence mechanism.
- A nonpreventable complication is enterocolitis.
- Constipation may also occur after these procedures. It is more common in patients in whom the aganglionic segment was resected, but a dilated portion of the colon was pulled down.

Surgical Management of Total Colonic Aganglionosis

- The current treatment consists of resection of the entire aganglionic colon and pullthrough of the normal aganglionic terminal ileum to be anastomosed to the rectum.

Surgical Treatment of Ultrashort Hirschsprung's

- The surgical treatment of the ultrashort-segment aganglionosis is as controversial as the existence of this condition.
- Some surgeons propose an operation called myectomy, consisting of the resection of a strip of smooth muscle from the anal verge up to the area where ganglion cells are found. The results of this procedure, again, are highly controversial and there is no scientific basis to explain why this may improve the condition.
- An internal sphincterectomy may yield a satisfactory result as performed after a failed pullthrough procedure.

Neuronal Intestinal Dysplasia

- Neuronal intestinal dysplasia (NID) refers to a histologic condition that includes hypertrophy of ganglion cells, immature ganglia, hypoganglionosis, hyperplasia of the submucosal and myenteric plexus, giant ganglion cells, as well as hypoplasia or aplasia of the sympathetic innervations of the myenteric plexus. The diagnosis has appeal to explain patients who have undergone a technically correct operation for Hirschsprung's, disease and still suffer from symptoms of enterocolitis or constipation. It was also expected that these histologic abnormalities would explain the pathophysiology of other colonic motility disorders.
- The histologic diagnosis of NID requires a high index of suspicion as well as the availability of special histologic techniques and expertise. Not all pathologists agree as to the existence of this condition.

- Unfortunately, a precise correlation between histology and clinical manifestations is lacking and the precise options for therapy have not been clearly established.

B. Anorectal Malformations (Imperforate Anus)

- Anorectal malformations represent a spectrum of defects characterized by the absence of an external anal orifice.
- The overwhelming majority of the patients have an abnormal communication between the rectum and the perineum (perineal fistula), the vestibule (vestibular fistula), or the vagina (vaginal fistula) in the female.
- In some female patients, rectum, vagina, and urethra are fused together forming a common channel (cloacal malformation) which opens into a single external orifice.
- In the male, the communication is with the urethra (rectourethral fistula), or the bladder (rectobladder neck fistula).
- Anorectal malformations occur in about 1 in every 5,000 newborns. Males seem to have this condition slightly more frequently than females.
- The most common type of defects seen in boys is a rectourethral fistula and the most common type in girls is vestibular fistula.
- Table 51.1 shows our proposed classification of anorectal malformations.

Table 51.1. Current classification of anorectal malformations.

Male

Perineal fistula
 Rectourethral fistula
 Bulbar
 Prostatic
 Rectobladder neck fistula
 Imperforate anus without fistula
 Rectal atresia

Female

Perineal fistula
 Vestibular fistula
 Imperforate anus without fistula
 Rectal atresia
 Cloaca
 Complex malformations

Associated Anomalies

- Urogenital abnormalities occur in about 50% of all patients with anorectal malformations. The higher and more complex the anorectal malformations, the higher the incidence of urologic associated defects.
- Sacral and spinal abnormalities are also very common in patients with anorectal malformations.
- Twenty-five percent of patients with anorectal malformations have a defect called tethered cord.
 - In this condition, the cord is abnormally attached (tethered) to the spine.
 - During the natural growth of the baby, it is believed that the spine grows faster than the cord, producing traction on the nerve fibers that may produce functional disturbances in the motion of the lower extremities and may contribute to sphincter problems.
- Hemisacrum is sometimes associated with an anorectal malformation and there is always a mass located in the area of the sacral defect.
- About 30% of patients with anorectal malformations also have some sort of cardiovascular congenital anomaly. Most frequently seen are patent ductus arteriosus, atrial septal defect, ventricular septal defect, tetralogy of Fallot, as well as other more complex malformations.
- The main concern in a patient with anorectal malformation is whether or not the patient will have bowel control, urinary control, and sexual function in the future. The higher the malformation, the worse the functional prognosis will be.
- The higher the anorectal defect, the more likely the child will have fecal incontinence, but the lesser the chance of having constipation.

Description of Specific Defects

Males

Perineal Fistula

- This is the simplest of all defects. The rectum opens anterior to the center of the external sphincter in the area known as the perineum.

- The overwhelming majority of these patients have a normal sacrum, and less than 10% of them have associated defects.
- The ideal operation consists of moving the orifice back to the center of the sphincter creating a normal-sized anus.

Rectourethral Fistula

- In the most common subtype, the rectum opens into the lower part of the posterior urethra known as bulbar urethra and, therefore, the defect is called rectourethral bulbar fistula.
- Most of these patients require a colostomy at birth and subsequently (usually 1 month later) they receive the final repair of the malformation.
- In patients with rectourethral bulbar fistula, there is a recognizable midline groove as well as an anal dimple and in patients with rectoprostatic fistula, there is conspicuous tendency for the perineum to be flat.

Rectobladder Neck Fistula

- Ninety percent of these patients have important associated defects.
- These patients are the only ones that require a laparotomy or laparoscopy in addition to the posterior sagittal approach to be repaired.

Imperforate Anus Without Fistula

- This is a rather unusual anomaly that occurs in 5% of all children with anorectal malformations. Half of them also have Down's, syndrome.

Rectal Atresia

- This malformation occurs in only 1% of all cases. It consists of a complete or partial interruption of the rectal lumen located between the anal canal and the rectum.

Female Defects

Perineal Fistula

- In these female babies, the rectum opens in what is called the perineal body between the normal location of the anus and the female genitalia.

- These patients can be repaired at birth without a colostomy. The prognosis is excellent.

Vestibular Fistula

- This is by far the most common defect seen in female patients. The rectum opens in the vestibule of the female genitalia just outside the hymen.
- Most of the vestibular fistula cases are successfully operated on at birth without a colostomy.

Cloaca

- A cloaca is defined as a malformation in which the rectum, vagina, and urinary tract are fused together forming a common channel.
- This single channel opens where the normal urethra is located in females.
- Associated defects occur in about 90% of all patients with a common channel longer than 3 cm.

Initial Management

Male Babies

- Perineal inspection and urinalysis allows determination of the likely type of malformation in about 90% of the cases.
 - The presence of a perineal orifice, by definition makes the diagnosis of a perineal fistula. This is also true when the baby has an external defect called “bucket-handle” malformation that is a skin bridge in the midline in the area of the anal dimple.
 - The presence of a good midline groove and an anal dimple, as well as meconium in the urine, means that the patient has a rectourethral fistula.
 - A flat bottom and bifid scrotum are signs of a very high malformation.
- Diagnostic studies should be done after 24 h of life, but not later than 36 h. The reason for this is that it is necessary to wait until the most distal part of the rectum is distended in order for it to be seen by any of the diagnostic modalities

[magnetic resonance imaging (MRI), ultrasound, CAT scan, or simple X-ray films].

- Also, in order for meconium to be forced through a tiny distal fistula, it is necessary to wait until the intraluminal pressure is high enough to overcome the tone of the striated muscle that surrounds the distal rectum, which usually happens after 24 h.
- During the first 24 h, the clinician must try to answer two very important questions: Does the baby have an associated defect that threatens his/her life? Does the baby need a primary repair or a colostomy?
- The baby should be examined to rule out the presence of cardiovascular defects.
- The patient will remain with nothing by mouth, and insertion of a nasogastric tube is recommended to avoid vomiting and potential risk of aspiration.
- An ultrasound of the abdomen is indicated to exclude the presence of hydronephrosis. An ultrasound of the spine is also useful to exclude the presence of tethered cord. An X-ray film of the lumbar spine and the sacrum will rule out the presence of hemivertebrae and sacral abnormalities. A very abnormal sacrum is usually associated with a very high defect.
- If after 24 h the surgeon is still not sure as to the type of defect, a cross-table lateral film with the baby in prone position and the pelvis elevated should be performed. This image will show the location of gas inside a distended rectum.
 - If the rectum is visualized below the coccyx and the surgeons have experience with the neonatal repair of this malformation, the patient can be approached primarily.
 - However, if the rectum is located higher than the coccyx, or the surgeons have no experience with these neonatal operations, it is better to perform a diverting colostomy and to postpone the main repair for a later date.

Females

- It is also true in females that simple inspection of the perineum will allow the surgeon to make a correct diagnosis during the neonatal period in most cases.
- The presence of an anal opening in the perineum makes the diagnosis of perineal fistula.

- Sometimes it is difficult to see the opening of the rectum in the vestibule because the female genitalia are swollen at birth because of the effect of the maternal hormones. The presence of a fistula in the vestibule establishes that diagnosis.
- The presence of a single perineal orifice makes the diagnosis of a cloaca.
- If none of these signs are present after 24 h, the baby should have a cross-table lateral film in prone position. Most likely the baby has an imperforated anus with no fistula (which represents 5% of all cases).
- During the first 24 h of life, the baby should be subjected to the same tests described for the male patient.
- If the baby has a cloaca, an ultrasound of the abdomen should be performed not only in the upper abdomen to rule out hydronephrosis, but also in the lower abdomen to rule out the presence of hydrocolpos.
- Most babies with a cloaca need a diverting colostomy.

Colostomy

- Colostomies in babies with anorectal malformation should be totally diverting. Loop colostomies are contraindicated; they may allow the passing of stool from the proximal into the distal colon, producing direct fecal contamination of the urinary tract.
- The ideal colostomy should be created in the descending colon, with separated stomas.
- In cases of cloaca, the surgeon must also drain the hydrocolpos through the abdomen.
- Two weeks after the colostomy, a high-pressure distal colostogram should be performed. This consists of injection of hydrosoluble contrast material through the distal limb of the colostomy to delineate the anatomy of the distal colon and to establish an accurate anatomic diagnosis. This radiograph is, by far, the most important diagnostic study in anorectal malformations.

Main Repair

Males

- Perineal fistulas can be repaired performing a minimal posterior sagittal anoplasty.

- In cases of rectourethral fistulas, the patients are subjected to a posterior sagittal anorectoplasty.

Rectobladder Neck Fistula

- This is the only defect that requires a laparotomy or laparoscopic assistance in addition to the posterior sagittal operation.

Imperforate Anus Without Fistula

- These patients are approached posterior sagittally, the posterior rectal wall is opened in the midline, and multiple stitches are placed in the edge of the rectal wall to exert uniform traction and to facilitate the separation of the rectum from the urinary tract.

Rectal Atresia

- Both rectum and anal canal are opened posteriorly. The dilated proximal rectum is anastomosed to the anal canal and then the sphincter mechanism is meticulously reconstructed in the midline.

Female Defects

Perineal Fistula

- The repair of this malformation is the same that was described for male patients, except that the rectum is usually separated from the vagina so there is no risk of vaginal injury.

Vestibular Fistula

- The main technical challenge in the repair of this defect is represented by the common wall that exists between the rectum and vagina.
- One must make two walls out of one.

Cloaca

- Repair of Cloaca with a Common Channel Shorter Than 3 cm. These patients are approached posterior sagittally. The entire sphincter mechanism is divided in the midline and the posterior sagittal incision is extended down to the single perineal opening. The common channel is also opened in the midline

to expose the anatomy of the defect. The entire defect can be repaired through this incision without opening the abdomen.

- Surgical Repair of Patients with Cloaca with a Common Channel Longer Than 3 cm. We specifically recommend these patients to be referred to specialized centers dedicated to the treatment of complex malformations. The repair of these defects usually requires not only a posterior sagittal approach, but also a laparotomy and a series of decision-making steps that require experience and special training in urology.

Results of Treatment of Anorectal Malformations

- About 75% of all patients with anorectal malformations (when subjected to a good operation), have bowel control.
- The bowel control is not perfect. This becomes evident when the patients have severe constipation, which may produce overflow pseudoincontinence, and soiling. Also, a severe episode of diarrhea may show that the bowel control is not normal.
- Constipation is a problem in most patients with anorectal malformations in whom the rectum was preserved during the main repair of the defect. Constipation should not be underestimated as a problem. When not treated properly, the patients develop megacolon and chronic fecal impaction, which may end up producing overflow pseudoincontinence.

C. Medical Management of Fecal Incontinence

- The basis of this treatment is to teach the family or the patient to clean the colon every day with an enema or colonic irrigation.
- Because most patients have constipation, the cleaning of the colon with an enema will prevent the patient from passing stool for 24–48 h.
- The goal is to find the enema that is well tolerated by the patient, is easy to administer, and keeps the patient completely clean.
- When the patient complains about the rectal enema and feels embarrassed about their parents giving the enema, an operation called the Malone procedure (continent appendicostomy) is an option.

- This consists of creating a connection between the tip of the cecal appendix and the umbilicus.
- The cecum is plicated around the appendix, to create a one-way valve that allows the introduction of a catheter through the umbilicus into the colon and prevents the colon from passing stool through the orifice.

Relevant Aspects for Adult Colorectal Surgery

- Many adolescent and adult patients may still have fecal incontinence despite successful repair in infancy.
- Evaluation of these patients should include a detailed history and physical, i.e., type of defect with which the patient was born, bowel movement and voiding pattern, type of perineum, location of rectal opening, presence of an anal dimple, and strength of sphincter contraction.
- A water-soluble enema or defecography, voiding cystourethrogram, sacral films, MRI with a rectal coil to assess the location of the rectum are essential.
- Manometry, anal ultrasound, and pudendal nerve terminal motor latency may also be helpful.
- We then classify patients into four groups.
 - “Group one” appears untrainable. They have a poor sacrum, flat perineum, poor muscles, no sensation, and poor bowel movement pattern and usually are incontinent to both urine and all types of stool. These patients are good candidates for a bowel management program. A permanent stoma is usually best suited and truly appreciated by these patients.
 - “Group two” have clinical and MRI evidence of a mislocated rectum with a good sacrum and well-developed muscles. They benefit from a secondary pullthrough procedure by an experienced surgeon with the aid of the Peña stimulator.
 - “Group three” has severe constipation and a contrast enema shows a severely dilated mega rectosigmoid. They benefit from a sigmoid resection.
 - “Group four” are patients born of the good prognostic type and have a well-located rectum, good sacrum, and good muscles but are still incontinent. They may benefit

from biofeedback or other behavior modification programs to help them evacuate the rectum at controlled and predictable times.

D. Other Pediatric Colorectal Disorders

Idiopathic Constipation

- At least 6% of pediatric consultations are related to this particular problem.
- We consider this condition to be the result of a colonic hypomotility disorder with different degrees of severity, affecting mainly the rectosigmoid and sometimes the entire colon.
- Constipation means an incapacity to empty the colon on a daily basis or incapacity to empty it completely. As a consequence, the colon stores a large amount of stool, and becomes very dilated (megacolon).
- Megacolon produces constipation and constipation produces more megacolon, creating a vicious cycle. The final result is what we call chronic fecal impaction, which provokes overflow pseudoincontinence (encopresis).
- The treatment for this condition consists of trying to find the amount of laxatives that is capable of producing a bowel movement that empties the colon completely every day.
- When the laxative requirement is so high that it creates a problem in terms of quality of life, we offer the patient a surgical treatment consisting of the resection of the most dilated portion of the colon (usually the rectosigmoid), creating an anastomosis between the nondilated part of the descending colon and the rectum.
- By doing that, even when we are aware of the fact that we do not cure this mysterious condition, we make the problem more manageable and reduce significantly the amount of laxatives that the patient needs.

Rectal Prolapse

- Rectal prolapse occurs in children because of well-known conditions such as myelomeningocele and spina bifida. The lack of sphincter tone explains the severe prolapse from which

these patients may suffer. Also, patients with cystic fibrosis or some patients with inflammatory bowel disease or intestinal parasites may have rectal prolapse.

- More recently, a perineal rectosigmoidectomy (modified Altemeier procedure) has emerged as a treatment option in these children mimicking a one-stage pullthrough for Hirschsprung's, disease.

Perianal Fistula

- Perianal abscess and fistula in pediatrics seems to be a completely different condition to that seen in adults.
- During the first year of life, many babies (mainly males), have perianal abscesses that eventually become perianal fistulas. The orifice seen externally next to the anus communicates with one of the crypts of the pectinate line.
- Our experience has been that this is a benign condition that does not require any treatment.
- All fistulas disappear after 1 year of age.

Juvenile Polyps

- Around 4 years of age, patients might have polyps in the rectum and in the colon. These polyps are benign. They grow and eventually amputate and disappear.
- The symptoms in these patients are the presence of blood surrounding the fecal matter.
- Histologically, these are benign inflammatory polyps. Once the diagnosis is made, they can be predicted to have a benign course.

Anal Fissure

- Anal fissures in pediatric patients are always a consequence and not a cause of constipation. The fissure represents a laceration that was produced with the passage of a hard large piece of fecal matter.
- The main treatment for this condition is to make the parents understand the nature of the problem. It is necessary to give enough laxatives so as to guarantee that the patient will have soft stool passing through the rectum for several weeks until the fissure heals.

- No surgical treatment is necessary in fissures in children.
- Recently, 0.2% NTG (glyceryl trinitrate) ointment has been used for intractable cases to cause a reversible chemical sphincterotomy.

52. Healthcare Economics

A. Introduction

- Healthcare expenditures are forecasted to grow more than 7.0% per year over the next 10 years (Fig. 52.1).
- Multiple interrelated events have led to the current state of healthcare finance. With the advent of the resource-based relative value system (RBRVS), physicians have shifted from price setters to price takers.
 - Technology costs, although providing an improvement in patient care, have skyrocketed.
 - Although the life expectancy of the population has not increased dramatically over the past decades, the “baby boomers” are here and continue to shift the average age of the American population to one that requires increased utilization of healthcare resources.
 - In 2003 it was estimated that forty-five million or 15.6% of Americans had no health insurance, and millions more were underinsured, putting a strain on state and federal budgets to provide care.
 - Last but not least is the current professional liability crisis, resulting in increased malpractice rates and driving specialists from specific locations.

B. The Reimbursement Process

Medicare

- Medicare Part A, also known as hospital insurance, helps pay for inpatient hospitalizations, skilled nursing care (SNF), home health

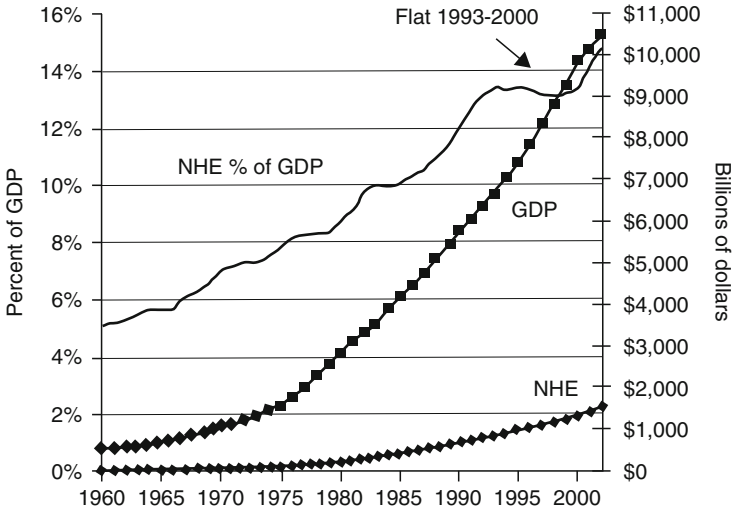


Fig. 52.1. Healthcare expenditures. The green line shows the percentage of the gross national product going to national health expenditure. The scale on the left axis measures it. The purple line, for gross domestic product (GDP), and the blue line, for national health expenditure (NHE), in billions of dollars, measured by the right axis scale. <http://hsphm.sph.sc.edu/Courses/Econ/Classes/nhe00/>.

and hospice care. Part A is financed primarily through federal payroll taxes (FICA) paid by both employees and employers.

- Individuals who receive social security benefits or railroad retirement benefits are automatically enrolled in Part A. Individuals under 65 who receive social security disability or those with end-stage renal disease for more than 24 months are also eligible for Part A.
- Although there is no monthly premium (Part A), Medicare enrollees are responsible for copayments associated with the services provided.
- Medicare Part B, also known as Medical Insurance, provides coverage for payments to physicians for services provided. This includes outpatient medical and surgical services, supplies, diagnostic testing, and some home health care.
- Part B is funded by a combination of the federal government's general revenues (75%) and individual monthly premiums (25%).

- Part B covers screening for breast cancer, cervical cancer, prostate cancer, and colorectal cancer.
- Medicare covers fecal occult blood testing every 24 months, flexible sigmoidoscopy every 48 months, colonoscopy for high-risk individuals once every 24 months or for average risk individuals every 10 years. Medicare also covers barium enemas every 24 or 48 months depending on your risk stratification. Coinsurance or copayment may be required.
- New in 2004 was a prescription drug benefit plan available to Medicare beneficiaries in 2006.
- Unlike Part A, Medicare Part B has monthly premiums.
- If one enrolls at eligibility, this premium is deducted from your social security or railroad retirement check.
- One can opt out of Part B. Similar to Part A, Part B enrollees are responsible for copayments and deductibles.
- Whereas Part A and B are considered traditional Medicare, Medicare Part C or Medicare + choice is the government's plan to shift the cost and risks of Medicare patients to the private sector. In Part C, private payers receive a monthly payment per covered individual (capitated amount) to provide all of Part A and B services.
- Private payers then tailor these plans to cover anticipated needs. These plans often provide benefits not seen in traditional Medicare, such as prescription drugs, routine physicals, preventative care, eyeglasses, and hearing aids.
- However, because these plans are privately administered, individual choice is often severely limited with regard to physicians and hospitals.
- Medicare Part D, prescription drug coverage, was signed into law in December 2003. This program will provide for prescription drugs with an initial deductible of \$250 dollars and a monthly premium of \$35. New to Part D is the institution of means testing. Individuals with incomes \$160,000 and above will be subjected to higher Part B and Part D premiums.

Medicare Resources

- According to the Office of Management and Budget, Medicare in 2004 had a budget of \$302 billion forecasted to grow to more than \$317 billion by 2008. That budget is determined

by legislation and is formula based. It involves the Medicare Economic Index, a weighted index, and the sustainable growth rate.

Hospital (Part A) Reimbursement

- In response to sharply increasing hospital costs, the federal government instituted a prospective payment system.
- This was modeled after a system developed by Fetter and associates at Yale University that categorized patients based on primary and secondary diagnosis, primary and secondary procedures, age and length of stay, and then set a uniform cost for each category.
- These diagnostic related groups (DRGs) set a maximum amount that would be paid for the hospital care of Medicare patients for a specific problem.
- Each DRG contains a list of specific diagnoses and procedures based on the International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM).
- ICD-9 is a coding system that lists specific diseases, diagnoses, and medical acuity. By using this system, Medicare has grouped related ICD-9 codes that use similar hospital recourses in specific DRGs.
- Private payers have followed Medicare's lead and began using a prospective payment system.
- Although the reasons for the continued increase in hospital costs are multifactorial, the failure of DRGs to truly control cost can best be summed up this way: "Hospitals prefer management strategies that are designed to enhance revenues over cost control measures that may be resisted by the physician staff."
- Medicare has developed a prospective payment system called the ambulatory payment classification (APC). APCs, similar to DRGs, are specific reimbursement groupings that Medicare pays to facilities.
- For these outpatient services, Medicare pays a specific rate per procedure determined by the APC in which the procedure is grouped.
- In 2004, four APC classifications covered the majority of outpatient anorectal procedures. APCs reimburse facilities between \$209 (APC 148, lateral internal anal sphincterotomy) and \$1210 (APC 150, hemorrhoidectomy) with a patient copayment between \$41 and \$437.

Physician Reimbursement

- Currently physician reimbursement from Medicare is a three-step process: (1) appropriate coding of the service provided by utilizing CPT®; (2) the appropriate coding of the diagnosis using ICD-9 code; and (3) CMS determination of the appropriate fee based on the RBRVS.
- CPT® is a uniform coding system that was developed by the American Medical Association (AMA).
- To receive consideration for a new code, a procedure must meet certain requirements: it must be done by a reasonable number of the specialty that presents the code, be performed at reasonable frequency, be done throughout the country, and have peer-reviewed literature supporting its efficacy.
- The code then moves to the Relative Value Update Committee (RUC) where it receives a value relative to other codes (RVU).
- CPT® also uses a series of modifiers in addition to the original code to better describe the service provided. This allows not only for better data collection regarding the frequency and complexity of services but also for appropriate reimbursement by Medicare.
- The Medicare fee schedule was based on the work of a research team led by William Hsiao, a Harvard economist under contract to CMS. The Harvard study ranked procedures and services relative to each other based on the amount of physician work necessary to perform the procedure or service.
- Work was defined as a combination of the time used to perform the service and the complexity of service (mental effort, knowledge, judgment and diagnostic acumen, technical skill, physical skill, psychological stress, and potential iatrogenic risk).
- Work was then broken down into three time periods, preservice, intraservice, and postservice.
 - Preservice work for surgical procedures has come to be defined as the physician work provided from the day before, until the time of the operative procedure (i.e., skin incision). This may involve any or all of the following: hospital admission work-up, the preoperative evaluation including the procedural work-up, review of records, communicating with other professionals, patient and family, and obtaining consent; and, dressing, scrubbing, and waiting before the operative procedure, preparing patient and needed equipment for the

operative procedure, positioning the patient, and other non-“skin-to-skin” work done in the operating room before incision.

- Intraservice work includes all “skin-to-skin” work that is a necessary part of the procedure. The time measurement for the intraservice work is from the start of the skin incision until the incision is closed.
- Unlike preservice work, postservice work varies depending on the magnitude of the procedure. There are currently three postprocedural global periods: 0 days, 10 days, and 90 days. For a surgical service with a global period of 10 or 90 days, the postservice work includes all of the above, and in addition postoperative hospital care, including the intensive care unit if needed; other in-hospital visits; discharge day management services; and office visits within the assigned global period of 10 or 90 days.
- For nonsurgical services such as office evaluation and management (E&M) services, the preservice work includes preparing to see the patient, reviewing records, and communicating with other professionals.
- The intraservice work includes the work provided while the physician is with the patient and/or family. This includes the time in which the physician obtains the history, performs a physical evaluation, and counsels the patient.
- The postservice work for nonprocedural services includes arranging for further services, reviewing results of studies, and communicating further with the patient, family, and other professionals, including written and telephone reports as well as calls to the patient.
- According to federal law, the relative value of codes is reviewed every 5 years by the RUC allowing for corrections in the relativity of the codes.
- Currently, physician work is not the only value used to calculate an RVU. Whereas the work RVUs (wRVU) makes up the majority of the total RVUs (tRVU) for a specific CPT® code, RVUs are also calculated for practice expense (peRVU) and malpractice (mRVU) for each code.
- Final physician reimbursement by CMS is then multiplied by a geographic practice cost index (GPCI), which is supposed to adjust payments for differences in physician practice costs across geographic areas.

- For a given service, multiplying the service-specific Physician Work, Practice Expense, and Malpractice Expense RVUs by their respective GPCIs determines the payment amount in a given geographic area. Next, these three products are summed, yielding a geographically adjusted RVU total for the service.
- This number is then converted to dollars by a conversion factor, which in 2004 was \$37.3374 per RVU.
- Most private payers today use CPT® codes to identify physician services.
- Again using CPT® terminology, companies will adjust payment based on the individual service provided; for example, paying E&M codes 105% of Medicare, office-based procedures 110% of Medicare, and surgical procedures 115%. This is often modified regionally based on the rules of supply and demand. In areas with a paucity of a specific specialty, reimbursement is high as opposed to a saturated market where the insurance company can play one physician or group against another to obtain a favorable contract.
- Hospital payments are similar. Private payers reimburse hospitals either as a percentage of the DRG or on a per diem based on the service provided. For outpatient procedures, hospitals are often reimbursed as a percentage of the APC.

Private Payers

- The majority of people obtain health insurance through some type of group. This allows for cheaper individual payments as group purchasing allows the insurer to spread the risk over a larger number of people.
- Group insurance can be obtained through employers, professional societies (ACS, etc.), or other organizations (AARP, etc.).
- Regardless of how insurance is purchased, the types of insurance plans are distinctly different. The most costly is the fee-for-service plan, also known as an indemnity plan in which individuals are free to seek care from any physician or hospital they choose.
- These plans are often structured so that there is a copayment for all services.
- In traditional fee-for-service plans, an individual may be responsible for 20% of the bill.

- To help control increasing healthcare costs and stimulate a more efficient use of healthcare resources, managed care organizations were developed.
- They use a variety of tools to manage preauthorization functions, control healthcare costs, and share the risks associated with group coverage.
- Health maintenance organizations (HMOs) were designed to meet these ends. Although HMOs are still in the process of evolution, they characteristically represent the most restrictive type of health maintenance organization.
- In this model, the HMO restricts patient access in nonemergency incidents to HMO-contracted physicians and hospitals. Out-of-pocket costs for individuals are traditionally low for HMO physicians; however, individuals are responsible for all costs for non-HMO physicians.
- Most HMOs initially used a “gatekeeper” or primary care physician for specialist referral.
- The next iteration of managed care organizations is the preferred provider organization (PPO). Similar to HMOs, PPOs enter into contracts with healthcare providers and hospitals to provide member care. Often more choice and flexibility are available to the patient than in the traditional HMO model but at the cost of higher beneficiary premiums.
- Unlike HMOs, PPOs do not own physician practices. To have access to the PPOs beneficiaries and be listed in the “network,” physicians often agree to reduce their normal fees. PPOs traditionally do not use a “gatekeeper,” thus allowing patients increased access to self-referred specialty care.
- The most recent variation in managed care organizations is the development of “Point of Service” plans, a mixture of traditional HMO and PPO plans. In this type of plan, if a patient first sees their primary care physician to receive a referral, much like an HMO, the copay, if present, is negligible.
 - Patients are also able to see “network” physicians with minimal financial responsibility.
 - Patients may seek care from someone outside the “network” without a referral. In these instances, the physician is paid a rate less than is characteristically billed, usually the same rate as in network physicians, and the patient is responsible for the difference. This provides increased patient flexibility but at increased cost.

C. The Future

- Despite hopes that managed care would provide cost stability to health care in America, after costs initially slowed, they have continued to increase at a rate higher than the consumer price index and personal income (Table 52.1).
- Experts now tout a “consumer-centric” or “consumer-driven” healthcare model as the future of healthcare delivery.
- Similar to making any large purchases, individuals are given the opportunity to choose from specific benefit packages that will fit their particular need.
- With the increasing number of consumers in need of healthcare resources, these experts see the Internet as a way of rapid dissemination of healthcare information.
- Although consumer-centric health care and health reimbursement arrangements (HRAs) seem to be recreating the way health care is funded, there are potential problems. This model assumes that consumers are sophisticated enough to make sound healthcare choices, not just those based on cost.
- The bottom line is that consumers lack the information necessary to use the money wisely. So consumer driven health care, as it is being discussed today, will be a market failure.”
- Another potential problem is that individuals will feel obligated to use all of their HRA or employer contributions, especially as the year end approaches and individuals run the risk of losing their contributions.
- Despite the many and varied attempts to control healthcare costs, an unacceptably large number of Americans are still unable to obtain adequate healthcare coverage.

Annual percent change continues																
Gross domestic product																
Billions of dollars	5.9	2.9	3.8	4.8	2.7	2.4	2.4	3	3.4	4.4	4.2	3.9	4	5.4	6	6.7
Personal income																
Personal income in billions	8	3.4	2.3	3.3	3.8	2.5	2.4	1.6	2.6	2.5	2.4	2.8	2.6	3.5	4.3	5.2
Prices ^a																
Consumer price index, all items	3.4	2.8	1.6	2.3	3.4	2.7	1.9	1.3	1.3	1.6	2.2	2.9	2.1	2.2	1.9	1.8
All items less medical care	3.3	2.7	1.4	2.2	3.3	2.6	1.7	1	1.1	1.4	2.1	2.7	2	2.1	1.8	1.7
Medical care	4.1	4.6	4.7	4	4.6	4.5	4.7	4.5	4.6	4.8	5	4.5	4	3.9	3.7	4.2

^aBase period = 1982–1984, unless noted

Note: Q designates quarter of year. Quarterly data on GDP, personal income, and disposable personal income, are seasonally adjusted at annual rates

Sources: U.S. Department of Commerce, Bureau of Economic Analysis; Survey of Current Business. Washington. U.S. Government Printing Office. Monthly reports for January 1998–October 2003; U.S. Department of Labor, Bureau of Labor and Producer Price Indexes. Washington. U.S. Government Printing Office. Monthly reports for January 1999–March 2004. <http://www.cms.hhs.gov/statistics/health-indicators/t7.asp>

53. Ethical and Legal Considerations

A. Considerations for Surgeons

General Concepts

Defining the Problem

- Professional responsibilities have been a concern of surgeons since antiquity; however, the last 25 years have displayed a dramatic growth of both professional and societal attention to moral and ethical issues involved in the delivery of health care.
- This increased interest in medical ethics has occurred because of such factors as the greater technologic power of modern medicine, the assigning of social ills to the responsibility of medicine, the growing sophistication of patients and the information available to them, the efforts to protect the civil rights of the increasing disadvantaged groups in our society, and the continued rapidly escalating costs of health care including medical malpractice costs.
- The terms *ethics* and *morals* are often used interchangeably to refer to standards regarding right and wrong behavior.
 - Morals refer to conduct that conforms to the accepted customs or standards of a people. They vary with time and with the nature of society at that time.
 - Ethics is the branch of philosophy that deals with human conduct, and can be described as applied morals.
 - Medical ethics refers to the ethics of the practice of medicine.
 - Clinical ethics refers to the ethics of delivering patient care.

- The term bioethics includes the ethics of all biomedical endeavors and encompasses both medical and clinical ethics.
 - The law serves to delineate the formal rules of society. It expresses a kind of minimal societal ethical consensus, which society is willing to enforce through civil judgments or criminal sanctions. The law does not always prohibit behavior deemed unethical, however it will usually set a minimal standard for conduct.
- It should be stated from the outset that it is more important to understand the process of dealing with these issues than to assume that anyone can clearly state what is ethically right or wrong in a complex medical/surgical dilemma.
- Our society seems willing to accept flaws from many sources, but not from physicians and the medical delivery system. This situation is made even more complicated by a system in which individuals purchase their healthcare coverage when they are well and willing to buy the cheapest plan possible; but they utilize their coverage, especially for surgical problems, when they are sick and want the maximum that the system can deliver, without regard to time and cost.
- We must learn and apply the ethical principle of truth telling and the doctrine of informed consent for the effective care, which has taken us so long to master. We must also take into account that high-speed communication via the Internet will necessitate reevaluation of issues such as patient's rights and confidentiality.

What Makes the Surgeon Special?

- There are special ethical considerations for surgeons. These include: Rescue, Proximity, Ordeal, Aftermath, and Presence.
 - Rescue is the first pillar of surgical ethics. It deals with the fact that surgery conveys power, and that power is socially endorsed and may be reinforced by the surgeon's individual charisma; but as with all power it must be constantly renewed and revalidated. Accepting rescue as a legitimate principle justifies respect for dependence in the surgical relationship.
 - Proximity occurs in surgery as in no other act. To operate on persons involves entering their bodies and becoming privy to secrets even denied to the owner of the body. This proximity carries with it the penalties of closeness, and particularly the pains of failure.

- Ordeals are periods of extreme experience, capable of disrupting our lives.
- Aftermath deals with the reality that surgery leaves physical and psychological scars that may persist for life.
- Presence, as a virtue and a duty, is what the patient desires of the surgeon during all phases of the surgical encounter.

Unique Problems of Surgery

- The surgeon and the surgical team take on the continued responsibility of the operative procedure itself, the postoperative care, and usually the long-term follow-up and management of any complications and dilemmas that may result from the initial encounter. This intense relationship is often established very quickly and under frequently adverse circumstances.
- The bottom line for surgeons who work under the same kinds of time pressures is to do what you think is best. You must use your judgment, based on your medical knowledge and your experience.
- However, you also want to be as scrupulous as possible in making sure that bioethical and legal guidelines are followed, both for the benefit of the patient, and, frankly, as protection for yourself.
- It is important for surgeons to have a working knowledge of general medical ethical principles and how these principles affect decisions involved with treating patients.
- For specific dilemmas, time permitting, surgeons should obtain an opinion from the hospital ethics consultation service and/or from hospital counsel. By doing so, one can gain the experience and imprimatur of opinions from those who have dealt with such issues and whose training gives them the experience to deal with them in a knowledgeable way.
- Surgeons should do all they can for the patient, while at the same time, doing what they need to do to protect themselves from personal risk and possibly from negative legal ramifications.
- Similarly, doctors have a duty to themselves to avoid situations that violate their own personal beliefs, whether religious or medical. This includes thinking a step or two ahead of the current situation to know what the ramifications of a course of treatment may be. If the anticipated actions may violate a doctor's own personal tenants, he or she should refer the patient to another physician.

B. Principles of Bioethics

General Concepts

Philosophical Principles

Respect for Autonomy

- Adult patients with decision-making capacity have a right to their preferences regarding their own health care.
- This right is grounded on the legal doctrine of informed consent. This means that patients must give their voluntary consent to treatment after receiving all appropriate and relevant information about the nature of their problem, the expected consequences of the recommended treatment, and treatment alternatives. This is probably the most crucial legal concept in bioethics.
- Touching someone without his or her consent is, in legal terms, a “battery,” which could result in a lawsuit for damages. Therefore, the principle is: medical treatment without consent is a battery.
- This is true except in cases of emergency where the patient is unconscious and where it is necessary to operate before consent can be obtained.”
- The courts now require the patient not only to consent to the procedure, either themselves or through a proper surrogate, but to be given sufficient information to make an informed decision. The courts have held that the quality and quantity of information given to the patient must be sufficient for the reasonable patient to understand, not the doctor.
- Doctors are duty bound to respect the autonomy of each competent patient. The patient is the ultimate decision maker about what he or she wants.
- If the patient is unable to make his or her own decision, the treating surgeon must respect the decision made by a surrogate decision maker, such as one designated in a healthcare durable power of attorney.

Beneficence

- The principle of *beneficence*, simply stated, involves the duty of the physician to act in the best interest of his or her patients.
- Beneficence, or doing good, is probably the universal tenet of the medical profession.

Nonmaleficence

- *Nonmaleficence* is essentially the old philosophical principle, “first, do no harm.”
- This concept also incorporates the principle of *avoiding killing*.

Justice

- *Justice* is *fairness*. It is required to ensure that medical decisions are made with reason and honesty.
- *Distributive justice* implies that all individuals and groups should share in society’s benefits and burdens. This presents an ethical challenge for the surgeon, dealing with an individual patient, who mistakenly believes that she should limit or terminate care based on a need to limit healthcare resource expenditures for the *good of society*.

Religion and Medical Ethics

- Clinical bioethics, in fact, uses many decision-making methods, arguments, and ideals that originated from religion. It is also important for the individual clinician to understand his or her own personal spirituality in order to relate better to patients and families, representing a broad diversity of religious and ethnic backgrounds.
- Problems frequently arise when trying to apply religion-based rules to specific clinical, ethical situations.
- As previously described, we have come to rely instead on the four ethical principles of autonomy, beneficence, nonmaleficence, and fairness. These are the principles that have guided medical ethical thinking and have become instrumental in forming healthcare policies in the United States and other Western countries over the past three decades.
- It is known that religion is one of the most common ways by which patients cope with medical illness.
- Religious beliefs are known to be significant influences on medical decisions, especially those made by patients with serious illnesses.
- We must be extremely cautious about prescribing religion to nonreligious patients, forcing a spiritual history on patients who are not religious, causing patients to believe our practice and specific ways, attempting to provide spiritual counsel to patients, and arguing with patients over religious matters.

- It is also imperative for us as surgeons to be comfortable enough with our own beliefs to allow our patients to pray for us, according to the faith of their own religion.

C. Legal Principles

General Concepts

Types of Law

- There are three kinds of law that affect the practice of surgery: statutes, regulations promulgated by an administrative agency, pursuant to a statute, and case law.
- The legislatures are the designated policy-making entities in our system; regulations are written to comply with legislative directives; and the courts are charged with resolving disputes between parties, usually as directed by statute, if there is a relevant one.
- Doctors should be generally familiar with state law. There are different state laws on many bioethical matters, such as definition of death, competency, organ donation, and now the use of embryonic stem cells, even for research only.
- Many doctors move from state to state during their careers, and general understanding of state laws governing situations that may confront them in surgical situations is crucial.

Statutory Law

- Statutory law is made by legislatures and includes such issues as the statute of limitations, which defines how long after an adverse event a patient is able to sue a physician for malpractice, and, in some states, statutes on informed consent.
- The Emergency Medical Treatment and Labor Act (EMTALA) is another example of a federal statutory law.
- The Act requires that a basic screening examination be provided to all patients seeking care. It therefore became illegal, as well as unethical, to withhold therapy from the poor just because they do not have the ability to pay.

Regulatory Law

- These administrative laws are created by regulatory agencies including State Medical Boards.

- HIPAA, as EMTALA, was intended to protect patients' rights of privacy and to guarantee them continuation of health insurance coverage should they change employers.
- Also, like EMTALA, HIPAA has taken on many ramifications threatening a huge economic impact on the escalating costs of delivering medical care.

D. A Familiar Case-Management System

Physician-Based Ethics

The Clinical Ethics System

- Jonsen and his colleagues suggest that every clinical case, especially those raising an ethical dilemma, should be analyzed by means of the following four topics: (1) medical indications, (2) patient preferences, (3) quality of life, and (4) contextual features, defined as the social, economic, legal, and administrative context in which the case occurs.
- Their intent is to show clinicians that these four topics provide a systematic method of identifying and analyzing the ethical problems occurring in clinical medicine. See Table 53.1.

Table 53.1. The four topics: case analysis in clinical ethics.

Medical indications	Patient preferences
The principles of beneficence and nonmaleficence	The principle of respect for autonomy
1. What is the patient's medical problem? history? diagnosis? prognosis?	1. Is the patient mentally capable and legally competent? Is there evidence of incapacity?
2. Is the problem acute? chronic? critical? emergent? reversible?	2. If competent, what is the patient stating about preferences for treatment?
3. What are the goals of treatment?	3. Has the patient been informed of benefits and risks, understood this information, and given consent?
4. What are the probabilities of success?	4. If incapacitated, who is the appropriate surrogate? Is the surrogate using appropriate standards for decision making?
5. What are the plans in case of therapeutic failure?	5. Has the patient expressed prior preferences, e.g., Advance directives?

(continued)

Table 53.1 (continued)

Medical indications	Patient preferences
6. In sum, how can this patient be benefited by medical and nursing care, and how can harm be avoided?	6. Is the patient unwilling or unable to cooperate with medical treatment? If so, why? 7. In sum, is the patient's right to choose being respected to the extent possible in ethics and law?
Quality of life	Contextual features
The principles of beneficence and nonmaleficence and respect for autonomy	The principles of loyalty and fairness
1. What are the prospects, with or without treatment, for a return to normal life?	1. Are there family issues that might influence treatment decisions?
2. What physical, mental, and social deficits is the patient likely to experience if treatment succeeds?	2. Are there provider (physicians and nurses) issues that might influence treatment decisions?
3. Are there biases that might prejudice the provider's evaluation of the patient's quality of life?	3. Are there financial and economic factors?
4. Is the patient's present or future condition such that his or her	4. Are there religious or cultural factors?
5. Is there any plan and rationale to forego treatment?	5. Are there limits on confidentiality?
6. Are there plans for comfort and palliative care?	6. Are there problems of allocation of resources? 7. How does the law affect treatment decisions? continued life might be judged undesirable? 8. Is clinical research or teaching involved? 9. Is there any conflict of interest on the part of the providers or the institution?

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E. Specific Dilemmas of Colon and Rectal Surgery

Special Considerations for Colon and Rectal Surgeons

- We understand, however, that we have chosen a surgical career that includes resolving perplexing problems of anal-rectal disease, pelvic floor malfunction, and incontinence which cause daily

significant discomfort for the patient and have frequently been mismanaged, for a long period of time, by our nonspecialized colleagues.

- This places us, frequently, in the position of not only having to resolve the technical surgical aspect of the problem, but also having to explain the previous misdiagnosis or mismanagement by other physicians, a challenging ethical dilemma.
- Thus, we become actively involved with screening, preventive measures, understanding genetic predisposition to disease, and even the need for what has come to be called preemptive surgery. Because of the diseases that we treat, we must understand the science of current genetics as well as the appropriate clinical utilization of genetic testing, including the challenges of respecting confidentiality and requesting genetic counseling to deal with the long-term aspects involving not only the patient but family members who may not wish to be included in the discovery of genetic predisposition to disease.
- In fact, because of our experience and expertise in the construction and management of intestinal stomas, we are often confronted with such quality-of-life issues as body image and impairment of sexual function.
- Because of the complexity of the diseases on which we operate, including those in areas with difficult access and high risk of postoperative complications and recurrence of malignant processes, we often find ourselves on the leading edge of surgical innovation and instrumentation. This creates the ethical challenges of differentiating acceptable surgical innovation from truly investigative ventures that require research protocols and institutional approval.

F. Categories of Patient Encounters

Severe Emergency: Life in Immediate Jeopardy

- Certainly there is no preestablished doctor-patient relationship, there is little chance that there will be a reliable surrogate, and many ethicists have questioned if a patient in such dire straits ever has decision-making capacity.

Urgent: Serious Problem Needing Surgery

- In a case such as this, in which there is some but not much time, the presence of a surrogate and clearly described advance directives would be extremely helpful.

Semi-elective: Will Probably Need Surgery

- An example would be an elderly patient with known extensive intraabdominal cancer who presents with a significant, unresolving intestinal obstruction. It is clear that the obstruction can only be relieved by surgery, but it is not clear that this will be beneficial to the patient.
- In this case, determination of decisional capacity, the existence of advance directives, or the presence of a reliable surrogate is very important; and there is enough time to pursue the intended desires of this patient.

G. Autonomy/Decision-Making Capacity/Competency

General Concepts

Autonomy Versus Paternalism: Trust Is the Bridge

- Individual freedom is one of the basic tenets of modern bioethics. This freedom is usually referred to as autonomy. This principle implies that a person should be free to make his or her own decisions. It is somewhat the antithesis of the medical profession's long practiced paternalism whereby the physician acted on what he or she thought was good for the patient, whether or not the patient agreed.
- However, experienced surgeons know that their patients significantly rely on them for guidance through complicated choices, often where life itself is on the line. This is, of course, a form of paternalism which our patients request and to which they are entitled. The key to accomplishing this ethically and successfully is based on the principle of trust.
- For surgeons, the establishing of this trust must begin at the inception of the relationship, and sometimes must be very quickly accomplished.

- The crucial issue for the surgeon seeking autonomous informed consent is the decision-making capacity or competence of the patient involved.
- The determination of decision-making capacity involves more than just completing a mental status examination and includes the ability of the patient to take in information, to evaluate a decision based on personal values, to make a decision, and to communicate the choice of decision to the physician.
- The concept of medical decision-making capacity is one based on the evaluation by the team providing medical and surgical care. This is distinguishable from a legal determination of incompetence. A patient is always assumed to be legally competent unless a court has declared otherwise.
- The determination of decision-making capacity varies in stringency with the seriousness of the impact of the decision. For example, the more severe the risk posed by the patient's decision, the more stringent should be the standard of determining capacity.

Refusal of Treatment

- The Courts have, however, identified four *state interests* that override the refusal or termination of medical treatment on behalf of competent and incompetent persons, including the preservation of human life, the protection of the interests of innocent third persons, the prevention of suicide, and the maintenance of the integrity of the medical profession.
- In exercising their rights under the autonomy principle, each competent patient has a right to refuse treatment, even if the results of such refusal will be their death.
- For sure, *refusal* of a life-sustaining medical treatment should be accompanied by a full assessment of *decision-making capacity* and by an understanding from the patient of the consequences of refusal. If uncertainty prevails, the surgeon on the firing line should still "err on the side of life."

H. Telling the Truth/Disclosing Errors

General Concepts

- If the physician believes that telling the patient everything about the condition in question, which is a duty, will have a

dramatic negative effect on the patient's well being, the physician must decide which duty is more important in each particular situation.

Prognosis: Balance Between Giving False Hope and Removing All Hope

- Discussing prognosis with our patients and their families is one of the situations that forces us most carefully to choose our words precisely. Even when we are forced by patients and families to use specific statistics, we must use them in a manner that is helpful and not totally destructive of hope.
- It helps to explain that statistics are better for 100 people rather than for any given individual. It can be very expeditious for us to use statistics as a form of *truth dumping*, but such an act can be devastating to a terrified, desperate, and inadequately informed patient who is desperately clinging for any possible hope.

I. Patients with Impaired Decision-Making Capacity

- Examples of patients having impaired decision-making capacity include minors, mentally handicapped persons, those with organic brain disease or in toxic states, and those with psychiatric conditions, including suicidal risk.
- Determining the point at which a minor has the capacity to make medical decisions is often very complicated and varies with the laws of an individual state. For example, an “emancipated” minor can make his or her own medical decisions. This includes individuals younger than the age of majority who are living on their own, are married, or are in the military.

Suicidal Patients

- Generally, surgeons intervene with the suicidal patient based on the assumption that the person is suffering from mental illness and impaired judgment. This assumption is usually correct, with 90% of suicides being found to be associated with mental illness such as depression, substance abuse, or psychosis.

- Therefore, relying on the principle of beneficence, surgeons almost always treat the injuries inflicted by suicidal patients despite their expressed intention to die.
- The conflict arises when the reasons for suicide appear “good,” such as in the case of the terminally ill cancer patient with severe, uncontrollable pain.
- Thus, although some patients might make a rational decision to commit suicide, in most cases, the surgeon delivering care must assume that the person’s judgment is impaired, and proceed with full indicated, lifesaving measures.

J. Advance Directives

General Principles: Talking About Death

- Facility in routinely addressing end-of-life issues with surgical patients is critical because it allows the surgeon to raise difficult questions with patients during the earlier phases of their disease process. Often the issues that are most difficult to address when patients near the end of life are those that have not been attended to earlier in the patients’ course of treatment.
- When a patient does not have the decision-making capacity to give informed consent, or there is no time to ask the patient or his or her surrogate about treatment preferences, advance directives express in written form what the patient’s choices would have been if he or she had decision-making capacity.
- Advance directives include living wills, durable powers of attorney, and other written documents.
- An advance directive is any proactive document stating the patient’s wishes in various situations, should they be unable to state their own wishes.
 - Some states have specific language for each of these documents and provide reciprocity for other states.
 - Both the *living will* and a *durable power of attorney* can be prepared without the benefit of state-approved language as long as the intention of the person executing the document is clear.

Living Will

- The *living will*, which was adopted by many states in 1990, is a document suitable for *terminally ill patients* in which the treating physician accepts the patient's wishes regarding withholding of care, including requests restricting heroic resuscitative efforts, in advance.
- In a *living will*, the signatory indicates what his or her choices would be for medical treatment in the situation in which *death is imminent*, and the individual's wishes are unable to be communicated to the treating physician.
- Under most state laws, *living wills* indicate the signatory's desire to die a natural death and indicate unwillingness to be kept alive by so-called "heroic measures." This usually amounts to a "Do Not Resuscitate" order.
- In most states, the activation of the terms of a living will require an *imminent demise* and a second physician's opinion corroborating that determination.

Durable Power of Attorney

- A *durable power of attorney for health care* specifies a surrogate decision maker in the event that the patient no longer has the capacity to make medical decisions. The *durable power of attorney* is a written document that gives the authority to another person, usually a spouse or relative, to make decisions regarding health care if the patient is incapacitated and unable to make decisions for himself or herself.
- The reason it is called "durable" is to ensure that the signatory knows that it can be revoked and/or changed at any time. This provides the freedom to change both who the surrogate is and what the patient's stated wishes, if any, are. This is important in situations such as divorce in which the person executing the power of attorney may want to change the surrogate before the divorce becomes final or in those family situations in which dynamics create a desire to change the surrogate.
- The *durable power of attorney* works best when the patient has discussed with a surrogate his or her values and beliefs, because these would apply in making complex decisions regarding healthcare issues.

- If there is no durable power of attorney, surrogate decision makers may be sought based on state laws. There is usually a defined hierarchy regarding surrogate decision makers: spouses, adult children, siblings, and so forth.
- The *durable power of attorney* is a better form of advance directive than the *living will* because, in the former, a surrogate can be educated about the nuances and options regarding each stage of treatment or nontreatment.

Problems

- All persons, when naming a surrogate decision maker, have a responsibility to fully explain what they would want in certain medical treatment situations.
- A further problem with advance directives that limit full implementation of medical care is the application of such directives in situations for which they were not intended.
- There must also never be confusion when the patient is able to relate his or her preferences to healthcare providers. *Verbal communication takes precedence over any written advance directive.*
- In addition, when there is any confusion about the advance directive, disagreement among family members, or concern that it was not meant for the clinical circumstance at hand, *advance directives limiting treatment should be ignored in favor of prudent medical care.*
- In general, it is always wise for healthcare providers to err on the side of life and to begin standard medical treatment.
- Treatment options, such as mechanical ventilation and hemodynamic support, can always be withdrawn at a later time once issues are resolved and the family is present. In such situations, the hospital *ethics consultation service* can often prove very helpful.

K. Informed Consent

General Concepts

- The laws dealing with informed consent require the surgeon to describe to the patient the nature of the procedure, risks, benefits, and alternatives, including no treatment at all.

- The current interpretation of the law requires several elements to constitute *informed consent*. These are the *criteria* that the physician must disseminate to the patient or acting surrogate to meet that standard:
 - What is the treatment that the doctor wishes to pursue, including a full explanation of the procedure and what it involves, including the necessity for anesthesia and other support functions?
 - For what reason has the doctor selected this particular treatment, including the doctor's judgment as to why this procedure is chosen to alleviate, cure, or minimize the medical/surgical problem?
 - What are the risks of the recommended treatment, including an explanation of both the risks of the treatment itself and of any corollary threats to the patient? Surgeons should, in satisfying this requirement, include discussion of their own particular *experience with the procedure* as well as that of the hospital and the medical/surgical colleagues who will be assisting.
 - What benefits will the patient receive from the proposed treatment? This is similar to the choice of treatment information previously described in that it requires the doctor to explain what the potential benefits will be from the procedure.
 - What are the chances that the proposed treatment will remedy the problem? This is similar to the information included when describing "benefits and risks" and should also include a description of the *past experience* of the surgeon in performing this specific procedure, as well as the *outcomes* that the surgeon has obtained.
 - What alternative treatment options exist for the given problem? This is similar to explaining the choice of treatment but emphasizes what other treatment options are available, and why this surgeon has chosen this particular procedure.
 - What effect will refusal to accept the proposed treatment have on the patient? This must entail a frank discussion of the ramifications of failure to receive the suggested treatment and whether it is life threatening, or of a lesser degree of medical difficulty. This is the part of the dis-

cussion in which the surgeon must be most sensitive to the patient's religious, cultural, and ethnic background.

- Here the law requires that the sufficiency of the level of information will be judged from the *patient's point of view*, not the doctor's.
- Every profession has its own terms of terminology or jargon. Physicians must strive to ensure that the language they use is clearly understandable.
- As with every rule of law, there are certain *exceptions* to the requirement for informed consent.
 - When there is an emergency situation that could result in the death of the patient, time is of the essence, and there is no surrogate decision maker present, the *consent requirement is waived*.
 - Similarly, when the situation is not an emergency, but the patient is for one reason or another not able to give consent because of unconsciousness, coma, mental disability, or other cause of inadequate decision-making capacity, and there is no advance directive or surrogate, informed consent is not necessary.
 - There is also a *therapeutic exception* to the rule. If the physician believes that revelation of the normally required information would have a negative effect on the patient's health, fully informed consent is not necessary. This usually arises in the context of a psychiatric patient.
 - Also, when a competent patient *refuses* to receive information upon which to base a decision, this requirement is waived.
 - There can also be a waiver of the necessity for informed consent when the *government* requires certain medical tests or treatment in the face of possible medical or national security emergencies.
- A common misconception among those rendering emergency care is that anyone who presents to an emergency facility falls into the *emergency exception* to informed consent.
 - The *emergency exception* allows a physician to treat a patient without obtaining informed consent.
 - This exception requires the following: the patient must be unconscious or without the capacity to make a decision, and no one else legally authorized to make such a decision

is available; time must be of the essence in avoiding risk of serious bodily injury or death; and, under the circumstances, the action proposed would be that to which a *reasonable person* would consent.

- The emergency exception does not apply if the patient has decision-making capacity and is able to communicate a decision about medical care.

L. Patient-Surgeon Relationship

- Over the last few decades, the relationship between patients and physicians has been evolving from one of *paternalism*, in which surgeons make choices for their patients, to a more equal and *autonomous* relationship of shared decision making by which surgeons provide information that allows competent adult patients to make their own choices.

M. Communication and the Internet

- Most of us have learned not to deliver complicated or bad news by telephone, unless we have made a previous agreement with the patient and family to convey such information in order to save significant travel or other inconveniences that are significant enough to preclude a face-to-face personal communication. Such situations are now increasingly complicated because communication by the Internet is usually not secure, and the information delivered can become a permanent part of the patient's record.
- Currently, there are no guidelines available for the ethical transfer of confidential medical information via the Internet.
- Especially with the implementation of HIPAA requirements, until clearer guidelines are defined, surgeons should err on the side of no sensitive information to be delivered by e-mail or telephone.
- A new part of our responsibility, as surgeons, is to not only guide our patients to appropriate and helpful Web sites but to actively participate in the construction and quality control of electronic information provided by the Internet in our own areas of expertise.

N. Using Newly Deceased Patients for Teaching Purposes

- To our knowledge, there are no state statutes that specifically prohibit the teaching of procedures using newly dead patients, and no court has considered this issue.
- Although the law in this situation is very forgiving, compassionate and ethical considerations should supervene. Several medical studies have found that patients and families are likely to consent to such procedures but prefer to be asked permission first.

O. Special Concerns for Participation in Research/Innovation

General Concepts

- Special issues for informed consent arise when the surgical patient is asked to participate in a *research project*. The time for decision making is usually short, and the principle investigator of the project may also be the one administering care. This raises not only the issue of adequate informed consent but of the *risk for coercion* of the patient to participate in the study.
- All physicians must ensure that trials involving human subjects are of potentially significant value and are conducted ethically.
- When discussing the potential *risks* of a proposed procedure, it is essential for the person seeking consent to quantify minimal, low, or high-risk using examples from everyday life.
- When discussing the benefits of a proposed study, one must distinguish clearly between *therapeutic* and *nontherapeutic* research.
- Researchers must clearly differentiate, for the patient, the balance between *potential benefit* to the patient and any *potential risks* associated with the protocol.
- Especially for research, the principle still holds that for consent to be valid, it must be informed, understood, and voluntarily given.

P. Placebo Surgery

- As investigators sort out the mechanism for ensuring that surgical research is performed ethically and with true *informed consent*, the issue of the use of *placebo surgery* seems based on recently published trials. Horng and Miller, commenting on these trials in the *New England Journal of Medicine*, comment that the issue of using *placebo surgery* in clinical trials seems to violate the fundamental ethical principles of *beneficence* and *nonmaleficence*.

Q. Conflict of Interest: Industry and Drug Money

- Currently the lifeblood of clinical research is external support requiring a productive relationship with the biomedical industry. This potential conflict of interest can only be resolved by scrupulously implementing the principles of integrity, honesty, respect, and equity.
- Even the mere appearance of a conflict of interest could jeopardize the investigator's integrity and undermine public trust.
- Surgeon investigators involved with industry-sponsored research should meticulously divorce themselves from any personal or commercial conflict that could compromise patient loyalty or well being.
- However, it is not inappropriate for an investigator to receive economic rewards from a drug or device that is commensurate with his or her efforts involved in the development of the product.
- It is also acceptable for investigators to receive consultant and lecture fees from companies whose product they are testing, provided that the remuneration is proportionate with his or her efforts, and that it is clearly reported, in advance, of all presentations and is clearly stipulated in any publications.
- It is unethical, however, to sell or purchase stock or have a direct financial interest in the product under investigation until the relationship between the investigator and the company has been terminated, and the results of the research have been published or made public.
- Acceptance of individual gifts that did not benefit patients, such as trips and subsidies for medical educational conferences in which physicians are not speakers, are strongly discouraged.

- The acceptance of even small gifts has been shown to affect clinical judgment and to heighten the perception (or reality) of a *conflict of interest*.

R. Confidentiality

General Principles

- Surgeons are bound by the same rules of *confidentiality* as other doctors. Especially with the new restrictions and significant penalties imposed by HIPAA, all healthcare personnel must be very cognizant of preserving *confidentiality*.
- A surgeon's duty to maintain confidentiality regarding information disclosed by the patient has been a long-held medical precept.
- Although the law generally prevents the divulgence of confidential information, it also *mandates certain exceptions*, such as reporting patients with infectious disease and those who are likely to harm others.

S. Making and Managing a Genetic Diagnosis

- The ethical hazard involves obtaining the results of a genetic test without adequate counseling of the patient to determine what will be done with results once obtained. Clearly, this should all be determined before obtaining the information.
- Most of these unpleasant situations can be avoided by appropriate genetic counseling before any genetic information is acquired. This should ideally involve the use of professional genetics counselors because most of us surgeons have not been adequately trained in the skills required.

T. Abuse of the Elderly

- The first priority of the physician is to ensure this victim's safety. The surgeon should never hesitate to ask for social service consultation or to report suspicions to the appropriate

adult protective services. Such acts are not breaches of confidentiality; they represent implementation of the most sincere duty of the physician.

U. Futility/Withholding Treatment

General Concepts

- No physician has ever been successfully prosecuted for withholding or withdrawing of medical care from any dying patient in the legal history of the United States.
- Some clinicians and ethicists believe that the *withholding* of medical treatment is more problematic than later *withdrawal* of unwanted or useless interventions. This discrepancy in the urgent situation probably exists because the physicians involved usually lack the vital information about their patients' identities, medical conditions, and expressed wishes.
- The surgeon's decision to limit or withhold treatment can be based either on the patient's refusal or on the physician's determination that the treatment would not be of benefit.
- Withholding treatment because of a judgment of *futility* is even more of an ethical challenge. *Futility* has been defined as "any effort to achieve a result as *possible*, but that reasoning or experience suggests is *highly improbable*, and cannot be systematically produced."
- It should be noted that assertions of *futility* come about in two contradictory situations. One is where the patient or surrogate wants the doctor to refrain from a further treatment, which the doctor thinks is not futile; and the other is where the doctor wishes to refrain from treatment that he or she believes to be futile.
- Many ethicists agree that physicians are under no obligation to render treatments that they ascertain to be of little or no benefit to the patient.

V. DNR and the Need for Surgery

- There is, and should be, confusion regarding operating on a patient with existing "do not resuscitate" orders. Because there is no universal agreement as to how this situation is to be

handled, each surgeon must be aware of specific institutional guidelines.

- Most hospitals have a policy that allows suspension of the DNR order during the procedure and administration of anesthesia, only to have it resume when the surgery and required anesthesia have been concluded.

W. Withdrawal of Treatment

General Principles

- Taking into account the preceding discussion, an important line of reasoning for the moral and legal equivalents for the two actions of *withholding* or *withdrawing* is the important concept that if a medical intervention will not result in the desired or beneficial results intended for the patient, it makes no difference whether the clinician withholds the intervention before beginning it or discontinues its use after it has been started and found to be not effective.
- We must be willing to respect a terminally ill patient's wish to forego life-prolonging treatment, as expressed in a living will or through a healthcare surrogate appointed via a durable power of attorney for healthcare.

X. Euthanasia/Physician-Assisted Suicide/Terminal Sedation

- First is *euthanasia*, which literally means "good death." Its consideration arises when patients or surrogates claim that the quality of life is so diminished, the pain and suffering is so unbearable, or they have become such a burden on others that they request their physicians to *cause* their deaths quickly and painlessly.
- Such terms as "voluntary," "nonvoluntary," and "involuntary" have been applied in an attempt to clarify the various ramifications of this process, but, in fact, *euthanasia* is the act of killing by a physician and is *not legal* anywhere in the United States.

- *Physician-assisted suicide*, however, implies a death that a competent person, with decision-making capacity, chooses and *causes* by self-administration of drugs that a physician has prescribed but *did not administer*.
- *Terminal sedation*, another frequently misunderstood term, is the practice of sedating a patient to unconsciousness in order to relieve the horrible symptoms, which may occur during the process of dying, including pain, shortness of breath, suffocation, seizures, and delirium.
- As the sedating medication is administered, other life-sustaining treatments are withdrawn, including ventilatory support, dialysis, artificial nutrition, and hydration. It is critically important to understand that in this frequently used process, *no lethal doses of opiates or muscle relaxants are administered*.

Y. Applying the Principles

- The surgeon should ensure that the patient is given all the information necessary to allow proper informed consent regarding withdrawal of treatment, but once that is done, it is the ethical duty of the surgeon to withdraw the specified treatment.
- This is true no matter what the patient requests, whether it be withdrawal of feeding tubes, ventilators, or nutrition and hydration. As long as the patient is fully aware of the consequences, both short-term and long-term, his or her stated wishes should be respected and acted upon appropriately by the healthcare team.
- The same principle should be invoked if the patient is not able to understand but has provided, in an advance directive, an indicated desire with respect to withdrawal of treatment under specified circumstances.
- The duty of the physician is identical if a designated surrogate requests or demands the withdrawal of treatment.
- When the surgeon determines that withdrawal of treatment is appropriate and further treatment would be ineffective, consent of the family or surrogate should be sought.
- In this situation, it is very important and helpful to know what if any *surrogacy laws* exist. These do vary from state to state,

and those surgeons faced with potential decision making should know in advance the laws of their state

- Courts have upheld the principles of *autonomy* and *self-determination*, affirming the right to refuse life-sustaining treatment.
- Should the surgeon have moral or religious beliefs that would preclude her from *withdrawing* treatment, she should remove herself from the case.

Z. Palliative Care/Hospice

General Principles

- A brief definition of *palliative care* would be: the act of *total* care of patients whose disease is not responsive to *curative* treatment.
- The concept of *palliative surgery* refers to surgery for which the major intent is alleviation of symptoms and improving quality of life, *not necessarily cure*.

AA. Pain Relief and the Doctrine of “Double Effect”

Confusing Principles

- At the same time that we are criticized for not giving enough pain medication to our suffering patients, we are also challenged by the law for prescribing medication with the *double effect* of potentially *hastening death*. This doctrine of *double effect* is intended by the courts to recognize the difference between provision of adequate pain treatment that unintentionally causes death and the ordering of medication that intentionally causes a patient’s death.

Double Effect

- The application of the principle of *double effect* is controversial because it places significant weight on physician *intent*, which

is impossible to prove, and no weight on a patient's right to self-determination.

- In caring for dying patients, surgeons must acknowledge that they are one part of the often-fragmented medical team. They must accept the goal of providing care where they can, comfort always, consult when necessary, and coordination of the remaining end of life issues.

Hastening Death: The "Code"

- Because the overwhelming admonition to the physician is "above all do no harm," society has implored the surgeon, in life-threatening situations, to waive informed consent requirements and to act presumptively to save life or limb in situations in which the usual consent is impossible to obtain. This leads to our current default in dealing with the critically ill or moribund unknown patient: resuscitating with "a full code" and asking questions later. This practice is probably acceptable as long as the surgeon realizes that *withdrawing life support* is just as acceptable as *withholding life support* initially.
- The initial full resuscitation may make it possible to assess the patient's end-of-life desires more fully and carefully.
- If the initial intervention is unsuccessful or is inconsistent with the patient's preference, it can and should be withdrawn, consistent with the patient's identified goals.
- Although no ill is usually intended, the slow code is usually an indication that the surgeon has not realistically communicated with the patient and family to express the medical opinion that resuscitation, in the face of cardiac or respiratory arrest, would be inappropriate.
- The concept of "no code" should be clear, and is usually instituted at the request of the patient, his advance directive, or an appropriate surrogate.
- It is ethically inappropriate for the physician to disrespect the patient's autonomous decision even when faced with despairing surrogates requesting interventions over a clear directive to the contrary.
- In the absence of any directive, including a decisional patient, the physician must use *best interest standard*, which requires implementing what a *reasonable patient* would want done in a similar situation.

- *Passive euthanasia* is the result of withdrawing or withholding life support in situations judged to be medically futile. In the United States, this is both ethically and legally acceptable.
- *Physician-assisted suicide* occurs when a physician supplies a death-causing agent to a patient with the knowledge that the patient intends to use this agent to commit suicide. In the United States, this practice is legal only in the state of Oregon.

AB. Determination of Death

- The attending physician has the discretion and the responsibility to determine death.
- Most states use the brain death criteria.
- There is debate currently about whether the “whole brain” definition of death is no longer valid, and that the appropriate ethical standard for definition of death is cessation of “higher brain” function. Higher brain function includes the cognitive functions or the capacity for consciousness.
- Once there is irreversible cessation of that capability, a judgment usually made in consultation with a neurologist, then death can be declared.
- It should be noted that in some states the definition of death includes either the *cessation of cardiopulmonary function* or *irreversible cessation of all brain function*, including the brain stem.
- The healthcare team, however, should realize that no matter which criterion is being used, it may be appropriate to continue cardiovascular support for the purpose of maintaining perfusion during the eminent birth of a fetus, or to sustain viability of transplantable organs.

AC. Organ Donation

- Federal law requires most hospitals to make an inquiry of all patients, during their admission, for any procedure, whether emergency or elective, about their wishes to be a potential *organ donor*.

- However it is obtained, *informed consent* of the *donor* is required. Most states provide organ donor options on driver's licenses, and many people possess other documents such as donor cards, which indicate their desire to become organ donors.
- In fact, it is usually inappropriate for anyone on the treating team to initiate the discussion of organ donation. Most hospitals have in place a procedure whereby the discussion of potential organ donation is initiated by a person specifically trained for this purpose.
- In cases in which there are no previously expressed wishes by the potential donor, the family, as custodians of the body, may agree to organ donation.
- In cases with no directives at all, the best course of action, unfortunately, is to do nothing postmortem.

AD. Ethics/Legal Consultation

- Most of these institutions provide a mechanism for obtaining help in sorting out challenging ethical dilemmas. This help usually comes in the form of consultation from the hospital *Ethics Committee* or from in-house *legal consultation*.

AE. Good Samaritan

General Concepts

- Good Samaritan acts or deeds are defined as those in which aid is rendered to a person in need, where no fiduciary or legal obligation exists to provide such aid, and neither reward nor remuneration for the aid is anticipated.
- Briefly stated, in almost every state, an off-duty surgeon who comes across a person with an emergency medical condition has no *legal duty* to come to the aid of that person.
- All states in the United States have enacted so-called "Good Samaritan" statutes, which protect the physician from liability incurred for good-faith efforts to help at the scene of an accident or emergency. The ethical duty should far exceed the legal excuse for inaction.

AF. Previous Suboptimal Care

General Concepts

- Generally our surgical and specialty training does not prepare us for the ethical differentiation between “bailing out” and “condemning,” responding to patients’ pointed questions, communicating with the doctor responsible for the suboptimal care, and certainly not “blowing the whistle” on another surgeon and going to court, when requested, as an “expert witness.”
- Each of us must then rely on compassion and tact to tell our patients the truth without unduly condemning the other physicians.

AG. “Blowing the Whistle” and Going to Court

- We should understand that credibility in the medical-legal system should be based on true expertise and on telling the truth, be it for the plaintiff or for the defense of our colleagues, and, in fact, we can be of much greater help to inappropriately accused physicians by establishing such a record of credibility.

AH. Personal Challenges: Competition of Interests

Family

- The American Medical Association has issued a statement on “Self-treatment or Treatment of Immediate Family Members.” In essence it speaks against treating family except in emergent situations and for short periods of time.

Competence/Impairment/Insight

- More than one in every seven physicians is affected by substance abuse at some time in their careers.
- We should never hesitate to request intervention because correction of substance abuse in physicians is highly successful. If we stand by and allow patients to be mismanaged by inadequate physicians, we will not only see the patients suffer but will

allow our colleagues and friends to be destroyed professionally and perhaps devastated emotionally by malpractice suits, condemnation by institutions and colleagues, loss of licensure, and eventually the ravages of substance abuse or personal humiliation.

54. Critically Reviewing the Literature for Improving Clinical Practice

A. Study Designs: Case Series, Case Control, Cohort, and RCTs

Providing the Evidence

- Various hierarchies have been proposed for classifying study design. In simplest terms, studies can be classified as case series, case control studies, cohort studies, and randomized controlled trials (RCTs). The case series is the weakest and the RCT is the strongest for determining the effectiveness of treatment (Table 54.1).

Case Series

- Case reports (arbitrarily defined as 10 or fewer subjects) and case series are the typical surgical studies performed. There is no concurrent control group although there may be a historical control group.
- Patients may be followed from the same inception point and followed prospectively – not for the purpose of the study – but in the normal clinical course of the disease.
- Typically, data from patient charts or clinical databases are reviewed retrospectively. Thus, the outcome of interest is present when the study is initiated.
- However, results from case series should be likened to those observations made in the laboratory. Just as those observations should lead to generation of a hypothesis and performance of an experiment to test it, an RCT should be performed to confirm the observations reported in a case series.

Table 54.1. Types of study designs.

	Control Group	Prospective follow-up	Random allocation of subjects
Case series	No	No	No
Case control study	Yes	No	No
Cohort study	Yes	Yes	No
RCT	Yes	Yes	Yes

- Case series are plagued with biases such as selection and referral biases, and because data are not collected specifically for the study, they are often incomplete or even inaccurate. Therefore, incorrect conclusions about the efficacy of a treatment are common and surgeons should not rely solely on evidence from case series.

Case Control Studies

- The case control study is the design used most frequently to study risk factors or causation.
- There are typically two groups of patients: the case group, composed of subjects in whom the outcome of interest is present, and the control group in whom it is not.
- Controls are selected by the investigator rather than by random allocation so the likelihood of bias being introduced is real and thus there is a risk of making an erroneous conclusion.
- In case control studies, as in case series, data are collected retrospectively. Thus, the outcome is present at the start of the study.

Cohort Studies

- Cohort studies may be retrospective or prospective.
- There are two or more groups but subjects are not randomly allocated to the groups.
- However, the outcome is not present at the time that the inception cohort is assembled. There is less possibility of bias than a case control study because cases are not selected and the outcome is not present at the initiation of the study.
- However, the likelihood of bias is still high because subjects are not randomly allocated to groups.
- Retrospective cohort studies differ from prospective cohort studies in that data analysis and possibly data collection are performed retrospectively but there is an identifiable time point that can be used to define the inception cohort.

- Cohort studies typically are performed by epidemiologists studying risk factors where randomization of patients is unethical.

Randomized, Controlled Trials (RCT)

- The RCT is accepted as the best trial design for establishing treatment effectiveness.
- There are several essential components of the RCT.
 - First, subjects are randomly allocated to two groups: a treatment group (in which the new treatment is being tested) and a control group (in which the standard therapy or placebo is administered).
 - Second, the interventions and follow-up are standardized and performed prospectively. Thus, it is hoped that both groups are similar in all respects except for the interventions being studied. Not only does this guard against differences in factors known to be important, it also ensures that there are no differences as a result of unknown or unidentified factors.
- Where differences in treatment effect are small, the RCT may minimize the chance of reaching an incorrect conclusion about the effectiveness of treatment.
- There are, however, some limitations to RCTs.
 - First, RCTs tend to take a long time to complete because of the time required for planning, accruing, and following patients and finally analyzing results.
 - Second, clinical trials are expensive to perform, although their cost may be recouped if ineffective treatments are abandoned and only effective treatments are implemented.
 - Third, the results may not be generalizable or applicable to all patients with the disease because of the strict inclusion and exclusion criteria and inherent differences in patients who volunteer for trials.
 - In addition, not all patients will respond similarly to treatment.
 - Fourth, in situations whereby the disease or outcome is rare or only occurs after a long period of follow-up, RCTs are generally not feasible.
 - Finally, the ethics of performing RCTs is controversial and some clinicians may be uncomfortable with randomizing their patients when they believe one treatment to be superior even if that is based only on anecdotal evidence.

- There are elements common to all RCTs. The first and perhaps the most important issue in designing an RCT is to enunciate clearly the research question.
- Most RCTs are based on observations or experimental evidence from the laboratory. RCTs should always make biologic sense, have clinical relevance, and be feasible to perform.
- As one can see, the selection of subjects, the intervention, duration of the trial, and the choice of outcome measure may vary depending on the research question.
- Ultimately, however, investigators wish to generalize the results to clinical practice so the outcome measures should be clinically relevant. For this reason, QOL measures are often included.
- The issue of standardization of the procedure is of major importance in surgical trials. Standardization is difficult because surgeons vary in their experience with and in their ability to perform a surgical technique.
- There are two issues related to standardization of the procedure.
 - First, there is the issue of who should perform the procedure: only experts or surgeons of varying ability. Implicit in this is the definition of an “expert.”
 - Second, there is the issue of standardization of the procedure so it is performed similarly by all surgical participants and it can be duplicated by others following publication of the trial results.
- If the procedure is usually performed by experts, then it probably is desirable to have only experts involved in the trial. However, if a wide spectrum of surgeons perform the procedure, then it would be appropriate not to limit surgical participation.
- Regardless of the number of surgeons involved in the trial and their desire to mimic routine practice, there must be a certain amount of standardization so that readers of the trial results can understand what was done and can duplicate the procedure in their own practice.
- Assessments may be performed by an independent assessor who is unaware of the treatment group that the patient is in.
- Finally, if criteria used to define an outcome are explicitly specified a priori, it may minimize or eliminate bias (e.g., criteria to diagnose an intraabdominal abscess).
- Unlike the release of medical therapies, there is no regulating body in surgery that restricts performance of a procedure or requires proof of its efficacy.

In 2000, as part of the Food and Drug Administration modernization act, an on line trials registry was established at www.clinicaltrials.gov. In 2004, the international committee of medical journal editors met and agreed that in order for a study to be acceptable for publication,, it must have been reistered either prior to or at the time of commencement in order to be compliant with the requirements. Registration can be done on line at www.clinicaltrials.gov

B. Levels of Evidence: Grading the Evidence

Levels of Evidence

- There are several grading systems for assessing the level of evidence. The first was developed by the Canadian Task Force on the Periodic Health Examination in the 1970s (Table 54.2) and has been adopted by the United States Task Force.
- Studies in which there has been blinded random allocation of subjects are given highest weighting because the risk of bias is minimized. Thus, an RCT will provide Level I evidence provided it is well executed with respect to the issues discussed earlier in this chapter.
- In the American Society of Colon and Rectal Surgeons (ASCRS), the Standards Committee in 2003 decided to adopt the grading system shown in Table 54.3. This system identifies the level of evidence based on the available literature. Moreover,

Table 54.2. Canadian task force levels of evidence.

Level	Type of evidence
I	Evidence obtained from at least one properly RCT
II-1	Evidence obtained from well-designed controlled trials without randomization
II-2	Evidence obtained from well-designed cohort or case-control analytic studies, preferably from more than one center or research group
II-3	Evidence obtained from comparisons between times or places with or without the intervention; dramatic results in uncontrolled experiments (such as the results of treatment with penicillin in the 1940s) could also be included in this category
III	Opinions of respected authorities, based on clinical experience, descriptive studies, or reports of expert committees

Table 54.3. Levels of evidence and grade of recommendation used by the ASCRS Standards Committee.

Level	Type of evidence
I	Evidence obtained from metaanalysis of multiple, well-designed, controlled studies. Randomized trials with low false-positive and low false-negative errors (high power)
II	Evidence obtained from at least one well-designed experimental study. Randomized trials with high false-positive and/or false-negative errors (low power)
III	Evidence obtained from well-designed, quasi-experimental studies such as nonrandomized, controlled, single-group, pre-post, cohort, time, or matched case-control series
IV	Evidence from well-designed, nonexperimental studies such as comparative and correlational descriptive and case studies
V	Evidence from case reports and clinical examples
Grade	Grade of recommendation
A	There is evidence of Type I or consistent findings from multiple studies of Type II, III, or IV
B	There is evidence of Type II, III, or IV and findings are generally consistent
C	There is evidence of Type II, III, or IV but findings are inconsistent
D	There is little or no systematic empirical evidence

this system also provides a grade for the recommendation that depends on both the level of evidence and the consistency of the results from the different studies.

C. Assessing the Best Evidence

What Is the Quality of Evidence Evaluating Surgical Practice?

- Given the relative paucity of RCTs reported in the literature, Solomon and McLeod then wished to determine whether it should be possible to perform RCTs in more instances or whether it is not possible, as has been suggested by some.
 - To address this issue, they identified a sample of 260 questions in the surgical literature relating to the efficacy of general surgical procedures. From this analysis, it was estimated that it should be possible to perform an RCT to answer approximately 40% of questions.

- In contrast, only 4.6% of the articles reviewed reported results of RCTs and more than 50% of the articles were case reports or case studies.
- Although methodologic issues unique to surgical trials are frequently cited as the reason for not being able to do an RCT, in fact, they believed that methodologic issues would preclude doing an RCT only 1% of the time.
- However, although internists may criticize surgeons for not performing more trials, it is also important to realize that perhaps the greatest impetus for medical trials is the requirement by regulating agencies of evidence from clinical trials before release of new medication and, therefore, the availability of funding from industry to test them.
- A recent article examined the quality of reporting for RCTs in the Diseases of the Colon and Rectum. The authors found that 77% of 11 basic elements were reported appropriately. The best reported items were eligibility criteria, discussion of statistical tests, and accounting for all patients lost to follow-up. The worst reported item involved power calculations. Only 11% appropriately reported power calculations. For the critical reader, the reporting of appropriate methods, limitations, and data is important. To this end, standards have been recommended regarding the publication of RCTs (i.e., CONSORT – Consolidated Standards of Reporting Trials) and includes 22 items (Table 54.4). In 2008 the CONSORT guidelines were revised to include the specifics germane to nonpharmacologic (such as surgical intervention) trials

Systematic Reviews or Metaanalyses

- The terms systematic review and metaanalysis have been used interchangeably. However, systematic reviews or overviews are qualitative reviews, whereas statistical methods are used to combine and summarize the results of several studies in metaanalysis.
- In both, there is a specific scientific approach to the identification, critical appraisal, and synthesis of all relevant studies on a specific topic.
- They differ from the usual clinical review in that there is an explicit, specific question that is addressed. As well, the methodology is explicit and there is a conscientious effort to retrieve and review all studies on the topic without preconceived prejudice.

Table 54.4. CONSORT checklist for reporting RCTs.

1. Title and abstract – how participants were allocated to interventions
<i>Introduction</i>
2. Background – scientific background and explanation of rationale
<i>Methods</i>
3. Participants – eligibility criteria, settings, and locations of data collection
4. Interventions – details of interventions for each group
5. Objectives – specific aims and hypotheses
6. Outcomes – defined primary and secondary outcomes
7. Sample size – how sample size was determined, interim analyses, stopping rules
8. Randomization sequence generation – method used to generate randomization
9. Randomization allocation concealment – method used to implement randomization
10. Randomization implementation – who generated the allocation sequence, who enrolled participants
11. Blinding – whether or not blinding was performed (subjects, researchers, etc.)
12. Statistical methods – methods used to compare groups
<i>Results</i>
13. Participant flow – flow of subjects through each stage (strongly recommend diagram) such as numbers of subjects randomly assigned, receiving intended treatment, completing protocol, etc.
14. Recruitment – dates defining the periods of recruitment and follow-up
15. Baseline data – baseline demographic/clinical characteristics of each group.
16. Numbers analyzed – “denominator” of each group and whether analysis was performed by “intention to treat”
17. Outcomes and estimation – summary of results for each primary and secondary outcome for each group
18. Ancillary analyses – address added analyses and whether they were prespecified or exploratory
19. Adverse events – all important adverse events or side effects for each group
<i>Discussion</i>
20. Interpretation – interpretation of results, discussing hypotheses, bias, limitations
21. Generalizability – external validity of the trial findings
22. Overall evidence – general interpretation of the results in the context of current evidence

- The value of metaanalysis is that study results are combined so conclusions can be made about therapeutic effectiveness, or if there is not a conclusive answer, to plan new studies. They

are especially useful when results from several studies disagree with regard to the magnitude or the direction of effect, when individual studies are too small to detect an effect and label it as statistically not significant, or when a large trial is too costly or time consuming to perform.

- For the clinician, metaanalyses are useful because results of individual trials are combined so he or she does not have to retrieve, evaluate, and synthesize the results of all studies on the topic.
- However, because the rigor of the methodology of many published metaanalyses may be quite variable, the clinician should have some knowledge of metaanalysis methodology and be able to critically appraise them. Published guidelines are available (Table 54.5).
- Whereas some have embraced metaanalysis as a systematic approach to synthesizing published information from individual trials, others have cautioned about the results of metaanalysis and some have been completely skeptical of the technique.
- Others have pointed out that metaanalyses on the same clinical question have led to different conclusions. Some of these are attributable to methodologic problems.
- Finally, there is a strong association between statistically positive conclusions of metaanalyses and their quality (i.e., the lower the quality of the studies, the more likely that the metaanalysis reached a positive conclusion).
- In response to the problems in disseminating the results of individual RCTs, the Cochrane Collaboration was established to prepare, maintain, and disseminate systematic reviews of RCTs of healthcare interventions.

Table 54.5. Guidelines for using a review.

-
1. Did the overview address a focused clinical question?
 2. Were the criteria used to select articles for inclusion appropriate?
 3. Is it unlikely that important, relevant studies were missed?
 4. Was the validity of the included studies appraised?
 5. Were the assessments of the studies reproducible?
 6. Were the results similar from study to study?
 7. What are the overall results of the review?
 8. How precise were the results?
 9. Can the results be applied to my patient care?
 10. Were all the clinically important outcomes considered?
 11. Are the benefits worth the harms and costs?
-

- The Cochrane Library is available on CD ROM on a quarterly basis (The Cochrane Library. Update Software Inc. 936 La Rueda, Vista, CA 92084). It includes several databases including the Cochrane Database of Systematic Reviews. This is a valuable source of high-level information for practicing clinicians. Unfortunately, it is of somewhat more limited use to surgeons because of the paucity of published surgical RCTs and metaanalyses.

Practice Guidelines

- Practice guidelines have been defined by the Institute of Medicine as “systematically developed statements to assist practitioner and patient decisions about appropriate health care for specific clinical circumstances.”
- Guidelines are not standards that set rigid rules of care for patients. Rather, guidelines should be flexible so that individual patient characteristics, preferences of surgeons and patients, and local circumstances can be accommodated.
- Many clinicians are wary of guidelines and believe that they are simply a means to limit resources and inhibit clinical decision making and individual preferences.
- Guidelines have also been criticized for being too idealistic and failing to take into account the realities of day to day practice. The argument is that patients differ in their clinical manifestations, associated diseases, and preferences for treatments. Thus, guidelines may be either too restrictive or irrelevant.
- Also, clinicians may be confused because of conflicting guidelines.
- Finally, guideline development may be inhibited because there is a lack of evidence upon which to base guidelines.
- Evidence-based guidelines are the most rigorously developed guidelines. There should be a focused clinical question and a systematic approach to the retrieval; assessment of quality and synthesis of evidence should be followed.
- Because there are many guidelines available, including some with conflicting recommendations, clinicians require some skills to evaluate the guidelines and determine their validity and applicability (Table 54.6).

Table 54.6. Guidelines for assessing practice guidelines.

1. Were all the important options and outcomes clearly specified?
2. Was an explicit and sensible process used to identify, select, and combine evidence?
3. Was an explicit and sensible process used to consider the relative value of different outcomes?
4. Is the guideline likely to account for important recent developments?
5. Has the guideline been subject to peer review and testing?
6. Are practical, clinically important, recommendations made?
7. How strong are the recommendations?
8. What is the impact of uncertainty associated with the evidence and values used in guidelines?
9. Is the primary objective of the guideline consistent with your objective?
10. Are the recommendations applicable to your patients?

D. Critically Evaluating the Literature (How to...)

Critically Appraising the Literature

- Critical appraisal skills must be mastered before evidence-based practice can be implemented successfully. Critical appraisal skills are those that enable application of certain rules of evidence and laws of logic to clinical, investigative, and published data and information in order to evaluate their validity, reliability, credibility, and utility.
- Clinicians need critical appraisal skills because of the constant appearance of new knowledge and the short half-life of current knowledge.
- Critical appraisal requires the clinician to have some knowledge of clinical epidemiology, biostatistics, epidemiology, decision analysis, and economics.
- Sackett and colleagues have consolidated much of this information into a book entitled "Evidence Based Medicine."
- There are two potential sources of error, which may lead to incorrect conclusions about the validity of the study results: systematic error (bias) or random error.
- Bias is defined as "any effect at any stage of investigation or inference tending to produce results that depart systematically from the true values."
- The risk of an error as a result of bias decreases as the rigor of the trial design increases.

- Because of the random allocation of patients as well as its other attributes, the RCT is considered the best design for minimizing bias.
- In observational studies, including outcomes research (where patients have not been randomized), various statistical tests (e.g., multivariate analysis) are frequently used to adjust for differences in prognostic factors between the two groups of patients. However, it is important to realize that it is possible to adjust for only known or measurable factors.
- Random error occurs because of chance, when the result obtained in the sample of patients studied differs from the result that would be obtained if the entire population were studied.
- Statistical testing can be performed to determine the likelihood of a random error. The type of statistical test used will vary depending on the type of data. Some of the more common tests are shown in Table 54.7.
- There are two types of random error: Type I and Type II errors.
- The risk of stating there is a difference between two treatments when really there is not one is known as a Type I error.
- By convention, if the risk of the result occurring because of chance is less than 5% (a *P* value less than 0.05), then the difference in the results of treatment is considered statistically significant.
- One of the issues regarding Type I errors is that of multiple comparisons. Specifically, the more comparisons being performed with a given set of data, the higher the likelihood of a Type I error (finding a difference, when one truly does not

Table 54.7. Types of statistical tests.

Data type	Statistical tests (with no adjustment for risk factors)	Statistical tests (with adjustment for risk factors)
Binary (dichotomous)	Fisher exact test or chi square	Logistic regression
Ordered discrete	Mann-Whitney <i>U</i> test	
Continuous (normal distribution)	Student's <i>t</i> test	Analysis of covariance
Time to event (censored data)	Log-rank Wilcoxon test	Log-rank (Cox proportional hazard)

exist). Under these circumstances, a correction for multiple comparisons (e.g., a Bonferroni correction) should be performed by the authors.

- Although a result may be statistically significant, the clinician must determine whether it is clinically relevant or important. Typically, treatment effects can be written as absolute risk reduction (ARR) or relative risk reduction (RRR).
- The ARR is simply the difference in rates between the control group and the experimental group whereas the RRR is a proportional risk reduction and is calculated by dividing the ARR by the control risk.
- The advantage of the ARR is that the baseline event rate is considered.
- Recently, Cook and Sackett have coined the term “number needed to treat” (NNT) which may make more intuitive sense to clinicians rather than thinking in terms of ARR and RRR. It is calculated by dividing the ARR into 1.
- It is up to the judgment of the clinician to decide whether the treatment benefit is clinically significant. The statistician can only determine whether a treatment benefit is statistically significant.
- The other random error is the Type II error. A Type II error occurs when two treatments are, in reality, different but one concludes that they are equally effective.
- When investigators plan a trial, they minimize the risk of a Type II error by calculating a sample size to ensure that there is adequate power (1-Type II error) to show a difference if one really exists.
- Whereas a power calculation is performed a priori, a more useful measure for the reader interpreting the study results is the calculation of 95% confidence intervals (CIs). The 95% CI gives a range within which the true mean of the sample variable lies, with a probability of 95%.
- Moreover, one frequently sees CIs when odds ratios are reported. In this case, if CI for the odds ratio overlaps 1, then there is no significant difference in odds. If the CI of the odds ratio is greater than one, then there is a significant increase in odds (i.e., a positive association between the predictor variable and outcome). Finally, if the CI of the odds ratio is less than one, then there is a significant decrease in odds (i.e., a negative association between the predictor variable and outcome).

Risk Adjustment

- For the surgeon reading the literature, an issue that is inherently related to systematic error, or selection bias, is that of patient comorbidity. The methodology for controlling for differing patient disease severity is termed risk adjustment, and is an important issue for critically evaluating the literature – particularly when the study design is not an RCT.
- The techniques of risk adjustment need to account for both the health status of the patient before treatment as well as severity (and acuity) of the current (i.e., morbid) illness.
- Risk adjustment is generally accomplished by identifying and then accounting for the factors that determine, or are associated with, variations in outcomes.
- One of the most difficult issues in performing risk adjustment is deciding which comorbid diseases or conditions to adjust for in the analysis.
- Overall, a reader should examine whether or not risk adjustment was performed, and if so, is there a validated method being used, and is this method adequate?

Charlson Index

- One of the most common indices for risk adjustment currently being used is the Charlson Index.
- Overall, the Charlson method predicts the risk of dying by assigning a score to each comorbid factor. Several comorbid conditions are included. The method itself is simple: points are summed for each of the comorbid conditions that are present to generate an index score; this score can then be used as a risk adjustment score for a patient's level of comorbidity.
- Another method for risk adjustment in surgery is seen in the Veterans Affairs (VA) developed system used in the National Surgical Quality Improvement Program (NSQIP).
- In addition to collecting perioperative items for risk assessment, these data can all be used in a predictive manner.

Quality of Life

- The most common way of measuring QOL is through patient self-assessment surveys. These surveys (also called questionnaires, tools, or instruments) are organized into a series of items

that gather information on specific areas of interest related to QOL. For example, most surveys that address “overall” QOL include questions that cover the areas of physical, psychological, social, and overall well being.

- For a survey to be considered useful, the instrument should have reliability, validity, and responsiveness.
- Reliability refers to the extent that a survey produces reproducible results.
- Validity refers to the ability of a survey to accurately measure what it is designed to measure.
- Finally, responsiveness, or sensitivity to change, is the extent to which an instrument can detect true differences. In other words, it is a survey’s ability to change as the patient’s clinical status changes.
- For the critical reader, interpretability has been thus far the most elusive aspect of QOL measurement in the literature. Most of the difficulty in interpretation of QOL data stems from the fact that what is being measured is not observable.
- Survey instruments may be categorized broadly into two types – generic versus disease specific.
- Generic surveys attempt to measure the global relationship between a patient’s health and their well being.
- Examples of generic surveys that have been used in colorectal disease include Sickness Impact Profile (ulcerative colitis, colorectal cancer), Nottingham Health Profile (colorectal cancer), and the Short Form 36 (fecal incontinence, restorative proctocolectomy, familial adenomatous polyposis, and colorectal cancer).
- Another benefit of these surveys is comparison of results with normative data, such as aged matched, healthy, control individuals. The SF-36 survey, for instance, has this advantage because scores (overall and for each of its eight domains) are available for the general population, and can be subsetted by such things as age and gender.
- More clinically detailed than a generic survey, disease- or symptom-specific surveys offer the possibility of allowing the physician and patient to concentrate on the issues that can be expected to influence QOL in the context of the disease process in question.
- This improved sensitivity, however, comes at the cost of a lack of generalizability, in that the survey is only useful for those specific issues (e.g., disease, symptom, procedure).

Table 54.8. Attributes of well-performed QOL studies.

Trial design	Prospective
Survey choice	Depends on intent, usually combination of generic, disease-specific, and/or modular; must justify survey(s) chosen
Survey psychometric characteristics	Valid, reliable, sensitive to change, interpretable
Total survey length	<100 questions (<30 min to complete)
Source of information	Patient whenever possible
Method of administration	Self-administered, if not possible at least consistent approach
Missing data	Defined approach (imputed, deleted), report number missing all and/or part of data
Scoring	Report source of algorithm used
Analysis	Both univariate and multivariate, include potential confounders in model; correct for multiple comparisons
Reporting	Report both descriptive and traditional statistics

- Some examples of targeted surveys for colorectal surgery include the European Organization for the Research and Treatment of Cancer’s Quality of Life Questionnaire for ColoRectal cancer (EORTC QLQ-CR38), the Inflammatory Bowel Disease Questionnaire, and the Rating Form of Inflammatory Bowel Disease Patient Concerns.
- One of the more significant factors preventing more widespread acknowledgment of QOL as an outcome is lack of interpretability of the data.
- Table 54.8 provides a summary of some of the key attributes for critiquing reports of QOL research.

55. Surgical Education: A Time for Change

A. Introduction

- It would seem that lifestyle concerns dominate the landscape of resident choice and are at the heart of the reason surgical specialties are losing some of the best and brightest to specialties with a more controlled lifestyle.
- Further exacerbating this trend is the reality that surgical specialties no longer have a monopoly on interventional procedures, and levels of compensation that have historically favored surgical specialties no longer do.
- In concert with a diminishing attractiveness of the specialty, there is the global move toward a diminished workweek for surgical trainees.

B. Cognitive Learning

- Perceived as a valuable educational endeavor, even to the extent that M&M is a requirement by the Residency Review Committees (RRC) for accredited surgery programs, there are differing opinions on how the conference should be conducted.
- The role of M&M conference is to review the process of patient's medical care. Adverse events and errors are discussed with the goal of improving patient care. In this conference, the care of patients that have had a complication is reviewed to determine what factors likely contributed to this complication and what alternative interventions or management strategies could have been used to decrease the likelihood of the complication or its magnitude.

- Case presentation conferences are used to present clinical scenarios about patients recently cared for highlighting certain aspects of their presentation, diagnosis, and treatment. As the clinical scenario is presented, a Socratic approach is used to question the participants.
- With increasing access to patient information, and a decreasing emphasis on restricting attendance at conferences, some programs have found it necessary to pay stricter attention to what is said in fear of potential use or misuse of that information.

C. Technical Skills Acquisition

- There is a growing body of opinion that observational learning has its limits, and experiential learning results in a quicker ascent to competency.
- One method to alter learning curves for surgical procedures is to shift some the training from the traditional environment of the operating room into an “ex vivo” laboratory. In so doing, there may be great promise in the deployment of surgical simulations.
- Many residency programs in surgery today have begun to develop a Skills Training Program.
- In general, laboratory curricula parallel training via graded responsibility in the operating room.
- Even experienced surgeons benefit from skills training.
- Summarizing a growing body of literature, it would seem at present that the report card on simulator training is mixed. It seems to have its major benefit for novice learners, durability of effect is an issue, and results to date have not been validated in large-scale studies.

D. Educational Challenges

- The structure of Graduate Medical Education is changing dramatically. For example, in the United States, in 2003, the Accrediting Council for Graduate Medical Education (ACGME) approved new duty hour standards for all accredited programs

including an 80-h weekly limit, rest periods, and limits on continuous duty hours. This reflects a worldwide trend to a reduction in workweek in general, and the surgical workweek in specific.

- The main issue that arises from this situation is how residents will be able to obtain the volume of experience previously encountered before the current restrictions placed on the time in which the resident can participate in patient care.
- This reality will force us to rethink our curricula, especially with a view to diminishing hours spent on “pure service requirements.” It may also force us to depart from a long-held surgical tradition that aspiring surgeons need a broad base of experiences, opting for a more focused approach to training.
- The first major activity of the project was identifying six general competencies for residents. These were identified by attention to how adequately physicians are prepared to practice medicine in the changing Healthcare Delivery System.
 - Patient care
 - Medical knowledge
 - Professionalism
 - Systems-based practice
 - Practice-based learning and improvement
 - Interpersonal and communication skills

E. New Directions

Strategically Planned Curricula

- The tenets of a strategically planned curriculum include the following elements:
 1. A restructuring of the education system to one that is modular, each module linked to specific objectives, including: cognitive knowledge, clinical skills, judgment, technical surgery, ethics, professionalism, and evidence-based training.
 2. A linking of objectives to an appropriate curriculum that is characterized by the following: ensuring that most if not all competencies developed during residency training relate directly to the desired career outcome; an adherence to the principles of residency training as outlined

in regulatory bodies such as the ACGME; that the curriculum is populated to the fullest by activities aimed at satisfying specific educational objectives; that it is learner-based; that it makes liberal uses of technology such as Web-based curricular materials, access to point of care (wireless) information, and a focus on providing data for evidence-based decision making and that it reestablishes anatomy as a backbone of surgical teaching, and includes cadaver dissection, prosection, and the use of virtual reality-based anatomy training models.

3. Dramatically changing the pace of technical skill acquisition by: developing a “pre-program” of basic skills focusing on technical skills fundamental to surgery; dramatically ramping up skills laboratory (ex vivo) practice, using virtual reality models, cadavers, surrogate tissue, and inanimate training models; developing programs of structured and deliberate practice; placing a premium on participatory learning as opposed to observational learning; maximizing the number and focus of real-world operations performed by residents and ensure that all learners are actively engaged in each real surgical opportunity; maximizing each “real” patient experience by the use of preoperative technical sessions, by videotape review of self and experts, and by debriefing sessions; developing specific teaching teams for each module; developing programs of faculty development for teaching surgeons; creating a link of faculty compensation to educational deliverables; and maximizing the opportunities for resident involvement in surgery by strategic scheduling initiatives.
4. Diminish wasted time during residency (educational dead space) by: eliminating or minimizing time wasted secondary to a hierarchical model; minimizing time wasted doing noneducational activities; increasing support services, increasing nurse autonomy, rationalizing calls, and optimizing technologic solutions to service problems; critically assessing the need for and the context of night call and seriously addressing the issue of sleep deprivation.
5. Incorporate meaningful assessment into the day to day running of the residency program by: rigorous, reliable,

and regular assessment; liberal use of formative assessment; linking evaluation instruments to goals, objectives, and desired competencies; training the evaluators focusing effort on performance-based evaluation systems; using a diverse array of assessors, including self, other health professionals, patients, peers, and faculty and documentation of technical proficiency within a learning module by testing for technical proficiency using sentinel cases.

- The American Board of Colon and Rectal Surgery has identified 17 categories of operative procedures. Residents who display insufficient numbers in five or more categories are not allowed to enter the certification process until they are able to furnish sufficient case numbers to meet the requirements.
- As the list submitted and certified reflects their year of training, additional training would be required for a surgeon with five or more deficiencies in order to meet this requirement.

F. Technology and Efficiency

- We have gone from the problem in which the difficulty was trying to identify information and acquire knowledge, to the problem of having so much information that the volume is overwhelming.
- We must rely on technologic advances.
 - For example, there may be efficiencies that can be gained by computer-based training (CBT).
 - For a vast array of knowledge, ready retrieval with a device such as a handheld device that can be carried in a coat pocket may provide the answer.

New methods of more efficient, reproducible, and objectively quantifiable education such as surgical simulators and endoscopic trainers will be used. Validated skills testing such as Fundamentals of Laparoscopic Surgery (FLS) will also be more widely available. As of July 2008, the FLS module will be available to all 4th and 5th year general surgery residents and all colorectal surgery residents. These newer educational modalities will ideally help standardize education and allow objective verification of minimum requisite baseline skills.

56. Legal Considerations

A. Introduction

- The ever-increasing frequency and often crushing severity of malpractice claims and lawsuits, databank reporting, Web-based consumer claims data, new privacy requirements, increasing clinical demands, greater government regulation and enforcement activity, and spiraling malpractice premiums have caused many physicians to leave practice, retire early, or relocate to more defendant-friendly lawsuit jurisdictions.

B. Medical Malpractice

Elements of Malpractice

- The elements that must be proved by a plaintiff to prevail in a medical malpractice case are determined by the laws of the various states.
- In general, medical malpractice is established when it is proved, by a preponderance of the evidence, that a patient sustained an injury as a result of an act or omission of a physician or surgeon that would not have occurred had the physician or surgeon exercised ordinary skill, care, and diligence.
- What a “physician or surgeon of ordinary skill, care, and diligence would or would not have done under like or similar conditions or circumstances” is called the standard of care.
- The standard of care for a physician or surgeon in the practice of a board-certified medical or surgical specialty should be that level of care expected of a reasonable specialist practicing

medicine or surgery in that same specialty, regardless of geographical considerations or circumstances.

- Negligence occurs when the care falls below the standard of care. A case can include single or multiple allegations of negligence.
- When negligence is proved in the courtroom, the departure from the standard of care must also be a proximate cause of the injury to the patient for the plaintiff to prevail. Thus, there must be a cause and effect relationship between the care and the harm.
- For there to be a plaintiffs' verdict, the jury must believe that (1) there was a departure from the standard of care, *and* (2) that the departure from the standard of care was a cause of the patient's injury.
- For the defense to prevail, the jury must believe that either (1) or (2) above were *not* proved by a preponderance of the evidence – or that neither were proved.

Recurring Malpractice Themes

- A study of medical malpractice cases involving colon and rectal disease involved a retrospective review of all cases tried in the federal and state civil court system over a 21-year period from 1971 through 1991 remains instructive today. The study identified 98 malpractice cases over that period of time from a computerized legal database. The 98 cases included 103 allegations of negligence. The nature and frequency of allegations were as follows:
 - 43%: Failure to timely diagnose disease (principally cancer and appendicitis)
 - 24%: Iatrogenic colon injury
 - 15%: Iatrogenic medical complications during diagnosis or treatment
 - 10%: Sphincter injury with fecal incontinence from anorectal surgery or midline episiotomy
 - 8%: Lack of informed consent (usually regarding extent of procedures or endoscopy)
- Risk management suggestions relevant to colon cancer screening include using authoritative screening guidelines, documenting informed consent and refusals, assessing family histories, recommending that family members of at-risk patients

be contacted, repeating sigmoidoscopies and colonoscopies when the preparation is inadequate, and documenting both cecal intubation and careful withdrawal techniques.

Lawsuit Stress

- Communications with your attorney are confidential and are protected by a privilege similar to the physician–patient privilege. Attorneys representing physicians usually advise their clients not to discuss the case with others for fear of losing the protections available through the attorney–client privilege.
- Many insurance companies and medical institutions provide resources for defendant physicians that enable them to discuss their lawsuit and their feelings of uncertainty and isolation with counselors or colleagues in a protected manner. Conversations with psychotherapists are generally privileged and not admissible in the courtroom as evidence in the case.
- Remember that your emotional stability is critical to the successful defense of the litigation.

C. Informed Consent

- Informed consent is a patient’s agreement to a medical procedure or other treatment after the person has been informed of the likely benefits, significant risks, and the alternatives of the treatment.
- In reality, few cases are prosecuted exclusively on the issue of informed consent, and juries do not customarily award damages solely for a lack of informed consent.
- The informed consent discussion is at the heart of physician–patient communication and is usually an important component in the defense of the main medical or surgical issues in every case.
- The physician should discuss the procedure or treatment with the patient and obtain and document informed consent as close to the date of the procedure or treatment as reasonably possible, e.g., within days to several weeks.

Obtaining Informed Consent

- Obtaining informed consent is primarily a physician obligation.
- Obtaining a patient's informed consent involves more than securing a patient's name on a form. It is a communication process in which the physician should discuss the following information with the patient:
 - The patient's diagnosis, if known
 - The nature and purpose of the proposed treatment or procedure
 - The risks and benefits of a proposed treatment or procedure
 - Alternatives (regardless of cost or insurance coverage)
 - The risks and benefits of the alternatives
 - The risks and benefits of not receiving or undergoing the treatment or procedure

Proving a Case of Lack of Informed Consent

- Depending on variations in state laws, plaintiff attorneys typically must prove the following elements to establish a prima facie case of lack of informed consent by a physician:
 - The physician failed to disclose to the patient and discuss the material risks and dangers inherently and potentially involved with respect to the proposed therapy, if any.
 - The unrevealed risks and dangers which should have been disclosed by the physician actually materialize and were the proximate cause of injury to the patient, and
 - A reasonable person in the position of the patient would have decided against the therapy had the material risks and dangers inherent and incidental to the treatment been disclosed to him or her before the therapy.
- Whether risks are material is normally an issue decided by a jury.
- A risk that is either *severe*, such as death, or *frequent* are usually risks that are considered material.

Documentation of Informed Consent

- Informed consent is usually documented with formal consent forms requiring the patient's signature.
- Forms can be challenged and criticized in the courtroom. A form containing errors, or one that is incomplete, can distract a jury from the real issues involving informed consent.

- Claims of lack of informed consent are most successfully defended when a jury is persuaded that the physician had a meaningful conversation with the patient.
- In addition to a consent form, a chart notation made by the doctor, in the doctor's own words or handwriting, is usually very helpful.
- Producing a diagram that was drawn for the patient to explain the procedure can be persuasive for jurors. Similarly, patient information sheets or pamphlets are effective communication devices and serve well in the litigation defense.
- Listen carefully to your patients' questions. Answer questions in a friendly but candid manner. Note in the chart the presence of any family members who are present for the informed consent discussion.
- Patients who are minors – usually those less than 18 years of age – may not normally consent for themselves. There are limited exceptions to that rule, e.g., patients who are living apart from their parents, or patients who are sufficiently mature to provide consent.
- Regardless of a minor's emancipation or maturity, it is wise to always obtain parental or custodial consent for elective procedures performed on minors.

D. Documentation

- A patient's medical record is often the star witness in any medical malpractice lawsuit.

Defensive Charting

- “If it's not documented, it didn't happen.” This adage serves as a good rule of thumb for all caregivers.
- Examples of concepts to consider inserting, when applicable, include the following:
 - Descriptions of bedside visits, especially when the physician has been paged multiple times
 - When you were with the patient and what you did
 - Your thought process and differential diagnosis
 - Presence of family members

- “Patient states that she understands a change in bowel habits should be reported”
- “Patient refuses colonoscopy because ...”
- “Patient not able to perform fecal occult blood test because ...”

Etiology Speculation

- The charting of speculative opinions can be as damaging as charting too little information. Not uncommonly, one member of the medical team speculates as to the etiology of an adverse event, and the speculated etiology is adopted as fact by other members of the healthcare team.
- Remember that causation is one of the four elements of medical malpractice, and it is frequently the most difficult of the four elements for the plaintiff to prove.
- ALERT! – *Iatrogenic* means “caused by manner or action of physician, not by medical treatment.” Use this word only when you are sure it is applicable.

Plaintiff’s Preclaim Review

- Because most medical malpractice cases are tried before juries (as opposed to judges), attorneys representing patients look for flaws in medical record documentation that can be exploited at trial.
- Other items that attorneys and their reviewing physicians look for are missing laboratory reports, missing radiology interpretations, or the results of any tests or procedures that were ordered but not present in the chart.

Record Tampering and Deception

- Improper alteration of the medical record is grounds for punitive damages and may result in loss of licensure. It should *never* be done. Postevent recording in a medical record should be done with proper disclosure of the timing and reason for the entry.
- Remember that your medical records are copied for multiple reasons, including insurance, compliance, and quality-review issues. Copies of any given patient’s medical records may exist elsewhere, even at other healthcare facilities.

- Plaintiffs' attorneys routinely request copies of the same medical records from multiple sources. This is done to ensure that all records are gathered, and to determine whether discrepancies exist among the various copies, e.g., a late entry on one copy that does not appear on another copy.
- Evidence that a surgical error was known to the physician but concealed from the patient would almost certainly flame juror anger and result in a significant adverse verdict. Sponges, needles, and other "foreign objects" inadvertently left behind in the patient during surgery and later discovered by X-ray should be immediately disclosed to patients.

Computerized Medical Records

- All patient records, whether paper or electronic, are discoverable and admissible in medical malpractice lawsuits.
- Physicians who record entries in computerized medical records must become familiar with the use of electronic medical systems and should understand some dangers inherent in these computerized systems. For example:
 - BEWARE drop-down menus and checklists
 - BEWARE prefabricated medical descriptors
 - BEWARE prefabricated informed consent notations
 - BEWARE easy click-on techniques
- Physicians should use "free text" whenever necessary and appropriate. It is easier to explain and defend "your own words" in describing the care of a patient than the words of a computer programmer who has written a menu of typical patient diagnoses in drop-down menus or other coded formats.

E. Communication

Adverse Events, Bad News, and Apologies

- When an untoward and/or unexpected event occurs involving a patient, communication is critical for quality care and for responding to later claims of malpractice. First and foremost, the patient's medical needs must be promptly addressed. Coordination of ongoing care, including consultation and appropriate follow-up, is a critical first step.

- As soon as practicable after the event, the patient and family should be informed of the event and its potential consequences to the patient. This communication should be respectful and sympathetic.
- The discussion should be preliminary to a more detailed conversation that should occur after more facts are available.
- Without assigning blame or criticizing other practitioners, the patient and family should be informed that the event occurred, the current and future consequences of the event to the patient, and what steps have been taken to address the patient's medical condition.
- If the underlying causes for the event are not yet known, care should be taken not to speculate about those causes.
- The patient and family should be told that additional information will be conveyed to them as it becomes known, and that a more thorough discussion will occur within a set period of time, ideally 24 h.
- It is usually advisable to contact a risk manager or in-house legal counsel, if applicable, when the critical incident occurs in an institution where such personnel are available.
- It is advisable for one member of the institutional team to be designated as the liaison with the patient and family so that consistent information is being delivered.
- Physicians and institutions should be willing to express sympathy. An apology expressing sorrow that the patient experienced the event may be appropriate but should be carefully worded, e.g., "We are sorry you have experienced this complication."
- At family meetings, the family members should have an opportunity to ask all of their questions.
- All discussions with the patient and family members after the incident should also be clearly described, including the identity of persons present at the family meetings and what was said.

Electronic Mail

- The Federal Health Insurance Portability and Accountability Act (HIPAA) of 1996 provides regulation for electronic transmission containing protected health information such as confidential medical information.
- HIPAA provides that healthcare providers have in place appropriate administrative, technical, and physical safeguards to protect the privacy of protected health information (PHI).

- The HIPAA regulations do not provide a specific regulatory scheme for email communication, but they do require that providers have procedures that limit disclosures of PHI to the amount reasonably necessary to achieve the purposes of PHI disclosures.
- The Internet is not considered a secure medium for transmitting confidential data unless both parties use encryption technology.
- It is advisable for physicians to keep either paper or electronic copies of emails to and from patients that are relevant to patient treatment. These email copies should be maintained in the patient's medical records just as traditional paper correspondence would be.

Health Insurance Portability and Accountability Act

- HIPAA provides national privacy protection for patients.
- Generally speaking, PHI is any information that is created (or received) and maintained by a covered entity related to the health or health care of a patient (or payment related to the health care) that directly or indirectly identifies the patient.
- HIPAA provides that healthcare providers must make a good faith effort to give each patient a Notice of Privacy Practices that describes the privacy practices of the healthcare provider.
- HIPAA permits treating physicians to disclose to a patient's family members, other relatives, close personal friends, and others identified by the patient any PHI that is directly relevant to such person's involvement with the patient's care or healthcare payments.
- Before making any of these disclosures, a physician should either obtain the patient's agreement to the disclosure or reasonably infer from the circumstances that the patient does not object. Research and Innovative Surgery

Research Versus Innovative Practice

- It is often not clear when innovative therapy crosses the line into the research arena.
- Research is usually described in a formal protocol, and departures from standard practice are not necessarily "research."
- Regulation of the practice of medicine has historically been the exclusive province of the state medical boards and other state regulatory authorities.
- When medical practice crosses the line into "research" involving "human subjects" or investigational drugs, devices, or

other test articles, however, the activity becomes subject to the regulation of the federal Office for Human Research Protection (OHRP) or the FDA.

Database Registries

- In theory, physicians who engage in innovative treatment that does not involve a systematic design, a research protocol, a prospective intent to publish, or an investigational item are not regulated by either OHRP or FDA.
- Over the past decade, however, OHRP has expressed its view that the systematic collections of data performed off-chart, especially if published, may carry an implicit prospective intent and are considered research. These may include ongoing patient registries, including outcomes data; tissue banks; static databases, including ad hoc research from closed trials; and even retrospective studies, including chart reviews, if a prospective intent to publish was present.

Promotional Prohibitions

- Physicians who conduct FDA-regulated research are prohibited from representing in a promotional context that an investigational new drug, device, or other test article is safe or effective (or otherwise beneficial) before it has received regulatory approval.

Insider Trading

- If you are involved in clinical trials for pharmaceutical companies or biotechnology companies whose securities are publicly traded, you may have certain obligations to protect the confidentiality of sensitive information that you acquire.

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