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M.J. Stamos · S.R. Steele *Editors*

The ASCRS Manual of Colon and Rectal Surgery

Second Edition

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Preface

Similar to the first, the second edition of the American Society of Colon and Rectal Surgeons' (ASCRS) Manual is abstracted from and is a companion to the second edition of the *ASCRS Textbook of Colon and Rectal Surgery*, Beck DE, Wexner SD, Roberts PL, Saclarides TJ, Senagore AJ, Stamos MJ eds. New York: Springer; 2011. It is yet another resource representing ASCRSs ongoing major commitment to education. The purpose of the second edition 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 second edition of 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*), the ASCRS Textbook, and the ASCRS electronic efforts such as CREST.

Readers of the second edition of the ASCRS Manual are strongly encouraged to consult the second edition of the ASCRS Textbook for in-depth discussions, clarification of content, and appropriate citing 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

Jose Marcio Neves Jorge and Angelita Habr-Gama

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.

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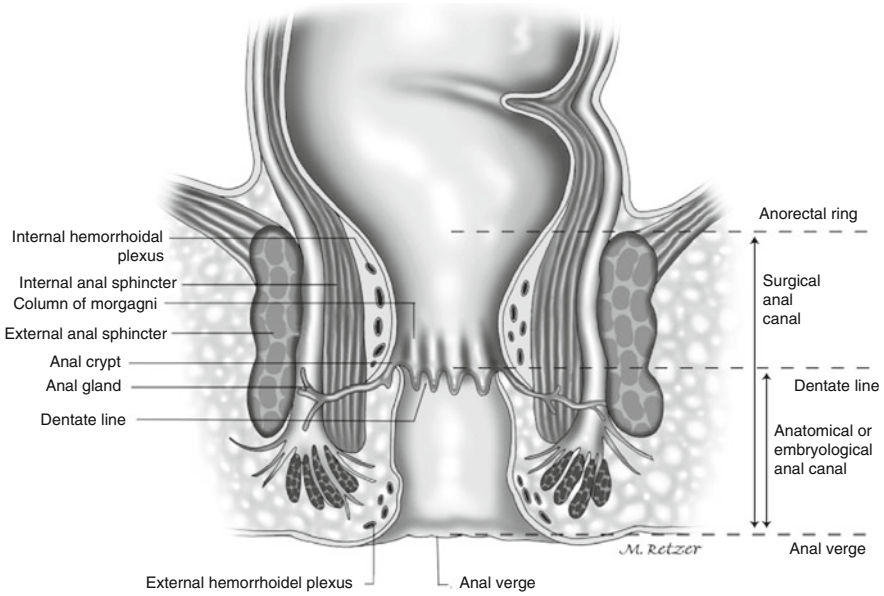

Fig. 1.1 Anal canal

Anatomic Versus 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).
- 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).

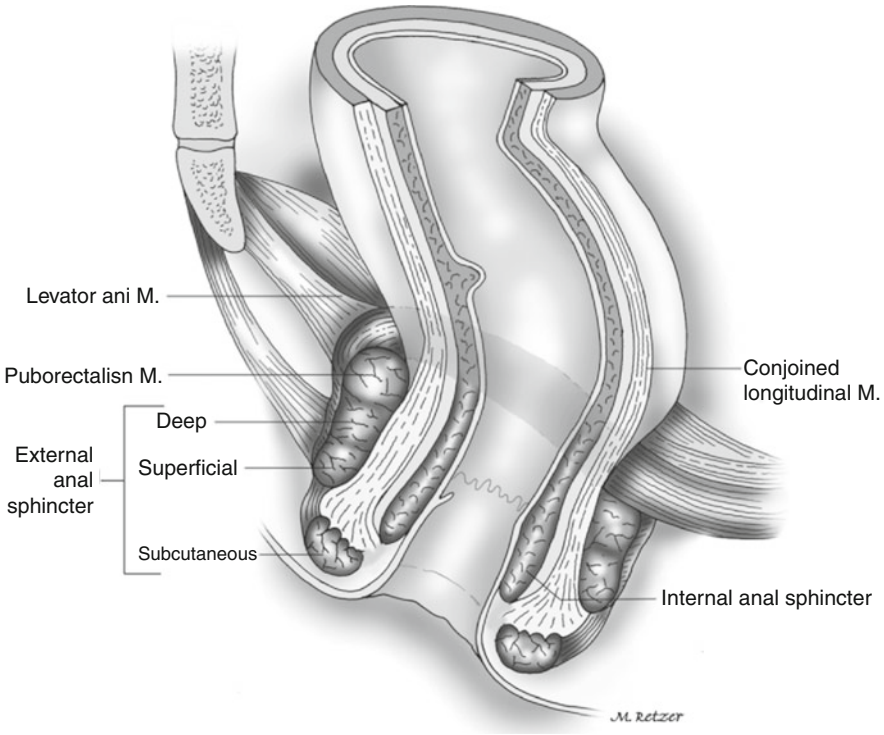

Fig. 1.2 Muscles of the anal canal

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.

- 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, and magnified by voluntary, reflex, and resting external anal sphincter contractile activities.
- In response to conditions of threatened incontinence, such as increased intra-abdominal 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 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.

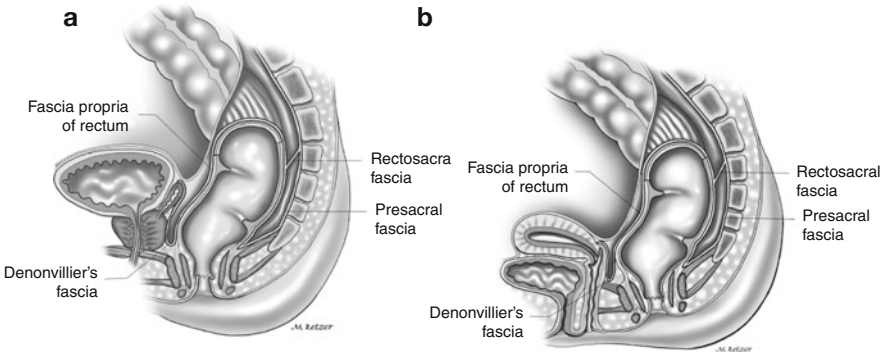

Fig. 1.3 Fascial relationships of the rectum: (**a**) male, (**b**) female

- 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 the 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 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 S4 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 S3 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 para-aortic 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 L1, L2, and L3 (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 (S2, S3, and S4).
- 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

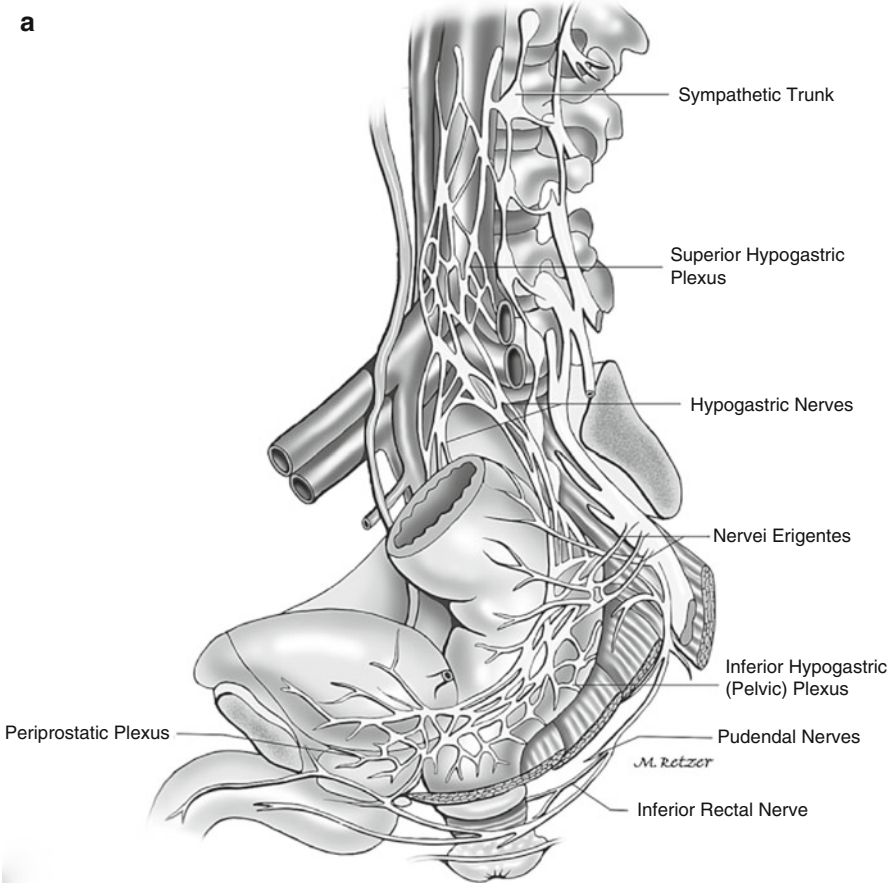

Fig. 1.4 (**a**, **b**) Innervation of the colon, rectum, and anal canal

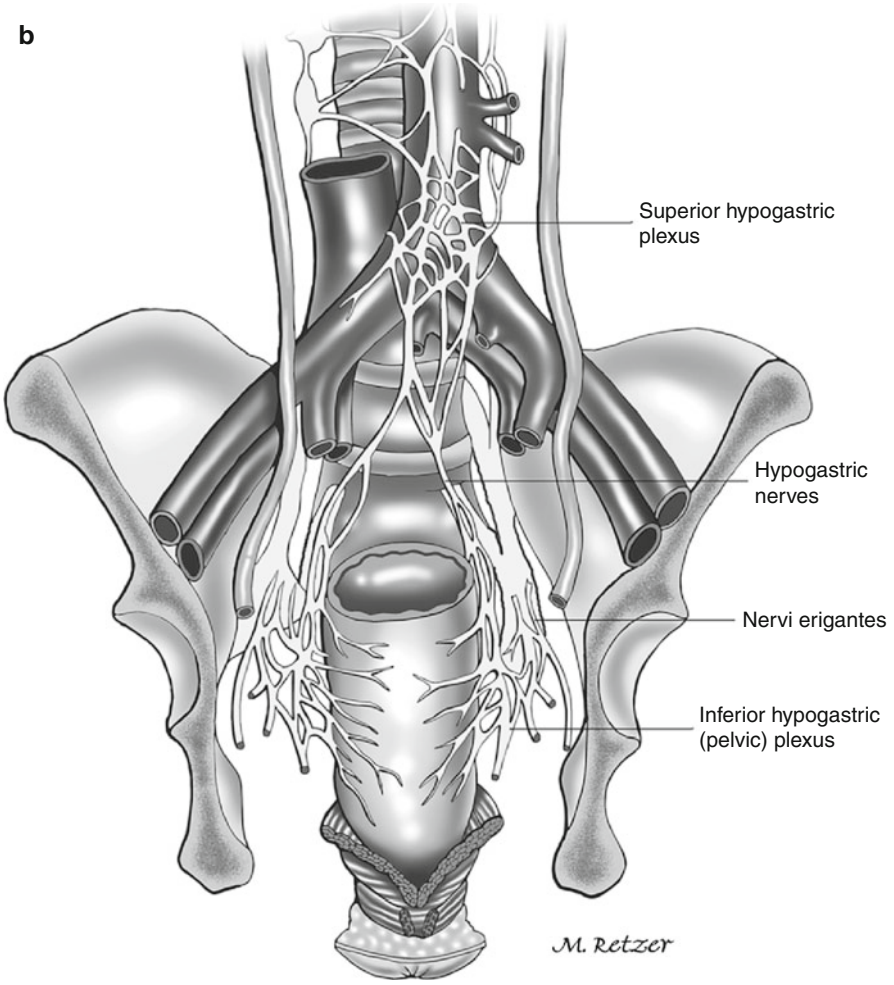

Fig. 1.4 (continued)

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 15to 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.

- 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 (L5) and parasympathetic nerves (S2, S3, and S4) 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 (S2 and S3) and by the perineal branch of S4. 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, supralevator, and retrorectal spaces (Fig. 1.5a, b).
- The ischiorectal fossa is subdivided by a thin horizontal fascia into two spaces: the perianal and ischiorectal.

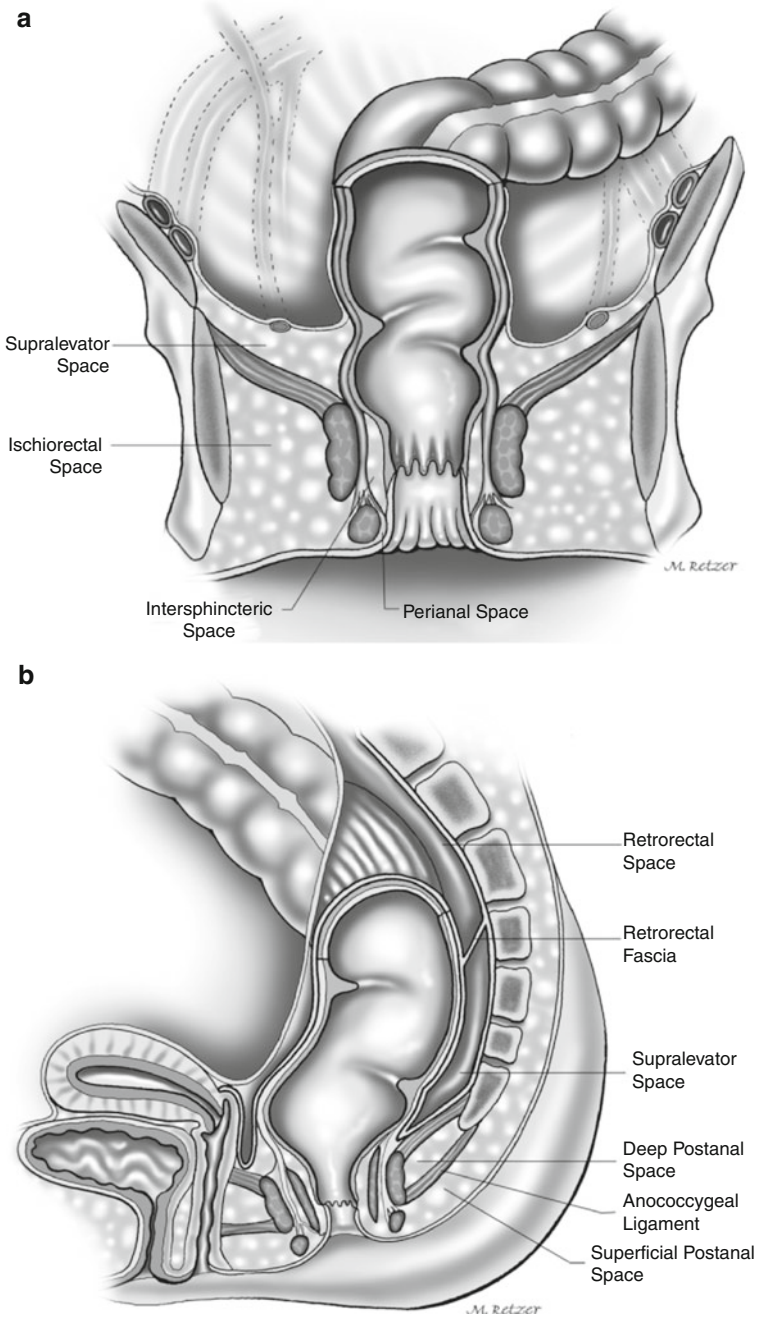

Fig. 1.5 Para-anal and pararectal spaces. (**a**) Frontal view. (**b**) Lateral view

- 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 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 retrosphincteric 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 supralevator spaces are situated between the peritoneum superiorly and the levator ani inferiorly.
- Supralevator 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.

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 or the vagina in women passes 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).

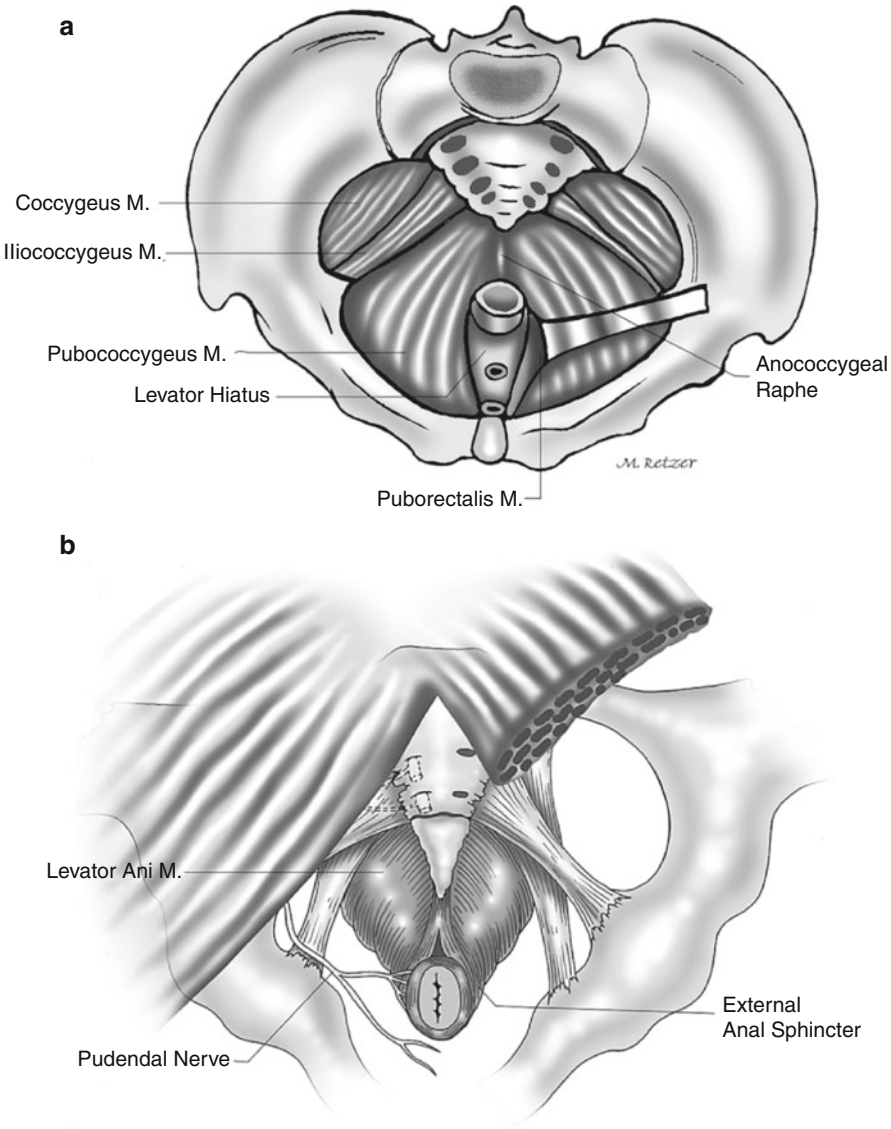

Fig. 1.6 Levator ani muscle. (**a**) Superior. (**b**) Inferior surface

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.

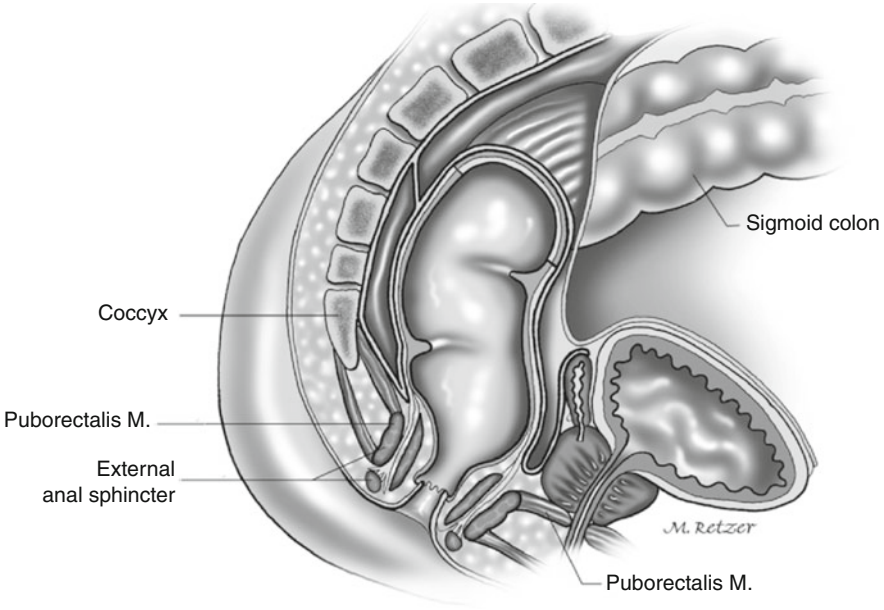

Fig. 1.7 The anteriorly directed pull of the puborectalis contributes to the angulation between the rectum and anal canal, the anorectal angle

- 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 the 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 rectosigmoid 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 L1 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–L3, 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 the 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, is 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 para-aortic 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.

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 S2, S3, and S4 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.

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

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.

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 to the 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 nonrotation, 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 S2, S3, and S4 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 (Littré'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 intrauterine 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. Colonic Physiology

Ursula M. Szmulowicz and Tracy L. Hull

Colonic Function

Salvage, Metabolism, and Storage

- The colon plays a role in digestion by fermenting complex carbohydrates and proteins that prove resistant to digestion and absorption in the more proximal intestine.
- Ten percent of ingested carbohydrates enter the cecum and are fermented by saccharolytic and proteolytic species of bacteria, the majority of which are obligate anaerobes.
- The diverse end products of bacterial fermentation include complex carbohydrates (fiber) and the short-chain fatty acids: butyrate [15 %], propionate [25 %], and acetate [60 %].
- Complex carbohydrates are fermented primarily in the ascending and proximal transverse colon, while proteins are fermented in the distal colon.
- Dietary prebiotics such as inulin result in saccharolytic fermentation.
- Fermented proteins are converted into short-chain fatty acids, branched-chain fatty acids, amines, ammonia, phenols, indoles, and sulfurs. Some of these products are considered potential etiologic agents for colon cancer and ulcerative colitis.
- Residual products of bacterial fermentation such as carbon dioxide, hydrogen, and methane are absorbed or passed with the feces.
- Dietary fats are usually expelled with the stool.

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- An average of 400 mmol/day (range of 150–600 mmol/day) of short-chain fatty acids is produced in the colon. More than 95 % of short-chain fatty acids are immediately appropriated by the colon.
- Reclamation of undigested matter in the colon provides 5–15 % of the total caloric needs of an individual.
- Short-chain fatty acids are incorporated as the basic elements for mucin synthesis, lipogenesis, gluconeogenesis, and protein production.
- Butyrate, the least abundant of the short-chain fatty acids, acts as the primary energy source for the colonocyte, supplying 70–90 % of its energy requirements. Colonocytes receive their nourishment solely from luminal substrates, not from the bloodstream.
- Butyrate also advances colonic cell proliferation and differentiation, repair, and immune function as well as promotes the absorption of water, sodium, and chloride from the colon, acting as an antidiarrheal agent.
- Fewer butyrate transporters are present in human colonic adenocarcinomas, resulting in a decrease in the utilization of the trophic butyrate by malignant cells. In vitro studies of cancer cell lines identified apoptosis, nonproliferation, and differentiation after the administration of butyrate.
- Prebiotics, primarily nondigestable oligosaccharides, are slowly fermentable foods that selectively propagate microbial proliferation and/or activity.
- In contrast, probiotics represent active bacterial cultures that benefit the host by replenishing the colonic microenvironment.
- Synbiotics combine the action of pre- and probiotics.
- The beneficial effect of these supplements is attributable to an increased production of butyrate, changes in mucin production, or interference in the binding of pathogenic bacteria to the colonic mucosa.
- Currently, probiotics are prescribed in cases of disturbed microbial balance, such as antibiotic-associated diarrhea.
- In the future, pre- and probiotics may become important supplements to promote health and to prevent illness.
- The colon demonstrates regional differences but does exhibit adaptability.
  - The proximal colon is more saccular and serves as a reservoir.
  - The distal colon is more tubular and performs as a conduit.
  - The character of the luminal contents impacts transit times. Large volumes of liquid quickly pass through the ascending colon but remain within the transverse colon for as long as 20–40 h; in contrast, a solid meal is retained by the cecum and ascending colon for longer periods than a liquid diet.
  - Salvage of water and electrolytes occurs primarily in the proximal colon.

Transport of Water and Electrolytes

- The colonic mucosal surface area is approximately 2,000 cm^2. The colonic mucosa assists in fluid homeostasis.
- The surface epithelial cells are primarily responsible for absorption, while the crypt cells are involved in fluid secretion.
- Water is passively absorbed along an osmotic gradient, enabled by a luminal sodium concentration lower than that of the epithelial cells.
- Normally, the colon is presented with 1.5–2 L of water daily.
- Approximately 90 % of this water is reclaimed by the colon, leaving 100–150 mL in the feces. Approximately 200 g of solid feces per day is produced following fluid and electrolyte absorption and secretion as well as bacterial activity.
- The ascending colon demonstrates the greatest absorptive capability.
- As a consequence, diarrhea more consistently ensues after a right as opposed to a left hemicolectomy.
- Fluid retention is promoted by the antidiuretic hormone.
- When challenged, the colon, with the additional contribution of the sigmoid colon and rectosigmoid, is able to save a further 5–6 L of intestinal water daily.
- This facility for fluid salvage is contingent upon the composition, rate of flow (less than 1–2 mL/min), and amount of the effluent.
- Fluid secretion in the colon only transpires in the presence of diverse secretagogues, such as laxatives, bacterial endotoxins, hormones (e.g., VIP), and endogenous substances (e.g., bile acids).
- Under normal conditions, the colon principally absorbs sodium and chloride but secretes bicarbonate and potassium.
- If required, the colon is able to increase its salvage of sodium to 800 mmol/L/day.
- The transport mechanisms for sodium absorption, located on the luminal surface of the epithelial cells, vary throughout the colon: a Na^+/H^+ exchange channel in the proximal colon and an electrogenic sodium-specific channel (ENaC) in the distal colon and rectum.
- The Na^+/H^+ exchange channels (NHE 2 and 3) are coupled to the Cl^--HCO_3^- exchange channels. The activity of the electrogenic sodium-specific channel in the distal colon and rectum is requisite for the desiccation of stool.
- These two types of transport channel allow for the passive diffusion of sodium into the colonic epithelial cells along an electrochemical gradient, consisting of a low intracellular sodium concentration (<15 mM) and a negative intracellular electrical potential difference as compared to the lumen.
- This favorable electrochemical gradient is created by the active extrusion of sodium via the Na^+/K^+ ATPase pump on the basolateral membrane of

the epithelial cell: three sodium ions are expelled in exchange for two potassium ions.
- Aldosterone, a mineralocorticoid secreted by the adrenal gland in response to sodium depletion and dehydration, enhances fluid and sodium absorption in the colon.
- The absorption of sodium is further promoted by somatostatin, α_2-adrenergic agents (e.g., clonidine), and the short-chain fatty acids.
- In the proximal colon, chloride is traded for bicarbonate via the Cl^--HCO_3^- exchange channel found on the luminal surface of the epithelial cells; the activity of this channel is linked to the Na^+/H^+ exchange protein.
- However, chloride also is absorbed through a Cl^--HCO_3^- exchange channel that is not associated with sodium.
- Chloride absorption is supported by an acidic luminal milieu. The transport mechanism for bicarbonate secretion is poorly understood.
- Potassium transport is primarily a passive process, following the movement of sodium across cell membranes.
- The H^+/K^+ ATPase actively conveys potassium into the epithelial cells of the distal colon and rectum.
- Potassium secretion, combined with potassium derived from bacteria and colonic mucous, may explain the relatively high concentration of this electrolyte—50–90 mmol/L—in stool.
- Approximately 0.4–1 g of urea enters the colon daily and is converted by colonic microorganisms into ammonia, which is then passively absorbed by the surface epithelial cells.
- Ammonia is also derived from dietary nitrogen, the sloughed mucosal lining, and bacterial waste.
- The majority of the ammonia that reaches the colon is returned via the enterohepatic circulation to the liver, where it is refashioned into urea.

Colonic Motility

Methods to Measure Colonic Transit

- Altered motility plays a role in various gastrointestinal disorders, but it is poorly understood due to the inaccessibility of the colon for direct study.
- Bowel questionnaires assess stool frequency and colorectal transit time (75 % of total intestinal transit time).
- Techniques to determine colonic motility begin with the calculation of colonic transit time via markers, scintigraphy, and wireless capsules.

Radiopaque Markers

- Total and regional colonic transit times are reflected by the number and the location of the markers on sequential abdominal radiographs.
- For men, the average total colonic transit is 30.7 h (SD 3.0) and for women, 38.3 h (SD 2.9).

- Various protocols for this type of examination exist, all of which suggest the cessation of all laxatives 48 h prior to swallowing the markers:
  - In one approach that focuses on total colonic transit, an abdominal radiograph is obtained 5 days after taking a capsule containing 20 markers. A normal study demonstrates evacuation of 80 % (14) of the markers. The retention of more than 20 % of the markers suggests slow transit constipation.
  - Currently commercial available markers (Sitzmarkers™, Konsyl Pharmaceuticals) contain 24 markers in the capsule.
  - A second variation involves ingesting the capsule on Sunday evening and obtaining abdominal x-rays on days 1, 3, and 5. The film on the first day provides evidence that gastric and small motility are grossly normal if all the markers are in the colon. A normal study shows the passage of 80 % of the markers by day 5.
  - In another alternative, patients ingest single capsules (containing 24 markers) on 3 successive days, with only one abdominal radiograph done on day 4 of the study. The number of markers present equals the colonic transit time in hours.
  - An accumulation of the markers in the rectosigmoid indicates a dyssynergic defecation pattern (outlet obstruction).
  - The reliability of the technique is affected by patient compliance as well as by differences in the interpretation of the results.

Scintigraphy

Colonic scintigraphy measures colonic transit by following the passage of a radioactive isotope that is ingested as a delayed release capsule or placed directly in the cecum by orocecal intubation. The delayed release capsule, coated with the pH-sensitive polymer methacrylate, is comprised of activated charcoal or polystyrene pellets labeled with either ^{111}In or ^{99m}Tc. The coating dissolves at the pH of 7.2–7.4 found in the distal ileum, after which the radioactive material is delivered into the colon.

- Images are taken with a gamma camera at specified intervals, usually at 4, 24, and 48 h after consumption of the isotope, although this can be performed as frequently as twice daily.
- Segmental transit is usually determined for the ascending, transverse, descending, and rectosigmoid regions of the colon. The proportion of the counts is calculated in each section and then multiplied by a weighing factor: 0 for the cecum, 1 for the ascending colon, 2 for the transverse colon, 3 for the descending colon, 4 for the rectosigmoid colon, and 5 for stool.
- The results are expressed as the geometric center of the isotope mass at any given time point, with a low count indicating that the isotope is close to the cecum and a higher count that it has progressed more distally.
- For clinical use, the total percentage of retained isotope as compared to normal data appears to be the most convenient reporting system.

- Scintigraphy correlates well with the radiopaque marker technique in assessing colonic transit, with a similar sensitivity in diagnosing patients with slow transit constipation.
- The total exposure to radiation is also equivalent. Due to its greater costs, in most cases scintigraphy serves as a research instrument.

Wireless Motility Capsule

- The wireless motility capsule (SmartPill®) uses a capsule containing miniature intraluminal pressure, temperature, and pH measurement devices.
- The capsule is ingested, after which continuous recordings are obtained in an ambulatory setting, with the data captured over 5 days via a wireless instrument.
- A drop in pH and a change in motility delineate the transition from the distal ileum into the cecum. From these data, whole gut transit and colonic transit can be separated and calculated.
- In one trial, the results from the capsule approach correlated well with those acquired from the radiopaque markers, with a similar sensitivity and specificity in detecting abnormal transit in those patients with constipation.
- The capsule is able to gauge phasic colonic contractions but not colonic motor patterns.
- This costly procedure is not widely employed but is attractive in that radiation exposure is avoided and patient compliance is facilitated.

Techniques to Record Colonic Motility

- Colonic motility is gauged by the monitoring of electrical activity using surface electrodes or of intraluminal pressure via a manometry or barostat apparatus.
- Indirect assessment of colonic motility has been hindered by the instruments available, colonic anatomy, the need for prolonged readings, and the absence of standardization.
- Placement of the intraluminal devices is difficult, requiring either oral or nasal intubation or colonoscopy; furthermore, application of the surface electrodes demands surgery.
- Additionally, the necessity to purge the colon of stool may impact the results, producing an increase in the number of high-amplitude propagated contractions, although these findings are conflicting.
- Determinations of colonic pressure are further influenced by artifact from extrinsic forces such as cough, straining, and sneezing.
- Recordings are usually obtained over 6 h in the laboratory and over 24 h in an ambulatory setting.
- Most of these approaches are in the researcher's domain.

Manometry

- Colonic manometry uses a flexible catheter (solid-state or a water-perfused catheter system) that is inserted into the colon. The water-perfused system increases the amount of fluid in the colon, which may alter results, while solid-state catheters are fragile, expensive, and sensitive to corrosive damage from colonic irritants.
- The validity of the readings depends upon the proper placement of the catheter. As noted, the introduction of the catheter occurs via an oral or nasal route, confirmed with fluoroscopy, or by colonoscopy.
- To adhere to more physiologic conditions, unprepared colons are currently advocated, despite the impediment presented by the retained stool to the retrograde placement of the catheters; in some cases, enemas are instead used.
- The patients are often asked to maintain a diary to mark events such as bowel movements, flatus, and meals.
- Manometry is well able to detect the changes in intraluminal pressure after eating or the administration of a colonic stimulant (e.g., bisacodyl).
- However, these variations in pressure do not consistently correspond to contractions, and contractions are not reliably identified. Measurements obtained from manometry are also affected by the luminal diameter at the location of the catheter tip.
- Manometry also recognizes patterns of motor activity due to the multiple recording sites along the catheter.

Barometry

- The colonic barostat device can record colonic tone, i.e., sustained contractions.
- The instrument includes a compressible polyethylene balloon, placed within the colonic lumen that is attached via tubing to a barostat—a cylinder containing a piston.
- The balloon is maintained at a low constant pressure such that it is continuously in close contact with the colon wall in a single location.
- Contraction of the colon constricts the balloon, reducing its volume by forcing air into the barostat; in contrast, colonic relaxation produces an increase in the volume of the balloon so as to sustain a constant pressure.
- Changes in the volume of the balloon reflect colonic tone, although phasic contractions are also assessed.
- However, patterns of colonic activity cannot be distinguished as measurements are obtained in only one site.
- Unlike the manometry technique, the barostat system is capable of detecting contractions that do not produce a significant pressure change, even in colonic segments wider than 5.6 cm.

Electrodes

- Electrodes placed on the serosal surface via surgery or on the mucosa by colonoscopy record the myoelectrical signals from the colon that result in muscular activity.
- The technique is seldom used due to ethical concerns.

Peristalsis

- Peristalsis represents the alternating waves of contraction and relaxation of the circular muscles of the colon wall.
- Fecal material is propelled antegrade through the colon by the contraction of the circular muscle proximal but the relaxation of the muscle distal to it, i.e., descending inhibition.
- During peristaltic activity, the saccular haustra—the product of circular muscle contraction—recede and then reform, first proximal to and subsequently at the level of the transferred material, again giving rise to colonic segmentation.
- The contribution of the longitudinal smooth muscle to colonic activity is unknown.
- The average rate of antegrade colonic transit is approximately 1 cm/h.
- The peristaltic reflex is thought to be initiated by luminal distention and, possibly, by chemical stimuli, which stimulate the enteric sensory neurons; ultimately, the enteric motor neurons—the effector cells—are activated via the intermediary of the enteric interneurons.
- The interneurons may also directly detect changes in smooth muscle length.
- The primary neurotransmitters involved in the peristaltic reflex include the excitatory acetylcholine and the inhibitory nitric oxide and adenosine triphosphate (ATP).
- Although the enteric nervous network primarily controls peristalsis, the extrinsic nervous system modifies the reflex, with the sympathetic nerves suppressing and the parasympathetic nerves promoting motility, especially during defecation.
- Interestingly, the parasympathetic nerves also assist in the synchronization of descending inhibition.
- The antegrade movement of the fecal bolus is further dependent upon the radius of the colonic segment, the consistency of the feces, and the pressure differential between segments.
- Colonic motility adheres to several patterns. Generally, contractions vary between tonic and phasic.
- The poorly understood tonic contractions are sustained events of slow onset, not necessarily inciting an elevation of the intraluminal pressure.
- Bassotti and colleagues further classify the briefer phasic contractile episodes as high- and low-amplitude propagated contractions and as segmental contractions.

- High-amplitude propagated contractions—also known as migrating long spike bursts, large bowel peristalsis, and giant migrating contractions—function to transport large volumes of feces over long distances.
- These contractions are believed to be the manometric equivalent of the mass movement—first identified on radiographic studies of the colon—whereby colonic contents are projected distally in seconds.
- The high-amplitude propagated contractions transpire between 2 and 24 times daily, with an average of approximately five to six times a day.
- These contractions, with an amplitude of 100–200 mmHg (average of 100 mmHg), persist for 20–30 s.
- The contraction usually begins in the proximal colon and is transmitted distally for 15 cm or longer, with the velocity gradually increasing to as fast as 1 cm/s as the impulse moves caudad.
- A contraction that starts in the proximal colon is conveyed farther than that commencing in the distal colon: 50 cm from the cecum and 20 cm from the sigmoid colon.
- More than 95 % of these contractions proceed antegrade; however, only one-third of these contractions result in the transit of fecal material.
- Moreover, not all instances of defecation, particularly those involving liquid stool, are incited by a high-amplitude propagated contraction.
- High-amplitude propagated contractions are considered the probable origin of the pressure spikes that occur upon morning waking (35 %) and after meals (50 %). The urge to defecate is likely attributable to these contractions.
- Borborygmi is thought also to arise from high-amplitude propagated contractions.
- The impetus for these contractions is incompletely comprehended. These contractions are elicited by cholinergic medications (e.g., neostigmine), eating, colonic distention, short-chain fatty acids, and laxatives (e.g., bisacodyl).
- However, only in 50 % of cases does colonic distention produce propagating activity.
- In patients with constipation, high-amplitude propagated contractions are decreased in number, amplitude, extent, and speed.
- The low-amplitude propagated contractions are still less understood. These contractions (5–40 mmHg)—also referred to as long spike bursts—last for 3 s.
- As with the high-amplitude propagated contractions, these contractions are strongly related to meals and the sleep-wake cycle.
- There may be an association with the passage of flatus and, in particular, liquid stool.
- Similar to the high-amplitude propagated contractions, these contractions are likely provoked by colonic distention.
- The mechanisms by which these two propagated contractions are regulated remain unclear. However, propulsive activity depends upon a functional enteric nervous system.

- Segmental contractions, presenting singly or in rhythmic or arrhythmic bursts, account for the majority of colonic activity, particularly at rest.
- These contractions appear with an amplitude of 5–50 mmHg.
- Found primarily in the ascending and transverse colon, this activity produces localized contractions of the circular and longitudinal muscles, in effect segregating the haustra.
- These segmental contractions, the correlate of myoelectrical short spike bursts, result in the slow, sequential antegrade or retrograde movement of colonic contents among the haustra, allowing for mixing of the material.
- Additionally, contact with the mucosal surface is maximized, which permits the absorption of intestinal water and electrolytes.
- Only 6 % of segmental contractions are rhythmic, with a frequency of 2–8 cycles/min; however, in the rectosigmoid region, a slower interval of 3 cycles/min is preeminent, possibly giving rise to a physiologic sphincter to aid in continence.
- Unlike other mammals, the human colon lacks cyclic motility.
- The human rectum has cyclic activity:
  - The rectal motor complex is comprised of phasic contractions with an amplitude of more than 5 mmHg.
- These phasic contractions appear at a cycle of 2–3/min, with each persisting for approximately 3 min. Yet, the interlude between these contractions ranges from 10 to 260 min.
- This phasic activity in the rectum and, potentially, the rectosigmoid may contribute to fecal continence, as it is correlated with an elevated anal canal pressure; this role is further suggested by the greater prominence of this activity at night.

Cellular Basis of Motility

- Colonic motor activity is driven and coordinated by the interstitial cells of Cajal, the intestinal pacemaker cells.
- In the absence of these cells, the intestinal smooth muscle is inactive.
- The interstitial cells of Cajal arise from smooth muscle precursor cells; that is, the cells are of mesenchymal, not neuronal, origin.
- These cells are classified by their location as ICC_{MY}—in the myenteric plexus, between the muscular layers; ICC_{SM}—in the submucosal surface of the circular muscle; and ICC_{IM}—within the circular and longitudinal muscles.
- The interstitial cells of Cajal are linked to the individual smooth muscle cells via intracellular gap junctions; the similarly coupled smooth muscle cells function as a single unit, or as a syncytium.
- The gap junctions allow for the passage of current—predominantly slow waves—from the interstitial cells of Cajal to the smooth muscle syncytium, leading to its depolarization.

- The interstitial cells of Cajal are believed to be mechanosensitive and able to transduce stretch stimulus from the distended colonic lumen into electrical activity.
- The ICC_{SM}—the primary pacemaker cells—continuously generate high-amplitude slow waves, at a frequency of 2–4/min, within the circular muscle layer.
- Unlike the other types of interstitial cells of Cajal, the ICC_{SM} are present only within the colon, solely in its proximal portion.
- A slow wave of sufficient charge produces a smooth muscle action potential, allowing for an influx of calcium into the smooth muscle cells via the L-type calcium channels and, thus, a brief contraction.
- The amplitude of the slow waves is greatest at the submucosal surface of the circular muscle, diminishing while traveling through the muscular wall.
- Slow waves migrate antegrade and retrograde along short segments of the colon, rapidly in the circumferential and slowly in the longitudinal axis; as waves of different inception meet, their propagation ceases, giving rise to non-propulsive mixing activity.
- A second pacemaker site may involve the $ICC_{MY.}$ In addition to the slow waves, the ICC_{MY} may initiate low-amplitude myenteric potential oscillations (MPOs) at a frequency of 12–20/min, which are conveyed to the circular and longitudinal smooth muscle.
- The MPOs possibly are the source of propagating contractions.
- Moreover, the ICC_{MY} synchronize the activity of the circular and longitudinal layers of the smooth muscle.
- As opposed to the ICC_{SM}, the ICC_{MY} are widespread throughout the colon.
- The etiology of the intrinsic electrical activity of the ICC_{MY} and ICC_{SM} is uncertain but may involve calcium-regulated nonselective cation channels or large-conductance chloride channels; the oscillations from the interstitial cells of Cajal remain even the absence of extrinsic neural input.
- The ICC_{IM} are thought to mediate such extrinsic input—from the enteric and autonomic neural networks—upon smooth muscle function; the release of acetylcholine and nitric oxide from excitatory and inhibitory neurons, respectively, results in alterations in the activity of the ICC_{IM}.
- Furthermore, the ICC_{IM} appear to augment the slow waves and MPOs from the ICC_{SM} and ICC_{MY}, respectively, as they are transmitted along the smooth muscle syncytium.
- Much still remains to be elucidated about the cellular basis of colonic motility.

Characteristics of Colonic Motility in Health

- Manometry studies have demonstrated a noncyclical pattern of colonic activity, which is mirrored by changes in colonic tone.
- The human colon follows a circadian rhythm in which sleep is associated with its relaxation and, thus, with a marked diminution of its pressure activity.

- However, as previously noted, the rectum and rectosigmoid display continued phasic activity during the night.
- Immediately after morning waking, a two- to threefold increase in colonic pressure activity—likely due to high-amplitude propagated contractions—occurs, inciting an urge to defecate in some cases.
- A similar rise in colonic activity transpires during brief nighttime arousals or during REM sleep.
- The mechanism by which the colon rapidly responds to these alterations in wakefulness is unknown.
- During the day, the transverse and descending colon reveal more pressure activity than the rectosigmoid colon. Moreover, less activity is seen in the transverse and descending colon of women, as compared to men.
- Oral intake also impacts colonic activity. Within 1–3 min of the initial bites of a meal, long before the food reaches the colon, segmental contractions begin in the proximal and distal colon, persisting for 2–3 h.
- This colonic motor response to eating, or gastrocolic reflex, also features a concomitant increase in the colonic smooth muscle tone, especially in the proximal colon, often affiliated with high-amplitude propagated contractions.
- The colon exhibits regional differences in its response to a meal: the proximal colon evinces a swifter but briefer duration of contractile activity than the distal colon.
- Although infrequently identified during scintigraphic studies, retrograde propulsion most commonly appears after meals as well as during morning waking.
- Colonic motility is instigated by a higher calorie meal (more than 500 kcal), fat, and, to a lesser degree, carbohydrates; in contrast, proteins inhibit motor function.
- The colonic response to eating includes two phases: an initial stimulation of the gastroduodenal wall mechano- and chemoreceptors, with a subsequent activation of receptors in the colonic wall.
- The means by which the gastrocolic reflex arises are unclear but may involve cholecystokinin, gastrin, serotoninergic input, or cholinergic stimuli.
- However, cholecystokinin antagonists do not block the reflex; also, infusions of high-dose cholecystokinin have no effect upon colonic activity although pancreatic exocrine secretion and gallbladder contraction are maximally stimulated.
- Interestingly, the colonic motor response to eating persists following a gastrectomy or spinal injury; yet, the colon must be in continuity for the reflex to take place.
- Stress, both physical and emotional, also influences colonic function. One study found that psychological stress induced a significant increase in propagating contractions, both in their frequency and amplitude,

throughout the colon, even in the absence of an appreciable autonomic response.
- Despite the withdrawal of the stressor, the augmented motor activity endured.
- In contrast, physical stress, consisting of exposures to extremes of temperature, precipitated a significant elevation in the frequency and amplitude of simultaneous contractions, which ceased immediately after the activity stopped.
- In some trials, low- and high-amplitude propagated contractions are stimulated by acute physical exercise.

Defecation

- The process of defecation involves the entire colon, not solely the anus and rectum.
- As already described, the majority of colonic activity—the segmental contractions—serves to retain fecal material so as to promote the salvage of intestinal water and electrolytes.
- However, periodically, colonic activity shifts in order to foster the expulsion of stool.
- Approximately 1 h prior to the act of defecation, an involuntary pre-expulsive phase is initiated, in which the frequency and amplitude of antegrade nonpropagating and, particularly, propagating contractions steadily increase throughout the whole colon.
- The early component of the pre-expulsive phase—the first 15–60 min—is characterized by propagating contractions that initially arise from the proximal colon but subsequently from the distal colon; this initial sequence is thought to transport stool into the distal colon, thus stimulating distal colonic afferent nerves, which in turn provoke further propagating sequences.
- During the late phase, consisting of the last 15 min, the point of origin of these contractions reverses from the distal to the proximal colon.
- Scintigraphic studies reveal that, in one bowel movement, 20 % of the ascending colon can be emptied; other evaluations indicate that nearly the entire colon may be evacuated of stool in a single defecatory action.
- A number of investigations identified antegrade high-amplitude propagated contractions in close temporal relation to defecation; yet, not all of these contractions necessarily precede or end in defecation.
- However, at least one high-amplitude propagated contraction of very high amplitude usually coincides with the urge to defecate.
- While the early activity is unnoticed, the late phase is often associated with the urge to defecate that occurs prior to the voluntary act of fecal evacuation.

Colonic Sensation

- Colonic sensation has proved a complicated, poorly understood topic.
- The colon itself contains no specialized sensory end organs. The normal physiologic processes of the healthy colon are largely unnoticed, with only fullness and an urge to defecate consciously perceptible.
- Naked nerve endings lie within the serosa, muscularis propria, and mucosa of the colon, while Pacinian corpuscles are found in the mesentery.
- Afferent nerve fibers reach the central nervous system via *parasympathetic* pathways and *spinal afferent nerves*, both of which display mechano- and chemosensitivity.
- The parasympathetic fibers convey sensory information from the proximal colon via the vagus nerve to cell bodies in the nodose and jugular ganglia and, from the distal colon, by the pelvic splanchnic nerves.
- The precise role of the parasympathetic afferent fibers remains unknown but likely involves unconscious reflex sensation, not painful stimuli.
- Sensory input from the colon is chiefly detected by spinal afferent neurons, primarily by those with their cell bodies within the lumbar dorsal root ganglia.
- These lumbar spinal afferent nerves travel with the sympathetic fibers within the lumbar splanchnic nerves from the colon by way of the inferior mesenteric ganglia.
- The lumbar spinal afferent fibers conclude in sensory endings throughout the entire large intestine, whereby pain, colorectal distention, mesenteric traction, and noxious mucosal stimuli are discerned.
- In contrast, the sacral spinal afferents, with their cell bodies in the sacral dorsal root ganglia of S2–S4, are thought to be concerned with a sensation of rectal fullness and an urge to defecate.
- These sacral spinal afferent fibers are borne along with the parasympathetic pelvic splanchnic nerves.
- Visceral pain sensation is carried by rapidly conducting Aδ fibers or by unmyelinated C fibers.
- The Aδ fibers are associated with the more localized “discriminative” pain, which persists for as long as the stimulus, and the C fibers in the diffuse “affective-motivational” pain, which continues beyond the duration of the catalyst.
- Sensory information is transported to the brain along the spinothalamic and spinoreticular tracts as well as by the dorsal column of the spinal cord.
- The spinothalamic tracts specifically transmit sensation from the Aδ and C fibers to the somatosensory cortex via the lateral thalamic nuclei or to the frontal, parietal, and limbic regions by means of the medial thalamic nuclei, respectively.
- The modulation of visceral sensation occurs through several methods. Enteroenteric reflexes mediated by the spinal cord produce variations in

the smooth muscle tone, leading to changes in the activation of the nerve endings in the intestine or mesentery.
- The perception of visceral pain is influenced by descending noradrenergic and serotonergic pathways that emanate from the reticular formation, hypothalamus, and frontal cortex.
- These fibers project to the dorsal horn of the spinal cord, where they modify noxious input from the visceral afferent nerves.
- The intersection of visceral spinal afferent nerves with somatic afferent nerves in the dorsal horn of the spinal cord produces the phenomenon of referred pain, in which visceral sensation is consciously recognized as somatic pain, located in a dermatome of the same embryologic origin as the visceral structure: T8–T12 for the midgut and T12–L2 for the hindgut.
- In addition, visceral afferent nerves from the colon relay information via collaterals to the reticular formation and thalamus, which induce alterations in affect, appetite, pulse, and blood pressure through autonomic, hypothalamic, and limbic system connections.

Disturbances in Colonic Physiology

Physiology of Constipation

- Constipation is a common complaint, with a prevalence of 2–28 % among Western populations.
- This disorder refers to infrequent bowel movements (fewer than three per week), hard or lumpy stools, incomplete evacuation, a sensation of anorectal obstruction, the need for manual maneuvers to facilitate defecation, and/or excessive straining.
- Individuals with constipation are an incredibly heterogeneous group, with wide variability in their clinical presentation and pathophysiologic etiology.
- The causes for constipation range from dietary, pharmacologic, structural to systemic.
- Many people become constipated due to dietary and lifestyle neglect. In the United States, fiber intake is overall low.
- Two primary roles of the colon, solidifying liquid chyme into stool and defecation, are dependent upon adequate dietary fiber: dietary fiber "normalizes" large bowel function.
- In particular, the bulkier stool produced by fiber supplementation stimulates propulsive activity, thus decreasing colonic transit time.
- The recommendation for adequate fiber intake ranges from 20 to 35 g/day for adults.
- For an individual on a 1,500–2,000 kcal/day diet, in order to include 15 g of fiber, 11 servings of refined grains and 5 servings of fruits and vegetables must be consumed.

- Fiber is classified as either soluble or insoluble, acting by differing mechanisms to increase stool weight.
- Soluble fibers such as oat bran provide rapidly fermentable material to the proximal colon, which allows for sustained bacterial growth.
- The consequent higher bacterial content of the stool results in the greater fecal mass. In an average bowel movement, 50 % of the stool weight consists of bacteria.
- Also, soluble fibers cause a rise in the excretion of lipid and fat, further boosting stool weight.
- In contrast, poorly fermentable insoluble fibers such as wheat bran, cellulose, and lignin augment stool weight by providing more undigested plant material for evacuation.
- One gram of wheat bran generates 2.7 g of stool.
- Wheat bran also promotes fat excretion, but not to the extent of oat bran.
- The outcomes of fiber supplementation as a treatment for constipation have yielded conflicting data.
- Constipation may be seen more commonly in sedentary individuals.
- During exercise, phasic and propagating motor activity is diminished in the colon, with the effect more pronounced with more vigorous effort; however, after the physical exertion is completed, an increase in the frequency and amplitude of the propagating pressure waves is demonstrated, possibly due to the restoration of parasympathetic input. This post-exercise pattern may precipitate the propulsion of feces.
- Idiopathic slow transit constipation involves ineffectual colonic propulsion, resulting in a measurable delay in the movement of fecal material through the colon.
- The severity of the presentation is variable, with the most intractable cases referred to as colonic inertia.
- These patients with slow transit constipation, usually women, have fewer than one bowel movement per week, often in association with abdominal pain, a lack of an urge to defecate, malaise, fatigue, or bloating.
- Little benefit is gained from dietary fiber supplementation in patients with slow transit constipation.
- Retarded colonic transit in these individuals is either pan-colonic or segmental.
- Slow transit constipation is consistently affiliated with a blunted colonic motor response to eating (i.e., gastrocolic reflex), including both propulsive and segmental contractions.
- In contrast, in patients with colonic inertia, there is *no* colonic response to a meal.
- A significant decrease in the frequency as well as the amplitude of high-amplitude propagated contractions is demonstrated in slow transit constipation, leading to reduced colonic propulsive activity.

- Histological evaluations reveal a marked decrease in the population of myenteric plexus neurons; however, of the neurons present in the myenteric plexus, those that produce the potent inhibitory neurotransmitter nitric oxide are vastly predominant, especially as compared to controls.
- Slow transit constipation also features a significant reduction in the interstitial cells of Cajal either throughout the colon or solely in the sigmoid colon.
- Moreover, the morphology of the existing cells is seen to be strikingly abnormal, demonstrating few dendrites and an irregular surface.
- Colonic transit studies of slow transit constipation reveal retention of more than 20 % of the radiopaque markers 5 days after their ingestion.

Obstructive Defecation

- Obstructed defecation usually results from abnormalities in pelvic as opposed to colonic function. Typically, this disorder is associated with failure of the puborectalis muscle to relax during defecation, producing a functional—not a physical—obstruction.
- Anatomic abnormalities also causing obstructed defecation include rectocele, enterocele, excessive perineal descent, and rectal intussusception. These patients report inordinate straining, incomplete evacuation, painful defecation, infrequent bowel movements, and the need for digital anal disimpaction.
- Among the diagnostic tests for obstructed defecation are anorectal manometry or electromyelography, balloon expulsion, barium defecography, and dynamic MRI.
- A defecogram may identify retention of 50–100 % of the instilled barium in the rectum.
- Colonic transit studies in these patients demonstrate collection of six or more radiopaque markers in the distal colon, indicating partial evacuation of the rectum.
- Two-thirds of patients with obstructive defecation may display a concurrent pattern of slow transit constipation.
- Obstructed defecation rarely arises from a colonic source—a sigmoidocele. In this variant, a redundant sigmoid colon descends into the rectovaginal pouch (of Douglas) during defecation, impinging upon the rectum during attempted evacuation.
- Defecography is the primary method of diagnosis of a sigmoidocele. The severity of a sigmoidocele is determined by the extent of its decline into the pelvis, as compared to the pubococcygeal and ischiococcygeal lines.
- Sigmoidoceles that descend into the pelvis below the pubococcygeal line may benefit from a sigmoid colectomy.
- The clinician should also be cognizant of concomitant pelvic floor disorders in these patients.

Irritable Bowel Syndrome

- Irritable bowel syndrome (IBS) is a functional disorder with multiple manifestations: constipation-predominant (IBS-C), diarrhea-predominant (IBS-D), and mixed (IBS-A).
- Irritable bowel syndrome is characterized by altered bowel habits and chronic, recurring abdominal pain directly related to defecation, in the absence of an anatomic abnormality.
- Extracolonic complaints include lower back pain, lethargy, nausea, urinary symptoms, dyspareunia, and dysmenorrhea.
- The etiology of irritable bowel syndrome is unclear but is believed to involve visceral hypersensitivity to intraluminal stimuli.
- Aberrant motility, inflammation, anomalies in extrinsic autonomic innervation, abnormal brain-gut interaction, and the role of psychosocial factors have also been extensively investigated.
- Hormonal factors may be involved, as symptoms are often increased perimenstrually; however, the complaints persist even in the absence of menses.
- The treatment of IBS is based on the nature and severity of symptoms. Education, reassurance, and the elimination of foods that incite the typical complaints are the initial interventions. In some patients, fiber supplementation exacerbates the IBS.
- For those who do not respond to conservative measures, medication is considered. However, the pharmacologic therapy of IBS-A has not been well studied.
- In approximately one-third of patients with irritable bowel syndrome, constipation is the main feature (IBS-C).
- Women are primarily affected by IBS-C. The majority of these patients demonstrate normal colonic transit and motility patterns, although there is a possible overlap with slow transit constipation.
- Tegaserod, an agonist of the 5-HT_4 receptor that is involved in the metabolism of serotonin, showed promise as a treatment of IBS-C, but was withdrawn by the Food and Drug Administration in 2007 due to a high incidence of myocardial infarction, stroke, and unstable angina.
- In some studies, probiotics such as *Lactobacillus* and *Bifidobacterium* produce variable degrees of alleviation of IBS symptoms such as pain.
- Lubiprostone (Amitiza®, Sucampo Pharmaceuticals, Inc., Bethesda, MD), a prostaglandin E1 analogue, activates type 2 chloride channels on the apical membrane of colonic epithelial cells.
- This medication promotes intestinal fluid secretion and, indirectly, colonic motility in patients with IBS-C.
- Studies of lubiprostone revealed significant improvement in stool frequency and consistency, abdominal discomfort and pain, straining, and bloating.
- Cholecystokinin, found in elevated levels in the plasma and sigmoid colon of IBS-C patients, has been implicated in the pathogenesis of IBS:

infusion of cholecystokinin induces typical symptoms of irritable bowel syndrome.

- However, in a randomized trial, the CCK-1 receptor antagonist dexloxiglumide led to no amelioration in IBS symptomology; moreover, overall colonic transit was unchanged, although emptying of the ascending colon was delayed.
- However, a pilot study of a similar CCK-1 receptor antagonist, loxiglumide, yielded some improvement in IBS symptoms.
- A randomized trial of neurotrophin-3, a protein growth factor integral to the development of the enteric nervous system, in constipated patients revealed more frequent spontaneous bowel movements, a more rapid colonic transit time, and a reduction in associated symptoms.
- Approximately one-third of subjects experienced transient injection site reactions after subcutaneous administration.
- Diarrhea-predominant irritable bowel syndrome is encountered in approximately one-third of patients with IBS.
- The majority of men with irritable bowel syndrome experience the diarrhea-predominant type.
- This subtype is often affiliated with urgency and fecal incontinence.
- IBS-D may follow an episode of acute gastroenteritis, pelvic surgery, or emotional stress.
- Some patients with IBS-D display accelerated proximal colonic transit, with an increased frequency of high- and low-amplitude propagated contractions.
- Additionally, the colonic motor response to eating is enhanced in a proportion of these patients, resulting in an intense urge to defecate and abdominal pain immediately after meals.
- Rectal hypersensitivity is also a feature in some of these patients.
- Antispasmodics such as hyoscine are prescribed to be used as needed for those with abdominal pain and bloating, especially after meals. Low-dose tricyclic antidepressants (e.g., amitriptyline) are added when the pain is more constant and even disabling; these medications function not as mood stabilizers, but instead act directly on the gut and central pain processing.
- Loperamide is an antidiarrheal agent safe for long-term use.
- Diarrhea is effectively addressed by selective serotonin 5-HT_3 antagonists such as alosetron. This drug was initially FDA approved in March 2000, only to be retracted due to reports of ischemic colitis, severe constipation, and even death. In June 2002, it was adopted solely for women with chronic, severe IBS-D.
- However, the medication may only be supplied by physicians participating in the Prometheus Prescribing Program, after the patient signs a patient-physician agreement.
- Further investigation into these novel pharmaceuticals for IBS is required.

Ogilvie's Syndrome

- Ogilvie's syndrome, initially described in 1948, is also known as acute colonic pseudo-obstruction.
- This disorder is characterized by an imbalance of autonomic innervation to the colon: the inhibitory sympathetic input exceeds that of the excitatory parasympathetic nerves.
- A massively dilated colon—particularly the proximal colon—results from the consequent suppression of peristaltic activity.
- The specific source for the initial motor disturbance that allows for this scenario is unknown.
- One hypothesis ascribes this functional obstruction to impairment of the pelvic (parasympathetic) splanchnic nerves supplying the distal colon, giving rise to an atonic segment, lacking peristaltic function.
- Acute colonic pseudo-obstruction has been reported concurrent with infectious or inflammatory (e.g., acute pancreatitis), cardiovascular (e.g., myocardial infarction), metabolic (e.g., hypokalemia), postoperative (e.g., spinal or pelvic surgery), posttraumatic, neurologic (e.g., Alzheimer's disease), respiratory (e.g., pneumonia), and neoplastic causes (e.g., metastatic disease); drugs (e.g., antidepressants); and old age.
- As indicated by the law of LaPlace (wall stress = [(transmural pressure) × (radius)]/wall thickness), the cecum is at greatest risk of perforation in light of its thin wall and large diameter.
- Despite symptoms and signs consistent with a large bowel obstruction, no mechanical blockade is present.
- The management of Ogilvie's syndrome begins with eliminating the presence of a physical obstruction, for instance with a water-soluble contrast enema.
- In the majority of cases, colonic dilatation responds to conservative therapy, including nasogastric decompression, correction of fluid and electrolyte abnormalities, cessation of antimotility medications such as opiates, and remedy of the underlying illness.
- In the absence of peritoneal signs or a cecal diameter greater than 12 cm on radiographic studies, conservative measures may be continued for 48–72 h. This approach is associated with a 14 % mortality rate.
- The colon may also be mechanically decompressed via colonoscopy, although, in one study, this difficult procedure in an unprepared colon was affiliated with a 1.7 % morbidity and a 3.4 % mortality rate; colonoscopic decompression was successful in 79.3 % of cases, albeit with a recurrence in 20 % of patients.
- Pharmacologic treatment has become the mainstay of management for acute colonic pseudo-obstruction if conservative measures fail. Neostigmine (2–2.5 mg IV over 1–60 min), an acetylcholinesterase inhibitor, provides a surfeit of acetylcholine to the enteric neurons and the neuromuscular junctions, thus inducing propagating contractions, specifically

high-amplitude propagating contractions, and the prompt evacuation of stool and flatus.

- In a double-blind randomized trial, the initial clinical response to neostigmine was 91 %, as compared to 0 % among those receiving a placebo; colonic distention recurred in two patients (18 %), ultimately requiring a subtotal colectomy in one patient.
- Administration of neostigmine may produce bradycardia, abdominal pain, vomiting, and excessive salivation.
- Alternative, less studied pharmacologic treatments are comprised of 5-HT_4 receptor agonists (e.g., cisapride), motilin receptor agonists (e.g., erythromycin), muscarinic receptor agonists (e.g., bethanechol), neurotropins (e.g., NT-3), nitric oxide synthase inhibitors (e.g., nitro-L-arginine methyl ester), and somatostatin analogues (e.g., octreotide).
- Surgical treatment—a cecostomy tube or a subtotal colectomy—is a final option if less invasive techniques are unsuccessful. Even in a non-emergent setting, surgery has a 30 % mortality rate.
- However, failure to decompress the colon may yield cecal ischemia and/or perforation in 14–40 % of cases; the mortality of these patients increases to 40–50 %.

Implications of Colonic Physiology for the Surgeon

- Colonic motility frequently impacts surgeons with respect to the phenomenon of postoperative ileus.
- In a murine model of postoperative ileus, a reduction in the number of interstitial cells of Cajal was evident on both sides of the colonic anastomosis within hours of the surgery; as a consequence, fewer slow waves were identified in that particular segment, possibly giving rise to postoperative ileus.
- Various disorders of colonic motility may stem from abnormalities of the interstitial cells of Cajal. These cells are significantly depleted in the colons of patients with diverticulosis and with slow transit constipation.
- The resection of a portion or the entirety of the colon can have profound functional ramifications for the patient.
- This should be discussed with patients prior to surgery and managed postoperatively.
- A new ileostomy patient requires counseling regarding adequate fluid and salt intake to compensate for the loss of the colon.
- Defecatory dysfunction—frequent bowel movements, urgency, or soiling—may occur after a low anterior resection.
- The neorectum demonstrates a decline in compliance postoperatively, although the maximum tolerated volume returns to normal 6 months later. Yet, the volume needed to elicit the rectoanal inhibitory reflex is persistently reduced even 1 year after surgery.

Conclusion

- The colon has proven an enigmatic organ with major roles of the salvage of intestinal water and electrolytes, the storage of fecal material, and the production of short-chain fatty acids.
- The mechanisms underlying its physiologic and pathophysiologic processes remain difficult to define. Although not essential for life, its normal function is integral to our well-being.

3. Anorectal Physiology

Richard E. Karulf

Introduction

- Normal bowel continence and evacuation are complex processes that involve the coordinated interaction between multiple different neuronal pathways and the pelvic and perineal musculature.
- Understanding of anorectal anatomy and physiology is challenging due to the complex series of neural and behavioral-mediated interactions and the lack of ideal studies to evaluate the anatomy and physiology.
- Complicating this understanding are other factors such as systemic disease, sphincter integrity, bowel motility, stool consistency, evacuation efficiency, pelvic floor stability, and cognitive and emotional affects.
- Conventional anorectal physiology testing using techniques such as manometry, endoanal ultrasound, electrophysiologic studies, and defecography help to elucidate anorectal structures and function.
- However, diagnostic dilemmas occur when patients report normal function with grossly abnormal test results or abnormal function with a normal test profile.

Muscles of the Pelvic Floor and Sphincter Complex

- Control of stool can be thought of as a pressure vector diagram, with continence represented as a balance of propulsive and resistive forces.
- Contraction of the muscles of the pelvic floor and sphincter complex provides resistance, and tone is noted during periods of rest or deep sleep.

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- Voluntary contraction of the puborectalis and external sphincter increases resistance and defers defecation.
- The anal sphincter is not a paired muscle structure, like the biceps and triceps in the arm; there is no extensor ani muscle.
- Evacuation occurs when propulsive forces (increased intra-abdominal pressure and peristalsis of the colon and rectum) overcome the resistance of the pelvic floor and sphincter 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 attachments span from the pubic bone, along the arcus tendineus (a condensation of the obturator fascia), to the ischial spine.
- 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.
- Controversy continues regarding the innervation and origin of the puborectalis muscle.
- Cadaver studies differ from in vivo stimulation studies as to whether the puborectalis muscle receives innervation only from the sacral nerve or also from the pudendal nerve.
- Comparative anatomy and histological studies of fiber typing also support the inclusion of the puborectalis muscle with the sphincter complex and not as a pelvic floor muscle. In addition, electromyography (EMG) studies of the external anal sphincter (EAS) and puborectalis muscle indicate that the muscles function together with cough and strain.
- The rectal smooth muscle consists of an outer muscularis mucosa, inner circular muscle, and the 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).
- This is not a simple extension of muscle as there are histologic differences between the upper circular muscle and the IAS.
- For instance, the IAS is thicker than the circular muscle due to an increased number of smaller muscle cells.
- The outer longitudinal layer surrounds the sigmoid colon coalescing proximally into thicker bands called taenia coli.
- This same layer continues down to the anorectal junction where it forms the conjoined longitudinal muscle along with fibers from the pubococcygeus muscle.

- Distally, this muscle lies in the intersphincteric plane, and fibers may fan out and cross both the internal and EAS muscles.
- In an ultrasound view of the anal canal, the longitudinal muscle is seen as a narrow hyperechoic line in the intersphincteric space.
- The puborectalis muscle, EAS, and IAS muscles are easily viewed with endoanal ultrasound. In the hands of an experienced ultrasonographer, the technique is highly sensitive and specific in identifying internal and external sphincter defects.

External Anal Sphincter (EAS)

- Anatomical and sonographic studies indicate that the EAS begins development, along with the puborectalis muscle, at 9–10 weeks gestation.
- At 28–30 weeks it is mature, and the anal sphincter then consists of three components, the striated puborectalis muscle, the smooth IAS muscle, and the smooth and striated EAS muscle.
- Further differentiation of the EAS into two or three components is highly debated.
- In 1715, Cowper described it as a single muscle. Later, Milligan and Morgan promoted the naming of the components as subcutaneous, superficial, and deep. Recently, Dalley makes a convincing point that the three components can only be seen in the exceptionally dissected specimen, and, in most cases, the muscle is one continuous mass and should be considered as such.
- The EAS is innervated bilaterally by the pudendal nerve arising from S2 to S4. Motor neurons arise in the dorsomedial and ventromedial divisions of Onuf's nucleus in the ventral horn of the spinal cord.
- Crossover of the pudendal innervation was first suggested in studies by Swash and Henry on rhesus monkeys.
- Hamdy and associates evaluated corticoanal stimulation of humans and found variable crossover which was symmetric in some and either right- or left-sided dominant in others.
- This has been offered as one possible explanation for the inconsistent relationship between unilateral pudendal neuropathy and fecal incontinence.
- The EAS maintains tonic activity at rest due to monosynaptic spinal reflex.
- The tone can be abolished with spinal anesthesia and in conditions such as tabes dorsalis, where large-diameter afferent sensory fibers are destroyed, and over distension of the rectum, due to the inflation response.
- Maximum tone, due to phasic activity in the EAS, can be maintained for only about 1 min, before fatigue is encountered.
- Of interest, the only other striated muscles that maintain continuous low-level resting activity are the abductor of the larynx, the cricopharyngeus, and the external urinary sphincter.

Internal Anal Sphincter (IAS)

- The IAS is an involuntary smooth muscle. It is the major source of anal resting pressure and is relatively hypoganglionic.
- There are nerve fibers expected in an autonomic muscle – cholinergic, adrenergic, and nonadrenergic noncholinergic fibers.
- It receives sympathetic innervation via the hypogastric and pelvic plexus. Parasympathetic innervation is from S1, S2, and S3 via the pelvic plexus.
- There is considerable evidence that the sympathetic innervation is excitatory but conflicting information regarding the parasympathetic effect.
- The IAS contributes 55 % to the anal resting pressure.
- The myogenic activity that contributes 10 and 45 % is due to the sympathetic innervation.
- The remainder of the resting tone is from the hemorrhoidal plexus (15 %) and the EAS (30 %).
- Spinal anesthesia decreases rectal tone by 50 %, and the decreased resting tone seen in diabetic patients may be due to an autonomic neuropathy.
- The IAS has slow waves occurring 6–20 times each minute increasing in frequency toward the distal anal canal.
- Ultraslow waves occur less than two times a minute and are not present in all individuals occurring in approximately 5–10 % of normal individuals.
- Ultraslow waves are associated with higher resting pressures, hemorrhoids, and anal fissures.
- The occurrence of anal slow-wave activity with rectal pressure waves exceeding anal resting pressure suggests a role for anal slow waves in preserving continence.
- Ultrasound examination of the anal canal shows the hypoechoic IAS ending approximately 10 mm proximal to the most distal portion of the hyperechoic EAS.

Sensory Factors

- Conventional concepts of the sensory innervation of the rectum have been challenged by data from continent patients following sphincter-saving surgery and ileal pouch-anal anastomosis (IPAA).
- Anal canal sensation to touch, pinprick, heat, and cold are present from the anal verge to 2.5–15 mm above the anal valves.
- This sensitive area is thought to help discriminate between flatus and stool, but local anesthesia does not obliterate that ability.
- The rectum is only sensitive to distention. Rectal sensation may be due to receptors in the rectal wall but also in the pelvic fascia or surrounding muscle.
- The sensory pathway for rectal distention is the parasympathetic system via the pelvic plexus to S2, S3, and S4.

- Below 15-cm rectal distention is perceived as flatus, but above 15-cm air distention causes a sensation of abdominal discomfort.
- Anal canal sensation is via the inferior rectal branch of the pudendal nerve that arises from S2, S3, and S4.
- This is the first branch of the pudendal nerve, and along with the second branch, the perineal nerve arises from the pudendal nerve in the pudendal canal (Alcock's canal).
- The remainder of the pudendal nerve continues as the dorsal nerve of the penis or clitoris.
- Many articles report daytime continence following low rectal resections with coloanal or IPAA. The reports of nighttime soiling following these procedures suggest that the ability to interpret sensory input from the neorectum requires conscious thought and not simple reflex contraction and relaxation.
- It is not clear if the decreased continence rate at night is solely due to impaired sensation (and subsequent defective discrimination of solid stool and gas) or if other factors limit fine control.

Reflexes

- There are a great number of reflexes that end with the name "… anal reflex."
- The reason for this is, in part, that the EAS is readily accessible and represents a convenient end point for recording during electrophysiological study.
- Consequently, there are a number of ways that one can assess the integrity of neurological connection through or around the spinal cord.

Cutaneous-Anal Reflex

- The cutaneous-anal reflex was first described by Rossolimo in 1891, as 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. Both afferent and efferent pathways travel within the pudendal nerve.
- If a cauda equina lesion is present, this reflex will usually be absent. Henry et al. recorded the latency of the anal reflex in 22 incontinent patients as compared to 33 control subjects.
- The mean latency was 13.0 ms vs. 8.3 ms, respectively. The mean latency was within normal range in only three (14 %) of the incontinent patients.
- However, Bartolo et al. have suggested that latency measurement of the cutaneous-anal reflex may be an inadequate means of demonstrating nerve damage in patients with fecal incontinence.

- 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

- Chan et al., using intercostal, rectus abdominis, and EAS electrodes, studied the latencies in response to voluntary cough and sniff stimulation.
- When compared to latencies from transcranial magnetic stimulation, it appeared that the EAS response was consistent with a polysynaptic reflex pathway.
- Visible contraction of the subcutaneous EAS as a consequence to cough and sniff stimulation is a simple nonintrusive validation of the pathways involved in the anal reflex.
- This response can also be displayed during anal sphincter manometry. Amarenco et al. demonstrated that the greater the intensity of the cough, the greater was the electromyographic response within the anal sphincter.
- 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 equina lesions.
- The mechanism of the cough-anal reflex contributes to the maintenance of urinary and fecal continence during sudden increases in intra-abdominal pressure as might also be seen with laughing, shouting, or heavy lifting.

Bulbocavernosus Reflex

- The bulbocavernosus reflex (BCR) is pelvic floor contraction elicited by squeezing the glans penis or clitoris.
- The EAS is used as the end point, because it is easily accessed either for visual assessment or by concentric needle electromyography (EMG) recording.
- The BCR latency will be prolonged by various disorders affecting the S2–S4 segments of the spinal cord.

Rectal Anal Inhibitory Reflex

- The rectoanal inhibitory reflex (RAIR) represents the relaxation of the IAS in response to distension of the rectum.
- It is felt 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.

- The 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 appears 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 amplitude of sphincter inhibition is roughly proportional to the volume extent of rectal distension.
- The RAIR is primarily dependent upon intrinsic nerve innervation in that it is preserved even after the rectum has been isolated from extrinsic influences, following transaction of hypogastric nerves and the presence of spinal cord lesions.
- The inhibition response is in part controlled by nonadrenergic, noncholinergic (NANC) mediators.
- The reflex matures quite early in that it is generally present at birth and has been detected in 81 % of premature infants older than 26 weeks postmenstrual age.
- The reflex is destroyed in Hirschsprung's disease when myenteric ganglia are absent. In addition, the reflex is lost after circumferential myotomy and after generous lateral internal sphincterotomy.
- Saigusa et al. found that at an average of 23 months following closure of ileostomy after IPAA, only 53 % of patients maintained a positive RAIR as compared to 96 % preoperatively.
- The incidence of nocturnal soiling was significantly greater, 72 % in those who did not have preserved or recovered RAIR as compared to those 40 % who had postoperative preserved RAIR.
- The RAIR appears to be nearly abolished in the early postoperative period following LAR resection for cancer. It often reappears with time.
- Loss of the RAIR is often a consequence of restorative proctocolectomy.
- Preservation of the RAIR correlated with less nocturnal soiling.
- The RAIR in children can be elicited even when general anesthetic agents or neuromuscular blockers are used. Glycopyrrolate, an anticholinergic, appears to inhibit RAIR.
- Disturbances in the RAIR appear to be involved in the incontinence that is associated with systemic sclerosis.

Rectal Anal Excitatory Reflex

- The rectal anal excitatory reflex (RAER) or inflation reflex is the contraction of the EAS in response to rectal distension.
- Rectal distension sensation is most 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 RAIR.
- Common methodologies for assessing the integrity of the pudendal nerve involve both single fiber density (SFD) of the EAS and pudendal nerve terminal motor latency (PNTML).
- However, derangement of the distal RAER was shown by Sangwan et al. to compare favorably with these more traditional and discomforting methodologies as an indicator of neuropathic injury to the EAS.
- It would appear that patients that have both an abnormal PNTML and an abnormal distal RAER do not require further study with SFD.

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 felt to be more involved with gross fecal continence.
- Parks postulated a mechanism by which this takes place.
- As intra-abdominal pressure is increased – such as with sneezing, coughing, or straining – 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.
- Bannister et al., in a study of 29 patients including 14 patients with incontinence, found no evidence of a flap-valve in the normal subjects by using manometric measurements during rising intra-abdominal pressures.
- However, in the incontinent patients, the manometric pressures were consistent with a flap-valve.
- Yet subjects still had leakage of stool, questioning the contribution to overall continence.

- Bartolo and colleagues also used manometric and EMG measurements in 13 subjects both at rest and during Valsalva, demonstrating a similar rise in rectal and sphincter pressures and puborectalis EMG recordings.
- Yet, with concomitant barium studies the anterior rectal wall separated from the mucosa, allowing contrast to fill the rectum.
- The authors proposed that the puborectalis functions more like a sphincter rather than contributing to the flap-valve mechanism.
- Furthermore, quantifying the anorectal angle and relating that to patient symptoms have resulted in mixed views.
- One study noted significant interobserver variation in anorectal angle measurements between three interpreters but good intraobserver consistency, suggesting that variation in anorectal angle measurements may be due to subjective interpretation of the rectal axis along the curved rectal wall.
- In another study assessing the reproducibility of anorectal angle measurement in 43 defecating proctograms, the authors found significant intra- and interobserver variations and concluded that the anorectal angle is an inaccurate measurement.
- Jorge and associates measured the anorectal angle during rest, squeeze, and push in 104 consecutive patients and also found highly significant differences in each measurement category.

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 rising 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.
- In addition, Bharucha and associates in a study of 52 women with fecal incontinence demonstrated that the rectal capacity was reduced in 25 % of women, and these lower volume and pressure thresholds were significantly associated with rectal hypersensitivity and urge fecal incontinence.
- Furthermore, following 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 awareness of the need to defecate occurs in the superior frontal gyrus and anterior cingulate gyrus.
- 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 stimulates 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."

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 internal or EAS muscles occur due to 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, due to 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 due to inflammation or radiation can result in hyperacute sensation.
- The rectum fails to accommodate, and the reservoir function is impaired leading to urgency and frequent stools.

- Fragmentation of stools is commonly 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, due to a large rectocele, megarectum, or neurogenic disorders, the rectum becomes over-distended and overflow incontinence occurs.
- The majority of patients with rectal prolapse are incontinent.
- Chronic stretching of the anal sphincters from full thickness prolapse leads to a patulous anus through which gas and liquid stool easily leak.
- A reflex relaxation of the IAS may also occur as the rectal wall descends toward the anal canal.
- Patients with mucosal prolapse may have seepage of mucus or small amounts of liquid stool.
- Correction of the prolapse can resolve the incontinence if the anal sphincter tone sufficiently returns.
- Age and duration of prolapse can affect this.

Obstructed Defecation

Suspected Enterocele or Rectocele (Obstructed Defecation)

- Patients with symptoms of enterocele or rectocele describe prolonged straining at defecation, with a sensation of partial or complete blockage (frequently a "closed trap door" preventing passage of stool).
- Defecography can demonstrate the presence of a rectocele or enterocele, suggest the presence of a peritoneocele, and clarify contributing disorders such as a nonrelaxing pelvic floor, rectal intussusception or prolapse, and potentially uterovaginal prolapse.

Rectocele

- A rectocele is defined as greater than 2 cm of rectal wall outpouching 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 commonly complain of the need for frequent sequential episodes of defecation and the need for manual compression or splinting of the anterior perineum or posterior vagina in order to completely evacuate.
- Additionally, patients may experience incontinence with relaxation due to reduction of the rectocele and return of the sequestered stool to the lower rectum.
- Van Dam and associates documented that there was no association between defecography measurements and outcome of the repair. However they concluded that defecography serves three major purposes in the

evaluation of a rectocele: preoperative evidence of its presence and size, documentation of additional pelvic floor abnormalities, and an objective assessment of postoperative changes.

- An abnormal increase in perineal descent (typically greater than 2 cm) has been described among both incontinent patients and continent patients who strain during defecation.
- These conflicting data underscore the poor relationship between neuropathic pelvic floor damage and symptomatology.
- Bartolo and associates evaluated patients with perineal descent using manometric, radiographic, and neurophysiologic studies and found no significant difference in the extent of perineal descent or neuropathic damage to the EAS.
- Patients who were incontinent had lower manometric pressures (both resting and squeeze pressures), while those with obstructed defecation had normal manometric pressures.
- In a separate study, these authors also found that incontinent patients with increased perineal descent had severe denervation of both the puborectalis and the EAS compared to continent patients with increased perineal descent, who had partial denervation of the EAS only.
- Miller and colleagues found that patients who were frankly incontinent actually had less perineal descent than continent patients with descent but had severely impaired anal sensation.
- Perineal descent may be a predictor of incontinence among patients with denervation of both the EAS 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.

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 botulism toxin injections into the puborectalis muscle with limited success.

Continence

- The interplay of all the aforementioned anatomy and physiology ensures continence, but a deficit in any one area does not lead to incontinence.
- An intact and functional puborectalis muscle can provide continence in the pediatric imperforate anus patient, but incontinence can ensue during adulthood.

- Even profound deficits do not necessarily lead to incontinence if stool consistency is solid, while minor deficits can easily lead to incontinence to gas.
- Diagnosis and management of abnormal fecal incontinence 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.

Summary

- Understanding the anatomy, innervation, and reflexes of the pelvic floor and anal sphincters is the key to assessing disorders of continence.
- Further work in this area remains promising.

4. Physiologic Testing

Anders F. Mellgren

Introduction

- Normal anorectal physiologic function is complex and relies on a multiplicity of factors, including an intact anatomy and an intact link between somatic and visceral function of the anus, rectum, and colon.
- Consequently, a comprehensive evaluation of anorectal function demands a combination of several tests that complement each other as well as a proper patient history, physical examination, and frequently other tests including endoscopy and other imaging studies.
- The patient history may be complemented by use of questionnaires and quality of life instruments. The clinical utility of some physiologic testing is limited because of a lack of reference data from healthy individuals and lack of standardization.
- Several of the existing physiologic tests are proven to improve diagnostic yield and to directly influence clinical management (Table 4.1).

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Table 4.1 Anorectal and colonic physiologic tests

Type of test	Measured modality	Primary indication
Test of function		
Anorectal manometry	Function of anal sphincter Rectoanal reflexes Anorectal sensation Rectal compliance Rectal motor function and coordination (balloon expulsion test, defecatory maneuver)	Fecal incontinence, nonrelaxation of the pelvic floor, Hirschsprung's disease
Vector volume manometry	Pressure profile and function of the anal sphincter	Fecal incontinence, sphincter injury
Saline infusion test	Rectal continence	Incontinence
Perineometry	Position of the pelvic floor	Pelvic floor laxity
Pudendal nerve terminal motor latency (PNTML)	Pudendal nerve terminal motor latency	Pudendal nerve injury or neuropathy
Electromyography (EMG)	Muscle activation. Motor unit potentials and fiber density (needle EMG)	Sphincter injury, biofeedback, imperforate anus
Test of structure		
Endoanal ultrasound	Two-dimensional or three-dimensional assessment of the internal and external anal sphincter, pelvic floor, and rectum	Fecal incontinence, fistula, tumors
Endoanal magnetic resonance imaging (MRI)	Assessment of the internal and external anal sphincter, pelvic floor, and rectum	Fecal incontinence, fistula, tumors
Test of function and structure		
Dynamic defecography	Rectal evacuation and dynamic assessment of the rectum and vagina	Fecal outlet obstruction, pelvic prolapse
Dynamic MRI	Rectal evacuation and dynamic assessment of the pelvis	Fecal outlet obstruction, pelvic prolapse
Marker study	Global transit time	Constipation
Radionuclide gamma scintigraphy	Global segmental colon transit	Constipation
SmartPill®	Stomach emptying, small bowel transit, colonic transit	Constipation, functional disorders of the stomach and small bowel

Anorectal Manometry

Indications

- Anorectal manometry measures the pressures in the anal canal (internal anal sphincter [IAS] and the external anal sphincter [EAS]) and the distal rectum and screens for functional outlet obstruction (nonrelaxing pelvic floor), Hirschsprung's disease (absence of rectoanal inhibitory reflex

[AIR]), and damage to sacral reflex arc (absence of cough reflex and predicting responses to biofeedback training and to objectively evaluate pressures before and after surgical intervention).

Equipment and Testing

- There are four essential components in anorectal manometry equipment: (1) a probe for measuring intraluminal pressure, (2) a pressure-recording device (amplifier/recorder, pneumohydraulic pump, and pressure transducers), (3) a balloon for inflation inside the rectum, and (4) a monitor/printer/storage system.
- The probes can be of different types, including solid state, water perfused, air charged, or microballoon. The diameter of the probe should not exceed 5–6 mm and the probe usually includes sensors radially distributed to measure several pressures at each level. Calibration of the probe and the recorder is critical for accurately measuring and obtaining reproducible results.

Bowel enema before the test is optional, but if formed stool is found at digital examination, an enema is advisable to avoid interference with the testing. Any manipulation of the rectum, such as digital rectal examination or administration of enema prior to a test, should be followed by a minimum of 5 min of rest to allow sphincter activity to return to baseline:

- The stationary pull-through technique is common and measures the resting and squeeze pressures in increments from 6 to 1 cm from the anal verge by pulling the probe out 1 cm at a time. Allowing a waiting period between each measurement minimizes artifacts.
- The dynamic pull-through technique measures pressures as the catheter is withdrawn in a continuous motion. It may create a reflex sphincter contraction, due to the stimulation generated by the probe, potentially resulting in an artificial increase of anal pressures.

Anal Resting Tone

- The anal resting pressure reflects the tonic activity of the IAS (55 %), the EAS (30 %), and the anal cushions (15 %).
- The IAS has an oscillating tonic activity with both slow waves of low amplitude and ultraslow waves of high amplitude.
- The anal resting tone is usually measured with the stationary pull-through technique and the maximum resting pressure (MRP) is usually defined as the highest recorded resting pressure.
- Due to radial asymmetry in different parts of the anal canal, the pressures in the four quadrants are averaged. The pressure profiles also vary according to gender, age, and measuring technique (Fig. 4.1).
- The length of the functional anal canal or high pressure zone is defined as the length of the anal canal with resting pressures exceeding 30 % of the rectal pressure.

Center for
Pelvic Floor
Disorders

Anorectal Manometry Report:

Patient Name:
Patient ID#:
Referring Physician:
Physician:
Date of Test:

Radial Pressure Analysis
Resting Level

Resting Average (mmHg)

	Post	Right	Anter.	Left	Min	Max	Median	HPZ	Mean	M Z
6.0 cm	4	4	3	7	3	7	4		5	
5.0 cm	15	3	3	12	3	15	8		8	
4.0 cm	20	4	10	20	4	20	15		14	
3.0 cm	55	23	14	44	14	55	34		34	
2.0 cm	45	45	20	48	20	48	45	x	40	
1.0 cm	51	84	78	71	51	84	75	x	71	55.5

Squeeze Increase

Squeeze Increase (mmHg)

	Post	Right	Anter.	Left	Min	Max	Median	HPZ	Mean	MZ
6.0 cm	13	4	4	13	4	13	8		8	
5.0 cm	49	10	17	44	10	49	30		30	
4.0 cm	40	22	20	42	20	42	31		31	
3.0 cm	62	24	17	21	17	62	23		31	
2.0 cm	55	48	39	51	39	55	50	X	48	
1.0 cm	79	88	86	76	76	88	82	X	82	65

Sensation/RAIR

Sensation	Measured Values	Normal Values
First Sensation	50 ml	40-80 ml
Max Tolerable Volume	150 ml	120-180 ml

RAIR	Measured Values	Normal Values
RAIR present	50ml	
RAIR nor present	ml	

Fig. 4.1 Anorectal manometry report. Resting pressures and squeeze increases at different levels are found in the columns "Mean"

- Patients with fecal incontinence tend to have lower anal resting tone than continent patients or normal controls. The clinical value of measuring basal anal canal pressures alone is limited, since patients with low pressures may have normal continence and patients with incontinence may have normal pressures. There is also a lack of defined values of what is the normal range for the anal resting tone.

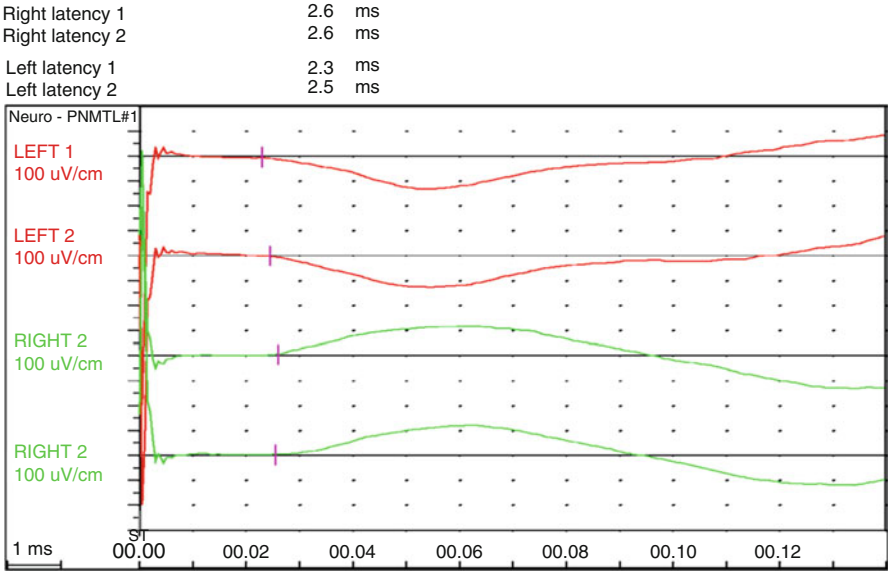

Fig. 4.2 Pudendal nerve motor latency measure twice on each side

Squeeze Pressure

- Squeeze increase of the anal canal pressure is generated by contraction of the EAS and can be calculated as the increase in pressure from the anal canal resting tone during maximal anal squeeze (Fig. 4.2).
- The squeeze increase is usually measured with the stationary pull-through technique, by asking the patient to maximally squeeze the sphincter at each level and hold this squeeze for 3 s. Instructing the patient to avoid contraction of accessory muscles, particularly the gluteal muscles, or to avoid increasing the intra-abdominal pressure reduces the risk of measuring false high squeeze increase.
- The maximum voluntary squeeze pressure (MSP) is usually defined as the highest pressure recorded above the baseline (zero) at any level of the anal canal during maximum squeeze effort. An alternative measurement is the highest pressure recorded above the resting pressure during maximum squeeze effort (the increment of pressure above the resting tone).
- Decreased squeeze pressures are frequently correlated to injuries in the EAS, neurologic damage, or just poor patient compliance/voluntary control. If the latter problem is suspected, the results of decreased squeeze pressure can be interpreted in context with the EAS response to coughing (see the section "Cough Reflex").
- The susceptibility for fatigue of the EAS can be estimated by measuring the patient's ability to sustain the squeeze effort over time. The squeeze

duration is often reduced in patients with incontinence. The squeeze durability can be measured as a fatigue index (the coefficient of maximum squeeze pressure and the gradient of decay).

Rectoanal Inhibitory Reflex (RAIR)

- Rectal distension or attempted defecation results in an inhibition of the tonic activity of the IAS and reflex relaxation of this muscle. The RAIR is mediated via the myenteric plexus and it is modulated by the spinal cord.
- This reflex facilitates rectal emptying and it is also believed to serve as a discriminatory function of the rectum, as it can facilitate discrimination of gas from fecal substance and allow rectal contents to be "sampled" by the sensory area of the anal canal.
- Concomitant with the relaxation of the IAS, there is sometimes a reflex EAS contraction during rectal distension that is automatic and not reflex mediated. By asking the patient to relax, this contraction sometimes can be limited.
- The RAIR can be tested by inflation of a balloon in the distal rectum and simultaneously measuring the pressure in the anal canal. Normally, a temporary decrease of the resting tone is observed and is indicative of a normal RAIR. The anal canal probe is usually positioned at the level of the highest recorded anal resting pressure, as this positioning facilitates the recording of a normal RAIR.
- Presence of an intact RAIR is dependent on an intact myenteric plexus and is usually impaired in patients with Hirschsprung's disease. An absence of RAIR may indicate a diagnosis of Hirschsprung's disease and should be followed by a full-thickness rectal biopsy to confirm an aganglionic segment diagnostic of Hirschsprung's disease. Hirschsprung's disease is usually diagnosed in early childhood and therefore rarely newly discovered in adults. The prevalence and the clinical relevance of ultra-short Hirschsprung's disease in adults are controversial.

Cough Reflex

- A normal response following a rapid increase in intra-abdominal pressure is a contraction of the EAS. This reflex, the cough reflex, maintains continence in case of a rapid increase in intra-abdominal pressure.
- The cough reflex can be assessed with a probe supplied with an intrarectal balloon (estimating the intra-abdominal pressure) and sensors located in the anal canal. If the increment of the anal canal pressure is higher than the rectal pressure, the reflex is considered to be normal.
- A sphincter defect or innervation injury may result in a weaker anal pressure increase and an abnormal cough reflex. Even though the clinical use of this test is limited, it can serve as an instrument to measure compliance in patients with attenuated voluntary squeeze pressures without evidence of spinal damage.

Rectal Sensation and Compliance

- Rectal sensation (and rectal compliance) can be measured by intermittent balloon distension in the distal rectum while simultaneously monitoring the patient's response.
- The first sensation, the first urge, and the maximal tolerable volume are usually recorded. Rectal compliance can also be assessed by measuring the pressure and volume relationship when a balloon is inflated in the rectum. This method is associated with a significant intersubjective variation, but some studies have demonstrated a good reproducibility of the recorded sensory thresholds.
- Some data supports that the sensory perception of the rectal distension is directly related to the rectal wall tension. Reduced sensory threshold levels of the rectum (rectal hypersensitivity) in patients with fecal incontinence could indicate a presence of urge fecal incontinence and increased frequency of defecation, whereas incontinent patients with increased sensory threshold levels (rectal hyposensitivity) may suffer from passive (overflow) incontinence.

Vector Volume Manometry

- Using equipment measuring pressures in multiple radial directions can provide a three-dimensional picture of the pressure profile in the anal canal.
- Pressure asymmetry corresponding to any sphincter defects can possibly be located by this method. The clinical utility of vector volume manometry has largely been replaced by endoanal ultrasound.

Other Tests of Anorectal Function

Balloon Expulsion Test

- Rectal expulsion ability can be evaluated by inflation of a water-filled rectal non-latex balloon. The main purpose of this test is to identify patients with obstructed defecation.
- Normal subjects can usually expel a balloon containing 50–150 mL, but patients suffering from constipation with megarectum are frequently unable to expel the balloon even though the intrarectal pressures are within the normal range.
- A variation of the technique uses a detachable water- or air-filled balloon that is inserted into the rectum. The patient is then allowed to sit on a commode in a private bathroom to pass it. This method may be more physiological then trying to pass a balloon attached to a catheter in the lateral position.
- There are several factors that may lead to overdiagnosis of functional outlet obstruction, including the inability of the balloon to accurately

mimic patient's stool, technical challenges to standardize the test, and embarrassment experienced by the patients in the test setting.

- The volume of the balloon may also influence the ability to expel the balloon. The utility of the balloon expulsion test alone is limited, but in addition to other physiologic tests, it may assist in the evaluation of patients with a nonrelaxing pelvic floor.

Saline Continence Test

- The saline continence test evaluates the ability of the sphincters to remain continent with continuous infusion of saline into the rectum. The time and volume at first leak and total leaked volume are assessed.
- Approximately 1.5 L can be infused in normal subjects without any significant leakage. Patients with fecal incontinence due to weak sphincter function or reduced rectal compliance usually start leaking after infusion of 250–600 mL saline.
- This test is used sparingly, but may be useful for objectively evaluating patients with fecal incontinence or for assessing improvement to surgical or medical treatment.

Perineometry

- There is a relation between increased perineal descent (pelvic floor laxity) and fecal incontinence. The pelvic floor should descend <1.5 cm during normal defecation. The perineometer measures the level of the perineum with respect to the ischial tuberosities and is used to estimate the perineal descent.
- This test has limited clinical utility because of poor reproducibility and comparatively more accurate radiologic methods for evaluating the movement of the pelvic floor are available.

Neurophysiologic Tests

Pudendal Nerve Terminal Motor Latency

- The pudendal nerve innervates the EAS, urethral sphincter, perineal musculature, mucosa of the anal canal, and the perineal skin. The nerve carries both afferent and efferent information originating from the nerve roots S2, S3, and S4 and travels along the lateral pelvic floor and exits the pelvis at the ischial spine into the pudendal canal (Alcock's canal).
- Pudendal nerve terminal motor latency (PNTML) is measured with a disposable finger-mounted electrode (St Mark's electrode) with a distal stimulating electrode at the fingertip and a recording electrode located at the finger base. By placing the fingertip as close as possible to the pudendal nerve at the ischial spine, the nerve conduction velocity (latency) from the ischial spine to the EAS (at the finger base) can be measured. PNTML

provides an estimation of the fastest conducting fibers in the pudendal nerve with a risk of showing a normal PNTML in a damaged nerve as long as some of the fast conducting fibers remain intact.

- The use of this test is controversial because of suboptimal test sensitivity and specificity. However, knowledge of any existing neuropathy or injury of the pudendal nerve may be of importance before sphincter surgery or biofeedback. PNTML is usually used as a complementary tool in the physiologic evaluation of anorectal function.
- The American Gastroenterological Association does not recommend PNTML for evaluation of patients with fecal incontinence on the basis of its unknown test reproducibility, age-dependent results independent of continence status, operator dependency, and high rate of false-negative result. However, the test is widely performed and relied upon by surgeons who operate on patients with fecal incontinence, constipation, and rectal prolapse.

Electromyography

- Anal electromyography (EMG) can be used to sample the activity of striated pelvic floor muscles. In the clinical setting, EMG is primarily used to identify EAS activity and whether appropriate sphincter relaxation and contraction exists. This information can be obtained using surface electrodes and can identify patients with nonrelaxing pelvic floor (Figs. 4.3 and 4.4) and it is also used in biofeedback therapy.
- Needle EMG can also provide information about possible nerve injury (denervation-reinnervation potentials) and locate muscle in the EAS. The latter indication has today largely been replaced by endoanal ultrasound.
- Surface electrodes (anal plug and skin electrodes) are associated with less patient discomfort and a lower risk of infection. Surface electrodes are frequently used to measure EAS activity to determine appropriate sphincter relaxation and contraction (Fig. 4.5).
- Anal plug electrodes are frequently used in biofeedback training. Using this technique, patients suffering from fecal incontinence or nonrelaxing sphincter are able to obtain a visual or audible signal as a response to sphincter contraction.
- Needle electrodes can be either single-fiber electrodes or concentric needle electrodes.
- Single-fiber needle electrodes record a single motor unit at a time. Increased fiber density (motor unit grouping) can be detected as evidence of nerve denervation with reinnervation. Single-fiber EMG results have shown a high degree of repeatability among independent investigators.
- Concentric needle EMG, which measures approximately 30 motor units at a time, is useful for detecting polyphasic or prolonged duration of the motor unit potentials as evidence for reinnervation in the EAS. In patients with fecal incontinence, high fiber density and longer motor

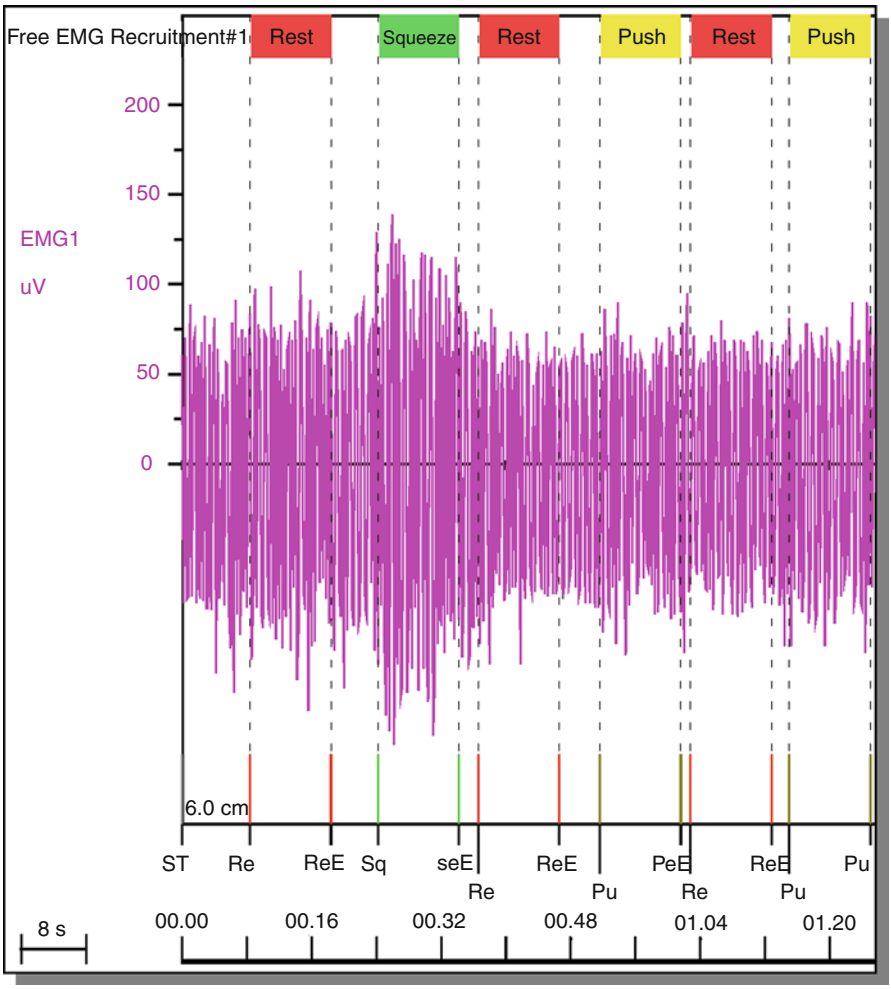

Fig. 4.3 Electromyography recruitment demonstrating equivocal reaction, since the activity is unchanged at "push"

unit potentials are more commonly detected in EMG than in controls, but the extent of denervation measured by EMG in the EAS does not appear to influence the severity of incontinence.

- The clinical utility of EMG has diminished since mapping of the EAS has been replaced in many centers by endoanal ultrasound; EAS is less painful and provides the examiner with a two- or three-dimensional picture of the anal canal and the anal sphincters.
- According to the American Gastroenterological Association, EMG still has a role in confirming imperforate anus before surgical placement of the bowel if endoanal ultrasound is not possible or not available and in biofeedback therapy.

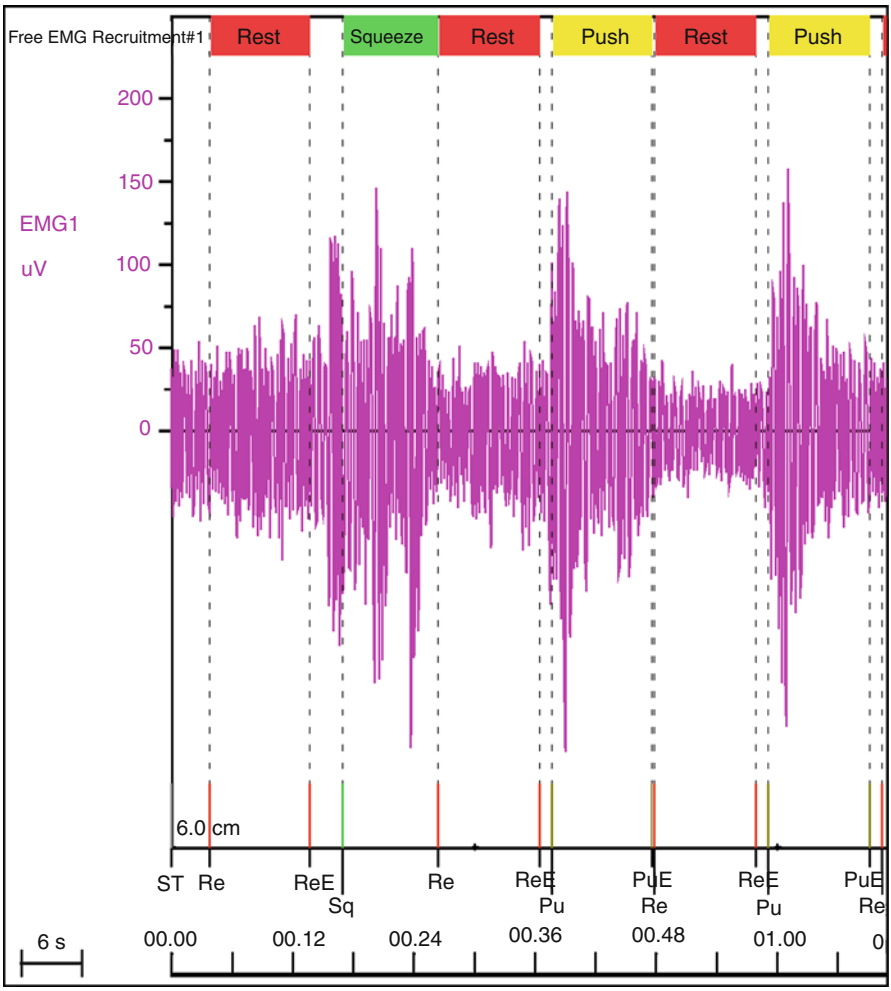

Fig. 4.4 Electromyography recruitment demonstrates paradoxic reaction, since the activity is increased at "push"

- Many colorectal surgeons find that anal ultrasound compliments rather than replaces EMG. The former test offers gross anatomic information while the latter evaluation reveals more about function rather than structure.

Anatomic Assessment

Endoanal Ultrasound

- Endoanal ultrasound (EUS) (see Chap. 7) is one of the most reliable tests in identifying anatomic defects (Fig. 4.6) in the anal sphincters with a high sensitivity and specificity.

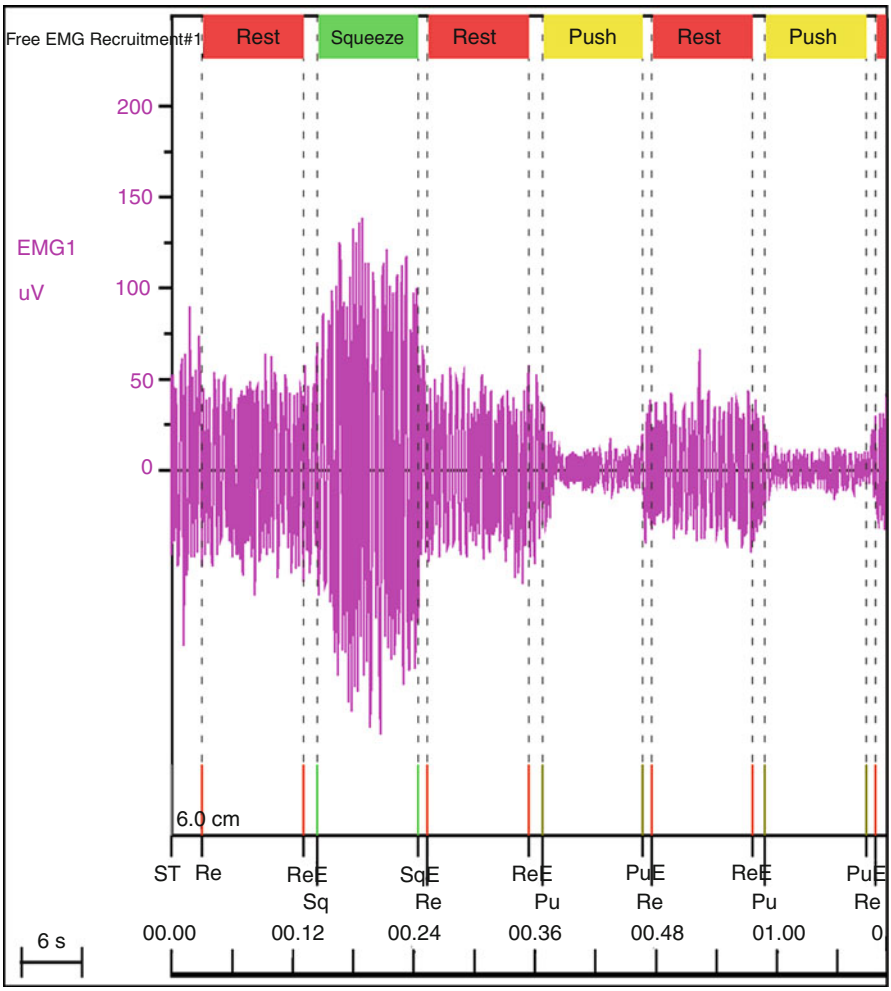

Fig. 4.5 Electromyography recruitment demonstrates normal reaction, since the activity is increased at "squeeze" and decreased at "push"

- A 7- or 10-MHz frequency endoanal probe is usually used for imaging of the sphincters. The latter provides a higher resolution and hence a superior picture quality. The transducer provides a 360° view of the anal canal.
- The main indication for EUS is to diagnose defects in the IAS and/or EAS with a high correlation between histologic and intraoperative findings. Ultrasound is also used to document injuries to the pelvic floor and pelvic prolapse.
- The investigation and the interpretation of the procedure is operator dependent, but three-dimensional endoanal ultrasound has improved results.
- EUS is used to select patients for surgical repair and to assess postoperative results.

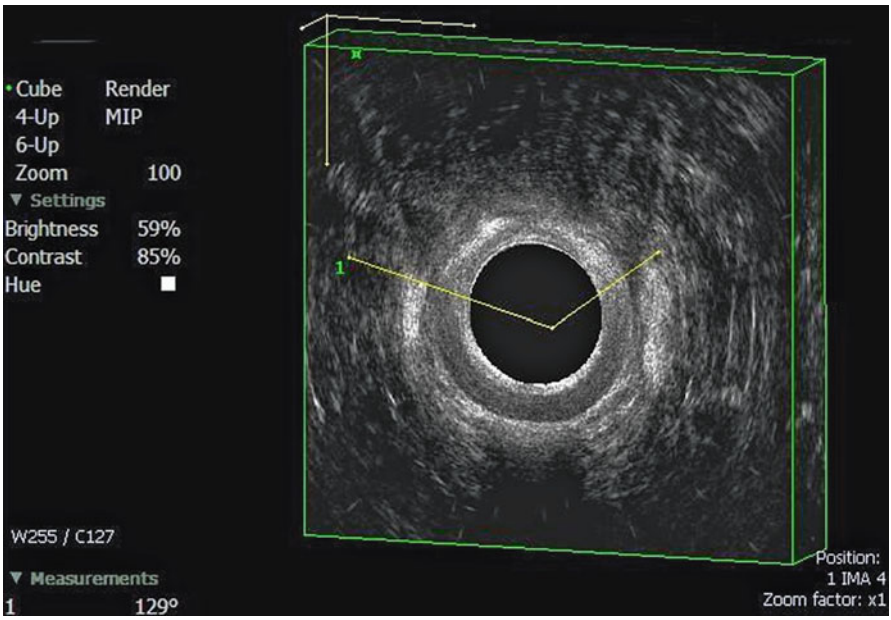

Fig. 4.6 Sphincter defect in the anterior aspect

Magnetic Resonance Imaging (MRI)

- MRI is used to image the anal canal and the pelvic floor muscles.
- Images can be generated either with an endoanal coil or external phased-array coil. These two techniques are comparable in diagnosing anal sphincter defects and EAS atrophy, but there is some discomfort when the endoanal coil is introduced.
- There is no consensus regarding the use of MRI vs. EUS. Because of availability and costs, EUS is usually preferred as the first-line method for anatomic assessment.

Tests of Function and Structure

- Fluoroscopic defecography, MR defecography, and pelvic floor ultrasound can provide information about dynamic anorectal disorders, such as rectal intussusception and rectal prolapse.

Dynamic Fluoroscopic Defecography

- Fluoroscopic defecography is a dynamic radiologic test providing morphologic information about the anal canal, rectum, vagina, and the pelvic floor during the defecation maneuver.
- Defecography involves contrast in the rectum and preferably in the vagina. Occasionally, contrast in the small bowel, bladder, and even the peritoneal

cavity is used. The primary indications are evaluation of outlet obstruction and prolapse, visualization of the defecation process, identification of nonrelaxation, and visualization of various anatomic abnormalities.

- Patient's embarrassment of the test may result in a false-positive test result of pelvic floor relaxation and a false-negative assessment of anatomic abnormalities because of insufficient rectal emptying. Other limitations are interobserver variation and a high incidence of "abnormal findings" in both patients with and without symptoms.

Anorectal Angle and Rectal Emptying

- The anorectal angle is the angle between the anal canal and rectum.
- The action of the puborectalis muscle during straining decreases this angle from 75–90° in resting to 90–110°, and the angle increases to 110–180° at evacuation.
- The anorectal angle is believed to play a role in maintaining continence.
- The quantification of the anorectal angle in defecography has somewhat limited clinical value due to a high interobserver variation.
- The ability to relax the puborectalis muscle, and increase the anorectal angle, is pivotal for the evacuation process. A persistent contraction of the puborectalis muscle during the evacuation process is consistent with nonrelaxing pelvic floor, which is also named anismus or paradoxic contraction of the pelvic floor.
- Rectal emptying should be rapid (<30 s) and complete (<10 % residual contrast).
- In patients with evacuation difficulties, emptying is frequently achieved in small portions.
- Perineal descent during emptying is measured relative to a line drawn in between the tip of the coccyx and the pubic bone (the pubococcygeal line). During squeezing the pelvic floor will rise, and during straining and evacuation it will descend.

Rectal Intussusception and Rectal Prolapse

- Rectal intussusception is a circumferential infolding of the entire thickness of the rectal wall not extending beyond the anal verge, while a rectal prolapse is a protrusion of the entire thickness of the rectal wall extending through and beyond the anal verge.
- Rectal intussusception is difficult to diagnose at clinical examination.
- Defecography can help in the differentiation between a small rectal prolapse from large hemorrhoids and identify patients with concomitant enterocele or vaginal prolapse in patients with rectal prolapse.

Rectocele

- Rectocele is a herniation of the anterior rectal wall into the vagina. To diagnose a rectocele, the bulge in the anterior part of the distal rectum should be ≥3 cm.

- Rectoceles are common and may not always cause symptoms. Barium trapping in the rectocele or facilitation of emptying by digital support of the posterior vagina wall is used by some surgeons to define surgical candidates for rectocele repair.

Peritoneocele, Enterocele, and Sigmoidocele

- A peritoneocele is a peritoneal herniation extending the pouch of Douglas below the upper third of the vaginal length and at the same time increasing the distance between the rectum and vagina.
- An enterocele is formed when small bowel descends into the peritoneocele and a sigmoidocele is formed when the sigmoid colon descends into the peritoneocele.

Dynamic MR Defecography

- Dynamic MR defecography is a nonionizing investigation that uses fast MRI sequences to provide a dynamic picture of the complete pelvic floor and pelvic organs during rest, squeezing, straining, and evacuation. The test is also helpful in preoperative planning and best results are obtained when contrast (usually sonographic gel) is used.
- Dynamic MR defecography can be performed with open- or closed-configuration units.
- The open-configuration MRI unit, where the patient is sitting during the investigation, is superior to the closed-configuration unit. This equipment is expensive, not readily available in most institutions, and the image quality is inferior to open-configuration units.
- Closed unit MRI permits evacuation only in a supine position. This may influence the results, but this limitation is debated.

Pelvic Floor Ultrasound

- Ultrasound using probes employed in the perineum and/or the vagina can provide information on most of the anatomic and dynamic abnormalities that are visualized at defecography and MR defecography.

Gastrointestinal Transit Studies

- Transit studies provide an objective evaluation of the gastrointestinal motility, which is of paramount importance for stool consistency and in facilitating defecation through the "rectocolic reflex."
- Small bowel transit can be evaluated with oral lactulose ingestion followed by measurement of breath hydrogen excretion. The lactulose ferments in the cecum to release hydrogen allowing inexpensive, safe, rapid, and reproducible measurement of orocecal transit time.
- Colonic marker studies, radionuclide gamma scintigraphy, and the SmartPill® were covered in Chap. 2.

5. Endoscopy

Charles B. Whitlow

Anoscopy

- Anoscopy is the examination of the anal canal. The lower part of the rectal mucosa, upper anal mucosa, anoderm, dentate line, and internal and external hemorrhoids can be seen through this examination.
- There are two types of anoscopes:
  - Beveled: Buie or Hirschman scope (Fig. 5.1) and the lighted Welch-Allyn scope (Fig. 5.2)
  - Slotted or side opening: Vernon-David scope with Hirschman handle (Fig. 5.3) and Hinkel-James anoscope (Fig. 5.4)

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 other endoscopic examinations.

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Fig. 5.1 Buie anoscope

Fig. 5.2 Lighted Welch-Allyn anoscope

Contraindications

- Anal stricture or severe anal stenosis.
- Patients with severe anal pain (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 may be used in patients with anal pain.

Fig. 5.3 Vernon-David with Hirschman handle anoscope

Fig. 5.4 Hinkel-James anoscope

Preparation

- No preparation is required.

Positioning

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

Technique

- Inspect the anal area and then gently spread the buttock cheeks with good lighting to gain exposure.
- Look for skin tags, excoriation, and change in color or thickness of the anal verge and perianal skin.
- 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 too far during straining – a feature of the perineal descent syndrome.
- A digital examination is performed with a well-lubricated index finger. The finger is pressed on the anal aperture to "warn" the patient and 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 (normal, tight, or loose) is estimated and the canal is assessed for any stricture or narrowing or for a defect in the internal or external sphincters.
- A fibrous cord or induration in the anal area and the anal canal may indicate a fistulous tract. The external sphincter, puborectalis, and levator ani muscles can also be appreciated by digital examination.
- When the puborectalis is pulled in the posterior quadrant, the anus will gape but will close immediately when the traction is released. Persistence of the gaping indicates an abnormal reflex pathway in the thoracolumbar region frequently seen in paraplegic patients.
- The finger should press gently on these muscles for signs of tenderness. With good anal function, the examiner not only feels the squeeze of the muscle on the examining finger but also feels the finger pulled forward by the puborectalis muscle when the patient is asked to contract the muscles.
- 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. In patients with redundant mucosa, reinsertion of the obturator may cause discomfort if the mucosa gets trapped between the obturator and the anoscope. However, if the beveled type of endoscope is used, the endoscope can be rotated without having to reinsert the obturator.
- If an inverted (jackknife) position is used, the examination table need not be tipped down more than 10–15°. If a left-lateral position is used, an assistant needs to pull up the right cheek of the buttock for exposure.
- 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.
- Biopsies may be taken via the anoscope. Local anesthesia may be necessary for biopsies in the sensate area distal to the dentate line.

Complications

- Anal tear, especially at the posterior midline, can occur in patients with anal stenosis.
- Friable hemorrhoids may bleed from trauma from the anoscope.

Rigid Proctosigmoidoscopy

- Three sizes of rigid proctosigmoidoscope are available (Fig. 5.5):
  - A 19 mm × 25 cm scope is the standard size for a general examination and for polypectomy or electrocoagulation. A disposable standard-size rigid proctosigmoidoscope is available.
  - A 15 mm × 25 cm endoscope is an ideal size for general examination. 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 11 mm × 25 cm endoscope should be available for examining the patient who has anal or rectal stricture, such as Crohn's disease.

Indications

- Rigid proctosigmoidoscopy has largely been replaced by flexible sigmoidoscopy but remains useful as it allows evacuation of blood clots or stool and can identify the precise site and size of rectal neoplasm.

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

Contraindications

- Severe anal pain (from an acute fissure, thrombosed external hemorrhoids, and perianal abscess).
- Anal stricture.
- Patients with acute abdomen of any cause or a rectal or sigmoid anastomosis less than 2 weeks postoperatively should have a rigid proctosigmoidoscopy with caution.

Preparation

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

Positioning

- Prone jackknife is preferred but the 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 and some apprehensive patients.

Technique

- Although a standard proctosigmoidoscope is 25 cm in length, the average distance that the scope can be passed is 20 cm. In men, the scope can be passed to 21–25 cm half of the time, and in women, it can be passed that distance one-third of the time.
- Rigid proctosigmoidoscopy is suitable only to examine the rectum and, in some patients, the distal sigmoid colon.
- Properly performed, rigid proctosigmoidoscopy produces only mild discomfort. Some 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 will be helpful. Pain is produced by excessive stretching of the mesentery by direct scope pressure or by air insufflation.
- With the obturator in place and held steady with the right thumb, the well-lubricated rigid proctosigmoidoscope is gently inserted into the anal canal, aiming toward the umbilicus for a distance of about 4–5 cm. Then the endoscope is angled toward the sacrum and advanced another 4–5 cm into the rectum. The obturator is removed and the bowel lumen is negotiated under direct vision.
- Air insufflation is limited to the amount necessary to open the lumen.
- When an angle is encountered, the endoscope is withdrawn 3–4 cm and then readvanced. This may be repeated several times to straighten the angulation.

- If further advancement is unsuccessful, the procedure is terminated. The length of insertion should be measured from the anal verge without stretching the bowel wall.
- Careful examination is done as the instrument is withdrawn. The instrument should be rotated on withdrawal to ensure examination of the entire circumference, and it is usually necessary to insufflate a small amount of air for good visualization of the lumen.
- The mucosal folds in the rectum (valves of Houston) can be flattened with the tip of the endoscope to see the area immediately proximal to them.
- The appearance of the mucosa, depth of insertion, and the size, appearance, location, and level of any lesion should be accurately recorded.
- If a biopsy is performed, the location, level, and number of biopsies and whether electrocoagulation is necessary should be noted.
- A rigid cautery snare (Frankfelt snare) and cautery tip attachments are useful for excision or ablation of rectal neoplasms.
- During the entire procedure, suction and water irrigation should be available.

Complications

- The tip of the endoscope can tear the mucosa producing hemorrhage.
- Perforation from diagnostic rigid proctosigmoidoscopy is extremely rare (1 in 8–20,000 examinations).

Flexible Sigmoidoscopy

- The flexible videosigmoidoscope (FFS) is 60 cm in functional length (Fig. 5.6) and visualizes the entire sigmoid colon in some cases up to the splenic flexure.
- For screening, the FFS has a three to six times greater yield over rigid proctosigmoidoscopy.

Indications

- In acute diarrhea, to exclude Clostridium difficile colitis, acute bacterial colitis, amebic colitis, and ischemic colitis particularly after aortic aneurysm repair.
- With rectal bleeding, to identify nonspecific proctitis, radiation proctitis, anorectal Crohn's disease, rectal ulcer, and anorectal neoplasms.
- Postoperative evaluation (anastomotic strictures and local recurrence of neoplasms).
- Colorectal cancer screening in conjunction with tests for fecal occult blood and to complement a barium enema examination. CO_2 may be useful insufflation if a barium enema is to follow.

Fig. 5.6 Flexible videosigmoidoscope

Contraindications

- Severe anal pain
- Anorectal stricture
- Acute sigmoid diverticulitis, toxic colitis, and patients with an acute abdomen

Preparation

- Bowel preparation with two fleet enemas given within 2 h of examination is adequate. Patients with diarrhea may not require the enemas.

Positioning

- Left-lateral recumbent or prone jackknife position

Technique

- Sedation is unnecessary.
- The anal canal is lubricated by digital examination.
- A well-lubricated flexible sigmoidoscope is then inserted and advancement is performed under direct vision.
- Pushing the endoscope blindly, through a bend in the bowel, is a poor technique. Instead, the endoscope should be withdrawn to straighten the bowel.

- The key to success is short withdrawal and advancement of the endoscope or a to-and-fro movement ("dithering"), together with rotating (torquing) the instrument clockwise and/or counterclockwise as needed.
- Air insufflation should be kept to a minimum.
- The procedure should be completed within 5–10 min.
- If a lesion is detected and proved by biopsy to be a neoplasm, a complete colonic investigation is indicated, ideally by total colonoscopy at some other date.
- A polyp up to 8 mm in size can be sampled and frequently completely excised with cold biopsy forceps.
- Alternatively, cautery forceps (hot biopsy) and fulguration can be used. To prevent possible explosion, due to hydrogen or methane gas in the lumen, air should be exchanged in the colon and rectum with repeated insufflation and suction.
- For larger polyps and in those cases when a full colonoscopy is planned, delay in treatment until time of colonoscopy with full bowel preparation is preferable.

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.
- Too rough and improper technique can cause perforation or mucosal laceration with associated bleeding.
- The most common site of perforation is in the distal sigmoid colon where it is angulated from the relatively fixed rectum at promontory of the sacrum.
- Reported perforation rates have ranged from 1 in 11,000 to 54,000.
- In multivariate models, complications were significantly more common in men than in women (odds ratio, 3.34; confidence interval 95 %).

Ileoscopy

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

Indications

- To rule out Crohn's disease, find an abnormality in patients with high ileostomy output evaluation of ischemia or hemorrhage.

Contraindications

- Skin-level stricture of the stoma

Preparation

- Not required, but a clear liquid diet for 1 day is helpful. Sedation is not required.

Positioning

- Supine

Technique

- A digital examination gently dilates the stoma. The well-lubricated scope is introduced directly into the ileostomy. The terminal ileum is quite active with frequent spasm and requires more air insufflation than proctoscopy. The distance traversed by the endoscope is usually limited to 12–15 cm. In patients with a large para-ileostomy hernia, the endoscope is rarely passed beyond 10 cm.
- 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. Flexible ileoscopy is easier to perform.

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.

Pouchoscopy

Kock Pouch or Continent Ileostomy

Indications

- Valve evaluation (slippage or extrusion [difficult or impossible intubation])
- Decompression of an obstructed pouch and passage of a drainage tube
- Crohn's disease and pouch complications (fistulas and high output)

Contraindications

- Stricture of the stoma

Preparation

- Bowel preparation is unnecessary and sedation is not usually required. If possible, the pouch should be emptied or irrigated immediately prior to the examination.

Positioning

- Supine

Technique

- The endoscope can usually be passed easily into the pouch with inspection of the stoma being performed on insertion or withdrawal.
- A general inspection of the pouch is performed noting the mucosal appearance, the pouch size, distensibility, and the status of suture lines. If possible, the afferent loop of ileum should be intubated, especially in patients presenting with pouch inflammation.
- The endoscope must be retroflexed within the pouch to check valve length, symmetry, and fixation.
- A careful search for foreign material should be made, particularly around the base of the valve. If mesh was used to reinforce the nipple valve, a fistula may form at this area. In patients with slippage or extrusion of the valve, passing the endoscope will be difficult.
- For an obstructed pouch from a slipped valve, a rigid endoscope may be placed over the flexible endoscope, which is inserted into the pouch. Then the rigid endoscope is advanced over the flexible endoscope into the pouch. Now the flexible endoscope can be withdrawn and a drainage catheter inserted to temporarily relieve the obstruction.
- Another option is to pass a guide wire or forceps through the biopsy channel of the flexible endoscope that has been inserted through the valve into the pouch. The wire or forceps (with the handle removed) is then left in the pouch and the scope is withdrawn, a drainage catheter can then be passed into the pouch over the wire or forceps, and surgical repair of the nipple valve is almost always required.

Complications

- Perforation can occur, particularly when there is an obstruction of the pouch.

Ileoanal Pouch

Indications

- Patients with bleeding, diarrhea, recent onset of fecal incontinence, obstructive symptoms, pouchitis, and surveillance 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 or prone jackknife position

Technique

- The examination starts with a digital examination to evaluate the anal canal and the anal anastomosis. A stricture is dilated with a finger or Hegar dilators.
- The well-lubricated flexible sigmoidoscope or a colonoscope is introduced into the anal canal and advanced into the pouch and proximal terminal ileum.
- The mucosa of the pouch and anal canal are examined for edema, granularity, bleeding, erosion, fibrin exudate, ulceration, plaque, or masses. Abnormalities may be biopsied (cold).

Complications

- Tear of the anal canal or anastomosis, bleeding (which usually stops spontaneously), and perforation

Colonoscopy

- Colonoscopy is the gold standard for diagnosis and an increasing option for therapy.

Indications

Diagnostic

- Evaluation of virtually all symptoms associated with benign, malignant, acute, or chronic diseases of the colon and rectum; resolution of abnormalities seen on other imaging modalities; investigating otherwise unexplained symptoms such as anemia; the evaluation of chronic and acute bleeding per annum; for screening and surveillance for colon adenomas or carcinoma; localization of nonpalpable lesions at open or laparoscopic operation

Therapeutic

- Removal of lesions (polyps), decompression, control of bleeding, and stenting

Contraindications

Absolute

- Suspected bowel perforation, established peritonitis, or fulminant colitis

Relative

- Suspected ischemia and acute colitis, a recent anastomosis, and significant active bleeding

Preparation

- Thorough mechanical cleansing of the colon is absolutely essential for efficient, safe, and complete endoscopic examination. Should perforation occur, the empty colon certainly poses less risk of significant peritoneal contamination.
- Several methods of mechanical cleansing are in current use:
  - Lavage solutions (high- and low-volume PEG)
  - Sodium phosphate tablets
  - Stimulate laxatives
  - Enemas

Monitoring

- Pulse oximetry, heart rate, blood pressure, and electrocardiography; observation of the patient's level of awareness; respirations; and abdominal distention

Bleeding Prophylaxis

- Recommendations for periprocedural management of anticoagulants take into consideration the risks and consequence of a thromboembolic event and procedural bleeding.

Current Recommendations

- Aspirin: may be continued.
- Antiplatelet drugs: hold for 5–7 days prior to procedure.
- Warfarin: hold for 3–5 days prior to procedure and evaluation of INR preprocedure. "Bridging" anticoagulation with heparin (intravenous unfractionated heparin or subcutaneous low-molecular weight heparin), for higher-risk patients.
- Resumption of medication 1–3 days after procedure depending on therapy.

Technique

- Equipment is verified to be working prior to the procedure and a time-out is performed.
- With the patient in the left-lateral recumbent position, the examination is initiated by a perianal inspection followed by a careful digital rectal examination.
- The instrument tip is gently inserted as the right index finger is withdrawn. The examiner then grasps the head (handle) of the instrument in the palm of the left hand, leaving the thumb and index finger free to manipulate the knobs for tip deflection. The index or 3rd finger manipulates the air and water insufflation as well as suction buttons. The right hand manipulates the instrument shaft.
- The main objective on insertion is to reach the most proximal point desired as expeditiously as possible, leaving detailed inspection for withdrawal of the endoscope. However, biopsy or removal of a small lesion is often performed on insertion as identification may be difficult on withdrawal.
- Techniques to efficiently advance the colonoscope include:
  - Insertion of the scope with the lumen in view, attempting to keep the colon straight and avoidance of looping. This is aided by torquing (clockwise turn with the right hand on the shaft of the instrument), application of suction, change in the patient's body position, abdominal pressure by an assistant, and jiggling of the shaft (back and forth motion). This pleating or "accordioning" of the bowel over the instrument with alternating release allows for efficient advancement with one-to-one motion.
  - These actions explain the difficulty in estimating the extent of intubation or the location of a lesion, the least accurate determination is measuring on the shaft of the instrument.
  - Cecal intubation is confirmed by visualization of the appendiceal orifice and the ileocecal valve. Photographic documentation of these landmarks is common.
  - On withdrawal the entire mucosa is visualized.
  - Luminal material (fluids or stool) is irrigated and aspirated by suction through the instrument channel, or the patient's position is changed to allow the fluid to shift to another area.
  - As the endoscope is withdrawn through each segment of the colon, it is useful to decompress each examined segment with suction so that at the conclusion of the examination the abdomen is minimally distended.

Abnormal Findings

- Exophytic lesions: polyps and adenocarcinomas.
- Submucosal lesions (lymphoid hyperplasia, stromal tumors, lipomas, carcinoids, endometriomas, hemangiomas, neurofibromas, or lymphoma).
- Metastases from other organs (e.g., prostate, pancreas, or kidney).

- The diagnosis of most lesions can be made by endoscopic visualization or sampling. Some, being of no clinical consequence, require only recognition (lymphoid, hyperplasia, and lipoma).
- Chromoendoscopy, narrow-band imaging, and use of a retroscope have been described to improve polyp detection rate and differentiation of polyp type. However, none has proved to be clinically useful.
- Inflammatory or degenerative conditions (various colitides [bacterial, viral, ulcerative, granulomatous], ischemia, radiation proctopathy [formerly called "proctitis"], melanosis coli [laxative pigment deposition], angiodysplasia [vascular ectasias, arteriovenous malformations]).
- Intestinal anastomoses, stenosis, and stricture (secondary to benign conditions [previous resection and anastomosis, diverticulitis, colitis, radiation injury] or malignancy).
- Other findings to be recognized include colitis cystica profunda, pneumatosis, and Behçet's syndrome.
- Diagnostic techniques vary:
  - A tiny sessile lesion (e.g., a diminutive polyp) may be removed in its entirety with the biopsy forceps (with or without cautery).
  - A pedunculated lesion suspected of being a benign adenoma may be removed by snare polypectomy. Larger sessile lesions may be elevated with submucosal injection with saline and then excised with a snare completely or piecemeal.
  - Fulguration with monopolar cautery or argon plasma coagulator may be used to ablate tissue.
  - A sessile lesion suspected of being a carcinoma 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.
  - A lesion that appears vascular and friable may be simply photographed.
  - A submucosal lesion may be exposed by disrupting the overlying mucosa with sequential bites from biopsy forceps.
  - Lesions which are not located near a definitive landmark (cecum, ileocecal valve, rectum) and are likely to require colonic resection should be marked with a submucosal (India ink) tattoo placed in all four quadrants of the colonic lumen approximately 2–5 cm distal to the lesion.

Complications

- The most common serious complication of diagnostic colonoscopy is perforation with a reported incidence of 0.03–0.7 % and a mortality rate of 7–26 %.
- In diagnostic colonoscopy, perforation may be instrumental (instrument, overtube, or accessory device), 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 and with hernia incarceration.

- Perforation during diagnostic colonoscopy tends to be detected earlier when it is from instrumental causes, whereas perforation from therapeutic procedures is frequently related to thermal injury and is often delayed.
- Avoidance of perforation is related to training, skill, and experience.
- Techniques include 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, insuring that abdominal and inguinal hernias remain reduced, avoiding over insufflation, and looping in the splenic flexure region.
- There should be constant identification of the location of the lumen with avoidance of "slide by" (sidewise passage of the instrument without direct visualization of the lumen).
- Symptoms of perforation include undue and sustained pain (especially shoulder discomfort), absence of liver dullness on percussion, demonstration of pneumoperitoneum on upright chest film, and subcutaneous emphysema. Signs and symptoms are related to factors such as adequacy of bowel preparation, size of injury, and underlining pathologic state of the colon.
- Nonoperative management is successful in a subset of patients (localized peritoneal signs in the absence of sepsis, irrespective of a pneumoperitoneum).
- An uncommon presentation of a contained perforation may be the presence of retroperitoneal or mediastinal air and even subcutaneous emphysema which usually resolves without treatment.
- Perforation with generalized peritonitis suggests continuing contamination of the peritoneal cavity and therefore demands operative management. With early surgical intervention of a mechanical perforation, primary closure with or without protective proximal stoma is usually feasible. However, the surgeon must use good judgment in assessment of such factors as adequacy of tissue perfusion, degree of spillage, and colon tissue free of inflammation. Adverse findings may suggest resection of the perforated segment and proximal diversion.
- Other reported complications include abdominal distension, dehydration, respiratory depression, vasovagal reaction, thrombophlebitis, incarcerated hernia, splenic capsular tear and subcutaneous/mediastinal emphysema, and equipment failure.

6. Radiology

Jamie L. Bohl and Alan E. Timmcke

Introduction

- In order to extract the maximal amount of information from an abdominal plain film, the position of the patient, the number of views needed, and the known sensitivity of this modality for various diagnoses should be considered.

Plain Films

- An abdominal plain film is referred to as a KUB (kidneys, ureter, and bladder). An acute abdominal series is comprised of an upright chest, supine abdomen, and upright, decubitus, or cross table lateral of the abdomen. The series of radiographs with the patient in various positions is meant to maximize the diagnostic yield of plain films.
- Whether two or three abdominal films are obtained is of secondary importance. The most important goal is to image the entire abdominal cavity and ensure that the diagnostic question is addressed.
- The American College of Radiology suggests the use of abdominal plain films by the colon and rectal surgeon (Table 6.1).

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Table 6.1 Indications for abdominal radiography

Abdominal, flank, or pelvic pain
Vomiting
Abdominal distention, bloating, or increased girth
Evaluation for and follow-up of bowel obstruction or nonobstructive ileus
Constipation
Diarrhea
Palpable abdominal mass or organomegaly
Follow-up of the postoperative patient
Blunt or penetrating abdominal trauma
Search for foreign bodies
Assessment of the GI tract for residual contrast which can interfere with another imaging study
Evaluation of medical device position
Evaluation of pneumoperitoneum

- It is important to remember that plain films are not used as a screening tool and when used as such may contribute to increased radiation exposure for little diagnostic yield. If the clinical scenario suggests a diagnoses which is better imaged with a different radiologic modality, the alternate imaging study should be used as the initial or only examination for that patient.
- Plain abdominal films are useful to the colon and rectal surgeon to identify foreign bodies, check the position of drains and catheters, evaluate changes or abnormalities in intestinal gas distribution, and occasionally identify skeletal or mucosal changes associated with inflammatory bowel disease.
- Plain abdominal films not only document the proximal extent of the object but can determine the number, size, and shape of the foreign body (Fig. 6.1a, b). Gas collections may be extraperitoneal or intraperitoneal. Extraperitoneal collections in the soft tissue of the abdominal wall may reflect a necrotizing infection or recent intervention such as surgical incision.
- Intraperitoneal air may be located outside the intestinal lumen (free air), within the wall of the bowel, or within the confines of the bowel wall.
- Appropriate localization of abdominal gas collections along with clinical correlation assists the clinician in distinguishing a benign condition from a surgical emergency.
- Pneumoperitoneum or air outside the confines of the bowel wall is diagnostic of a perforated viscus and can be diagnosed with high sensitivity using an upright chest film.
- If the patient has peritonitis or is extremely ill and cannot sit upright, a left lateral decubitus film can be obtained.
- The left lateral decubitus film in the expiratory phase or the upright chest in the midinspiratory phase have a high sensitivity and can be diagnostic of as little as 1 cm^3 of free intraperitoneal air.

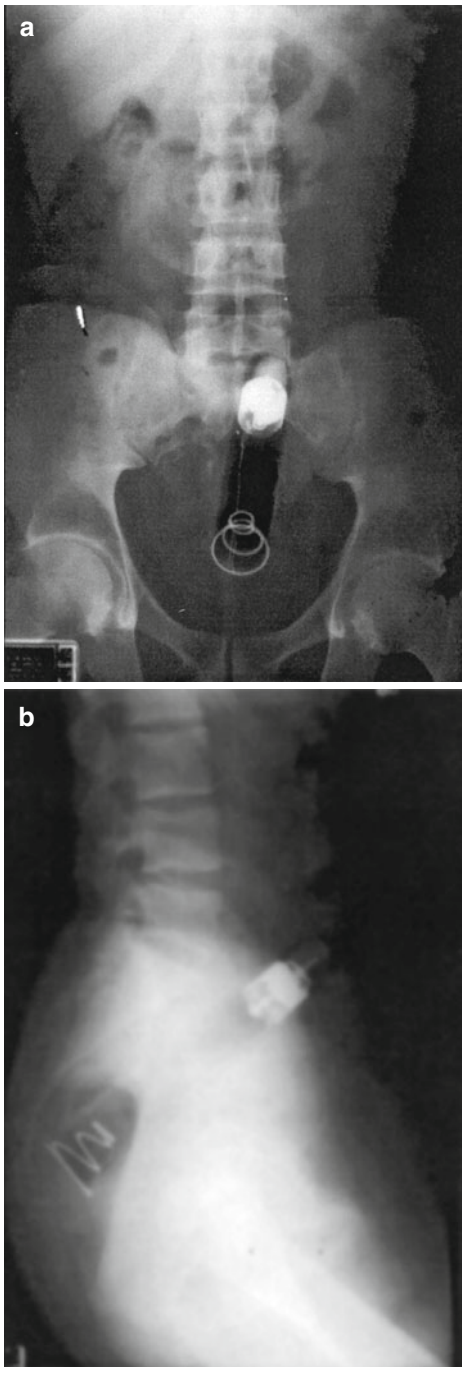

Fig. 6.1 (**a**) Radiograph of rectal foreign body (anterior posterior). (**b**) Radiograph of rectal foreign body (lateral)

- The left lateral decubitus film is preferred to the right, because it allows air movement between the liver and right hemidiaphragm where it is easily imaged and not confused with the gastric bubble.
- It is important to maintain the left lateral decubitus position for at least 5–10 min prior to imaging in order to allow migration of air.
- Diagnostic signs of free intraperitoneal air include:
  - A right upper quadrant gas sign (Fig. 6.2a) is a triangular or linear gas collection which has an oblique (superomedial to inferolateral) orientation between the liver and right hemidiaphragm.
  - Rigler's sign (Fig. 6.2b), outlining of both the mucosal and serosal sides of the bowel wall with associated bowel wall thickening (1–8 mm), is also indicative of free intraperitoneal air.
  - Other less commonly seen diagnostic signs include the falciform ligament sign (a thin linear soft tissue density in the right upper quadrant caused by free intraperitoneal air lining both sides of the falciform ligament), the football sign (visualization of gas anterior to loops of bowel within the central abdomen), and the inverted V sign (visualization of the medial umbilical folds in the pelvis).
- A diagnosis of free intraperitoneal air must always be correlated with the clinical condition of the patient. For instance, free intraperitoneal air can be a normal finding after surgery.
- Free air is typically reabsorbed over several days following surgery but reabsorption may be delayed in the recumbent or thin patient.
- Increasing amounts of air imaged over time or in association with increasing abdominal pain may be indicative of an anastomotic leak or intestinal perforation.
- In addition, various conditions may be mistaken for free air:
  - Chilaiditi syndrome is the interposition of the colon between the liver and diaphragm and can mimic the finding of pneumoperitoneum on plain abdominal films.
  - Extraluminal air may also be located within a loculated abscess cavity, within solid organs that do not typically contain air, in the venous system, or within the bowel wall.
  - Portal venous air is peripherally located air, which may have entered the portal venous system as a result of bowel ischemia and necrosis or a gas-producing bacterium.
  - In contrast, pneumobilia or air within the biliary tract is centrally located and can result from a cholecystoduodenal fistula or from an endoscopic sphincterotomy.
  - Finally, linear air within the bowel wall (pneumatosis intestinalis) may result from bowel ischemia and necrosis, while cystic air collections within the bowel wall signify a benign condition called pneumatosis cystoides.
- Determination of intraluminal bowel gas patterns can help differentiate a small from large bowel obstruction or a bowel obstruction from a paralytic ileus.

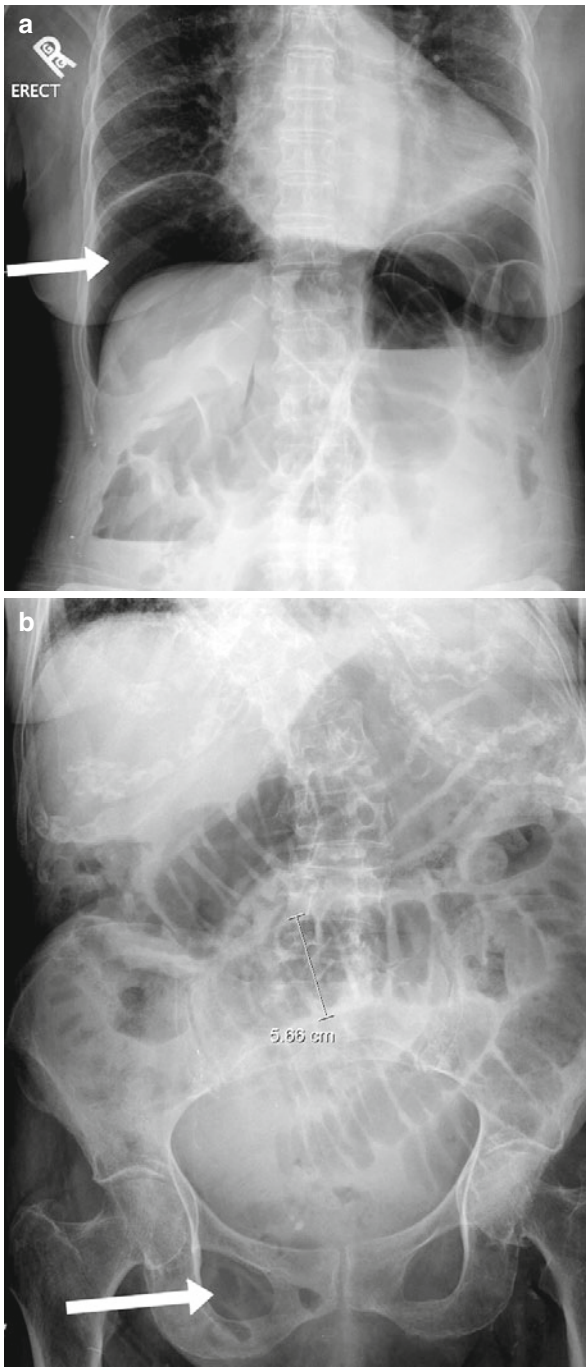

Fig. 6.2 (**a**) Upright radiograph of the abdomen demonstrates a collection of air within the peritoneal space between the liver and the diaphragm (*white arrow*). (**b**) Plain radiograph demonstrates the "Rigler" sign or "double lumen" sign (gas on both sides of the bowel wall (*white arrow*))

Fig. 6.3 Plain film of small bowel obstruction with dilated small bowel loops, forming a stepladder

- Bowel dilation is identified by the 3, 6, 9 rule. The small bowel is dilated when the diameter is 3 cm, the colon when it reaches 6 cm, and the cecum when it dilates to 9 cm.
- The small bowel can be differentiated from the colon by valvulae conniventes which cross the entire bowel loop and are more narrowly spaced compared to the haustra of the colon which are thicker, further apart, and only extend halfway across the colon diameter. In addition, dilated small bowel loops may form a stepladder appearance when dilated from obstruction (Fig. 6.3).
- The valvulae conniventes may trap air between them as the obstructed small bowel fills with fluid giving a string of beads appearance. This finding is sensitive for a high-grade small bowel obstruction (SBO). However, other signs of obstruction can be misleading.
- Air-fluid levels may be indicative of an SBO, gastroenteritis, or paralytic ileus. Ileus may be differentiated from obstruction by air found throughout the small bowel and colon (Fig. 6.4).
- In contrast, a completely obstructed bowel may be void of air distal to the obstruction. In a partial or early bowel obstruction, distal air evacuation may not be present and the distinction between ileus and obstructions is impossible.

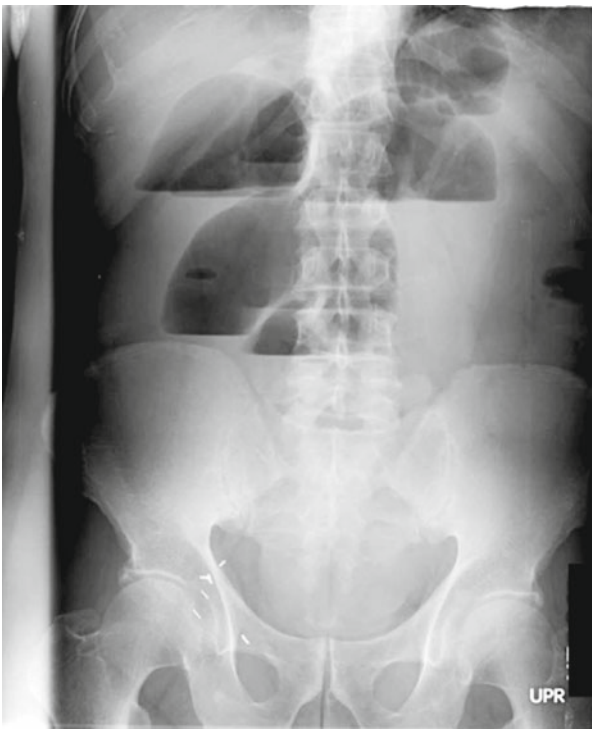

Fig. 6.4 Small bowel obstruction air-fluid levels

- Large bowel obstructions clinically appear like a distal SBO. On plain abdominal films the colon alone may be dilated if the ileocecal valve is competent (Fig. 6.5). This causes the cecum to dilate. Acute cecal dilation beyond 12 cm places the patient at risk of perforation. In the setting of an incompetent ileocecal valve, air refluxes proximally into the small bowel which can make it difficult to distinguish between a paralytic ileus and distal bowel obstruction (Fig. 6.6).
- Volvulus in the cecum or sigmoid gives rise to a closed loop obstruction within the colon and can result in characteristic findings on abdominal plain films.
- The classic finding of a sigmoid volvulus is a U-shaped loop of colon projected toward the right upper quadrant in the shape of a "bent inner tube." In the middle of the sigmoid loop, the medial walls of the obstructed sigmoid colon point into the pelvis (Fig. 6.7). These findings are also associated with a dilated colon and small bowel proximal to the sigmoid.
- Cecal volvulus is characterized by a dilated cecum in the upper left quadrant with a "coffee bean" or "kidney" shape because of the medially placed ileocecal valve (Fig. 6.8).

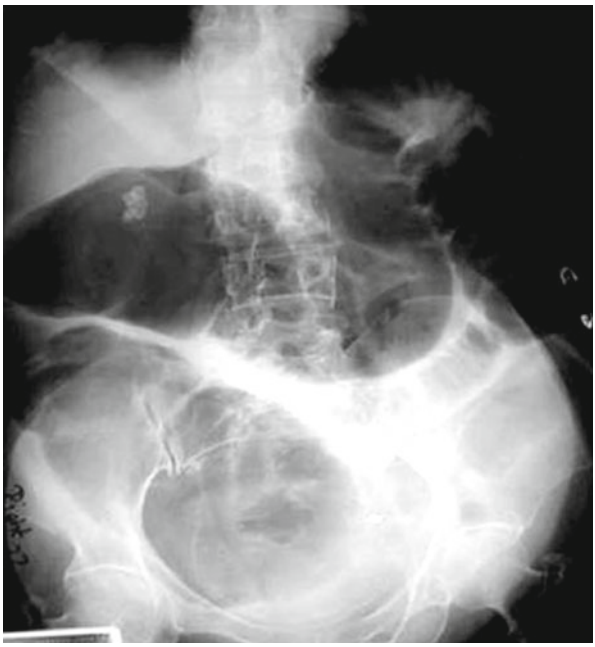

Fig. 6.5 Large bowel obstruction secondary to sigmoid cancer. Competent ICV

- Finally, the abdominal radiograph can reveal changes in mucosal contour and thickness. Normal bowel wall thickness is less than 2 mm. However, various forms of colitis may give rise to bowel wall thickening and mucosal irregularity.
- Thumbprinting is a radiographic sign that signifies bowel wall and mucosal edema and in the setting of colon dilation may signify the presence of toxic megacolon with risk of impending perforation.
- Chronic mucosal inflammation may lead to haustral blunting and a tubular burned out colon from longstanding colitis (Fig. 6.9).

Contrast Studies

Contrast Enemas

- Contrast enemas can be performed as a single-contrast or double-contrast enema.
- The single-contrast enema is performed by filling the colon and rectum with barium or a water-soluble agent through a rectal catheter.
- In double-contrast enemas or air-contrast enemas, barium is instilled into the colon and rectum until the mid-transverse colon is reached. The colon is then drained of excess barium and air is instilled to allow luminal distention and prevent mucosal wall apposition.

Fig. 6.6 Large bowel obstruction secondary to sigmoid cancer. Incompetent ICV

Fig. 6.7 Plain film of sigmoid volvulus

Fig. 6.8 Plain film of cecal volvulus

Fig. 6.9 Plain film of chronic burned out colitis

- The radiologist can then change the position of the patient and use fluoroscopic guidance to obtain images of the colonic and rectal mucosa throughout its length and in multiple projections without overlap. The double contrast provides mucosal coating and detail that cannot be seen in single-contrast studies.
- Careful technique with mucosal coating, adequate distention, and numerous projections allow discrimination of mucosal abnormalities with the double-contrast enema.
- The limitations of a contrast enema need to be considered prior to subjecting the patient to this study. In order to visualize the mucosa, the patient must undergo a complete bowel preparation.
- If a patient does not have mobility to change position on the fluoroscopy table or does not have enough rectal tone to hold the contrast enema, the mucosal coating and projections obtained will be of limited diagnostic value.
- An incompetent ileocecal valve may allow reflux of contrast into the small bowel and further obscure colonic findings.
- The rectal catheter may obscure the distal rectum so that internal hemorrhoids or a distal rectal cancer cannot be appropriately discriminated.
- Finally, there is a risk of perforation with this study. Because barium causes an intense inflammatory response within the peritoneal cavity, in clinical situations for which intestinal continuity is in question or when the bowel wall may be weakened, a water-soluble contrast agent should be used.
- These scenarios include question of anastomotic integrity, evaluation of a large bowel obstruction, acute colitis, recent snare or forceps biopsy of the colon wall, and suspicion of colonic fistulas. In comparison to barium studies, water-soluble enemas do not coat the mucosa and do not discriminate mucosal changes.
- The double-contrast technique can be used to detect mucosal disease in an elective setting (the evaluation of colonic polyps and cancer, inflammatory bowel disease, diverticulosis, and other mural abnormalities like lipomas, lymphoma, and endometriosis).
- The double-contrast enema has a sensitivity of 50 % for polyps and cancer less than 1 cm in size and 90 % sensitivity for those greater than 1 cm.
- Increasing size, ulceration, and circumferential involvement increase the possibility that a polyp has an underlying malignancy.
- Semiannular lesions, which are seen on contrast enema with abrupt transition from normal to irregular mucosal patterns, shelf-like overhanging borders, and circumferential bowel narrowing, are characteristic of an apple core lesion and are diagnostic of cancer (Fig. 6.10). In comparison, benign strictures from ischemic, infectious, or inflammatory etiologies have smooth tapering borders.
- Overall, double-contrast barium enema has a positive predictive value of 96 % for a malignant stricture and 84–88 % for a benign stricture. Double-contrast barium enema has been recommended as one screening modality for patients greater than 50 years of age at average risk of colon and rectal cancer.

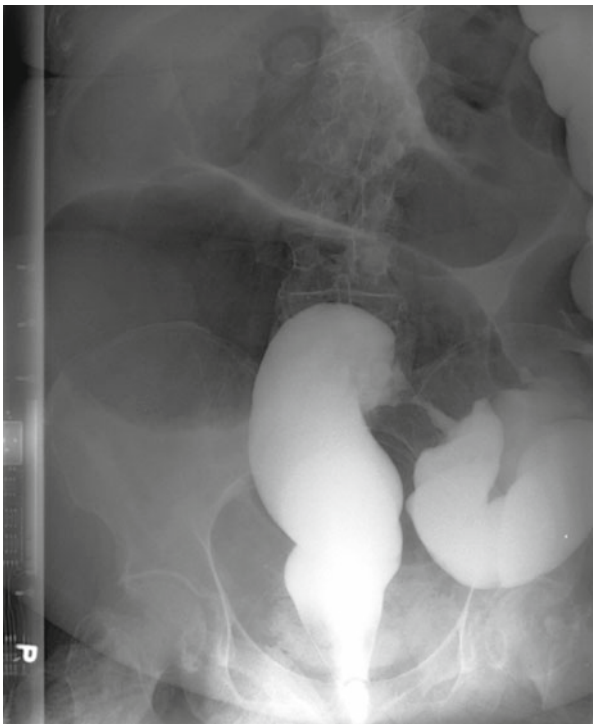

Fig. 6.10 ACE of annular cancer and "apple core sign"

- Double-contrast barium enema can also be diagnostic in the setting of inflammatory bowel disease. It can be used to differentiate Crohn's disease from ulcerative colitis, define the extent and severity of disease burden, as well as visualize complications of the disease. In acute ulcerative colitis, the mucosa appears stippled with shallow punctuate ulceration (Fig. 6.11a).
- As the inflammation progresses, the ulcers enlarge as crypt abscess ruptures and exposes the submucosa leading to pseudopolyps, which appear as irregular mucosal projections on the contrast enema (Fig. 6.11b).
- Eventually, there is loss of mucosal detail and haustral folds, which cause a tubular or lead pipe appearance of the colon (Fig. 6.12).
- Strictures from ulcerative colitis appear as smooth, symmetric, and circumferential colonic narrowing.
- In Crohn's disease, the mucosal changes are not continuous and are deeper than the changes seen in ulcerative colitis. Early aphthous ulcers appear as shallow depressions with a radiolucent halo (Fig. 6.13a).
- As Crohn's disease progresses, the ulcers widen and coalesce as the muscle in the bowel wall is penetrated. This leads to cobblestoning, which appears as irregular white stripes within the colon wall on contrast enema (Fig. 6.13b).

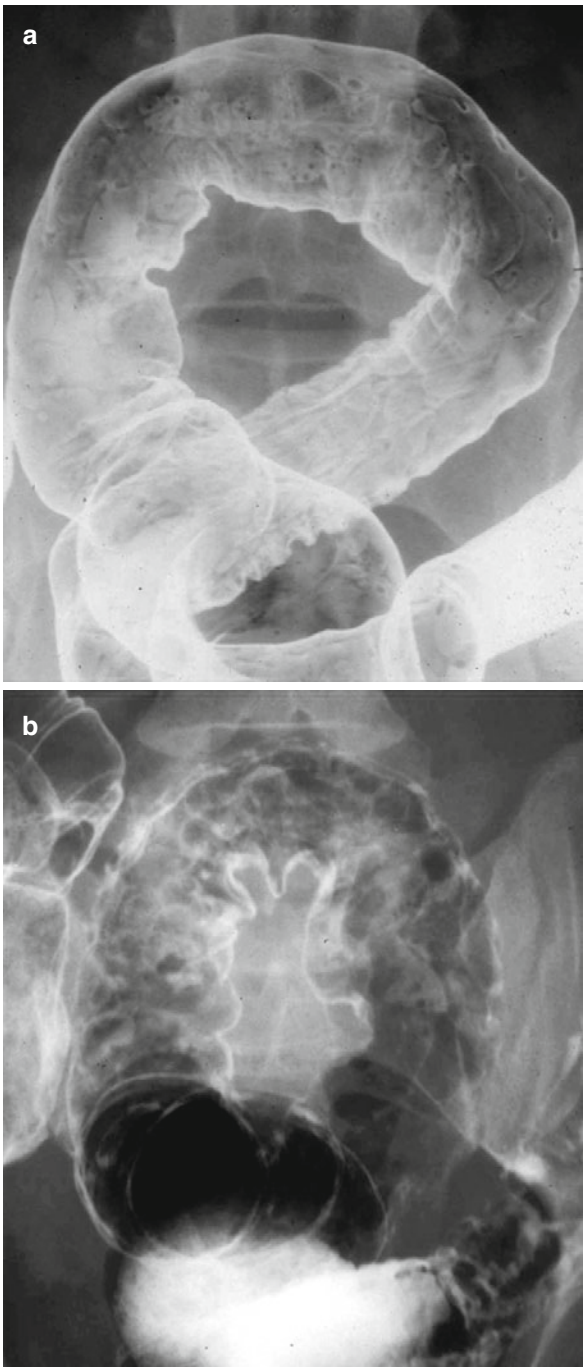

Fig. 6.11 (**a**) Contrast enema of ulcerative colitis showing stippling ulcers or early colitis. (**b**) Contrast enema of ulcerative colitis with pseudopolyps

Fig. 6.12 Contrast enema of chronic ulcerative colitis

- Deep linear ulceration along the mesenteric border causes “rake” or “bear claw” ulcers that can cause stricturing from transmural fibrosis.
- Strictures from Crohn’s disease appear as noncircumferential, irregular areas of narrowing that are centered at the mesenteric edge (Fig. 6.14).
- Complications of Crohn’s disease such as strictures and fistulas are well imaged with the double-contrast barium technique. In contrast, other complications of inflammatory bowel disease are not easily diagnosed with enema studies. In both ulcerative colitis and Crohn’s disease, it is difficult to distinguish inflammatory polyps from dysplasia or cancer.
- Diverticular disease can also be well characterized with contrast enemas. The size, shape, number, and location of diverticuli are well imaged.
- In profile, diverticuli appear flask shaped with a neck, which points away from the colonic lumen. En face diverticuli appear as a white spot or meniscus within the colon lumen (Fig. 6.15). With acute diverticular inflammation, secondary signs of inflammation such as narrowing of the colon lumen from extrinsic compression and mucosal edema are evident.

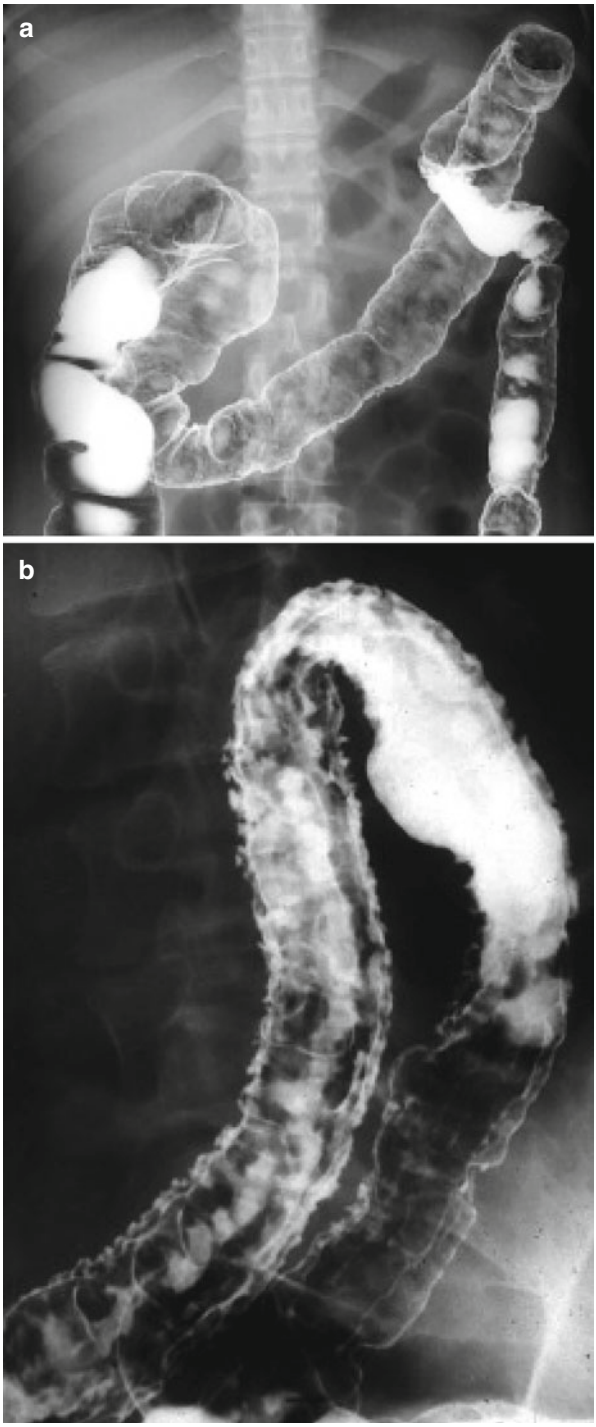

Fig. 6.13 (**a**) Contrast enema of Crohn's disease showing ulcers. (**b**) Contrast enema of Crohn's with fissures and long linear ulcers

Fig. 6.14 Contrast enema of Crohn's disease showing a stricture

- Complications of diverticulitis can also be seen. Diverticular perforation results in leaking of extraluminal contrast into the peritoneal cavity, a contained cavity, or a blind sinus that drains back into the colon lumen.
- Strictures appear as smooth transitions in colon caliber with intact mucosa.
- Abscesses are suggested by a smooth contour defect within the colon lumen, which does not distend with additional air or contrast instillation.
- Fistulae between proximal intestinal loops, the vagina, and bladder may also be seen. Barium contrast enema is safe to perform with active diverticular inflammation in the absence of peritonitis. However, the sensitivity of the contrast enema is low and may not be diagnostic in a patient with complicated diverticulitis.
- Double-contrast enemas may also reveal colonic lipomas, endometriosis, and lymphoma. Lipomas are seen as a submucosal mass or polypoid lesion with smooth overlying mucosa. The soft pliable nature of the lipoma may be imaged in real time as the barium and air are instilled and show compression of the mass known as the "pillow sign."

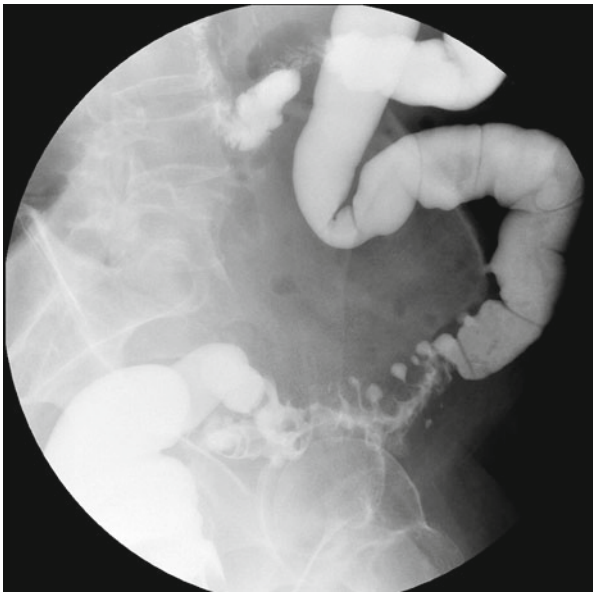

Fig. 6.15 Barium enema demonstrates a deformed colon wall with diverticular sacs (From Blanchard TJ, Altmeyer WB, Matthews CC. Limitations of colorectal imaging studies. In: Whitlow CB, Beck DE, Margolin DA, Hicks TC, Timmcke AE, editors. Improved outcomes in colon and rectal surgery. London: Informa Healthcare; 2010. p. 97–131. With permission)

- Endometriosis appears as an extracolonic process with intact but bunched up mucosal folds that result in luminal narrowing and in extreme cases scarring and luminal contracture (Fig. 6.16).
- Lymphoma appears different from adenocarcinoma on a double-contrast enema. In contrast, lymphoma does not narrow the lumen but causes folding and thickening of the mucosa from bowel wall infiltration.
- The mucosa maintains a smooth appearance (Fig. 6.17). All these findings on double-contrast enema while, suggestive of a specific diagnosis, require correlation with clinical information to be diagnostic of the condition.
- Water-soluble enemas do not result in the same mucosal coating and colonic distention that can be achieved with double-contrast enemas. However, water-soluble contrast is not toxic to the peritoneal lining and can therefore be used in clinical situations in which bowel integrity may be compromised.
- This includes clinical situations suspicious for colonic obstruction caused by cancer, acute episodes of inflammatory bowel disease, intussusception, volvulus, and fecal impaction.
- Water-soluble enemas may also be used for evaluation of anastomotic integrity.
- A water-soluble contrast enema demonstrates a spring-coil appearance or crescent sign as contrast gets trapped between the lumens of the two

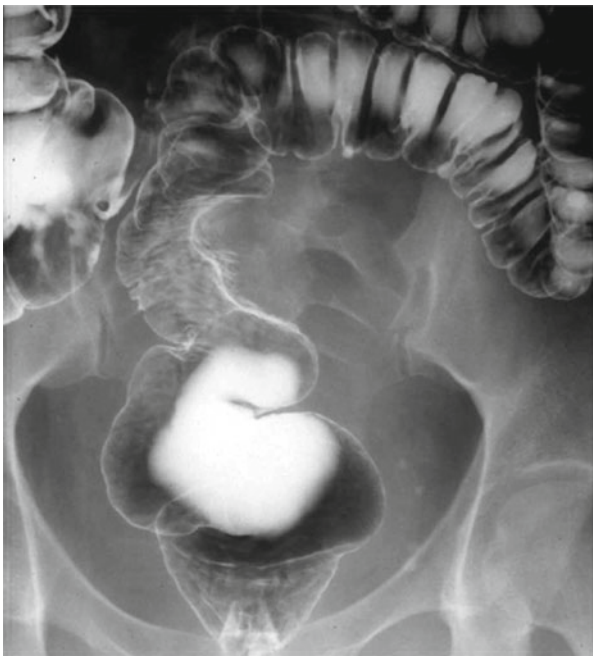

Fig. 6.16 Contrast enema showing endometriosis

bowel segments and leaves a thin circular line that outlines the proximal bowel in the distal bowel lumen (Fig. 6.18).

- While barium, air, and water-soluble enemas have been used to hydrostatically decompress an intussusception, this is not typically attempted in the older child or adult because the cause is usually a pathologic lead point.
- Water-soluble enemas can be used to diagnose and occasionally spontaneously decompress a colonic volvulus.
- Sigmoid volvulus appears as a "bird's beak" as the mucosal folds spiral into the point of obstruction.
- In cecal volvulus there is abrupt contrast cutoff distal to the torsed colonic segment with a dilated ectopic cecum. This is known as the "column cutoff sign" (Fig. 6.19).
- In the setting of fecal impaction, water-soluble contrast is instilled up to the site of obstruction under fluoroscopic guidance.
- The high osmolality of the substance allows it to emulsify stool and release impacted stool into smaller pieces that can be passed per anus.
- Water-soluble enemas are also useful prior to takedown of a diverting stoma, when a colonic stenosis is suspected or in the early postoperative period when a leak is suspected (Fig. 6.20a, b).
- Views of the colon should be obtained in the anteroposterior and lateral views during early luminal filling, full colonic distention, and after evacuation of contrast.

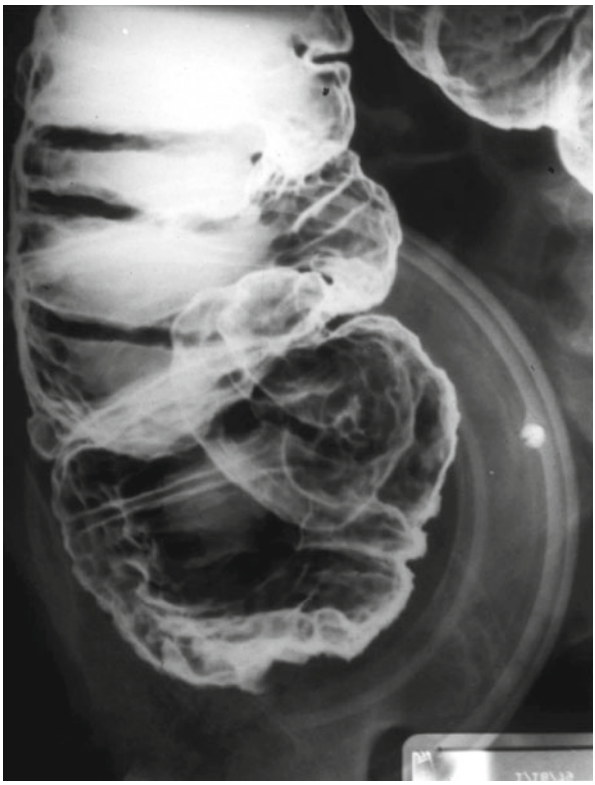

Fig. 6.17 Contrast enema showing colonic lymphoma

- Multiple colon projections with varying degrees of contrast distention allow for the diagnosis of subtle leaks that may be obscured by full colonic distention with contrast.

Small Bowel Series and Enteroclysis

- The small bowel can be imaged using several methods. To obtain a small bowel series, a patient drinks a large volume of dilute barium, and contrast is followed as it advances through the small bowel with fluoroscopy images taken every 15–30 min.
- In order to improve visualization of small bowel loops, abdominal pressure and compression can be used to flatten bowel loops and decrease small bowel loop overlap.
- Transit of contrast through the small bowel normally takes 90–120 min. In comparison, small bowel enteroclysis is a more labor- and time-intensive method for imaging the small bowel.
- The patient must undergo colonic cleansing to decrease both the time needed for contrast to reach the terminal ileum as well as the amount of contrast needed to fill the small bowel.

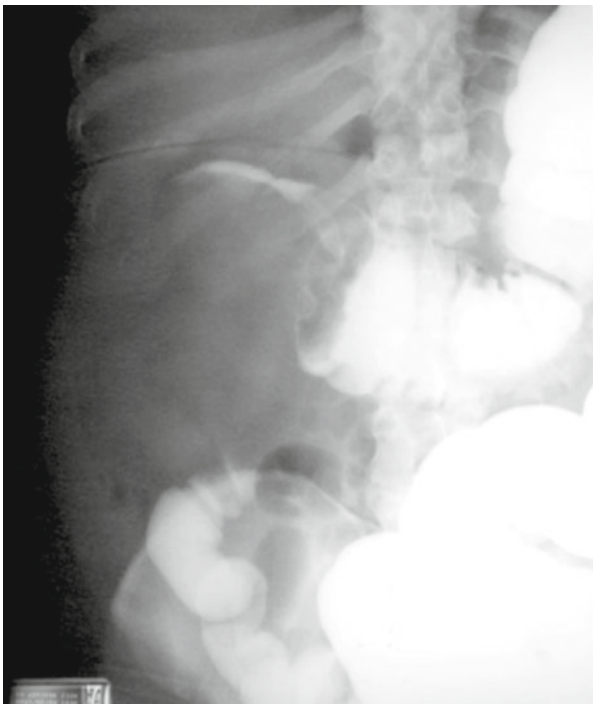

Fig. 6.18 Contrast enema showing colonic intussusception

- With this method, two contrast agents are instilled into the duodenum at separate points in time through a tube inserted through the nose and advanced into the proximal duodenum. The rate of contrast instillation is modified according to the amount of small bowel distention achieved and patient tolerance.
- Administration of barium in addition to air or methylcellulose allows the barium to act as an interface with the small bowel mucosa for detection of mucosal lesions or subtle mucosal changes. Serial images are obtained with enteroclysis as is done with small bowel series. In comparison to small bowel series, small bowel enteroclysis requires placement of a nasogastric tube, high radiation doses (up to 21 mSv), and administration of a hyperosmotic contrast agent.
- Small bowel imaging is typically useful for patients with unexplained gastrointestinal bleeding, suspected small bowel tumors, Crohn's disease, and partial SBOs.
- For patients with Crohn's disease, the severity and distribution of disease can be determined (Fig. 6.21a, b).
- In addition, the site of small bowel complications such a fistula and stricture can be located.

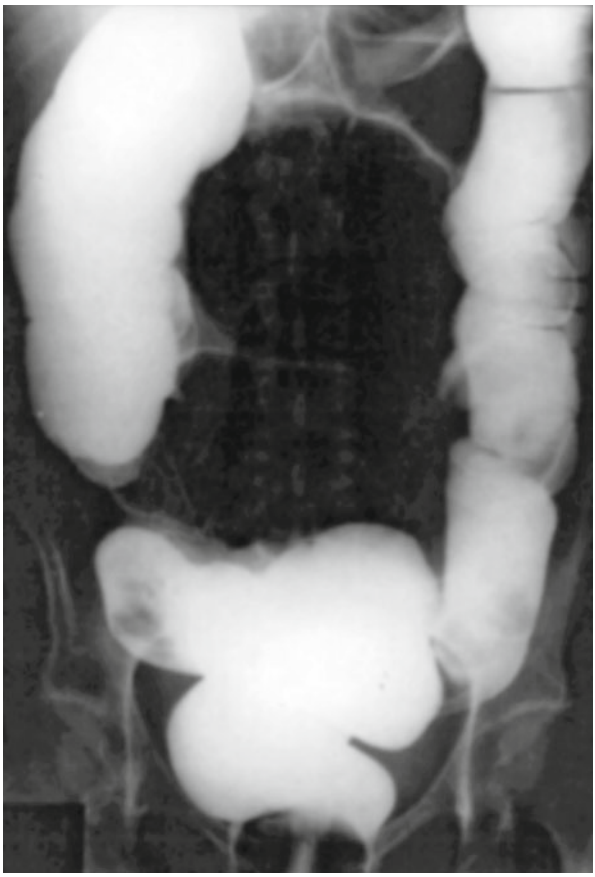

Fig. 6.19 Water-soluble contrast enema showing cecal volvulus (From Blanchard TJ, Altmeyer WB, Matthews CC. Limitations of colorectal imaging studies. In: Whitlow CB, Beck DE, Margolin DA, Hicks TC, Timmcke AE, editors. Improved outcomes in colon and rectal surgery. London: Informa Healthcare; 2010. p. 97–131. With permission)

- For patients with suspected SBOs, dilute barium can be used to image the small bowel when there is unclear etiology of the obstruction or when localization of the obstructing point is important.

Computed Tomography (CT)

- CT provides detailed and high-resolution cross-sectional images of hollow viscous and solid organs.
- Accurate interpretation requires optimal opacification of the gastrointestinal tract and vascular structures.

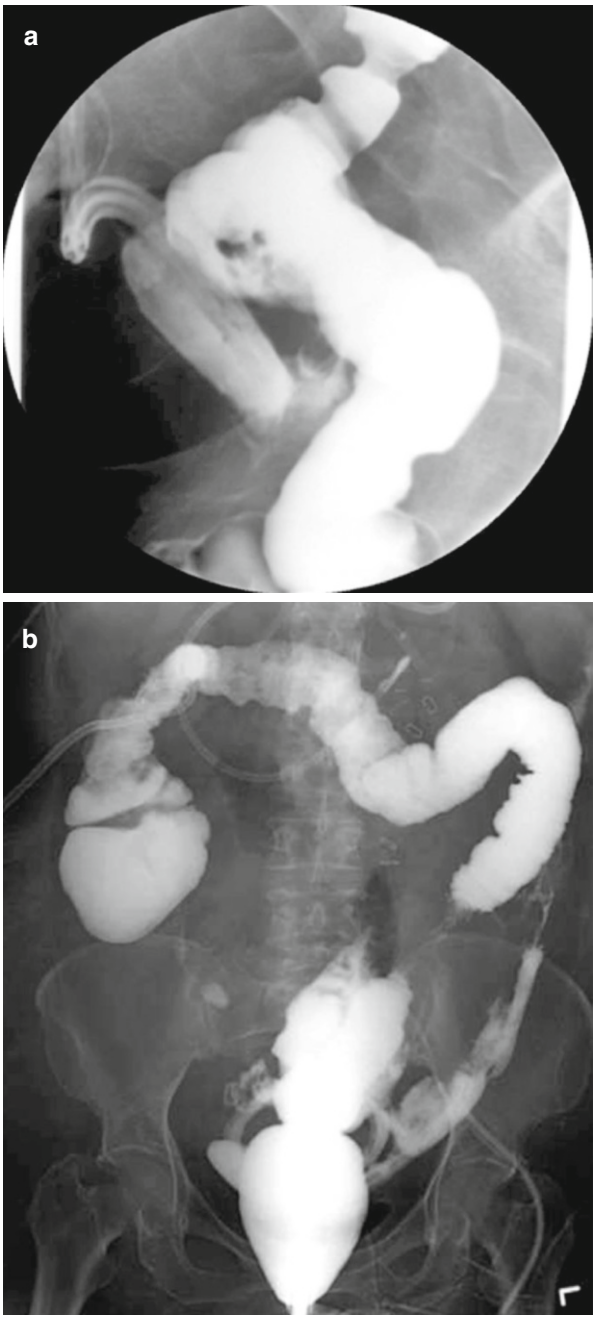

Fig. 6.20 (**a**) Contrast enema showing a contained anastomotic leak. (**b**) Contrast enema showing a free-flowing leak

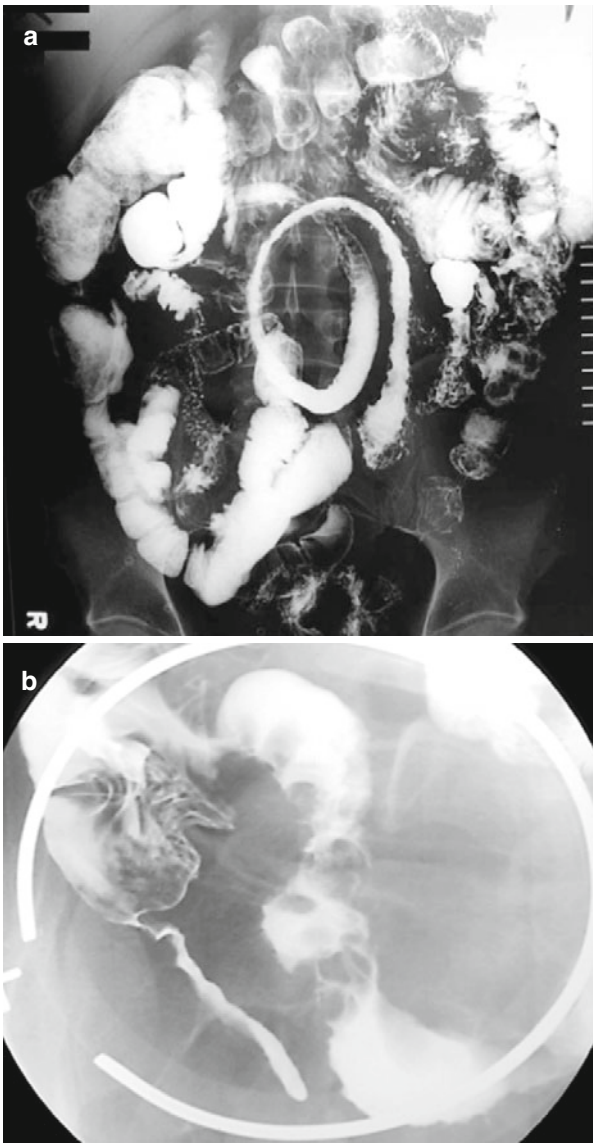

Fig. 6.21 (**a**) Small bowel series showing terminal ileum Crohn's disease strictures. (**b**) Small bowel follows through showing cobblestoning

- The bowel is opacified by administering a water-soluble oral contrast agent. The density of barium interferes with the acquisition of data during the scan and thus should be avoided as a contrast agent.
- The oral contrast is typically administered 45–60 min before scanning to allow the contrast to opacify as much of the bowel as possible.

- 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.
- Anaphylactic reaction to the iodinated contrast is a contraindication for administration, but simple allergies such as hives can be prevented with steroids and diphenhydramine.
- Iodinated contrast is administered as a bolus at the time of the examination. The reason for the examination dictates the exact timing between when the contrast is administered and when the CT images are acquired (i.e., venous vs. arterial phase).
- The CT scan uses ionizing radiation to acquire the images with 5- to 10-mm collimation. Smaller collimation allows for sharper, more detailed images.
- Radiation exposure to the patient varies depending on protocol design and the type of CT scanner used. However, the average radiation dose for a multidetector CT of the abdomen and pelvis is 13.3 mSv and for a CT of the chest is 6.8.
- CT is sensitive for the staging of colon and rectal cancer and diagnosis of inflammatory and infectious conditions of the colon, bowel obstruction, and postoperative complications.

Colon and Rectal Cancer

- CT assists the surgeon in determining the location of the primary tumor, involvement of adjacent organs, enlargement of regional lymph nodes, and the presence of distant (liver) metastases.
- CT accuracy for predicting tumoral extension beyond the muscularis propria can be as high as 70–82 %; however, inaccuracies result from the inability to distinguish gross tumor extension from peritumoral desmoplastic reaction (Fig. 6.22).
- Lymph nodes are considered pathologic if they are >1 cm in size on CT scan. Accuracy in detecting lymph node involvement can be limited by normal size of tumor-bearing nodes and enlargement of lymph nodes in the peritumoral region without nodal metastases.
- CT scan is an accurate imaging modality for the detection of hepatic metastases as well as hepatic recurrence of colon and rectal cancer.
- Preoperative CT scan is 85 % sensitive for colon and rectal hepatic metastases.
- The ASCRS practice parameters do not recommend routine abdominal imaging as part of a cancer surveillance program.

Other Tumors of the Colon

- Lipomas can be easily diagnosed by demonstrating a 2–3-cm, round or ovoid, sharply defined tumor with homogenous fat density.

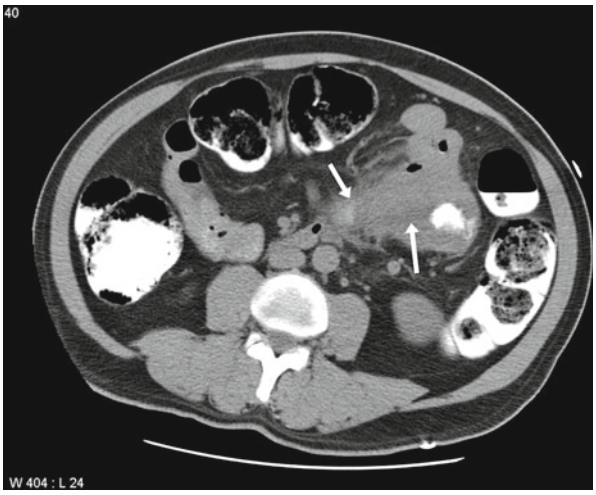

Fig. 6.22 CT showing a large colonic mass in the descending colon (*white arrows*) that narrows the lumen. CT cannot differentiate tumor extension through the wall from pericolonic edema or desmoplastic reaction (From Blanchard TJ, Altmeyer WB, Matthews CC. Limitations of colorectal imaging studies. In: Whitlow CB, Beck DE, Margolin DA, Hicks TC, Timmcke AE, editors. Improved outcomes in colon and rectal surgery. London: Informa Healthcare; 2010. p. 97–131. With permission)

- Colonic lymphoma usually appears as either a marked thickening of the bowel wall that often exceeds 4 cm, or a homogeneous soft tissue mass without calcification.
- Owing to the softness of the tumor, the lumen is commonly dilated or normal, rather than constricted, and bowel obstruction is uncommon.
- The absence of desmoplastic reaction and diffuse lymphadenopathy help to differentiate lymphoma from adenocarcinoma.
- GISTs can appear as an exophytic or intraluminal mass, and size varies from few millimeters to 30 cm (Fig. 6.23).
- Sarcomas that arise in the bowel, anorectum, or omentum are indistinguishable from malignant GIST. Tissue types include leiomyosarcoma, fibrosarcoma, and liposarcoma.

Diverticulitis

- CT scan is the most accurate imaging modality for the diagnosis of diverticulitis and its complications.
- CT findings of diverticulitis include soft tissue stranding of the pericolonic fat, diverticula, colon wall thickening, and abscess formation.
- Normally, the colon mesentery and pericolonic tissues are hypodense secondary to the high water content of fatty tissue. This creates sharp boundaries between the colon, colonic mesentery, and adjacent organs.

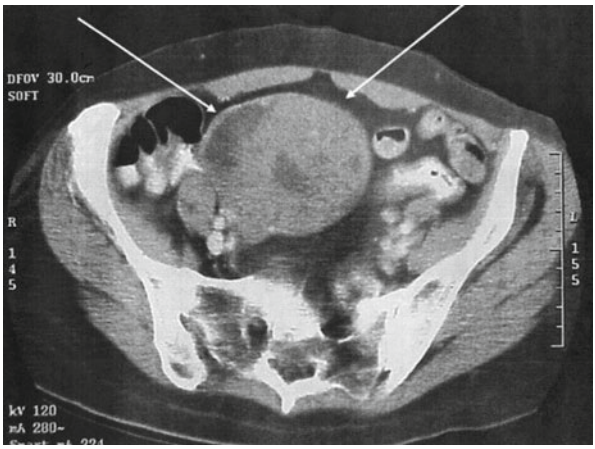

Fig. 6.23 CT showing a large heterogenous exophytic mass with cystic degeneration (*white arrows*) and necrosis that communicates with the lumen of adjacent colon and small bowel (From Blanchard TJ, Altmeyer WB, Matthews CC. Limitations of colorectal imaging studies. In: Whitlow CB, Beck DE, Margolin DA, Hicks TC, Timmcke AE, editors. Improved outcomes in colon and rectal surgery. London: Informa Healthcare; 2010. p. 97–131. With permission)

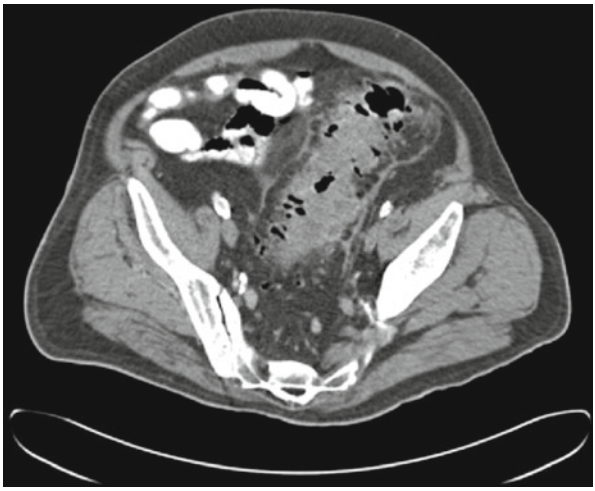

Fig. 6.24 CT showing uncomplicated diverticulitis

- As the inflammatory process develops, the mesentery becomes edematous and hypervascular. The sharp contrast between tissue planes is obscured resulting in so-called dirty fat.
- When the mesenteric and pericolonic inflammation is associated with colon wall thickening within the sigmoid mesentery, the diagnosis is diverticulitis (Fig. 6.24).

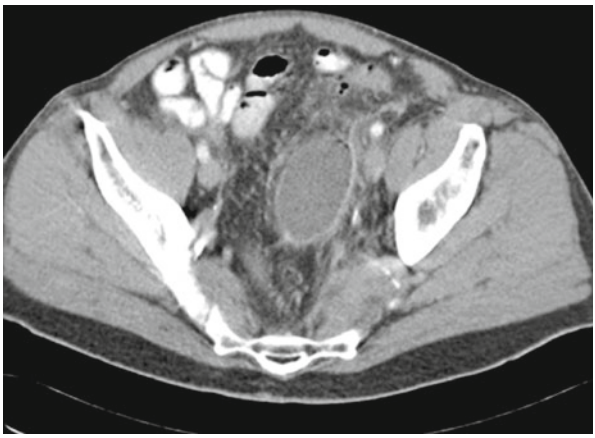

Fig. 6.25 CT showing a diverticular abscess

- Depending on the size of diverticular perforation, there may be small flecks of extraluminal air within the mesentery or in the upper abdomen above the liver.
- The identification of diverticula within the colon is not mandatory for the CT diagnosis of diverticulitis.
- Overall, the CT diagnosis of diverticulitis is based on a thickened short segment of colon with surrounding pericolonic inflammation.
- Pericolonic abscesses are fluid collections adjacent to the inflamed colon (Fig. 6.25).
- Abscesses are best visualized when surrounding loops of bowel are opacified with oral or rectal contrast, and the rim of the abscess is enhanced with intravenous contrast.
- A colovesicular fistula, an abnormal connection between the colon and bladder, can be diagnosed in several ways. Air within the bladder without previous catheterization is diagnostic (Fig. 6.26).
- In addition, thickening of the bladder wall with adjacent inflamed sigmoid colon can be suggestive of bladder involvement. If the fistula is large enough, enteral contrast may enter the bladder via the intestinal segment.
- Diverticulitis is more likely to involve a longer colonic segment (>5 cm), and produce pericolonic inflammation, perivascular engorgement, and fluid at the root of the mesentery. Conversely, colon cancer is more likely to be associated with an intraluminal mass, asymmetric wall thickening, and enlarged lymph nodes.

Inflammatory Bowel Disease

Crohn's Disease

- CT scan is useful for both the diagnosis of Crohn's disease and evaluation of established Crohn's disease.

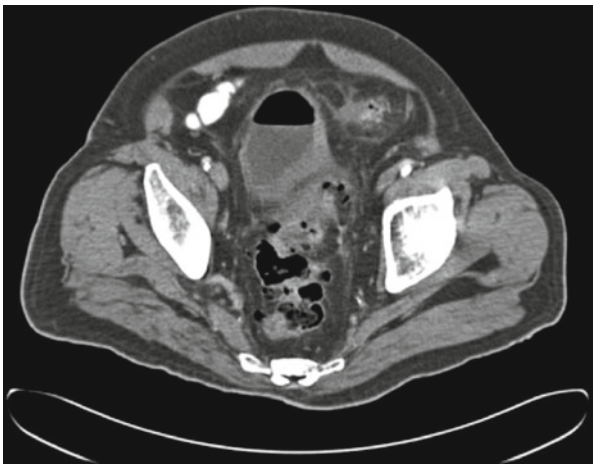

Fig. 6.26 CT demonstrating a colovesical fistula

- The most common findings associated with Crohn's disease are bowel wall thickening, peri-intestinal inflammation, and regional lymphadenopathy.
- The bowel wall can reach 11–13 mm 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.
- The transmural nature of the inflammatory process allows it to extend into the mesentery and adjacent structures so there is often an extensive inflammatory response centered on the affected bowel (Fig. 6.27a, b).
- The presence of creeping fat or fat proliferation within the mesentery separates bowel loops. This can give a characteristic appearance of a predominance of fat and inflammation on one side of the abdomen and a shift of unaffected, healthy bowel on the other side of the abdomen.
- Complications of Crohn's disease may also be seen on CT scan and include abscesses within mesentery, bowel loops, psoas muscle, pelvis, and abdominal wall (Fig. 6.28).
- Fistulae between bowel loops, the abdominal wall, vagina, and bladder may also be seen on CT. Finally, intestinal strictures with homogenous enhancement from chronic inflammation and fibrosis may also be seen on CT.

Ulcerative Colitis

- Like Crohn's disease, ulcerative colitis is characterized by thickening of the colon wall on CT scan. However, ulcerative colitis is not a transmural disease and, therefore, results in a lesser degree of bowel wall thickening (7–8 mm) in comparison to Crohn's disease (10–20 mm).
- Although ulcerative colitis can cause luminal narrowing of the colon from pseudopolyps, the outer bowel wall tends to remain smooth. In contrast,

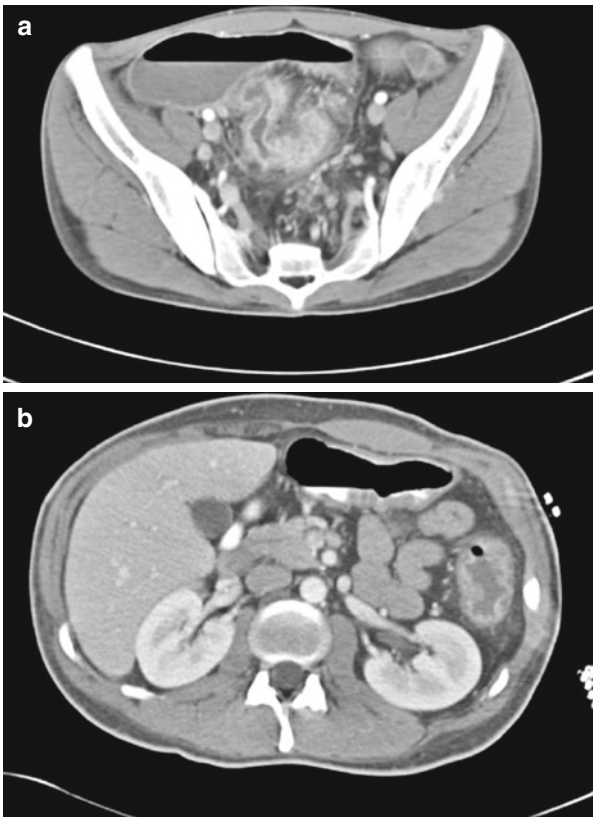

Fig. 6.27 (**a**) CT showing terminal ileum Crohn's disease with abscess. (**b**) CT showing Crohn's colitis

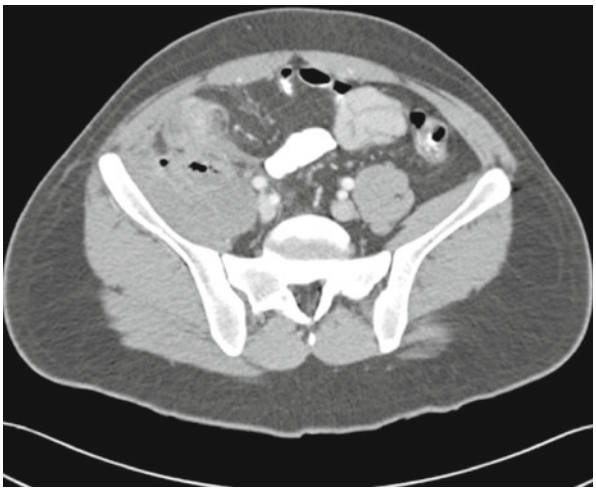

Fig. 6.28 CT showing a psoas abscess related to Crohn's disease

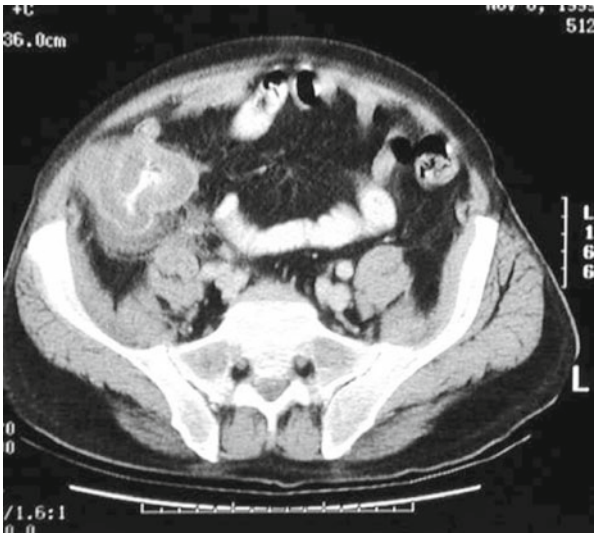

Fig. 6.29 CT showing neutropenic enterocolitis

bowel that is affected by Crohn's disease can be irregular on both the inner and outer bowel wall lining. Finally, ulcerative colitis is not typically associated with abscesses and fistulae.

Other Colitides

- Colitis is characterized by colonic wall thickening and may be indicative of an infectious, inflammatory, or ischemic process.
- Neutropenic enterocolitis or typhlitis typically occurs in patients who are neutropenic either from cytotoxic chemotherapy or from severe immunosuppression.
- The terminal ileum, cecum, and right colon are most frequently affected. CT is the study of choice for the diagnosis.
- Circumferential thickening of the terminal ileum, cecum, and variably the right colon is the common CT findings consistent with typhlitis (Fig. 6.29).
- The bowel wall may become so thickened because of edema that a hypodense ring develops between the mucosa and musculature. Complications such as pneumatosis or perforation can also be detected.
- CT findings in ischemic colitis consist of thickened, edematous colon in these areas (Fig. 6.30). The typical "thumbprinting" in the colonic mucosa can be seen on CT scan as well as plain films. There may be a halo sign of either low attenuation caused by edema or high attenuation caused by hemorrhage within the bowel wall.
- A pericolonic inflammatory response is often present as well. Thrombus within the colonic mesenteric vessels may also be seen. Finally, pneumatosis or portal venous gas may be present indicating bowel infarction.

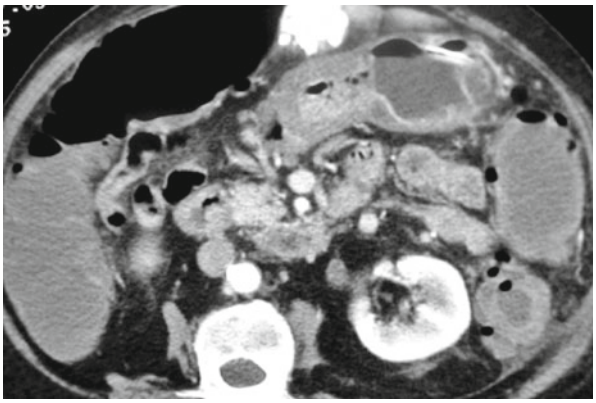

Fig. 6.30 CT showing of ischemic colitis

Fig. 6.31 CT showing pseudomembranous colitis

- Computed tomographic findings in pseudomembranous colitis include nonspecific thickening and edema of the colon and pericolonic inflammation. Generally, the edema and thickening of the colon is greater than that seen with infectious colitis or other inflammatory processes. The presence of pancolitis also tends to suggest pseudomembranous colitis vs. other colitides (Fig. 6.31).

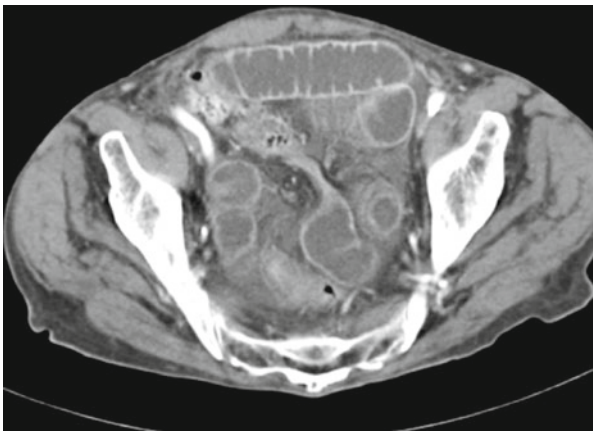

Fig. 6.32 CT showing a simple small bowel obstruction

Small Bowel Obstruction

- The use of CT in the evaluation of an SBO is expanding and in many cases can eliminate delays in diagnosis. CT has the advantages of being able to identify the site of obstruction and 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 intra-abdominal 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 augments the enhancement of the bowel wall after the administration of IV contrast, which can provide information regarding the flow of blood of the bowel.
- The CT diagnostic criteria of an SBO are based on the presence of dilated proximal small bowel (>2.5 cm) and collapsed distal bowel.
- When a transition between dilated and collapsed bowel is identified, then the diagnosis is confirmed (Fig. 6.32).
- When a transition point is not identified, it is difficult to distinguish between an SBO and adynamic ileus. In such cases, one must search for other clues to differentiate the processes.
- The presence of "small bowel feces," which are gas bubbles mixed within particulate matter and located in the dilated bowel, is a reliable indicator of an SBO.
- The presence of other intra-abdominal pathology, particularly inflammatory processes, would generally indicate an adynamic ileus.

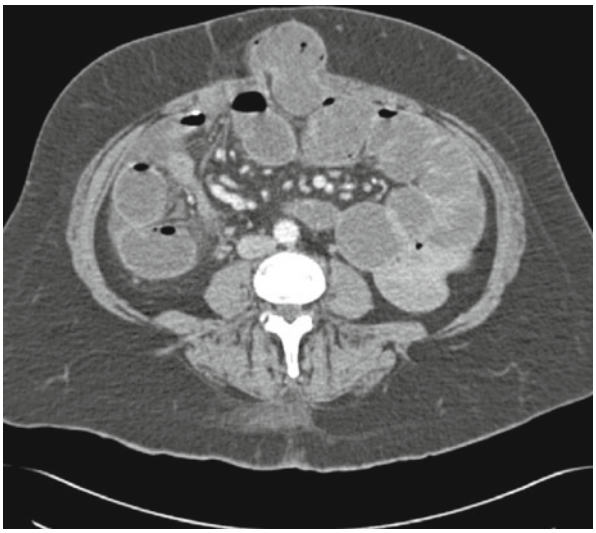

Fig. 6.33 CT showing an incarcerated hernia

- This is a case in which oral contrast may be particularly helpful because if contrast reaches the colon, a complete SBO is not present.
- A sharp transition from dilated to decompressed bowel in the absence of other findings, is highly suggestive of an SBO secondary to adhesions.
- CT does an excellent job identifying hernias such as inguinal, umbilical, incisional, or other atypical hernias. Often these hernias contain bowel but not all are obstructing.
- Clues indicating obstruction are dilated 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. 6.33).
- Thickened, congested bowel with increased attenuation at the site of obstruction associated with engorgement of the mesenteric vasculature is concerning for strangulation (Fig. 6.34).
- The mesentery may become hazy or the vasculature may be obliterated as the inflammation progresses, and it becomes filled with fluid or even blood.
- 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 is the more ominous signs of intestinal ischemia.
- Finally, a spiral pattern of engorged mesenteric blood vessels may indicate an internal hernia or rotation of small intestine around fixed adhesions.

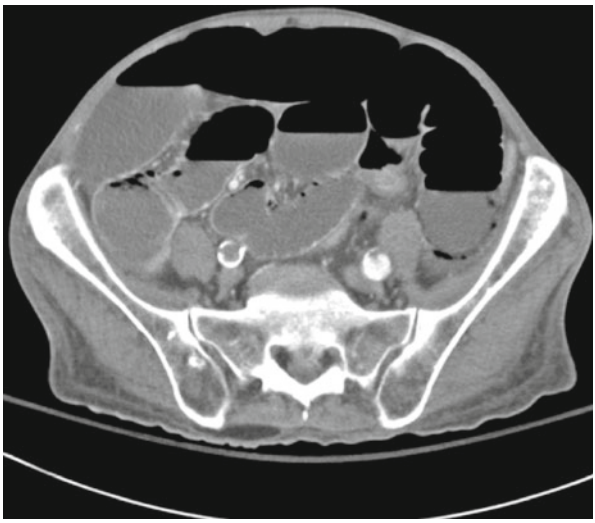

Fig. 6.34 CT showing a small bowel obstruction with evidence of ischemia

Postoperative Evaluation

- 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 and fluid from air and fluid that represent a leak from a hollow viscus or abscess cavity.
- It usually takes more than 5 days for an abscess to organize into a walled-off, contained collection.
- 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 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 CT with rectal contrast for the detection of a colonic anastomotic leak (Fig. 6.35).
- However, a CT is often more easily and readily obtained. An abscess is defined as an organized fluid collection with or without air that has an enhancing rim (Fig. 6.36).

Computed Tomography Enterography

- Computed tomography enterography (CTE) is a technique that uses multidetector row CT to examine the small bowel in a continuous fashion.

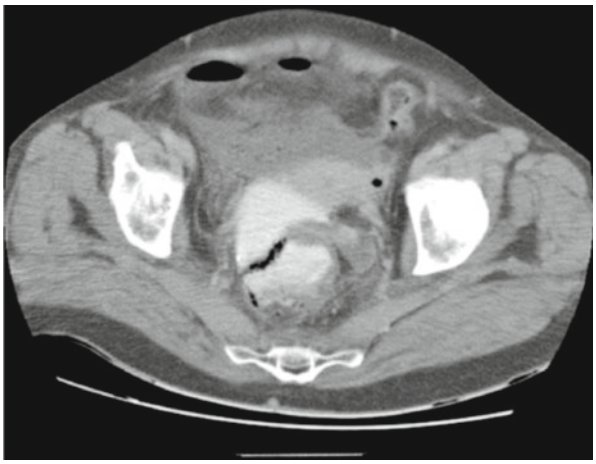

Fig. 6.35 CT showing a colorectal anastomotic leak

Fig. 6.36 CT showing an anastomotic leak. *Arrows* point to pneumoperitoneum and high-density ascites which represents extravasated oral contrast (From Blanchard TJ, Altmeyer WB, Matthews CC. Limitations of colorectal imaging studies. In: Whitlow CB, Beck DE, Margolin DA, Hicks TC, Timmcke AE, editors. Improved outcomes in colon and rectal surgery. London: Informa Healthcare; 2010. p. 97–131. With permission)

The volume of information produced can be reconstructed in any plane to produce high-resolution scans with superb image quality.

- For high-quality images the patient must ingest over a liter of oral contrast in a rapid fashion (<1 h) and intravenous contrast is administered for enhancement.
- Advantages of CTE include the ready availability of CT scanners, a straightforward technique, the speed of the exam (10–15 min), and the potential for

less radiation than a standard small bowel follow through. Intestinal and extraintestinal findings of Crohn's disease can be seen on CTE.

- Intestinal findings include wall hyperenhancement, wall thickening (generally >3 mm), and luminal narrowing (Figs. 6.37 and 6.38).
- Extraintestinal findings include peribowel vascular engorgement, peribowel fat proliferation, strictures, fistulae, and abscesses.

CT Colonography

- CT colonography or virtual colonoscopy is a method for imaging the colon and screening for advanced polyps and colorectal cancers.
- This technique requires cleansing of the colon to allow differentiation of polyps and haustral folds from fecal material.
- A newer method of stool tagging, which involves patient ingestion of low-density barium and water-soluble contrast the night before the study along with the colon preparation, increases the sensitivity of the exam.
- The colon is distended during the study through the manual or automated instillation of air or carbon dioxide.
- The colon is then imaged in two patient positions (supine and prone) using multidetector row CT with thin collimation.
- The images are then viewed in two- and three-dimensional views for interpretation by a computer and the radiologist.
- CT colonography allows detection of polyps based on size. Polyps which are >10 mm in size are considered high risk and the patient is referred for same day colonoscopy.
- Polyps between 6 and 10 mm in size are detected and reported but current treatment protocols call for variable management of these polyps.
- CT colonography has a poor sensitivity for flat lesions and may miss up to 66 % of flat lesions over 5 mm.
- Up to 1 in 5 patients undergoing CT colonography may be referred to optical colonoscopy.

Magnetic Resonance Imaging

- Magnetic resonance imaging (MRI) is an imaging technique that measures proton behavior after excitation by a radiofrequency pulse in a magnetic field. Protons within water dense or fat dense tissue can be selectively displayed so that adjacent tissues demonstrate different levels of intensity.
- MRI cannot be performed in patients with implanted devices, which may malfunction in a strong magnetic field (cardiac pacemakers, cerebral aneurysm clips, cochlear implants).
- In addition, patients with chronic renal insufficiency who will require gadolinium for MRI image acquisition are at risk for nephrogenic systemic fibrosis, a progressive fibrotic syndrome which affects the skin and other organs.

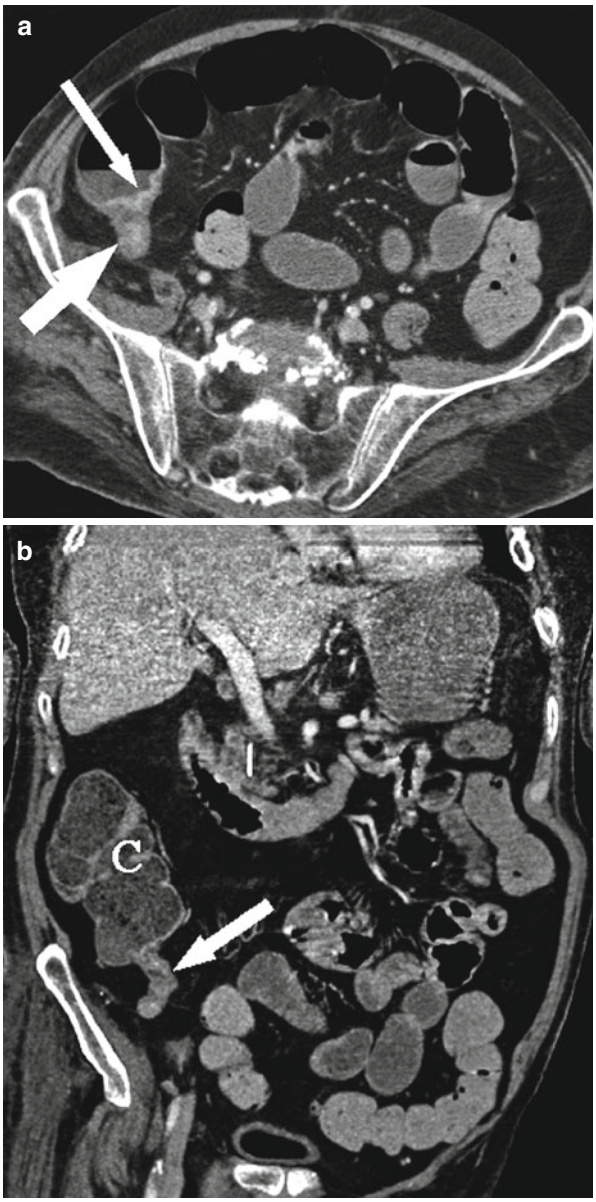

Fig. 6.37 (**a**) CT enterography of strictured ileal Crohn's disease. Axial scan through the pelvis shows narrowed, strictured neoterminal ileum (*large arrow*). Note the thin, inner wall hyperenhancement and the peripheral wall hypoenhancement giving a target appearance or mural stratification. Additionally, the inner portion of the wall of the immediate upstream ileum (*long small arrow*) also hyper-enhances. The stricture causes significant upstream obstruction. (**b**) CT enterography of strictured ileal Crohn's disease. Coronal, thin MIP scan through the pelvis shows narrowed, strictured neoterminal ileum (*arrow*) just proximal to the cecum (*C*) (From Baker ME, Veniero JC, Kiran RP. Computed tomography enterography and magnetic resonance enterography: the future of small bowel imaging. Clin Colon Rectal Surg. 2008;21:213–19. With permission)

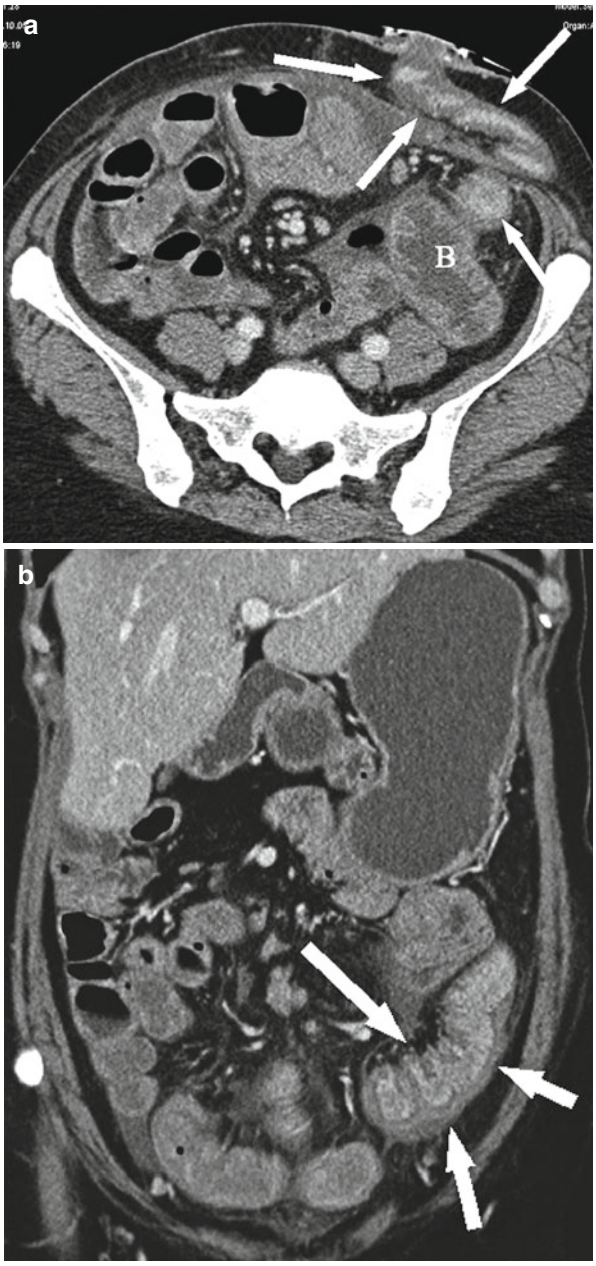

Fig. 6.38 (**a**) CT enterography of distal ileal Crohn's disease. Axial scan through the pelvis shows a long segment of disease proximal to an end ileostomy (*arrows*). There is mild-to-moderate upstream small bowel (*B*) dilation. Interestingly, the endoscopy was normal, but the pathology was positive for active disease. (**b**) CT enterography of distal ileal Crohn's disease. Coronal thin MIP reconstruction through the pelvis shows a long segment of disease proximal to an end ileostomy (*arrows*) (From Baker ME, Veniero JC, Kiran RP. Computed tomography enterography and magnetic resonance enterography: the future of small bowel imaging. Clin Colon Rectal Surg. 2008;21:213–19. With permission)

- Pretreatment staging of rectal cancer has been shown to have similar accuracy for detection of tumor depth and nodal involvement as endorectal ultrasound.
- Agreement between MRI and pathology staging is 94 % for tumor depth, 85 % for nodal involvement, and 92 % for circumferential margin involvement.
- Advantages of MRI for initial rectal cancer staging include accuracy that does not vary with the height of the rectal lesion and visualization of the entire pelvis. This allows surgeons to assess of the radial margin and pelvic sidewall prior to surgery.
- MRI images have a low sensitivity for diagnosing tumor persistence after chemoradiation therapy.
- Even as inflammation matures over time into fibrosis which appears as an area of low intensity and slow enhancement, the specificity of MRI remains low (29–86 %) and can lead to a diagnosis of recurrence when there is not.
- MRI is now increasingly used for the imaging of complex fistula in ano and fecal incontinence. Fistula in ano is often diagnosed and treated with an exam under anesthesia.
- MRI images may assist the surgeon in identifying primary and secondary fistula tracts and the internal anal canal opening with respect to the sphincter complex prior to definitive surgery.
- MRI may also be used for patients with fecal incontinence. While MRI demonstrates defects in the external and internal anal sphincters just as EAUS, MRI may be better for imaging external anal sphincter atrophy and other defects in pelvic musculature (puborectalis and levator ani). In all, MRI is an alternative to EAUS for image acquisition in patients with fistula in ano or fecal incontinence, and it offers some advantages over the ultrasound technique.

Radionuclide Imaging

- Radionuclide images are acquired based on physiologic rather than anatomic differences between tissues. These images have a wide spectrum of use in clinical medicine.
- Radiopharmaceuticals and gamma cameras are the mainstay of radionuclide imaging.
- Specific radionuclides are chosen based on their affinity for a particular organ system or ongoing physiologic process (i.e., glucose metabolism or GI bleeding). The image quality depends on the sensitivity of the radionuclide for the target organ or physiologic process.
- Gamma cameras then generate images based on the summed location and intensity of gamma photons emitted by the radionuclide substance.

Positron Emission Topography

- Positron emission topography (PET) is an imaging modality, which relies on the physiologic differences in glucose metabolism that exists between tissue types.

- Cells which have a higher baseline metabolic rate or increased mitotic activity will absorb glucose at a high rate. PET takes advantage of this difference as metabolically active cells will absorb a radioactive analog of glucose, 18-F-2-fluoro-2-deoxy-D-glucose (FDG) at a high concentration.
- However, structural changes in the FDG molecule prohibit further metabolic degradation and FDG accumulates in the intracellular space of metabolically active tissues. Images are then generated based on differential FDG uptake.
- PET image acquisition depends on differential glucose utilization by tissues. In order to maximize tissue differences, prior to the study patients should avoid carbohydrates, fast for 4–6 h immediately before, and control serum glucose (<200 mg/dl).
- Tissues that display increased FDG uptake include the urinary and gastrointestinal tracts, tissue with active inflammation secondary to leukocyte and macrophage activity, and malignant tissue.
- Because of increased FDG avidity of malignant cells, PET scans have become an invaluable tool for the staging of primary and recurrent cancers.
- PET is not recommended for primary staging of colon or rectal cancer where the likelihood of a change in surgical management is low.
- PET is more accurate in detecting extrahepatic disease and characterizing liver metastases than CT (Fig. 6.39).
- PET may aid in the initial staging of anal cancer by detecting inguinal lymph node involvement. However, the specificity of inguinal lymph node involvement is low and inguinal nodes may display FDG avidity with benign inflammation.

RBC Scintigraphy

- Radionuclide imaging studies are widely used in the diagnosis of lower gastrointestinal bleeding. The principle is that the intravascular tracer will be extravasated into the bowel lumen during active bleeding.
- Concentration of the radioactive tracer on the acquired images allows for identification of the bleeding site.
- Technetium 99mTc is the radionuclide used in bleeding scans. This radiopharmaceutical can be used to label colloid or patient red blood cells (RBCs).
- Radiolabeled colloid is readily available and requires less preparation time. However, the colloid is rapidly metabolized resulting in a lower sensitivity for the detection of gastrointestinal bleeding.
- RBCs take longer to label but they are metabolized slower and can remain active up to 24 h after injection.
- Therefore, the use of labeled RBCs is preferred as multiple scans can be obtained in patients with intermittent bleeding episodes.
- Tagged RBC scans are considered positive if the tracer pattern conforms to bowel anatomy, uptake increases in intensity over time, and the tracer propagates in an antegrade or retrograde fashion (Fig. 6.40). These criteria

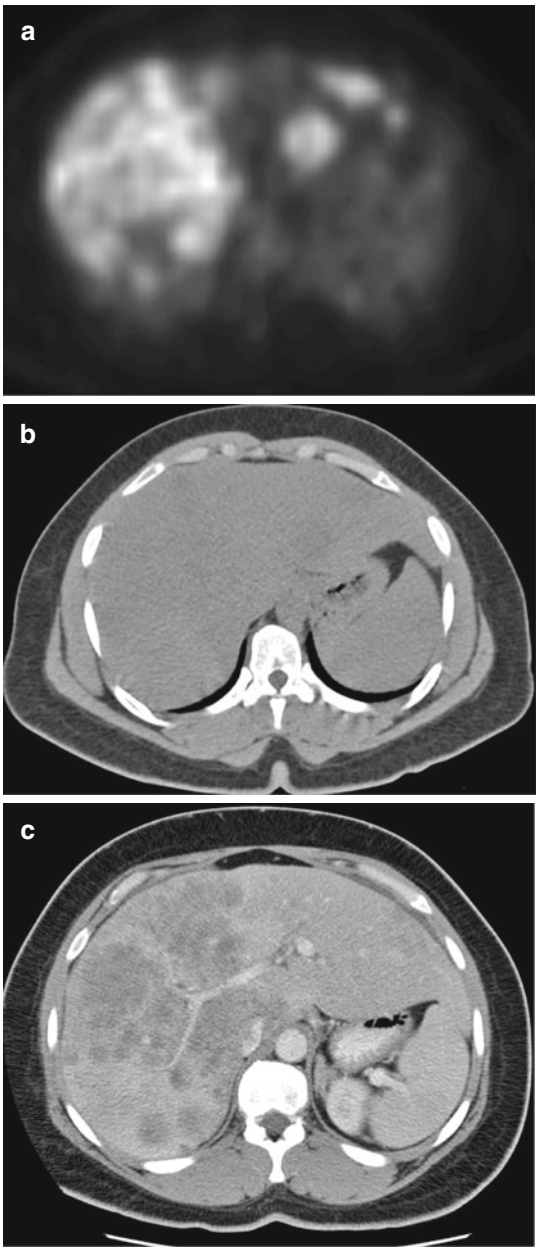

Fig. 6.39 (**a**) PET scan showing multiple discrete areas of hypermetabolism within the liver, representing metastatic colon adenocarcinoma. (**b**) A noncontrast CT of the same patient. The multiple metastatic foci are nearly impossible to detect without contrast. (**c**) Iodinated contrast helps to delineate between normal hepatic tissue and hypodense metastatic disease (From Blanchard TJ, Altmeyer WB, Matthews CC. Limitations of colorectal imaging studies. In: Whitlow CB, Beck DE, Margolin DA, Hicks TC, Timmcke AE, editors. Improved outcomes in colon and rectal surgery. London: Informa Healthcare; 2010. p. 97–131. With permission)

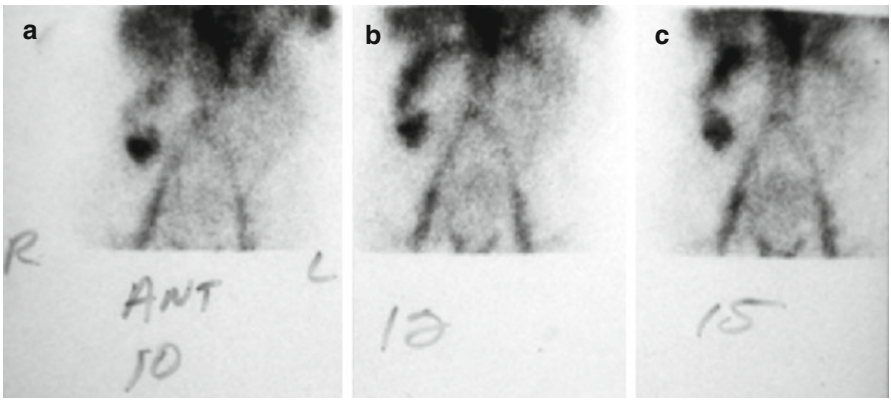

Fig. 6.40 (**a**) CT in a patient who had prior rectal resection for carcinoma shows soft tissue mass in the surgical bed of the perirectal fat. (**b**) Follow-up PET examination shows intense FDG uptake within this soft tissue mass consistent with recurrence. (**c**) ^{99m}Tc-tagged red blood cell study shows early blood pool activity within the ascending colon in this patient with bleeding after a recent polypectomy

help to distinguish true gastrointestinal bleeding from other lesions within the intestine with a high blood density (hepatic hemangioma, colonic angiodysplasia).

- Tagged RBC scans are sensitive for bleeding but may result in a false negative if the rate of bleeding is below 0.2 cm^3/min or the bleed is episodic.
- Patients who have an early positive scan (<2 min) are more likely to have a blush on arteriogram that can be treated compared to patients with a late positive scan who are more likely to benefit from resuscitation and colonoscopy if necessary.
- RBC scintigraphy is useful for the stratification of patients with active large volume gastrointestinal bleeding who will benefit from subsequent angiography and those who can be managed with less-invasive techniques.

Meckel's Scintigraphy

- A Meckel's scan, although not used as often as the tagged RBC scan, can be useful in the evaluation of young patients with occult gastrointestinal bleeding with no identifiable colonic source.
- 99Tc pertechnetate is a radionuclide which is actively concentrated and then excreted by mucous-secreting cells in gastric mucosa.
- Native as well as ectopic gastric mucosa will concentrate the radionuclide and be visualized within 30–60 min after injection (Fig. 6.41).
- Delayed images will obscure ectopic foci of uptake, secondary to rapid transit of the radiotracer through the gastrointestinal tract. The sensitivity of the Meckel's scan is 85 % and the specificity is 95 %.

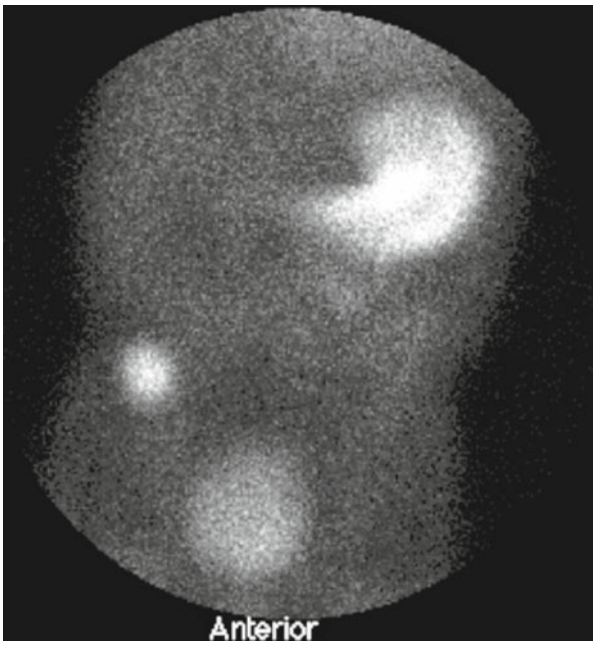

Fig. 6.41 99mTc-pertechnetate scan (Meckel's) shows a discrete focus of increased uptake in the right lower quadrant, with approximately the same intensity as the stomach indicating gastric mucosa is present within this Meckel's diverticulum

Arteriography

- The arteriogram is performed through a percutaneous approach under sterile conditions. The femoral artery is a preferred puncture site although axillary and brachial arteries may be used. Various catheters and guide wires allow the interventional radiologist to access the vessels in question.
- Arteriography is an invasive procedure with an overall mortality of 1 in 40,000.
- Complications from the performance of the procedure and manipulation of the wires and catheters are more common than reactions to the contrast itself.
- The most common complications are related to hematomas or pseudoaneurysms at the puncture sight, dissection, or embolization secondary to catheter manipulation.
- Contrast reactions and contrast toxicity (renal failure) occur in <1 % of studies done. Experience and technique can minimize many of the complications.
- Hydration and IV mannitol can reduce the nephrotoxicity. If the patient has allergies to iodine or has had a prior contrast reaction, premedication with methyl prednisolone is done 12 and 2 h before arteriography.

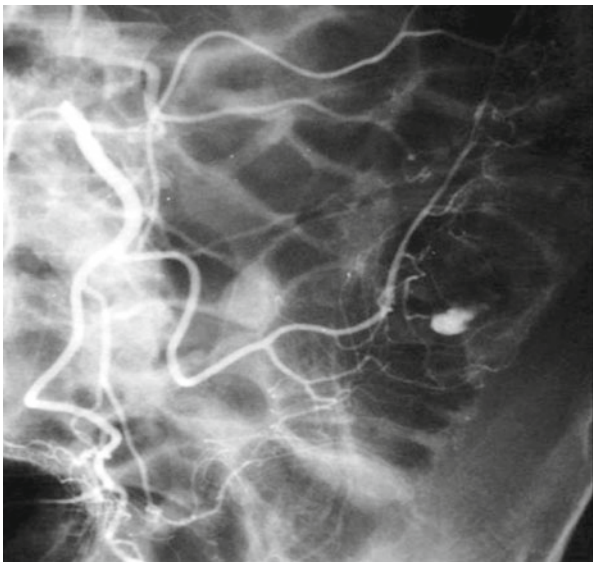

Fig. 6.42 Mesenteric angiogram shows pooling of contrast in the sigmoid colon in this patient with surgically proven diverticular bleeding

- 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. 6.42).
- Bleeding needs to occur at a higher rate for a positive angiogram (0.5 ml/min) than for nuclear imaging (0.1–0.2 ml/min). Because lower GI bleeding can be intermittent, the bleeding site is sometimes not identified at the time of the angiogram.
- Diverticular bleeds appear as a blush of contrast contained within a 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.
- Arteriovenous malformations are developmental in origin and are often seen in the small bowel as tortuous, dilated arteries and early prominent veins.
- Capillary telangiectasias (common in Osler-Weber-Rendu syndrome) appear as multiple, tiny areas of blush and no arteriovenous shunting.

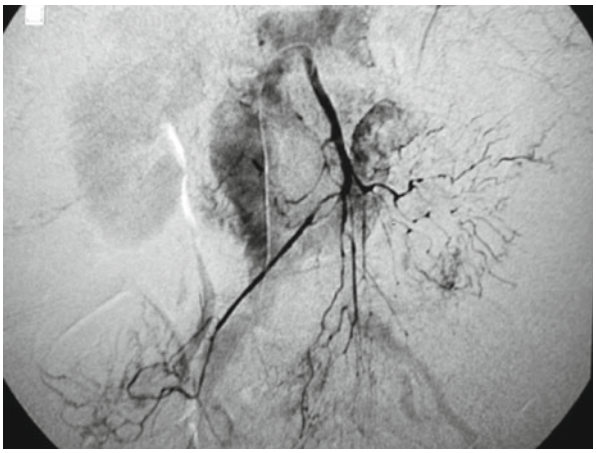

Fig. 6.43 Mesenteric angiogram shows vasoconstriction and pruning of the superior mesenteric artery and its branches in this patient who presented with mesenteric ischemia secondary to severe hypotension

- 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.
- Nonocclusive mesenteric ischemia arises from a "low flow" state typically secondary to reduction in mesenteric blood flow from cardiac failure or hypotensive shock.
- This diagnosis can frequently be made with clinical symptoms and computer tomography images.
- The typical early angiographic images show diffuse vasoconstriction of mesenteric arterial branches and decreased parenchymal vascularity (Fig. 6.43).
- In the late stage there is increased accumulation of contrast in the bowel wall.
- An arteriogram is the most useful diagnostic examination for patients in whom one has a high clinical suspicion of acute occlusive mesenteric ischemia.
- A catheter is inserted into the aorta and an aortogram is obtained.
- The celiac and superior mesenteric arteries are catheterized and injected with contrast in order to identify the level of occlusion and document collateral circulation.
- A superior mesenteric artery embolus typically lodges just proximal or distal to the takeoff of the middle colic artery and is seen as a meniscus at the site of occlusion and blockage of contrast (Fig. 6.44).
- Atherosclerotic occlusion will often involve the origin of the superior mesenteric artery seen as stenosis or plaque with a trickle of glow beyond.

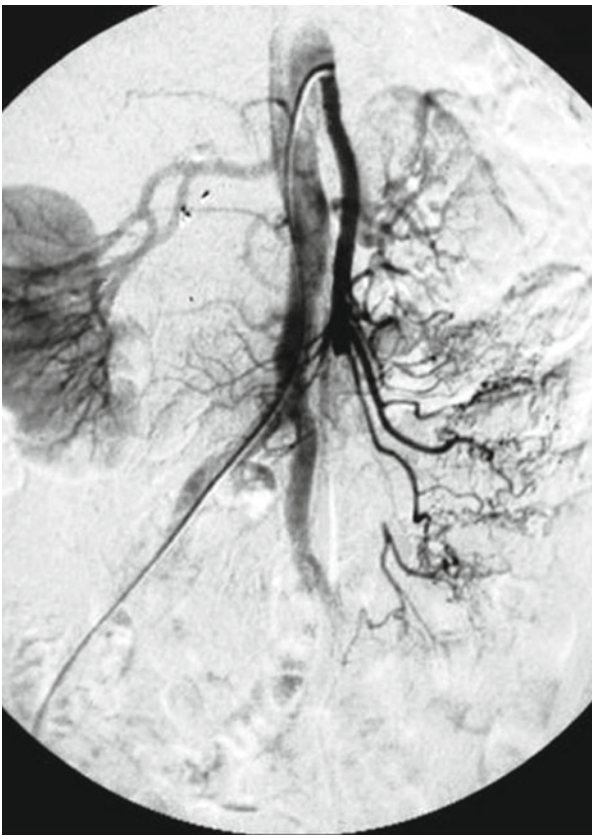

Fig. 6.44 Mesenteric angiogram shows a large filling defect within the proximal superior mesenteric artery consistent with an embolism in this patient with ischemic bowel

Acknowledgments This chapter was written by Matthew G. Mutch, Elisa H. Birnbaum, and Christine O. Menias in the first edition of this textbook.

7. Endoluminal Ultrasound

Donald G. Kim and W. Douglas Wong

Equipment and Technique

- Equipment used for endoluminal ultrasonography includes a handheld endocavitary probe with rotating transducer which acquires a 360° image. Most investigators use a BK Medical scanner with a rigid handheld type 1850 rotating probe and a 7- or 10-MHz transducer (BK Medical, Peabody, MA).
- Transducers of 7 and 10 MHz provide a focal length of 2–5 and 1–4 cm, respectively, rotating in a 90° scanning plane at 4–6 cycles/s to obtain a 360° radial scan of the rectal wall and surrounding structures. 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.

W. Douglas Wong was deceased at the time of publication.

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- Patients receive one or two phosphosoda enemas to cleanse the rectum before examination. The procedure is performed with the patient in the left lateral decubitus position without sedation.
- A digital rectal and proctoscopic examination is performed to assess the tumor size, appearance, location, and distance from the anal verge. Any residual stool or enema effluent that might interfere with the ultrasound is removed.
- 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.
- This approach is preferred to blind insertion of the ultrasound probe into the rectum. With blind insertion, distortion of the image can occur, and the proximal areas of a lesion as well as the adjacent mesorectum will often be missed.
- 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 ultrasound probe is oriented with the stopcock and syringe positioned upright to the patient's right. The proctoscope is slightly withdrawn keeping the ultrasound probe in place to expose the transducer protruding beyond the end of the proctoscope, above the rectal lesion.
- The latex balloon is filled with 30–60 ml of water providing an optimal acoustic environment surrounding the rotating transducer. Initial preparation of the ultrasound probe includes careful removal of all air bubbles within the latex balloon to minimize acoustic interference. The probe and attached proctoscope are slowly withdrawn together carefully scanning the rectum from proximal to distal. The ultrasonographer observes for alterations of the rectal wall and perirectal tissues to assess depth of invasion and perirectal lymph node involvement.
- Optimal evaluation often requires several passes back and forth across a lesion. 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.
- With the patient and ultrasound probe positioned as above, the images obtained are oriented radially similar to a computed tomography scan, looking up from the patient's feet. The patient's right side is oriented to the left of the image, anterior is up, and posterior is down. The studies can also be videotaped for further review.

Image Interpretation

- Most endorectal ultrasound (ERUS) images display a series of five distinct layers that can be identified in the rectal wall. They consist of three hyperechoic (white) layers separated by two hypoechoic (black) layers. Beynon and colleagues (1986) proposed a five-layer model based on an anatomic study, demonstrating that the five basic layers seen on an ultrasonographic scan of the rectal wall correspond directly to the anatomic layers present in the rectal wall.
- 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
  - *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
- To aid in memory, a "Big Mac" analogy has been suggested with three white areas representing the buns and two dark areas representing the meat (muscularis mucosa or propria).
- 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.

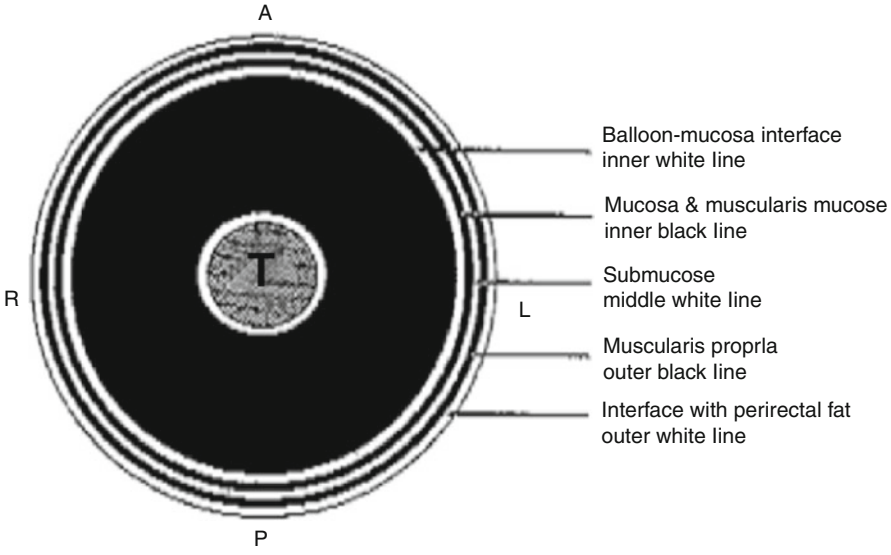

Fig. 7.1 Five-layer anatomic model of an ERUS scan. Three hyperechoic (*white*) layers and two hypoechoic (*black*) layers are visualized. *A* anterior, *L* left, *P* posterior, *R* right, *T* transducer

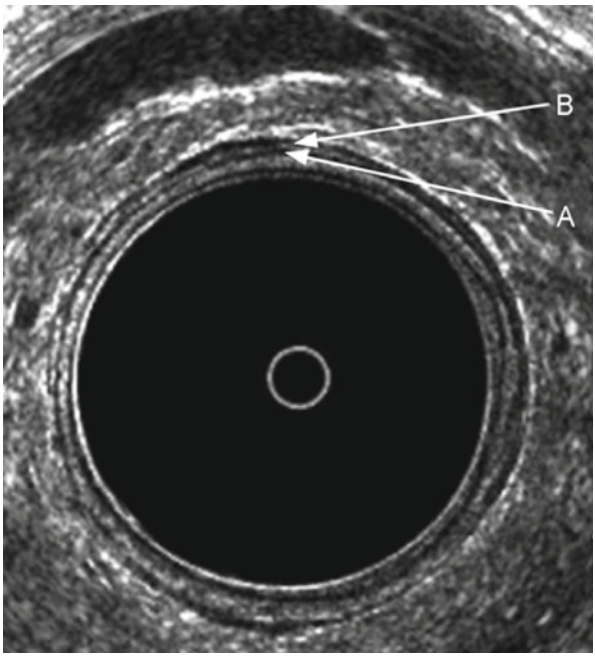

Fig. 7.2 The typical five layers of the rectal wall. Seven layers are depicted anteriorly, where an interface can be seen between the *inner circular A* and outer longitudinal *B* muscle layers of the muscularis propria

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

Assessment of Rectal Neoplasms

Depth of Invasion

- Ultrasound staging classification (uTNM) is presented in Table 7.1.

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, hyperechoic line) (Fig. 7.3).

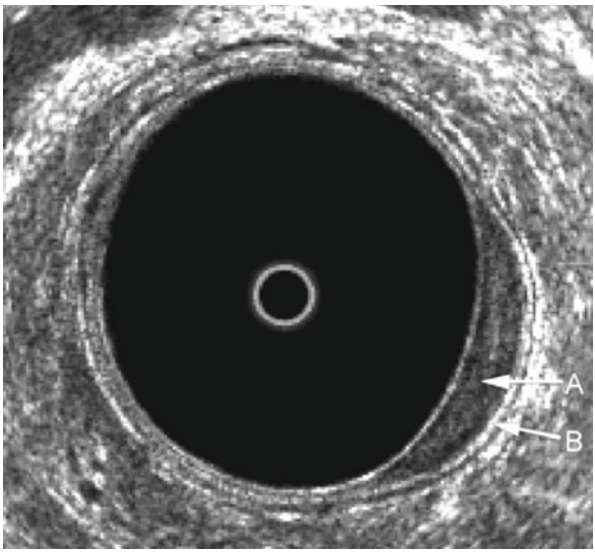

Fig. 7.3 A benign uT0 lesion in the left posterolateral aspect of the rectum. There is an expansion of the *inner black line* that represents the mucosa *A*, but the submucosa *B* is seen to be completely intact

- Benign rectal villous adenomas are classified as uT0 lesions and may be treated with local excision with excellent results. Important in this decision is to accurately exclude any focus of invasion.
- The accuracy of ERUS is probably highest for T0 lesions.

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.

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

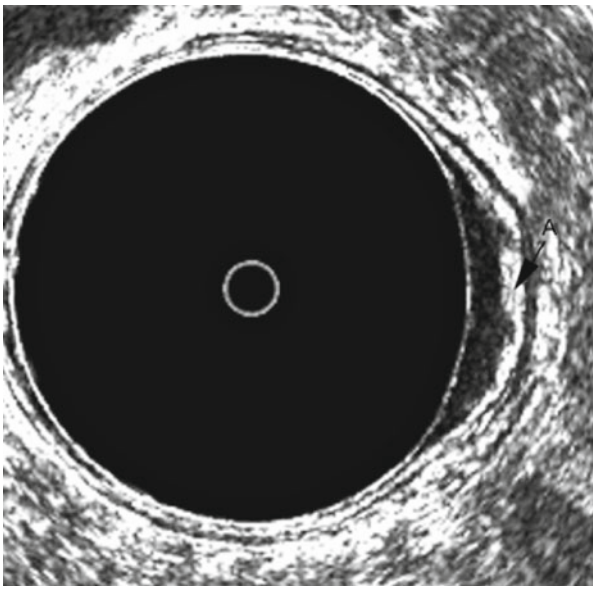

Fig. 7.4 A uT1 cancer in the left lateral wall of the rectum. The *middle white line* or submucosa is irregular and somewhat thickened *A* but not completely disrupted

perirectal fat (the outermost white line) remains intact. The expansion of the muscularis propria may be variable depending on the degree of invasion.

- "Early" uT2 lesions may just invade the muscularis propria with minimal expansion of the layer. "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.

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. 7.5). The recognition of perirectal fat invasion is an important determinant in the preoperative evaluation of the rectal cancer patient.

uT4 Lesions

- uT4 lesions are locally invasive into contiguous structures such as the uterus, vagina, cervix, bladder, prostate and seminal vesicles, or involve

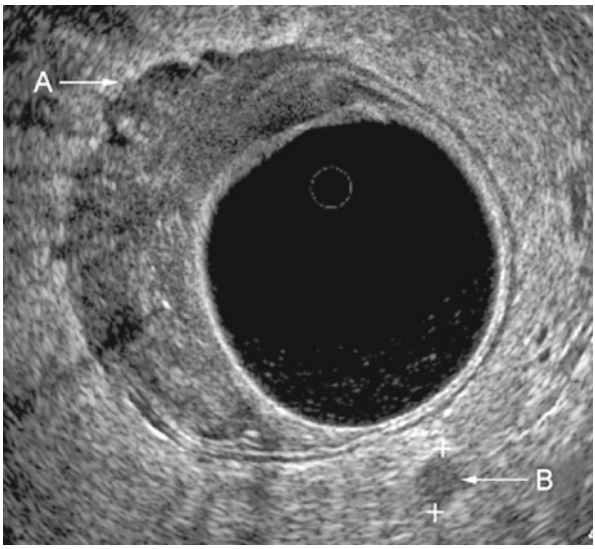

Fig. 7.5 A uT3N1 lesion. The tumor disrupts all layers of the rectal wall, with extensions evident into the perirectal fat *A*. A lymph node *B* is identified in the left posterior location within the mesorectum

the pelvic sidewall or sacrum. They are clinically fixed and tethered. Sonographically, there is loss of the normal hyperechoic interface between the tumor and adjacent organ (Fig. 7.6).

Nodal Involvement

- 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 83 %. ERUS determination of metastatic lymph nodes is certainly more accurate than clinical (digital) evaluation as well as other imaging modalities including computed tomography (CT).
- As indicated in Table 7.1, lymph node staging parallels pathologic TNM staging classifying tumors with (uN1) or without (uN0) lymph node involvement. 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.
- 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.

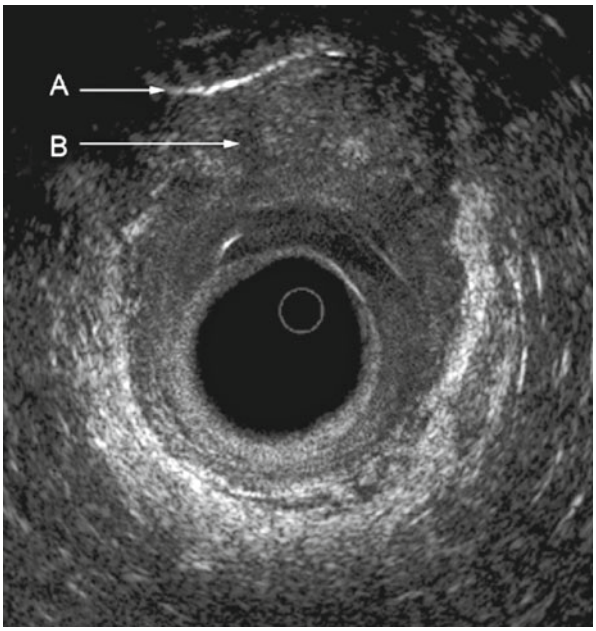

Fig. 7.6 A T4 lesion in the distal rectum and upper anal canal extending to the vagina. The *curved white line A* seen anteriorly represents the examiner's finger in the vagina, and the hypoechoic anterior tumor *B* can be seen to extend into the vagina

- ERUS differentiates two main groups of lymph nodes: hypoechoic and hyperechoic lymph nodes.
- Compared with pathologic findings, hypoechoic lymph nodes represent metastases, whereas hyperechoic lymph nodes are visualized because of nonspecific inflammation.
- There is no definitive size threshold to determine if an identified lymph node is malignant.
- Overall, 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-positive results may occur because of inflammatory lymph nodes or confusing the cross-sectional appearance of perirectal blood vessels for metastatic lymph nodes.

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
Saitoh et al.	1986	88	90	75
Holdsworth et al.	1988	36	86	61
Beynon et al.	1989	100	93	83
Rifkin et al.	1989	102	65	50
Glaser et al.	1990	86	88	79
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
Glaser et al.	1993	154	92	81
Herzog et al.	1993	118	89	80
Deen et al.	1995	209	82	77
Akasu et al.	1997	152	82	76
Adams et al.	1999	70	74	83
Kim et al.	1999	89	81	64
Garcia-Aguilar et al.	2002	545	69	64
Marusch et al.	2002	422	63	n/a
Kauer et al.	2004	458	69	68

- Scanning longitudinally will distinguish between blood vessels and lymph nodes because blood vessels will extend longitudinally, change direction, and/or branch. The sonographic continuity of the hypoechoic vessel over a distance greater than the cross-sectional area is the criterion used to distinguish the two. Three-dimensional imaging can help in making this distinction.
- 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 63–93 % (Table 7.2).
- Overstaging has been reported in approximately 11 % of patients and is believed to be the result of peritumoral inflammation beyond the leading edge of the tumor.
- Under-staging for depth of wall invasion has been reported to be approximately 5 % and is considerably more serious than overstaging because inadequate management may result. With overstaging, potentially more aggressive management is recommended than might be required.

- Detection of lymph node metastases with ERUS has been less accurate, ranging from 50 to 83 % in reported series (Table 7.2).
- ERUS is highly operator dependent, and thus accuracy is dependent on the experience and expertise of the examiner.
- Several factors can lead to the misinterpretation of ERUS images. These factors include a lesion in close proximity to the anal verge, improper balloon inflation with associated balloon-wall separation, a nonperpendicular imaging plane, shadowing artifacts caused by air or stool, reverberation artifacts, refraction artifacts, and a transducer gain setting that is too high.
- A technically difficult ERUS is likely to give an inconclusive or inaccurate result. Factors causing technical difficulties include stenotic lesions, patient discomfort, poor bowel preparation, and scarring from previous surgery.
- 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 for both depth of penetration and nodal status.
- 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.

Postoperative Follow-Up

- 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 %. In a series studying ERUS as a means to identify local recurrence, overall local recurrence ranged from 11 to 20 % with the proportion of local recurrences diagnosed exclusively by ERUS varying from 18 to 35 %. These ERUS-only recurrences represent only 3.2–5 % of the entire group of patients.
- Although local recurrence can occur within the lumen at the anastomosis, locally recurrent tumors more often extend from extrarectal lesions that invade through the rectum, often at the level of an anastomosis.
- Extrarectal tumor not involving the mucosa may be undetectable endoscopically but can be identified at an early stage with ERUS.
- 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. 7.7). Early postoperative changes,

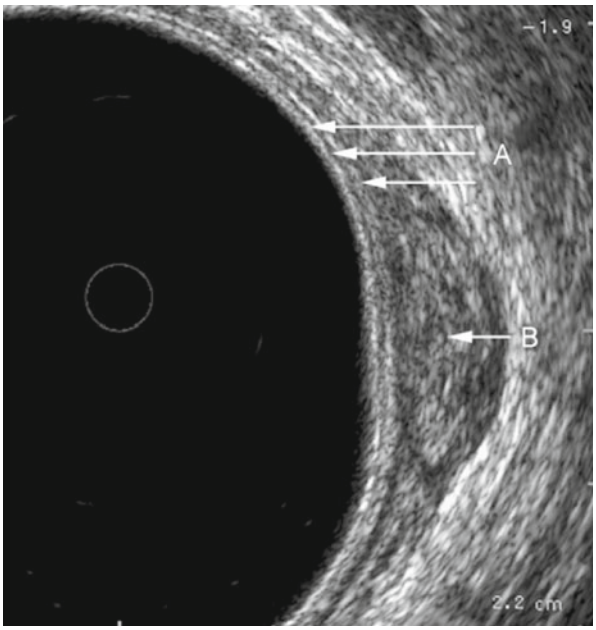

Fig. 7.7 A recurrent rectal cancer. It is located in the left lateral rectal wall. Note the intact *inner three lines A* on the ultrasound image, indicating no involvement of the mucosa or submucosa but an obvious abnormality at the level of the muscularis propria *B*, representing the recurrence

particularly adjacent to the anastomosis, can make the interpretation of the ERUS difficult.

- Interpretation is aided if a "baseline" ultrasound is obtained soon (3 months) after surgery and compared with subsequent surveillance images. A baseline examination is useful to document postoperative scarring and to evaluate that area for potential changes on serial examinations.
- Lesions that increase in size on subsequent examinations are more likely to represent recurrent tumor.
- 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.
- With respect to MRI, the accuracy of all MRI modalities for depth of penetration is 82 % (sensitivity, 86 %; specificity, 77 %). Nodal involvement accuracy for MRI was 74 % (sensitivity, 65 %; specificity 80 %). Of those cases staged by TNM classification, 13 % were overstaged and 13 % understaged.
- Subgroup analysis found that MRI with an endorectal coil was equivalent to ERUS for depth of penetration with an overall accuracy rate of 84 % (sensitivity, 89 %; specificity, 79 %). Overall accuracy for nodal status was 82 % (sensitivity, 82 %; specificity; 83 %).

Endoanal Ultrasound

- 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. The same BK scanner is used with the 1850 rotating probe and 10-MHz transducer (BK Medical). In place of the latex balloon, a translucent plastic cap (BK 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. There is a pinhole in the apex of the plastic cap that permits the escape of any air through displacement of the space with water.
- The examination technique for EAUS is similar to that of ERUS. Patients are examined in the left lateral decubitus position, again usually without sedation.
- A careful external examination of the perianal area followed by a digital rectal examination is performed. The probe is lubricated with a water-soluble gel and gently inserted into the anal canal until the plastic cap is no longer visible. This will usually ensure that the transducer is at the level of the upper anal canal.
- The probe is slowly withdrawn to image the full length of the anal canal. Images are typically obtained in the upper, mid, and distal anal canal.

Image Interpretation

- Normal anal canal anatomy is well visualized with EAUS. As with the rectum, the interpretation of these images must be based on a precise definition of normal endosonographic anatomy of the anal canal that correlates well with anatomy. EAUS of the anal canal and pelvic floor has been correlated with cadaveric anatomic dissections.
- 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. 7.8.
- 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.

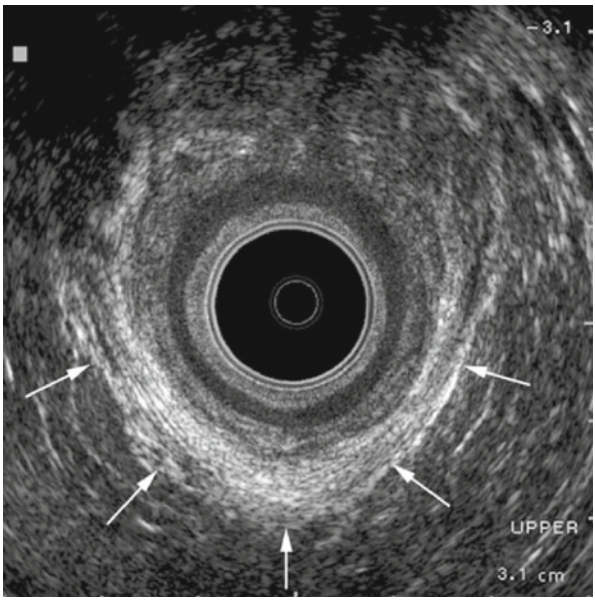

Fig. 7.8 The ultrasound appearance of the upper anal canal at the level of the puborectalis, which can be seen as the hyperechoic U-shaped structure seen posteriorly and laterally (*arrows*) in this image

- 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 tissue.
- Perineal body measurements can be made at the level of the mid-anal canal (Fig. 7.9). 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 as approximately 8 mm. This measurement is useful in the evaluation of women with fecal incontinence from anterior sphincter defects. The examining index finger not only better defines the perineal body but may accentuate an anterior sphincter defect that may otherwise appear intact.
- 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.

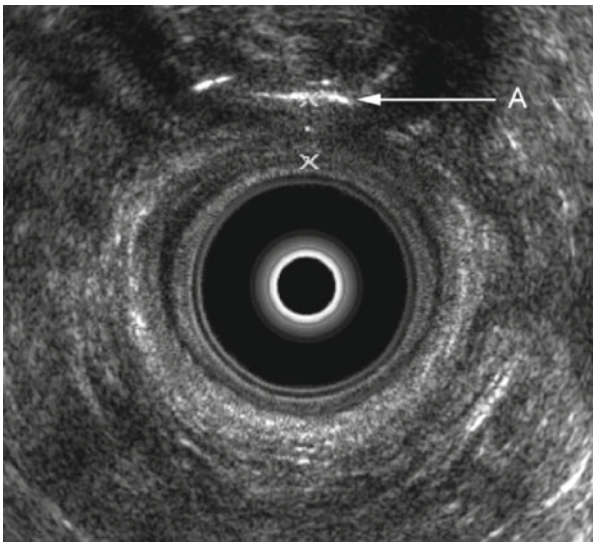

Fig. 7.9 The technique used to measure the anterior perineal body in a female patient. The examiner's finger is placed in the vagina, and the hyperechoic curvilinear structure *A* seen anteriorly delineates the examiner's finger. The two crosshatch between the examiner's finger, and the transducer measures 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.
- Anal incontinence is not restricted to patients with recognized third- or fourth-degree obstetric tears. Patients may also develop delayed symptoms of incontinence several years after an unrecognized sphincter injury.
- 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

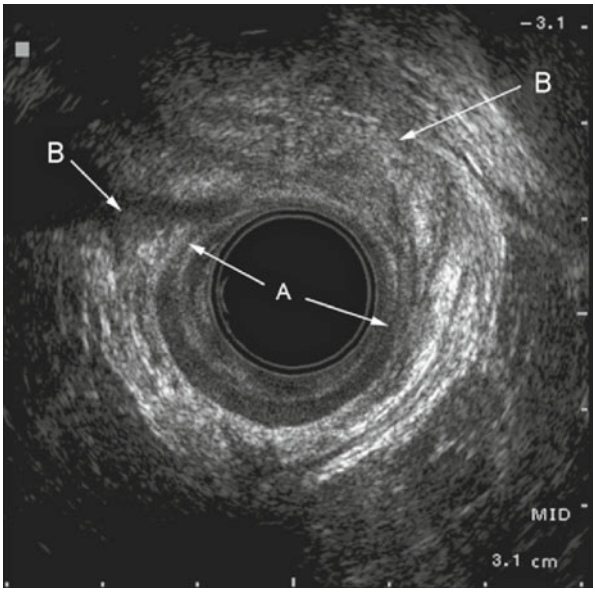

Fig. 7.10 A complete anterior sphincter disruption in a female patient. The hypoechoic internal anal sphincter can be seen completely disrupted in its anterior location (*A arrows*). Similarly, the hyperechoic external anal sphincter is completely disrupted anteriorly (*B arrows*)

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 levatorplasty. EAUS has become an accurate method to image the anal sphincters identifying anal sphincter defects that result in fecal incontinence.
- 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. 7.10).

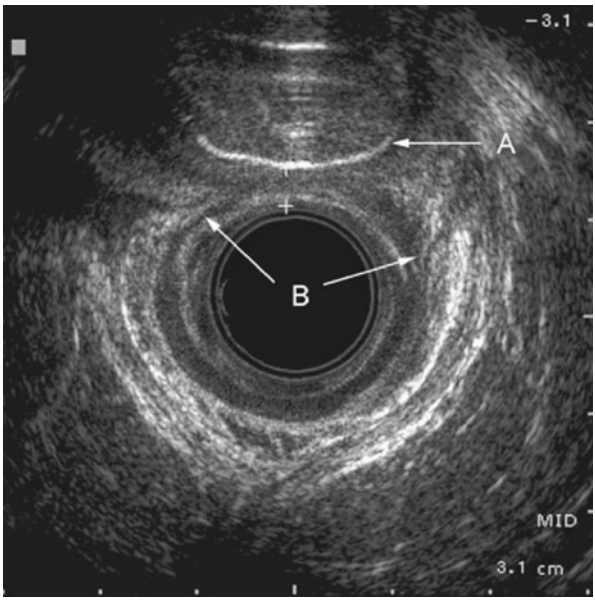

Fig. 7.11 The measurement of the anterior perineal body in this patient with an anterior sphincter disruption. The curvilinear hyperechoic structure *A* is the examiner's finger in the vagina. This technique can often accentuate the defect *B* seen in the internal anal sphincter and the external anal sphincter and documents the decreased thickness of the anterior sphincter and perineal body

- Many times, complete sphincter disruption is not seen, but attenuation of the sphincter mechanism is noted anteriorly, indicating a significant partial sphincter defect.
- An examining digit or vaginal balloon 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. 7.11).
- The identification of localized sphincter defects is important in the evaluation of the incontinent patient, because these defects may be amenable to surgical repair. EAUS can clearly and objectively image the anal sphincter mechanism and has replaced needle electromyography as the procedure of choice for anal sphincter mapping.
- EAUS is better tolerated and less painful than needle electromyography sphincter mapping. 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 (Fig. 7.12). Hydrogen peroxide causes a release of oxygen, accentuating the fistula and appears as a brightly hyperechoic image on the ultrasound image. With the instillation of hydrogen peroxide, the internal opening is identified in 62.5–94 % of patients. Lack of the use of hydrogen peroxide results in suboptimal results as is reflected in a recent meta-analysis.
- When evaluating an anal fistula with ERUS, it is important to use both the balloon-covered transducer to evaluate the perirectal region to assess for any supralevator extension as well as the plastic cap for evaluation of the anus and surrounding anatomy.

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.

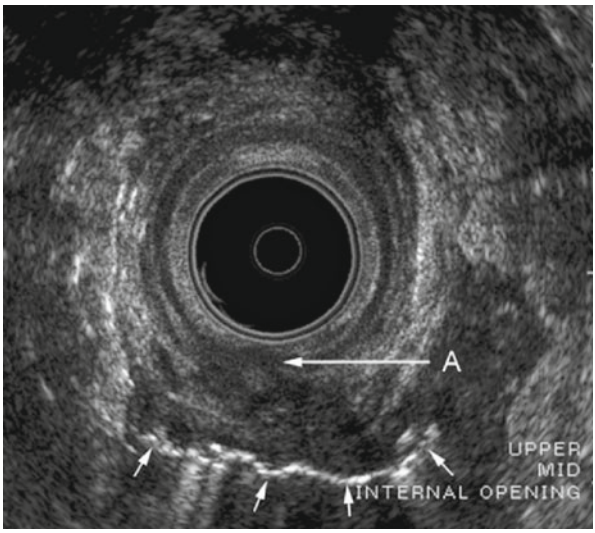

Fig. 7.12 A fistula in ano that has been enhanced by the introduction of hydrogen peroxide. The hyperechoic features posteriorly represent the hydrogen peroxide within the fistula tract (*short arrows*). There is an obvious hypoechoic defect in the internal anal sphincter in the midline posteriorly *A*, representing the internal fistula opening. The hypoechoic horseshoe tract can be seen extending toward the patient's left

- The normal anatomic structures are clearly defined, and any changes in the normal anatomy and their relationships with specific anatomic structures are clearly defined.
- 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.
- EAUS accurately stages the initial tumor and can be used in follow-up to detect residual tumors as well as early recurrences after treatment. Surgical treatment in the form of abdominoperineal resection is reserved as salvage surgery for those patients who fail standard chemoradiation 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).
- Tumor staging for anal cancer depends primarily on the maximal tumor diameter, which is accurately measured by EAUS. Additionally, the depth of invasion of the lesion can be measured in relationship to the sphincter mechanism.
- 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). The evaluation of squamous cell carcino-

Table 7.3 TNM staging classification for anal cancer

Primary tumor (T)	
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)
Regional lymph nodes (N)	
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
Distant metastasis	
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

mas of the anus should include an evaluation of the rectum with ERUS to determine the presence of metastatic lymph nodes within the mesorectum.

- The mesorectum as well as the anal canal can also be evaluated in follow-up after treatment. Any suspicious areas detected during follow-up may be biopsied if necessary.

Three-Dimensional Ultrasound

- Three-dimensional ultrasound allows for multiplanar imaging of both the rectum and the anal canal. This new technology is currently being evaluated to compare its efficacy relative to conventional two-dimensional ultrasound as well as to other modalities such as MRI.
- 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. An example of a three-dimensional ERUS image (3-D-ERUS) of a rectal cancer is shown in (Fig. 7.13).

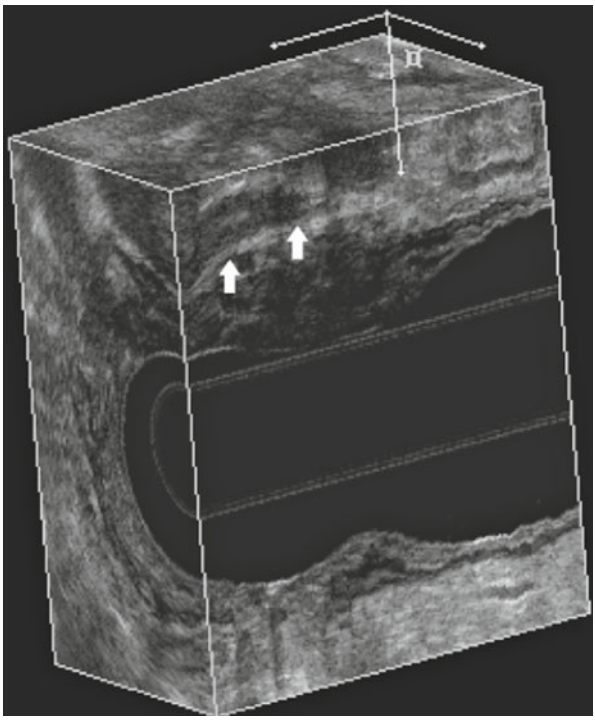

Fig. 7.13 This three-dimensional ultrasound image of an anteriorly based rectal cancer that extends full thickness through the rectal wall (uT3). However, a clear hyperechoic plane can be seen between the prostate gland and the rectal tumor, as depicted by the *arrows*

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8. Preoperative Management

Janice F. Rafferty

Risk Assessment and Management

Ambulatory Surgery

- "Ambulatory surgery" is defined as surgical procedures requiring at least local anesthesia, which are more complex than office-based procedures but less complex than operations requiring at least an overnight stay.
- Approximately 90 % of anorectal surgery to treat fissures, condyloma, fistulas, certain early tumors, hemorrhoids, and pilonidal disease may be suitable for the ambulatory setting.
- The Standards Committee of the American Society of Colon and Rectal Surgeons (ASCRS) has developed a Clinical Practice Guideline about Ambulatory Anorectal Surgery, for practitioners and health care workers, to provide current information from the literature upon which decisions can be made.
- Data from many nonrandomized trials suggest that most patients with American Society of Anesthesiologists (ASA) classifications I and II, and some class III, are suitable for ambulatory surgery from an anesthesia risk standpoint.
- Multiple factors must be considered to determine whether this is appropriate, including the estimation of the magnitude of the operation, type of anesthesia, patient compliance, distance of the patient's home from the surgical center, and availability of support once home.
- In general, the need for bloodwork, electrocardiogram (EKG), and other investigations of the ambulatory surgery patient can be predicted by information obtained with a thorough history and physical exam.

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Table 8.1 Operative scoring system

Preoperative	Physiologic
ASA grade	APACHE (I and II)
Goldman cardiac risk index	SAPS
Pulmonary complication risk	Sickness score
Prognostic nutritional index	POSSUM
Hospital prognostic index	P-POSSUM
	Sepsis score
	Therapeutic intervention score

Adapted from Kiran RP, Delaney CP, Senagore AJ. Perioperative management. In: Beck DE, editor. Clinics in colon and rectal surgery. 2003;16(2): 75–84

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	3–25	11	2
IV	≥26	22	56

Inpatient Surgery

- Objective assessment of patient risk for inpatient colorectal surgery is necessary for informed consent and favorable surgical outcome.
- Scoring systems have been developed to help differentiate those who are at high risk for perioperative complication from those who are not.
- Scoring systems can be classified as preoperative or physiologic (Table 8.1). Some are specific to colon and rectal surgery.
- The Goldman risk model determines cardiac risk for surgery. Point scores are assigned to each of nine clinical factors; patients are divided into four risk classes based on the total point score (Table 8.2).
- The risk for perioperative respiratory complications can be gauged by combining findings on chest examination, chest X-ray, Goldman cardiac risk index, and the Charlson comorbidity index. Risk reduction strategies initiated preoperatively, such as smoking cessation, lung expansion

Table 8.3 American Society of Anesthesiologists classification

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

teaching, chronic obstructive pulmonary disease (COPD) treatments, and asthmatic treatments, may positively influence outcome after surgery.

- The American Society of Anesthesiologists (ASA) classification system (Table 8.3) was initially developed to alert anesthesiologists to preexisting diseases. It has also been used to estimate operative risk and correlates directly with perioperative mortality and morbidity. This classification scheme also correlates with perioperative variables such as intraoperative blood loss, duration of postoperative ventilation, and duration of intensive care unit (ICU) stay.
- Abdominal surgery induces a catabolic response with stress hormone release and insulin resistance; therefore, nutritional parameters should be evaluated in certain chronically ill patients before surgery.
- Protein catabolism may be accentuated by prolonged fasting and bowel preparation. Increased nutritional risk can influence postoperative morbidity and mortality and anastomotic leak rates.
- The prognostic nutritional index (PNI) was devised in the 1970s to predict complications such as sepsis and death after surgery. The PNI evaluates four factors to predict complications (serum albumin, transferrin, triceps skinfold thickness, and cutaneous delayed-type hypersensitivity), but only albumin, transferrin, and delayed hypersensitivity are accurate predictors of postoperative morbidity and mortality. This index can theoretically be used to identify patients who may benefit from nutritional support in the perioperative period.
- The Acute Physiology and Chronic Health Evaluation (APACHE) scoring system was initially designed to assess risk for ICU patients but has been extended to assess patients with severe trauma, abdominal sepsis, postoperative enterocutaneous fistulas, and acute pancreatitis and to predict postoperative outcome.
- Scoring for emergency patients being admitted to the ICU is best performed before surgical intervention. This index does not take into consideration the nutritional status of the patient, extent of surgery, or cardiovascular findings that add to operative risk.
- Several simpler scoring systems have been developed from the APACHE system, including simplified acute physiology score (SAPS), which uses 14 of the 34 variables, and SAPS II, which also takes into consideration the urgency of the procedure and any associated chronic medical illness.

Table 8.4 Parameters for the calculation of the physiological and operative severity score for enumeration of morbidity and mortality (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 (mmHg)	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 Physiological and Operative Severity Score for enUmeration of Mortality and morbidity (POSSUM) calculates expected death and expected morbidity rates based on 12 physiologic variables and 6 operative variables (Table 8.4).
- Another modification of this index, the CR-POSSUM score, is advocated to assess the risk for patients undergoing major colorectal cancer surgery.
- Assessment of specific organ systems may be necessary and should be done for patients with identified preexisting dysfunction. In general, age, history of chronic heart disease, renal disease, emergency surgery, and type of operation are predictors of the risk of mortality.
- Fit, young patients undergoing minor and intermediate procedures do not need routine preoperative investigation, and, in the pediatric age group, a thorough clinical examination has been found to be of greater value than routine laboratory screening.
- A good history and physical examination are more important than laboratory data in the development of a treatment plan for anesthesia.
- Preoperative tests serve to complement the history and physical exam. 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. New guidelines have a significant impact on reducing preoperative testing and have not caused an increase in untoward perioperative events.
- Tests that need to be performed prior to major colorectal surgical procedures include hemoglobin for evidence of anemia and as a baseline level for postoperative management.
- Renal and liver function tests are not routinely carried out.

- Preoperative blood glucose determination is obtained in patients 45 years of age or older because current recommendations suggest screening of all over that age. In addition, impaired glucose control increases perioperative risks.
- A urine pregnancy test should be considered for all women of childbearing age.
- 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, even if transfusion is not expected. This may help to minimize the risk of later transfusion reaction.
- EKG is indicated in male patients older than 40 years and females older than 50 years. Those with a history suggestive of cardiac disorders, myocardial abnormalities, valvular disorders, conduction disorders, and hypertension may benefit from more intensive investigation prior to elective colorectal surgery.
- 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.

Bowel Preparation

- Bowel preparation for colon and rectal surgery has traditionally involved two components: mechanical cleansing and antibiotics. Mechanical bowel preparation (MBP) before elective colorectal surgery has its roots in history and has long been a cornerstone of surgical practice. Today, however, there remains little evidence that it is necessary.
- Bacteria represent a third of the dry weight of stool; uncontrolled leak of intestinal contents into the abdominal cavity can, therefore, be life threatening.
- The accepted rationale for MBP includes the evacuation of stool to allow visualization of the luminal surfaces as well as to reduce the fecal flora, which is believed to translate into lower risk of infectious and anastomotic complications at surgery.
- While the removal of stool permitting mucosal inspection at colonoscopy is well established and not controversial, the latter rationale – the reduction of infectious and anastomotic complications by MBP – has not been supported by evidence and has recently been challenged in the medical literature.
- Dietary restriction (5 days of clear liquids), cathartics, and enemas formed the original framework of colon preparation. However, patient discomfort, electrolyte problems, and inadequate caloric intake proved cumbersome as well as costly.

- Polyethylene glycol (PEG) lavage solution was first introduced in 1980. PEG solutions are iso-osmotic nonabsorbable electrolyte lavage solutions that cause little to no fluid shifts or electrolyte disturbances.
- Multiple studies have proven these lavage solutions to be safe, effective, and well tolerated when compared with traditional bowel preparative regimens.
- PEG solutions require ingestion of 3–4 L solution. The salty taste and high volume reduce patient compliance. Addition of bisacodyl, senna, or magnesium citrate to traditional 4 L PEG regimens has been shown to improve colonic cleansing for colonoscopy.
- Addition of these adjuncts has also allowed for lower-volume (2 L) PEG solutions to be administered with equivalent or increased efficacy and improved patient tolerability.
- Prokinetic agents and enemas when combined with oral lavage have not been shown to improve efficacy or decrease patient symptoms.
- PEG solutions are contraindicated in patients with any sensitivity to the components of the solution, gastrointestinal obstruction, gastric retention, bowel perforation, toxic colitis, toxic megacolon, or ileus.
- PEG solutions are considered Category C drugs in pregnancy and have not been well studied in this patient population.
- In 1990, sodium phosphate (NaP), a saline laxative, was introduced as a safe, more efficacious, and less costly form of bowel preparation when compared with PEG in initial and subsequent studies.
- A tablet form of NaP was developed in 2000 showing equal or improved efficacy and/or improved tolerance when compared with both liquid NaP, PEG, and PEG plus bisacodyl regimens.
- These tablet preparations offered an alternative to the solution-type NaP formulation.
- The tablet preparation regimen consists of 28–40 tablets given the day prior to the elective procedure or in a split dose manner, similar to the fluid formulation.
- Patients with impaired renal function, dehydration, hypercalcemia, hyperphosphatemia, congestive heart failure, or advanced liver disease could experience severe complications with NaP administration including phosphate nephropathy.
- This is especially true in hypertensive patients taking certain medications, namely, angiotensin-converting enzyme inhibitors or angiotensin receptor blockers.
- This led the Federal Drug Administration to issue a black box warning for the over-the-counter version of this preparation and the manufacturer to voluntarily remove the preparation from the market. As this preparation is hypertonic, significant fluid and electrolyte shifts can occur, and it is necessary to maintain adequate hydration while undergoing the preparation.
- Absolute contraindications to any bowel preparation include obstruction, ileus, perforation, diverticulitis, severe colitis, toxic megacolon, gastric retention, and gastric paresis.

Summary of Trials and Meta-analyses

- MBP need not be considered a "prerequisite of safe colorectal surgery." Despite these data, a 2003 survey of practicing colorectal surgeons revealed that 99 % of respondents continue to employ MBP, though 10 % did question its role in elective surgery (Table 8.5).

Antibiotics

- The use of antibiotic prophylaxis in elective colon surgery is mandatory to minimize infection complications.
- The first principle in prophylactic use of antibiotic administration is to provide coverage for the normal bowel flora [aerobic bacteria (*E. coli*) and anaerobic species (*Bacteroides* sp.)]. Oral antibiotics as used in the traditional Nichols–Condon antibiotic preparation have been shown to reduce intraluminal and mucosal bacterial count, while parenteral antibiotics have been shown to reduce systemic bacterial counts at the tissue level.

Table 8.5 Randomized controlled trials and Cochrane report relating to preoperative mechanical bowel preparation[a]

Author/year	No. of patients	Mechanical bowel preparation agent	Anastomotic leaks	Wound infections	Mortality
Brownson et al. (1992)	179	PEG	11.9 vs. 1.5[b]	5.8 vs. 7.5	0.0 vs. 0.0
Santos et al. (1994)	149	Mineral oil, agar, and phenolphthalein; enema; mannitol (3-day regimen)	10.4 vs. 5.3	23.6 vs. 11	7 0.0 vs. 0.0
Burke et al. (1994)	169	Sodium picosulfate	3.8 vs. 4.6	4.9 vs. 3.4	2.4 vs. 0.0
Fillman et al. (1995)	60	Mannitol	8.7 vs. 4.3	3.3 vs. 6.7	
Miettinen et al. (2000)	267	PEG	4.0 vs. 2.0	4.0 vs. 2.0	0.0 vs. 0.0
Tabusso et al. (2002)	47	Mannitol or PEG	20.8 vs. 0[b]	8.3 vs. 0	
Bucher et al. (2005)	153	PEG	6.4 vs. 1.3	12.8 vs. 4	
Ram et al. (2005)	329	NaP	0.6 vs. 1.3	9.8 vs. 6.1	
Fa-Si-Oen et al. (2005)	250	PEG	5.6 vs. 4.8	7.2 vs. 5.6	
Zmora et al. (2006)	249	PEG	4.2 vs. 2.3	6.7 vs. 10.1	1.7 vs. 0.8
Pena-Soria et al. (2007)	97	PEG	8.3 vs. 4.1	12.5 vs. 12.2	
Jung et al. (2007)	1,343	PEG, NaP, enema	1.9 vs. 2.6	7.9 vs. 6.4	
Contant et al. (2007)	1,354	PEG + bisacodyl or NaP	4.8 vs. 5.4	13.4 vs. 14.0	

PEG polyethylene glycol, *NaP* sodium phosphate
[a]All results as mechanical bowel preparation (MBP) vs. no MBP, %
[b]Significant result

- The dosing of 1 g of oral neomycin sulfate and erythromycin base at 2 p.m., 3 p.m., and 10 p.m. for an 8 a.m. case became and remains a standard oral antibiotic regime for elective surgery. Oral antibiotics may decrease surgical site infection when used in addition to a mechanical bowel prep.
- Unfortunately, the Nichols prep has its drawbacks. While this antibiotic combination is efficacious, it can cause significant gastrointestinal discomfort severely limiting patient compliance with the remainder of the antibiotic preparation and completion of their mechanical preparation.
- The standard for parenteral antibiotic prophylaxis in elective colon resections should include:
  1. *Timing*: Infusion of the first antimicrobial dose should begin within 60 min prior to surgical incision.
  2. *Duration*: Prophylactic antimicrobials should be discontinued within 24 h following surgery.
  3. *Dosing*: The initial dose should be adequate based on weight, adjusted dosing weight, or BMI. An additional dose should be administered, if the operation continues over two half-lives after the initial dose.
  4. *Selection* (*colon surgery*): Cefotetan, cefoxitin, cefazolin/metronidazole, and ampicillin/sulbactam.
     - Options for β-lactam allergic patients: clindamycin + gentamicin, ciprofloxacin, or aztreonam
     - Metronidazole + gentamicin or ciprofloxacin

Deep Venous Thrombosis Prophylaxis

- Deep venous thrombosis (DVT) and its embolic corollary and pulmonary embolism (PE) are a significant source of morbidity and mortality in the perioperative period.
- Due to the predominance of abdominal and pelvic surgery, colorectal surgery confers a higher risk of these postoperative complications than other general surgical procedures. Yet despite so much emphasis, DVT and PE continue to be the most common cause of preventable deaths during in-hospital admission, accounting for one out of every four hospitalized patients' deaths.
- Over 50 % of all DVTs are asymptomatic, while the vast majority of PEs are detected only after death.
- Symptomatic venous thromboembolism in the perioperative period is associated with male gender, malignancy, trauma, immobility, COPD, sepsis, low hematocrit, low albumin, and major surgery.
- Prophylaxis of venous thrombotic events centers on both mechanical and medical means. Mechanical methods include intermittent pneumatic compression stockings, while the current mainstays for chemical thromboprophylaxis are unfractionated and low-molecular-weight heparin.

- Unfractionated heparin works through antithrombin III to inactivate thrombin and other factors in the clotting cascade. Concerns about its increased bleeding events as well as its dose–effect relationship have led many to be wary of its use.
- Low-molecular-weight heparin has enhanced antifactor Xa activity and more predictable dose–effect relationships.
- Risk stratification is the mainstay for DVT prophylaxis recommendation. Young healthy patients undergoing routine anorectal surgery with minimal patient-specific risk factors do not require any additional therapy other than mechanical means via graduated compression stockings and/or intermittent pneumatic compression boots and early ambulation.
- Those patients with multiple risk factors and undergoing high-risk surgery such as pelvic operations warrant more aggressive means such as unfractionated or low-molecular-weight heparin in addition to the mechanical devices. Timing has been somewhat controversial with some studies demonstrating higher bleeding without undue increase in thrombotic events when given after the surgery and others stating that dosing should begin preoperatively.
- A concern in colorectal surgery is how to manage anticoagulated patients who require colonoscopy. Recent guidelines suggest that aspirin and other nonsteroidal anti-inflammatory drugs (NSAIDs) do not need to be withheld, with the rate of postpolypectomy bleeding around 2 %.
- Coumadin and other more potent antiplatelet medications (i.e., clopidogrel) are commonly held for 5–7 days prior to the procedure, especially when it is known that a polypectomy or other procedures are likely.

Beta-Blockade

- Preoperative beta-blockade is indicated in patients having intermediate risk surgery with one or more clinical risk factors or any patient having vascular surgery. It is not indicated in patients for low risk surgery or intermediate risk surgery without clinical risk factors.

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 ASCRS.
- Blood grouping and crossmatching are 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 crossmatching would not usually take place. This allows a double level of security when urgent samples are sent if bleeding occurs during surgery. This may help to avoid the risk of transfusion reaction, if there is concern about errors with sample labeling or source at any time.
- 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 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.71 techniques including acute normovolemic hemodilution and cell salvage may be more efficient; however, investigations still continue into their use.

Communication with the Patient and Establishing the Expectations for Postoperative Recovery

- No preoperative visit is complete without providing information on expected postoperative outcomes. This discussion helps the patient to build confidence and trust in the surgeon. Such discussion is likely to be an important component of any postoperative care pathway, and this may help lead to significant reduction in postoperative stay.
- Patients can 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.

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9. Postoperative Management

Sharon L. Stein and Conor P. Delaney

The Problem

- Postoperative care of the colorectal patient is focused on decreasing morbidity, mortality, and health-care costs.
- An estimated 161,000 Medicare patients undergo major intestinal surgery in the USA annually at a cost of 1.75 billion dollars.
- The average patient remains in the hospital 10.3 days after colorectal surgery, costing approximately $1,055/day.
- Advances and standardization of postoperative care have reduced perioperative morbidity and mortality.
- Estimates of overall morbidity are 24.3 % following colorectal surgery, with the incidence of serious morbidity including organ space surgical site infection, pulmonary embolism, and septic shock at up to 11.4 %.
- Recent NSQIP data estimates mortality at 1.4 % for elective procedures and 15.8 % for emergency colon and rectal surgery.
- Although some costs and complications are unavoidable in postoperative care, a substantial percentage results from prolonged hospitalization, complications including surgical site infections, postoperative ileus, and venous thromboembolic events.
- Numerous studies demonstrate that most patients can safely leave the hospital within 3–5 days following colon and rectal surgery without increasing rates of complications or readmission.

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- By decreasing the length of hospital stay, postoperative complications, and postoperative ileus, clinicians have the potential to save millions of healthcare dollars annually, as well as accelerate the recovery of patients after major surgery.

Standardized Fast-Track Protocols or Enhanced Recovery Pathways

- Standardized fast-track or enhanced recovery protocols have the ability to substantially reduce length of stay.
- Generally, patients with stable vital signs are deemed ready for discharge when ambulating, tolerating enteric nutrition, and pain is well controlled with oral analgesia and adequate discharge care (home or transitional facility) is available.
- In 2005, average length of stay following colectomy was 10.6 days. Using multimodal, enhanced recovery, or fast-track protocols, length of stay has dropped to a mean of 4–5 days in many series and as short as 2.5 days in the hands of some authors.
- Overall, 11 of 13 programs demonstrated a significant decrease in length of stay when compared to conventional care; 3 also found a decrease in complication rates. None of the studies documented an increased risk of negative outcomes in the clinical pathway group when compared to standardized protocol patients.
- Length of stay was significantly decreased in fast-track protocols (1.56–2.35 days shorter), and overall morbidity rates favored fast-track protocols.
- Meta-analysis has failed to show a significantly higher rate of readmission for fast-track protocols (RR = 1.17, 95 % CI 0.73–1.86). In addition, total hospital stay was analyzed including readmission in several studies and was still found to be approximately 2.5 days shorter than patients on conventional protocols.
- Data on increased use of posthospital services at time of discharge are scant.
- Implementing a fast-track protocol is not simple. Most fast-track protocols incorporate 8–12 elements, with ranges varying from 4 to 20 elements (Table 9.1).
- In a study center familiar with the fast-track protocol, the percentage of patients discharged upon meeting criteria was 66 % versus less familiar centers where only 26 % of patients were immediately discharged ($p < 0.001$).
- Many studies have now analyzed the cost-effectiveness of fast-track protocols.
- The mean cost per hospital stay was \$19,997.35 ± \$1,244.61 for patients in the historical control group, \$20,835.28 ± \$2,286.26 for those in the simultaneous control group, and \$13,908.53 ± \$1,113.01 for those in the enhanced recovery group ($p < 0.05$ vs. other groups).

Table 9.1 University Hospital Case Medical Center-enhanced recovery protocol guidelines

Day before surgery
1. Protein/glucose drink
2. Bowel prep as directed
3. Ibuprofen 800 mg tid
Preoperative holding area
1. Gabapentin 600 mg po 1–2 h prior to induction
2. Alvimopan 12 mg po 1–2 h prior to induction
3. Thromboprophylaxis low-dose unfractionated heparin 5,000 U SC
4. Antibiotics prior to induction 30–60 min prior to induction
Postanesthesia recovery unit
1. Morphine PCA for all patients
2. DC antibiotics unless therapeutic indication
Nursing floor – general orders
1. CBC, BMP POD #1, 3 unless otherwise indicated
2. Ambulate in hallway 5 times/day
3. Sit out of bed 4–6 h/day
4. Foley removed POD#1 if laparoscopic, POD#2 if open
5. Heplock IVF POD#1 if laparoscopic, POD#2 if open
Nursing floor – dietary orders
1. Clear liquids as tolerated
2. Protein/glucose drink 1 can BID
3. Soft diet POD#1 if laparoscopic, POD#2 if open
4. Chewing gum 1 stick TID × 60 min
Nursing floor medication orders
1. Gabapentin 300 mg po TID while in hospital
2. Alvimopan 12 mg po BID Å~7 days while in hospital
3. Ketorolac 15 mg IV Q6 h Å~72 h while in hospital
4. Ibuprofen 800 mg TID while in hospital
5. Heparin 5,000 U SC TID while in hospital. This may be continued following discharge in high-risk patients
6. Lactulose 10 mL po BID
Nursing floor – oral analgesia
1. Transition to oral analgesia – POD#1 if laparoscopic, POD#2 if open
2. DC PCA
3. Acetaminophen #3 1–2 pills po q4–6 h, first dose 30 min prior to stopping PCA
4. Hold morphine except break through pain

The above guidelines should be modified as clinically appropriate and do not replace clinical evaluation and experience
POD postoperative day, *PCA* patient controlled analgesia

- After implementation of a fast-track protocol, length of stay was reduced from 6.6 to 3.7 days ($p < 0.001$), and costs were reduced from \$9,310 ± \$5,170 to \$7,070 ± \$3,670 ($p = 0.002$).
- Kariv et al. looked exclusively at patients undergoing ileal pouch anal anastomosis and found shorter hospital stays (4 days vs. 5 days) ($p = 0.012$) and lower direct 30-day costs reduced from \$6,672 to \$5,692 ($p = 0.001$).

Fluid Management

- Postoperative fluid management is complicated by perioperative changes in homeostasis, and appropriate fluid management is essential to optimizing postoperative care.
- Basic fluid requirements are approximately 2,500 cc/day in a 70 kg adult. This allows for both insensible losses from respiration, perspiration, and feces as well as the 1,500 cc of urine necessary to excrete waste products including urea, potassium, and sodium.
- A basic formula for calculating fluid needs is 1,500 cc for the first 20 kg and 20 cc/kg for the rest of the weight.
- After 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 evaporation from exposed abdominal cavity, blood loss, diarrhea, nasogastric tubes, and abdominal drains; each of these must be accounted for.
- In recovering patients, fluid retention begins to resolve with a return of the hormones and sympathetic nervous system toward normal in approximately 72 h.
- Data have shown that insufficient perioperative fluid resuscitation increases the risk of hypotension, inadequate tissue perfusion, and renal failure.
- Over-resuscitation is associated with hypoalbuminemia, delayed gastrointestinal recovery, pulmonary complications, and increased cardiac demand.
- Transesophageal Doppler monitoring has been used to guide resuscitation. Monitoring of ejection fraction and stroke volume aids in assessing oxygen tissue delivery.
- Optimization of stroke volume as determined by Doppler is compared with typical postoperative hemodynamic parameters such as urine output, heart rate, and blood pressure.
- Several studies have shown reduced postoperative gastrointestinal and overall complications and earlier return of bowel function.
- Resuscitation with colloid versus crystalloid did not further improve length of stay.
- The rate of anastomotic leaks was not increased in the study groups.
- Three studies demonstrated a statistically reduced postoperative length of stay by 1.5–2 days confirmed in two separate meta-analyses in favor of Doppler-guided resuscitation.

Postoperative Gastrointestinal Recovery: Nausea, Vomiting, Feeding, Gum Chewing, and Ileus

Postoperative Nausea and Vomiting (PONV)

- Approximately 25 % of patients experience PONV within 24 h.
- Among high-risk patients, the incidence may be as high as 70–80 %.
- PONV delays recovery of patients after inpatient surgery and accounts for a significant proportion of unanticipated hospitalizations following ambulatory surgery.
- Consensus guidelines for managing PONV highlight patient, anesthetic, and surgical risk factors as listed in (Table 9.2).
- Instruments that predict PONV have been validated with a high level of correlation to patient outcome.
- Among the simplest is the Koivuranta score (Table 9.3), which uses only the five strongest risk factors – female gender, previous PONV, duration of surgery, history of motion sickness, and nonsmoking status – as predictors of PONV.
- Prevention of PONV is centered on reducing anesthetic and surgical risks while appropriately adding pharmacologic prophylaxis.
- Use of regional anesthesia, minimization of narcotics, and avoidance of nitrous oxide and volatile anesthetics have efficacy in reducing PONV.
- Propofol induction, increasing hydration, and use of supplemental oxygen are associated with reduction in risk in patients undergoing colorectal surgery.

Table 9.2 Risk factors for postoperative nausea and vomiting

Patient-specific risk factors
1. Female sex
2. Nonsmoking status
3. History of PONV/motion sickness
Anesthetic risk factors
1. Use of volatile anesthetics
2. Nitrous oxide
3. Use of intraoperative or postoperative narcotics
Surgical risk factors
1. Duration of surgery
2. Type of surgery

Adapted from Gan TJ. Risk factors for postoperative nausea and vomiting. Anesth Analg. 2006;102:1884–98

PONV postoperative nausea and vomiting

Table 9.3 Koivuranta score II for evaluation of postoperative nausea and vomiting

Scoring: Patient risk is calculated based on cumulative number of risk factors.
Risk factors:
Female gender
Previous PONV
Duration of surgery over 60 min
History of motion sickness
Nonsmoker

# of risk factors	Risk of nausea (%)	Risk of vomiting (%)
0–1 factor	17–18	7
2 factors	42	17
3 factors	54	25
4 factors	74	38
5 factors	87	61

Adapted from Koivuranta M, Laara E, Snare L, Alahuhta S. A survey of postoperative nausea and vomiting. Anaesthesia. 1997;52:443–9
PONV postoperative nausea and vomiting

- Many pharmacologic therapies for PONV are familiar to the colorectal surgeon. 5-HT_3A agents such as ondansetron, granisetron, and tropisetron are often chosen as first-line treatment. They are generally effective (NNT 5–7) with a favorable side effect profile which includes headaches, increased liver enzymes, and constipation.
- Typical dose of ondansetron is 4 mg IV every 8 h, but this may be doubled for increased efficacy.
- Steroids have also been shown to be effective, particularly if administered prior to induction. Dexamethasone is generally administered as a single dose intravenous of 8–10 mg, although doses as low as 2.5 have been found to be effective (NNT = 4).
- Side effect profile is more concerning to surgeons and includes wound infection and adrenal suppression, but these effects have not been reported after a single bolus dose.
- Droperidol was commonly administered at the end of surgery in doses of 1 mg IV with good effect (NNT = 5), but an FDA "black box" warning recently issued has diminished enthusiasm for this antiemetic.
- Acupuncture has been demonstrated to reduce the incidence of PONV when compared to placebo (23 % vs. 41 %, $p = 0.0058$).
- Economic and emotional costs of nausea and vomiting are often weighed against the cost of therapy. PONV prophylaxis was not found to be cost-effective in patients whose risk of nausea or vomiting are less than 20 %.
- Algorithms for management of PONV are well established.
- Patients should be assessed preoperatively for risk of PONV and if found to be low risk, no prophylactic dosage is generally given. A rescue dose of 5-HT_3A, such as ondansetron, may be given if the patient experiences PONV after emersion.

- Patients deemed to be at moderate to high risk of PONV are generally treated empirically. Monotherapy agents such as use of dexamethasone, droperidol, or ondansetron may be used, or combination therapy of multiple agents can be employed when deemed appropriate.

Early Refeeding and Use of Nasogastric Tubes

- Nasogastric tubes are associated with increased atelectasis and pneumonia and gastroesophageal reflux
- A recent meta-analysis demonstrated earlier return of bowel function after colonic surgery without a routine use of nasogastric tube.
- Early refeeding is believed to stimulate propulsive activity, decrease intestinal gut mucosal permeability, and induce secretions of gastrointestinal hormones to promote bowel motility.
- Feeding patients promptly after surgery is associated with decreased rate of infections (RR = 0.72, $p = 0.036$), and shorter length of stay (RR = 0.84, $p = 0.001$), but an increased risk of vomiting after surgery (RR = 1.27, $p = 0.046$).
- Approximately 5–15 % of patients will develop substantial postoperative ileus requiring return to NPO status or nasogastric decompression, but most patients tolerate early feeding without complications.
- For the majority of patients who tolerate early refeeding, decreased complications, earlier discharge, and patient comfort are significant benefits.
- Postoperative hyperglycemia and insulin resistance have been proposed as independent factors increasing hospital stay.
- Preoperative fasting of 8–12 h can deplete available carbohydrate reserves and promote a fasting metabolism.
- Administration of a preoperative carbohydrate drink does not increase risk of aspiration or complications on induction.
- A carbohydrate-rich drink, given the evening before surgery and 2–3 h prior to surgery, has been shown to significantly reduce patient thirst and hunger and improve well-being while also decreasing the loss of muscle mass postoperatively and significantly reducing length of stay by 1.2 days ($p < 0.02$).

Treatment and Prevention of Ileus

- Postoperative ileus is defined as the "transient cessation of coordinated bowel motility after surgical intervention, which prevents effective transit of intestinal contents and/or tolerance of oral intake."
- The average time until recovery of bowel function after major abdominal surgery is less than 24 h for the small intestine, 24–48 h for the stomach, and 48–120 h for the colon.
- In general, ileus should resolve within the fifth postoperative day after open surgery and by the third postoperative day after laparoscopic surgery.

- Failure to resume gastrointestinal function has many adverse effects including increased postoperative pain, nausea and vomiting, poor wound healing, delay in postoperative mobilization, increase in deconditioning, pulmonary complications and nosocomial infections, prolonged hospitalization, decreased patient satisfaction, and increased health-care costs.
- Health Care Financing Administration data estimates that postoperative ileus occurs in approximately 14.9 % of patients following large bowel resection and up to 19.2 % after small bowel resection.
- It is estimated that the total health-care cost of postoperative ileus is approximately $1.14 billion dollars annually or 6.24 % of all health-care costs in the USA.
- The average length of stay of patients with postoperative ileus is almost doubled to 11.5 from 6.5 days for patients without postoperative ileus.
- To reduce the incidence and duration of postoperative ileus, multiple pharmacologic interventions have been attempted.
- Newer drugs have been designed to selectively block peripheral (mu) μ-opioid receptors that contribute to postoperative ileus (POI).
- The ideal POI treatment is a peripheral opioid receptor antagonist that reverses GI side effects without crossing the blood–brain barrier and therefore is unable to compromise postoperative analgesia.
- Two novel peripheral (mu) μ-opioid receptor antagonists have been studied in patients undergoing abdominal and pelvic surgery.
- Alvimopan is a peripherally active (mu) μ-opioid antagonist, with affinity for human (mu) μ-opioid receptors and an active metabolite that appears to be absorbed systemically.
- Alvimopan speeded overall GI-2 (tolerance of solid food and first bowel movement) recovery by 12 h and accelerated time to discharge order ($HR = 1.35$, $p < 0.01$).
- Alvimopan has not been shown to have an increase in adverse event rates or complications.
- The first dose of 12 mg should be given orally prior to surgery, and continued 12 mg BID for 7 days, or until discharge.
- Alvimopan is contraindicated for patients on chronic opioids, with bowel obstruction or severe hepatic or renal disease.

Use of Gum Chewing

- Gum chewing has also been proposed to decrease the incidence of postoperative ileus.
- Chewing stimulates the cephalic phase of digestion and serves as a form of sham feeding stimulating neural and hormonal pathways.
- Mastication and salivation increase vagal cholinergic stimulation and promote the release of gastrointestinal hormones such as gastrin, neurotensin, and pancreatic polypeptide.

- Cephalic stimulation is accomplished without oral intake, thereby theoretically avoiding complications of food intolerance, which may occur in up to 20 % of patients after early oral intake.
- At least five meta-analyses on gum chewing exist in the literature, all of which demonstrate a statistically significant reduction in time to flatus and defecation. Cumulative time to flatus and defecation was reduced by as much as 20 and 29 h, respectively.

Early Ambulation

- Direct benefits of ambulation on postoperative gastrointestinal recovery are inconclusive.
- Early ambulation appears to be correlated with reduced postoperative respiratory and hematologic complications but may not have a direct effect on recovery of bowel function. Additional benefits include preservation of strength and conditioning.
- Ideally, patients ambulate on the evening of surgery. To accommodate early ambulation, lines and tubes are minimized after surgery. Foley catheters are removed by postoperative day 1 for laparoscopic surgery or day 2 after open surgery. Drainage catheters are not routinely left in place after surgery.
- By postoperative day 1, patients are encouraged to walk a minimum of 60 m and spend 5 or more hours out of bed.

Prevention of Pulmonary Complications

- Pulmonary complications are well established after surgery.
- Delayed ambulation has been directly correlated with worsening pulmonary function. Pain appears to be a factor in both ability to ambulate and pulmonary toilet.
- Appropriate pain control can be essential in moderating diminished lung capacity.
- Earlier return of forced expiratory volumes was one of the first benefits demonstrated from laparoscopic surgery. Several studies have demonstrated early recovery of pulmonary function as evidenced by incentive spirometry.
- Although all patients are at risk for pulmonary complications, there appear to be groups who are particularly susceptible.
- High-risk patients include those with chronic obstructive pulmonary disease, age greater than 60, American Society of Anesthesiologist (ASA) class II or greater, and cardiac failure. Emergency surgery, general anesthesia, abdominal surgery, and procedures longer than 3 h in length all further increase risk.
- Patients deemed high risk of complications benefit from deep breathing exercises or incentive spirometry, and the selective use of nasogastric tubes, though no single intervention was statistically superior.

- Preoperative smoking cessation may not be advantageous. Data regarding postoperative benefits of preoperative smoking cessation is generally inconclusive but appears to be most beneficial for patients who quit 4–6 weeks before surgery.
- Patients who quit smoking within 2 months of surgery may have a paradoxical increased risk of postoperative pulmonary complications, possibly from increased mucous production.

Prevention of Venous Thromboembolism

- Colon and rectal surgery patients are at risk for deep venous thrombosis (DVT) and pulmonary embolism (PE). Estimates are that between 20 and 40 % of patients undergoing abdominal surgery will experience DVT and 2–4 % will develop a pulmonary embolism.
- Fatal pulmonary embolism occurs in up to 1.0 % of hospitalized patients and accounts for 10 % of hospital deaths, making it the most common preventable cause of hospital death in the USA.
- Colon and rectal surgery patients often have multiple risk factors for venous thromboembolism (VTE), listed in Table 9.4, including diagnoses such as cancer or inflammatory bowel disease, advanced age, and prolonged surgical procedures.
- Patient risk should be stratified preoperatively, and use of prophylactic regimens including elastic stockings, mechanical sequential compression devices (SCDs), and pharmacologic agents should be employed.

Table 9.4 Risk factors for venous thromboembolism

Surgery
Trauma (major or lower extremity)
Malignancy
Cancer therapy (hormonal, chemotherapy, radiotherapy)
Previous venous thromboembolism
Increasing age
Pregnancy/postpartum
Estrogen-containing oral contraceptive/hormone therapy/modulation
Acute medical illness
Heart/respiratory failure
Inflammatory bowel disease
Nephrotic syndrome
Obesity
Smoking
Varicose veins
Central venous catheterization

Modified from Geerts WH, Bergqvist D, Pineo GF, et al. Prevention of venous thromboembolism. Chest 2008;133:381S–453S

Elastic Stockings and Sequential Compression Devices

- Elastic stockings and SCDs are mechanical methods of increasing venous outflow and reducing stasis in leg veins to decrease the risk of DVT.
- Graduated compression stockings function purely on a mechanical level to encourage venous return. SCDs are also believed to systemically increase the fibrinolytic activity by reducing plasminogen activator.
- For maximal benefit in patients undergoing surgery, elastic stockings or SCDs should be placed before the induction of anesthesia and function throughout the operation.
- Data on the effectiveness of elastic stockings and SCDs is limited. Both methods have demonstrated efficacy in reducing the risk of DVT, but neither have been shown to decrease the incidence of PE.
- Several factors limit the effectiveness of SCDs and elastic stockings including poor compliance, poor fit, and arterial insufficiency.

Low-Dose Unfractionated Heparin

- Unfractionated heparin has been used as a form of DVT prophylaxis since the 1970s and has been shown to be safe in the majority of surgical patients. It binds to antithrombin (ATIII) and accelerates the inhibition of thrombin and other coagulation factors, particularly factor X. Typically, pTT will be unchanged despite use of unfractionated mini-dose heparin. Heparin can be reversed with use of protamine. Recommendations are that the initial dose of low-dose unfractionated heparin (LDUH) be given 1–2 h preoperatively. Although the standard dosing regimen is 5,000 U subcutaneously every 8–12 h postoperatively, no study has compared dosing regimens directly.

Low-Molecular-Weight Heparin

- Compared to LDUH, LMWH has a longer half-life and may not be reversed with protamine infusion. The incidence of HIT is also lower than LDUH (2.7 % vs. 0 %). Dosing regimens for LMWH are varied. In Europe, LMWH (enoxaparin) is typically dosed 20–40 mg daily. Americans tend to prefer a 30 mg BID dosing.
- LMWH is at least as effective as LDUH in preventing DVT in postoperative general surgery and colorectal surgery patients.

VTE Prophylaxis and the Use of Epidural Analgesia

- A rare but potential complication of spinal or epidural analgesia is the risk of bleeding into the spinal canal or epidural space. This may result in spinal cord ischemia and paraplegia in patients. Risk factors for the development of hematoma include high level of anticoagulation and continuous use of epidural.

Duration

- Although thromboprophylaxis is traditionally terminated at the time of discharge from the hospital, the risk of DVT and PE continues.

Prophylactic Perioperative Antibiotics

- Significant literature has focused on the use of perioperative antibiotics for colorectal surgery. Surgical site infections account for 14–16 % of all hospital-acquired infection.
- Although patients who received antibiotics were less likely to develop surgical wound infections when compared to placebo (RR = 0.30, 95 % CI 0.22–0.41), there was no difference for short-term versus long-term prophylaxis (RR = 1.06, 95 % CI 0.89–1.27).
- Guidelines for perioperative antibiotics have been formalized by the Surgical Care Improvement Project, a partnership of organizations including the Centers of Medicare and Medicaid services (CMS) and US Centers for Disease Control.
- Currently, there are five recommendations relevant to prevention of surgical site infections in colorectal patients (see Table 9.5). Antibiotics should be given within a 60 min window of incision and within 2 h when using vancomycin or fluoroquinolones.

Table 9.5 Consensus recommendations of the surgical infection prevention guidelines for colorectal surgery

1. Antibiotic should be received within 1 h of surgical incision
2. Prophylaxis antibiotic should be discontinued within 24 h of surgical completion
3. Proper hair control (no clippers or hair removal)
4. Maintenance of normothermia in colorectal surgery patients
Oral antimicrobial prophylaxis
Neomycin + erythromycin
Neomycin + metronidazole
Parental antimicrobial prophylaxis
Cefotetan, cefoxitin
Ampicillin-sulbactam
Ertapenem
Cefazolin/cefuroxime + metronidazole
Parental antimicrobial prophylaxis with β-lactam allergy
Clindamycin + aminoglycoside
Clindamycin + quinolone
Clindamycin + aztreonam
Metronidazole + aminoglycoside
Metronidazole + fluoroquinolone

Adapted from material prepared by Stratis Health and the Oklahoma Foundation for Medical Quality, the Quality Improvement Organization Support Center for Patient Safety, under contract with the Centers for Medicare & Medicaid Services an agency of the US Department of Health and Human Services. 9SOW-QIOSC-6.2-09-36

- Prophylactic antibiotics should be discontinued within 24 h of surgery.
- Additional measures to prevent postoperative surgical site infections include appropriate preoperative hair removal, prompt removal of urinary catheters, and immediate postoperative maintenance of normothermia (greater than 96.8 °F/36 °C) for colorectal patients.

Postoperative Treatment of Adrenal Insufficiency

- Glucocorticoids and mineralocorticoids are important in the control of hemostasis including maintenance of blood volume and normal cardiovascular function. In addition to hemodynamic changes, use of chronic steroids may have other perioperative side such as water retention, delayed wound healing, and diabetes. After stress of trauma or surgery, endogenous steroids are increased up to six times from baseline to over 150 mg daily. Patients with adrenal suppression or insufficiency are unable to secrete sufficient corticosteroids.
- There are many causes of adrenal insufficiency including primary causes such as Addison's disease, tuberculosis, and HIV or secondary causes such as chronic exogenous administration. In addition to underlying medical illness, patients undergoing colorectal surgery may use steroids chronically as a component of treatment for their primary colorectal disorder; patients with inflammatory bowel disease are often treated acutely with steroids, and steroids may be a component of oncologic treatment as well.
- Patients treated with steroids chronically or with primary steroid deficiencies may suffer from adrenal insufficiency during times of stress, such as surgical intervention.
- Any patient on doses of 5 mg prednisone for any prolonged period up to 1 year prior to surgery has traditionally been believed to be at risk of postoperative adrenal insufficiency.
- 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.
- Symptoms 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.

Postoperative Analgesia

- Analgesia following colon and rectal surgery is of paramount importance in improving patient satisfaction, early ambulation, and minimizing sympathetic inhibition postoperatively.

- Narcotics are used to decrease pain after surgery by crossing the blood–brain barrier and binding to (mu) m-opioid receptors within the central nervous system.
- However, a secondary effect of narcotics is stimulation of (mu) m receptors in the gastrointestinal tract that contribute to inhibition of bowel function postoperatively.
- Narcotics have been shown to decrease peristaltic activity, delay gastric emptying, and play an important role in prolonging postoperative ileus.
- The use of epidural analgesia was proposed to minimize systemic narcotics, decrease inflammation, and create sympathetic blockade leading to earlier return of bowel function and decreasing need for narcotics.
- Notwithstanding the lack of evidence supporting use of epidurals, many centers still use them, particularly in European-enhanced recovery pathways.
- Although costs may be lower in patients with thoracic epidurals, difficulty inserting epidurals has been reported in up to 40 % of patients.
- Postoperative reduction of ileus and earlier return of bowel function are effective only with thoracic epidurals using local anesthetic alone without fentanyl, and several studies have demonstrated that epidurals should remain in place for 48 h to maximize benefits.
- Reducing the use of postoperative narcotics has a role in recovery of bowel function, avoiding postoperative ileus, and reduced length of stay. The use of thoracic epidural appears to reduce postoperative pain but not length of stay. Use of narcotic-sparing analgesia such as ketorolac and gabapentin may help improve pain control and reduce the incidence of postoperative ileus.

Conclusion

- The care of the postoperative colon and rectal surgery patient has undergone significant changes over the past 20 years.
- Optimization of perioperative fluids, early ambulation, timing of oral nutrition and gastric stimulation, prophylaxis for VTE, minimization of narcotics, and avoidance of postoperative ileus have led to substantial reductions in length of postoperative stay and improvements in postoperative care. A significant body of literature evaluating and testing various care options is now available. By combining care elements into standardized fast-track or enhanced recovery protocols, average length of stay can be reduced without compromising complication or readmission rates. Implementing a fast-track protocol requires multidisciplinary teams, with patient and provider education to be truly successful. However, patient care benefits as well as health cost savings may be substantial.

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10. Postoperative Complications

David W. Dietz

Unrecognized Enterotomies and Enterocutaneous Fistulae

- With any significant degree of adhesiolysis, there is an increased risk of enterotomies. Therefore, the entire bowel should be carefully inspected at the end of the procedure.
- All serosal tears should be repaired with imbricating seromuscular sutures in either a single- or two-layer closure.
- A bowel resection with anastomosis may be needed if there are multiple full-thickness enterotomies in a short segment of bowel. The viability of the ends should be confirmed if there was any mesenteric injury.
- Long longitudinal seromyotomies may be treated by conversion to a full-thickness laceration and closure in a strictureplasty fashion.
- Failure to recognize and repair an enterotomy may lead to peritonitis which may be difficult to detect in the first 24–48 h after surgery. A high index of suspicion with a low threshold for re-exploration is required as the usual markers of bowel perforation (leukocytosis, fever, and pneumoperitoneum) may not be reliable.
- At reoperation for a missed enterotomy in the early postoperative period, if the edges are viable, a primary repair can be done. If conditions are not favorable, a diverting stoma should be considered proximal to the repair.
- At relaparotomy, if bilious fluid is encountered and no enterotomy is found, a duodenal, gastric, or gallbladder injury must be excluded. Insufflation of the small bowel with gas via an NG tube and filling the abdomen with saline may help localize the enterotomy. If still no enterotomy is found, drains can be placed in each paracolic gutter and the pelvis in hopes of allowing a controlled enterocutaneous fistula to develop.

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- An unrecognized enterotomy, presenting with enteric drainage from the incision, may be nonoperatively managed if there are no signs of sepsis.
- Any reoperation after the first postoperative week is often extremely difficult as dense vascular adhesions may be encountered and the risk of making further enterotomies or a mesenteric vascular injury is high. Therefore, complete bowel rest, a nasogastric tube, nutritional support, and broad-spectrum antibiotics are initiated.
- A computed tomography scan is obtained to look for an abscess or undrained fluid. A collection >4 cm may be percutaneously drained.
- Assistance by an enterostomal therapist (WOCN) regarding skin care and pouching the fistula may be helpful.
- Total parenteral nutrition may be required if the fistula output is high. H_2 antagonists may be added to the TPN.
- Somatostatin analogs may be useful to decrease the volume of the fistula output but do not improve the rate of fistula closure.
- Spontaneous fistula closure is typically less than 50 %. Factors attributed to reduced fistula closure rates are high output (because of proximal location), distal obstruction, local sepsis, radiation exposure, short or epithelialized tract, malignancy, foreign body in the tract (such as mesh or sutures), Crohn's disease, and malnutrition.
- Enterocutaneous fistulas that close typically do so within the first month.
- Fibrin glue has been described. The success rate is low, but nothing is lost in trying this technique.
- Surgical intervention should be delayed until all sepsis is resolved, adequate nutrition is restored, and intra-abdominal adhesions have softened to allow for a safe reoperation. Surgery should be delayed at least 6 weeks from the time of the last laparotomy, but 3–6 months may be more appropriate. The longer one waits until reoperation the better. Delay must be balanced against the patient's medical and social condition.

Anastomotic Complications

- Anastomotic complications are usually related to technical factors such as ischemia, tension, poor technique, stapler malfunction, or preexisting conditions such as local sepsis, poor nutrition, immunosuppression, morbid obesity, and radiation exposure.
- Division of the lateral attachments of the descending colon, complete mobilization of the splenic flexure, high ligation of the inferior mesenteric artery, separation of the omentum from the distal transverse colon and mesocolon, and division of the inferior mesenteric vein at the lower edge of the pancreas are techniques to aid in the creation of a tension-free colorectal anastomosis.

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

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 inferior mesenteric artery 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

- To reduce the risk of anastomotic ischemia, adequate bleeding should be noted at the cut edge of the bowel along with pulsatile bleeding from the divided marginal artery.
- When the distal transverse colon is the proximal end of a colorectal anastomosis, additional length to obtain a tension-free anastomosis may be obtained by passing the colon through the ileal mesentery (behind the terminal ileum) before being brought into the pelvis.
- If severe malnutrition (albumin <2.0 or weight loss >15 %) or significant immunosuppression (chemotherapy, high-dose steroids, antitumor necrosis factor drugs) is present, an end colostomy and Hartmann stump or proximal ileostomy should be considered to minimize the risk of anastomotic complications.
- An ileostomy can be closed at 1.5–3 months. A laparotomy for a Hartmann reversal is generally deferred for 6 months.
- Before a Hartmann reversal, obese patients are encouraged to lose weight which allows for easier construction of a deep pelvic anastomosis.
- When operating on irradiated bowel, one end of an anastomosis should be from nonirradiated bowel. Intersecting staple lines (such as double-stapled technique) may have a higher predisposition to leak and a single-stapled or handsewn anastomosis may be considered.
- Table 10.1 lists the steps to minimize a leak from an anastomosis.

Bleeding

- Most anastomotic bleeding is minor and manifested by dark blood mixed in the first bowel movement after surgery.
- Bleeding can occur after a stapled or handsewn anastomosis but is probably more common after one is stapled. Careful inspection can allow intraoperative control of the bleeding and reduce the postoperative risk. Also stapling a side-to-side anastomosis using the antimesenteric border (avoiding inclusion of the mesentery) reduces the risk of bleeding.
- Bleeding points on a stapled anastomosis should be controlled with a suture rather than the Bovie as a deep burn injury may lead to a delayed

leak. Full-thickness staple line reinforcement with interrupted sutures can help ensure optimal hemostasis.

- Delayed detection of bleeding from a circular stapler or staple line of a J pouch (ileal or colonic) may need to be addressed on the ward. Steps to control bleeding include:
  1. Proctoscopy is done to evacuate all clots.
  2. A rectal tube (or Foley) is inserted and 1:100,000 epinephrine solution is instilled. The tube is clamped and the solution remains in the rectum/neorectum for 15 min.
  3. If the bleeding persists, the procedure is repeated. Endoscopic cautery or epinephrine injection is another option.
  4. If the bleeding continues to persist or the patient has hypotension, a transanal examination in the operating room is carried out.
- Treatment for delayed bleeding from an inaccessible anastomosis (such as an ileocolic) usually begins with supportive care including correction of any coagulopathy.
  - Angiography may be required to localize the site and allow selective vasopressin infusion.
  - Alternately using a colonoscope, if the bleeding site can be visualized, it can be treated with cautery, epinephrine injection, or endoscopic clips.
  - Rarely reoperation with oversewing is required.

Leaks

- The lowest leak rate is found after a small bowel or ileocolic anastomosis (1–3 %).
- The highest leak rate is after a coloanal anastomosis (10–20 %). The incidence of leak is strongly associated with the distance of the anastomosis from the anal verge.
- The ileal pouch-anal anastomosis has a leak rate of 5–10 %.
- Immunosuppressive drug therapy (prednisone >40 mg/day and antitumor necrosis factor alpha agents) is a significant risk factor associated with an ileal pouch-anal anastomotic leak.

Role of Fecal Diversion

- A proximal stoma minimizes the consequences of an anastomotic leak but does not reduce the actual incidence of a leak.
- A proximal stoma may reduce the need for surgical intervention should a leak occur.
- Table 10.2 lists indications when a diverting ileostomy should be considered.
- Patients with comorbidities who lack the “physiologic reserve” to tolerate an anastomotic leak should strongly be considered for proximal diversion even if other risk factors are not present.

Table 10.2 Indications for a diverting loop ileostomy

1. Coloanal or low colorectal anastomosis (<6 cm from anal verge)
2. Ileoanal anastomosis
3. Severe malnutrition
4. Significant immunosuppression (i.e., prednisone >40 mg/day, anti-TNF agents)
5. Hemodynamic instability
6. Excessive intraoperative blood loss
7. Purulent peritonitis
8. Pelvic sepsis
9. Neoadjuvant therapy

- Neoadjuvant radiation therapy in patients undergoing a low pelvic anastomosis for rectal cancer does not appear to increase the incidence of an anastomotic leak. However, surgeons tend to cover this anastomosis with a proximal stoma which may reduce the clinical manifestations of a leak.

Role of Pelvic Drains

- The use of a drain to minimize the risk of an anastomotic leak is controversial, and the use of a drain has been shown to neither harm nor benefit an anastomosis.
- One study did show the use of a drain reduced the incidence of clinical anastomotic leak after short-course neoadjuvant radiation therapy.

Diagnosis and Management of Anastomotic Leak

- *Free anastomotic leaks* are leaks with fecal contents spread throughout the abdominal cavity.
- Patients present with fever, tachycardia, hypotension, leukocytosis, and peritonitis.
- Feculent fluid may egress via the surgical incision (or pelvic drain if present).
- Radiological studies may localize the leak but should not delay reoperation.
- Patients with a free leak should be taken to the operating room after fluid resuscitation and intravenous antibiotics are administered.
- After a thorough washout, the treatment is dictated by the findings.
- Most colorectal anastomosis will require anastomotic takedown and an end colostomy.
- To minimize the effects of a friable rectal stump (that cannot be closed with staples or sutures nor brought to the skin surface as a mucous fistula), placement of transabdominal and transanal drains is indicated.
- Selective small bowel or ileocolic anastomotic defects can be repaired. However, resection of the anastomosis with creation of a new anastomosis or stoma is the most conservative option.

- Placement of the repaired anastomosis under the surgical incision will result in an enterocutaneous fistula instead of a second bout of peritonitis should a second leak occur.
- Any concern regarding viability of the bowel ends necessitates takedown of the anastomosis and creation of a stoma.
- Small defects in a colorectal anastomosis, in select circumstances, may be repaired and a proximal ileostomy created. This should be avoided when there is a large fecal load between the ileostomy and the repaired anastomosis.
- Creation of a stoma in the setting of peritonitis can be challenging due to a thickened rigid mesentery. If difficulty exists in creating the conventional stoma, two options exist:
  1. A loop end stoma provides extra mesenteric length and better blood supply than a traditional end stoma.
  2. Bringing the stoma up to the skin through the upper aspect of the midline incision can sometimes be the only alternative. In some severe cases, the bowel can only be wrapped in gauze and matured 5–7 days later to ensure viability and avoid complete mucocutaneous separation and retraction.
- A *contained anastomotic leak* is walled off and typically located in the pelvis presenting as an abscess.
- If the abscess is small and contrast flows freely into the bowel, the patient can be treated with intravenous antibiotics, bowel rest, and observation.
- Larger abscesses or those removed from the site of the anastomosis may require radiologically guided drainage.
- A contained leak rarely requires immediate operative intervention, but surgery may eventually be required if the patient develops a cutaneous fistula, anastomotic stricture, or chronic presacral cavity.

Fistulae

- *Colocutaneous fistula*s frequently close with conservative management (total parenteral nutrition or low residue diet and fistula pouching to protect the skin).
- Many patients do not require IV nutrition and can eat a solid diet while being monitored for fistula closure.
- After 3–6 months if the fistula persists, reoperation with reconstruction of the anastomosis can be performed.
- Successful injection of fibrin glue has been reported as an alternative to reoperation.
- *Colovaginal fistula* typically results from either an anastomotic leak that necessitates through the vaginal cuff (in a woman who has had a hysterectomy) or the inadvertent inclusion of the vaginal wall in the staple line. Spontaneous closure is rare in either of these circumstances.
- Intolerable or copious vaginal drainage may require proximal diversion. Alternatively a daily large-volume enema to evacuate colonic contents may defer a stoma until repair is undertaken.

- At 3–6 months reoperation can be performed. Options for repair include an advancement flap (colonic or vaginal), a rectal sleeve advancement flap, tissue interposition (labus majorum or gracilis), or laparotomy with a redo coloanal anastomosis.
- *Chronic presacral abscess or sinus* may be seen after a leak from a coloanal/rectal or ileal pouch-anal anastomotic leak.
- The presentation may be subtle with vague pelvic pain, fevers, increased stool frequency, urgency, or bleeding.
- A pelvic CT usually shows presacral inflammation. A contrast enema demonstrates the posterior midline sinus extending from the anastomosis into the presacral space.
- During an exam under anesthesia, a probe is placed in the posterior anastomotic defect, and the chronic cavity is laid open with cautery or the laparoscopic linear cutting stapler. Either process divides the luminal-cavity septum and allows free drainage and healing of the cavity by secondary intention.
- An endoscopically placed vacuum-sponge device has been described as a method to close early and late presacral sinuses.
- A redo coloanal anastomosis is considered for persistent sinuses after failure of other treatments.
- For redo coloanal anastomosis, the two-stage Turnbull-Cutait is a useful operation. During the first stage, the failed anastomosis is resected and the sepsis in the presacral space debrided. The descending colon is mobilized and brought out through the anal canal (Fig. 10.1a) and the exteriorized segment wrapped with gauze (Fig. 10.1b). After 5–10 days the patient returns to the operating room and the exteriorized segment is excised (Fig. 10.1c) and a delayed coloanal anastomosis is performed (Fig. 10.1d).

Stricture

- Anastomotic strictures can present 2–12 months after surgery with increasing constipation and difficulty evacuating.
- Causes of anastomotic stricture include leak, ischemia, or, if initially done for malignancy—recurrent cancer.
- For strictures after a cancer operation, recurrence must be excluded with a CT scan and positron emission tomography (PET) scan. For any mass or abnormality, biopsy is mandatory.
- Low colorectal, coloanal, or ileal pouch-anal anastomosis may be successfully dilated with a finger or rubber dilators. Dilatation is more successful if initiated within the first few weeks after surgery.
- Most coloanal and ileoanal anastomosis has some degree of stricture in the early postoperative period (particularly if a diverting stoma is present). Since most are soft, they can easily be dilated with an index finger. All these anastomosis should undergo digital examination 4–6 weeks after

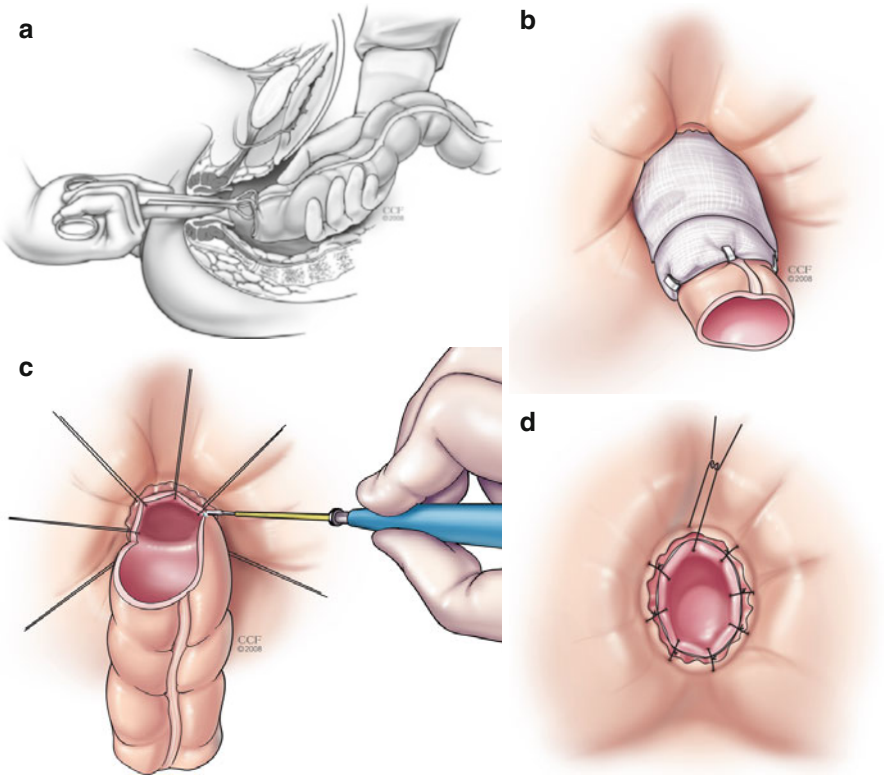

Fig. 10.1 (**a**–**d**) Turnbull-Cutait abdominoperineal pull-through procedure

surgery or just before stoma closure (which occurs usually around 2–3 months after initial surgery).

- Narrowed colorectal, colocolic, or ileocolic strictures may be treated with endoscopic balloon dilatation.
- If these measure fail, or if the stricture is extremely tight or long, revisionary surgery may be required. These operations are difficult and in some cases permanent fecal diversion is the only option.

Genitourinary Complications

Ureteral Injuries

- A ureter injury usually occurs at one of four specific points during pelvic dissection:
  - The first is high ligation of the inferior mesenteric artery between the upper and middle third of the left ureter. This is usually a transection injury and can be repaired primarily using an end-to-end repair over a stent.

  - The second is at the level of the sacral promontory; when mobilizing the upper mesorectum, the left ureter may be closely associated with the sigmoid colon or adherent to it. The injury may be tangential and not easily recognized, especially in the setting of a phlegmon or abscess. Ureteric stents help recognize an injury at this level but not prevent it. Injury at this level is managed by primary repair or ligation of the distal stump with creation of a ureteroneocystostomy with Boari flap or psoas hitch repair.
  - Mobilization in the deep pelvis may injure the ureter at the ureterovesical junction during the anterior-lateral dissection in the plane between the lower rectum, pelvic sidewall, and bladder base. The ureter may also be injured during lateral stalk division.
  - The final area of injury occurs during the most cephalad portion of the perineal phase of the operation. The ureter may be (unknowingly) divided near the ureterovesical junction. Limited exposure (obese patient, android pelvis) increases the chance of injury.
- Repair of the last two areas of injury requires reimplantation creating a ureteroneocystostomy. The ureter is tunneled through the bladder wall creating a mucosa-to-mucosa anastomosis.
- Figure 10.2 outlines the anatomic relations of the pelvic nerves.
- Immediate intraoperative recognition of a ureteral injury and repair is the key to minimizing the consequences. Less than 50 % of ureteral injuries are identified intraoperatively usually because an injury is not suspected.
- If a difficult pelvic dissection is anticipated such as in patients with prior pelvic surgery, inflammation, locally advanced tumor, recurrent Crohn's disease, chronic diverticulitis, leaked pelvic anastomosis, and pelvic irradiation, preoperative placement of ureteric stents should be considered. These may aid in localization of the ureters and facilitate identification and repair should an injury occur.
- If an intraoperative ureteric injury is suspected, indigo carmine can be administered intravenously. After several minutes the urine turns blue-green and the operative field can be inspected for staining.
- Ureteral stents should be used selectively due to potential complications (obstruction secondary to hematoma, perforation, or acute renal failure).

Urethral Injuries

- Iatrogenic urethral injuries occur during abdominoperineal resection or total proctocolectomy. A large diameter Foley may be useful to avoid injury in patients deemed at high risk for a urethral injury.
- The injury usually involves the membranous or prostatic portion of the urethra, and the bladder catheter may be visualized through the defect.
- An anterior rectal tumor with penetration close or into the prostate may obscure anatomic planes making this injury difficult to avoid. Also edema after neoadjuvant radiation therapy can also increase the risk of injury.

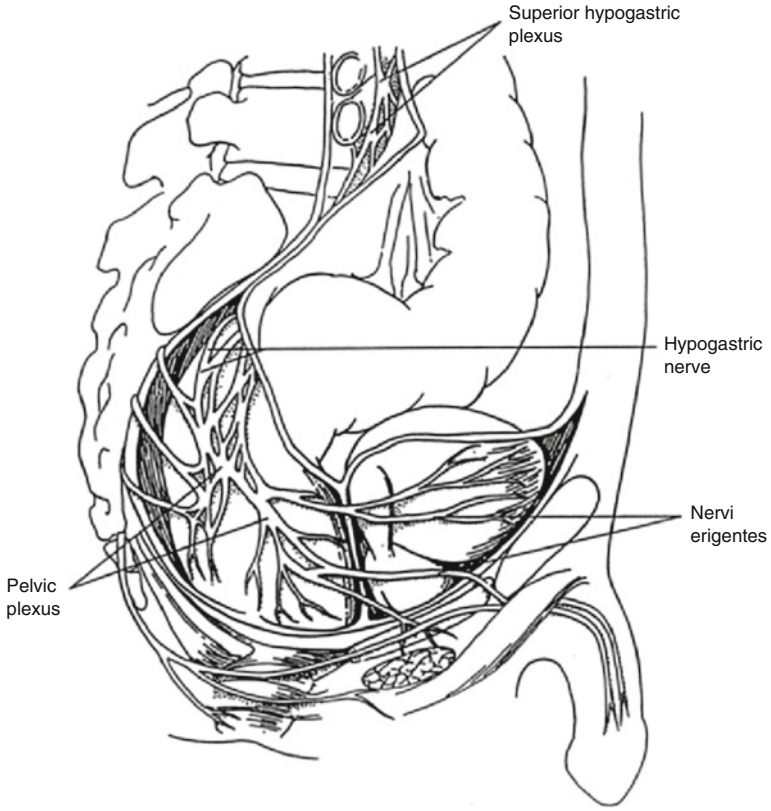

Fig. 10.2 Anatomic relations of the pelvic nerves. Damage to the superior hypogastric plexus during high ligation of the inferior mesenteric artery (IMA) or to the hypogastric nerves at the sacral promontory during mobilization of the upper mesorectum results in retrograde ejaculation. Damage to the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

- Small injuries can be repaired with 5-0 chromic sutures while leaving the Foley in place to stent the repair for 2–4 weeks.
- Larger injuries or those discovered in the postoperative period require proximal urinary diversion with a suprapubic catheter and a delayed repair. Repair of this type of injury requires a urologist experienced in urethral reconstruction and typically utilizes a gracilis muscle flap.

Bladder Injury

- Bladder injuries are frequent and can occur during resection of an adherent rectosigmoid cancer or diverticular phlegmon.
- Injuries to the dome of the bladder:
  - When recognized immediately, a two-layer repair while leaving the Foley in place for 7–10 days is sufficient to address the bladder injury.

  - A cystogram prior to Foley removal to confirm healing may be considered.
- Injuries to the base of the bladder:
  - Repair of injuries located at the base of the bladder carries a risk of occlusion of the ureteral orifice at the area of the trigone.
  - Opening the dome of the bladder to directly visualize the interior while performing the repair helps prevent occlusion.
  - Ureteral patency at the conclusion of the repair should be confirmed.
- Unrecognized bladder injuries:
  - Unrecognized bladder injuries will present in the postoperative period with urine in the abdominal cavity, pneumaturia, or fecaluria.
  - Urinary and fecal diversion may be needed to temporize the situation until repair can safely be done.
  - During takedown of the colovesical fistula with primary bladder repair, if possible, interposition of omentum between the bowel and bladder repair is performed.
  - Foley catheter drainage is continued for 1–2 weeks after surgery with confirmation of healing by a cystogram prior to Foley removal.

Urinary Dysfunction

- Temporary bladder dysfunction with some degree of voiding difficulty is nearly universal after an APR. This can persist 5–7 days and requires continuation of bladder catheterization.
- The inferior hypogastric nerves which control bladder contractility (via parasympathetic input) may be injured if the endopelvic fascia is breached.
- A small number of patients have permanent dysfunction and may need a urological consultation. Prostatectomy or intermittent self-catheterization may be required.

Sexual Dysfunction (Male)

- Fifteen to fifty percent of male patients have some degree of sexual dysfunction after an APR for rectal cancer. Factors attributable to this wide range include age, preoperative libido, adjuvant radiation therapy, definition of dysfunction, time of follow-up, and social barriers preventing a frank discussion of the topic.
- *Ejaculatory problems* such as retrograde ejaculation are the most common type of sexual dysfunction and the most likely to resolve within 6–12 months.
- Dysfunction results from damage to the superior hypogastric (sympathetic plexus) during high ligation of the IMA or to the hypogastric nerves at the sacral promontory during upper rectal mobilization.

- *Erectile dysfunction* results from injury to the nervi erigentes or cavernous nerves (branches of the pelvic plexus that course anterior to Denonvillier's fascia at the lateral border of the seminal vesicles). Parasympathetic innervation controls inflow and retention of blood within the corpora cavernosa.
- Injury occurs during lateral dissection or while dissecting in the anterior plane by Denonvillier's fascia.
- Tailoring the anterior dissection may decrease the risk of injury. For posterior tumors rectal mobilization on the rectal side of Denonvillier's fascia may protect the small cavernous nerves.
- Factors that also increase the risk of nerve injury are older age, poor preoperative libido, and a low rectal tumor requiring APR (this has a two to three times increased risk versus a low anterior resection).
- Sildenafil is an effective treatment for male patients with erectile dysfunction after proctectomy.

Sexual Dysfunction (Female)

- The incidence of sexual dysfunction after proctectomy in women is hard to quantify and reported to be 10–20 %.
- Symptoms include dyspareunia and inability to produce vaginal lubricant and achieve organism.

Female Infertility

- After restorative proctectomy, the postoperative infertility rate can exceed 50 % in women.
- This rate has implications regarding preoperative counseling and possible modification of surgical technique to minimize the effect of pelvic adhesions.
- The infertility is felt to be secondary to pelvic adhesions that interfere with transit of the egg from the ovary to the fallopian tubes.
- Measures to minimize pelvic adhesions such as tacking the ovaries to the anterior abdominal wall and wrapping the adnexa in anti-adhesion barrier are frequently used but not scientifically tested.

Trapped Ovary Syndrome

- After restorative proctocolectomy, the ovary and tube may become "trapped" in pelvic adhesions. With each menstrual cycle, fluid accumulates in the cavity and expands.
- Symptoms include pelvic or lower abdominal pain particularly on the side of the trapped ovary.

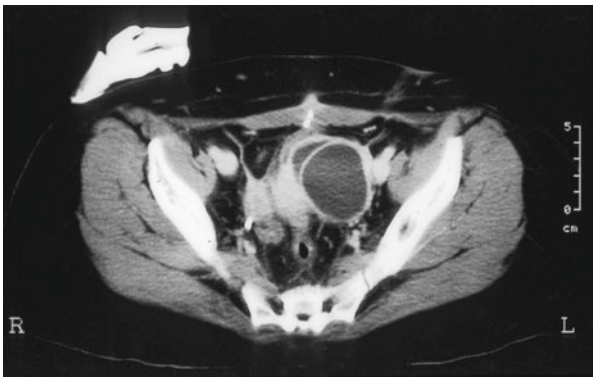

Fig. 10.3 CT scan demonstrating "trapped" ovary in the right pelvis

- CT scan or ultrasound reveals a cystic lesion with no air and no surrounding inflammation.
- Operative treatment consists of unroofing the cyst and fluid evacuation, pelvic adhesiolysis, and suspension of the ovary to the pelvic brim or iliac fossa with sutures. This condition may be prevented by ovary suspension at the time of initial surgery.
- Figure 10.3 shows a CT that demonstrates a "trapped" ovary in the right pelvis

Small Bowel Obstruction

- In managing patients with a small bowel obstruction, the critical component is operative intervention before bowel ischemia and necrosis develops.
- Finding nonviable bowel at laparotomy increases the risk of death fourfold.
- It is very important to distinguish between early (<30 days) and late postoperative small bowel obstruction.

Presentation and Diagnosis

- The most common signs of a small bowel obstruction are nausea, vomiting, colicky pain, abdominal bloating, and obstipation.
- The hallmarks of strangulated bowel are fever, tachycardia, leukocytosis, sepsis, peritoneal signs, and continuous (versus intermittent) pain. If any of these signs are detected, there should be a high suspicion for ischemia.
- Nearly one-third of patients with strangulated bowel are not diagnosed until laparotomy; therefore the traditional parameters are neither sensitive nor specific.

Radiographic Studies

Plain Radiographs

- Have 60 % sensitivity in detecting a small bowel obstruction.
- On supine and upright plain abdominal x-rays, dilated, air-filled loops of small bowel, air-fluid levels, and an absence or paucity of colonic air are typical findings of a small bowel obstruction.
- These findings may be absent in a proximal obstruction or if the dilated bowel is mostly fluid filled.
- Pneumatosis intestinalis or portal vein gas is worrisome for advanced bowel ischemia.

CT Scans

- Have 90–100 % sensitivity in diagnosing small bowel obstruction.
- Abdominopelvic CT is becoming the primary imaging modality for patients suspected of having a small bowel obstruction.
- This study can establish the diagnosis, precisely define a transition point, show a closed loop obstruction, and reveal secondary causes of obstruction (tumor, hernia, intussusception, volvulus, or inflammatory conditions such as Crohn's disease or radiation enteritis).
- This study can also show signs of progressing ischemia such as bowel wall thickening, pneumatosis, or portal vein gas.

Contrast Studies

- This study should be done with water-soluble agents.
- With a distal obstruction, a contrast enema can evaluate the colon.
- An antegrade study can differentiate a partial versus complete bowel obstruction. Failure of contrast material to reach the colon within 24 h is used by some surgeons as an indication for surgical exploration.
- An antegrade study may speed resolution of a partial small bowel obstruction presumably via an osmotic effect (but no definitive studies fully prove this).

Initial Therapy and Nonoperative Management

- For patients *with signs of perforation or ischemia*, rapid correction of fluid and electrolyte deficits is done prior to laparotomy. This also includes insertion of a urinary catheter, broad-spectrum antibiotics, and a nasogastric tube. It is important to decompress the stomach prior to general anesthesia to reduce the risk of aspiration.
- Expectant management in patients *without signs of perforation or ischemia* results in resolution of an adhesive small bowel obstruction in 80 %. The success rate is significantly lower in patients with a complete obstruction.

- Expectant management includes IV fluids and electrolyte replacement, bowel rest, and NG tube decompression.
- Nasoenteric (long) tubes have a balloon at the end (Gowen tube) and require endoscopic placement. Due to the special expertise needed to place these tubes, they are not typically used today.
- A nonoperative course includes serial exams for the first 24–48 h. Detection of increasing pain, peritoneal signs, or changes that suggest bowel ischemia mandate exploratory laparotomy. Obstructions that do not resolve beyond 48 h are unlikely to do so.
- Narcotic analgesia to comfort the patient without altering mental status is acceptable.

Decision to Operate

- Any patient with concern for bowel ischemia or strangulation should be operated upon.
- The distinction between partial and complete obstruction can be difficult. Patients with a complete obstruction have a low incidence of resolution with conservative management. There is a lower threshold to operate on patients with a complete bowel obstruction to avoid progression to strangulated bowel.
- Passage of flatus is not an accurate predictor of a partial bowel obstruction because a patient with a complete obstruction may continue to pass gas that is distal to the obstructed point.
- Bowel function beyond 12 h after the onset of obstructive symptoms decreases the likelihood of a complete obstruction.
- The onset of flatus after the initial period of obstructive symptoms usually signals resolution of the obstruction.

Surgical Technique for Small Bowel Obstruction

- Broad-spectrum antibiotics active against enteric pathogens are administered before the peritoneal cavity is entered via a midline incision.
- Bowel loops will be distended and often adherent to the undersurface of the abdominal wall, so great care is taken to avoid an inadvertent enterotomy entering the peritoneal cavity.
- When the fascia is encountered, gentle pressure with the bevel of the scalpel versus a cutting stroke may assist in identifying a bowel loop before an enterotomy occurs.
- Optimally, a single constricting band will be encountered that can be sharply divided and relieve the obstruction.
- If the peritoneal cavity is totally obliterated, the undersurface of the incisional scar is first cleared to allow opening of the entire incision.
- Next dissection is carried laterally to the paracolic gutters to allow placement of a self-retaining retractor.

- Needle decompression of dilated bowel loops may produce additional working space.
- With severe adhesions ("frozen abdomen"), injection of saline between bowel loops may facilitate adhesiolysis.
- Mobilization of the entire mass of small bowel loops which are stuck in the pelvis (versus individual loops) is helpful. Freeing the mass and then rolling it up and out of the pelvis is the optimal technique.
- Lysing adhesions from the small bowel mesentery to the retroperitoneum until the duodenum is encountered can be performed next.
- Lastly, individual loops are separated and all bowel is examined carefully for coexisting pathology, enterotomies, or serosal tears.
- Assessment of bowel viability involves examining the color, peristalsis, and mesenteric pulsations. If in doubt, the bowel should be wrapped in warm packs and reexamined after 15 min.
- If bowel viability is still in question, systemic injection of fluorescein dye followed by inspection of the bowel under a Wood's lamp or use of a Doppler probe may aid in decision making.
- If there is still a question of viability and the involved area is a short segment, resection may be the best option. If there is an extensive length of questionable bowel, before committing to a massive small bowel resection, a second-look operation in 24 h should be planned.
- Once the point of obstruction is addressed, it is debatable whether complete adhesiolysis is required. If the majority of adhesions can safely be divided, this can aid in inspection of the entire length of small bowel in order to look for serosal tears or an enterotomy. If an anti-adhesion barrier is to be used, complete adhesiolysis also may facilitate placement.

Special Situations

Early Postoperative Bowel Obstruction

- Bowel obstruction less than 30 days after a pelvic or abdominal procedure should generally not be managed with an operation unless there is concern for ischemic or necrotic bowel. The development of strangulation during this time frame is extremely rare.
- An intense inflammatory response begins 7–10 days postoperatively and leads to hypervascular adhesions that may obliterate the abdominal cavity.
- If patients undergo early reoperation between day 10 and 6–12 weeks postoperatively, the hypervascular adhesions may lead to extensive enterotomies with the risk of subsequent fistulization being extremely high. Additionally, a higher risk of vascular injuries or serosal tears may lead to massive bowel resections.
- Initial management of an early bowel obstruction is NG decompression and IV fluids for the first 5–7 days.

- If a bowel obstruction persists at postoperative day 10, a percutaneous gastrostomy tube may be placed for long-term decompression and the patient started on hyperalimentation.
- The patient is discharged on this conservative regimen. If the obstruction does not resolve, laparotomy is planned at least 6–12 weeks later (if not longer).
- During this period before relaparotomy, if signs of sepsis develop, 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 *before* postoperative day 10 can usually be done safely if a true obstruction is promptly recognized.
- There is a role for laparoscopic enterolysis in selected settings by appropriately trained skilled surgeons.

Anastomotic "Overhealing"

- Rarely, "overhealing" of an early adhesion between the linear cut staple lines for a side-to-side anastomosis can lead to obstruction.
- This can be prevented when placing the final stapler (that closes the anastomosis) by maximally distracting the two completed staple lines.
- This problem is diagnosed by a water contrast study and conservatively treated.
- Decompression with a long tube may be ideal as the balloon-tipped catheter may break the healing web.
- For an ileocolic anastomosis, colonoscopic balloon dilatation may be used.
- Operative intervention is the last resort and requires resection and reanastomosis.

Prevention of Adhesions

- Ninety percent of patients develop adhesions when the visceral or parietal peritoneum has been disturbed.
- There is a progression from early to mature adhesions that takes approximately 6 weeks.
- Strategies to minimize or prevent adhesions include gentle handling of tissues, use of powder-free gloves, and copious lavage of the peritoneal cavity at the conclusion of the operative procedure.
- If severe adhesion formation is expected, placement of a long intestinal tube (usually a Baker tube via a jejunostomy) to "splint" the bowel open during adhesion formation had been advocated.
- The use of a bioresorbable membrane (modified sodium hyaluronate and carboxymethylcellulose) has been reported to reduce extent, incidence,

and severity of adhesions. Whether this leads to a clinically significant reduction in reoperation for bowel obstruction is unclear.

- The use of anti-adhesion material may be justified for patients who are anticipated to be at high risk for future reoperation. The drawback of using this barrier material is that it only prevents adhesions between surfaces where it is applied.

Pelvic Bleeding

- Serious bleeding during pelvic surgery usually results from injury to the presacral venous plexus or the internal iliac vessels (or their branches). This can be a devastating event and could lead to death of the patient.
- If the bleeding is moderate, completion of the proctectomy may allow the bleeding to stop or slow. After the rectum has been removed, the area usually is better visualized and a bleeding point can be addressed.
- The fragility of the presacral venous plexus makes control of bleeding from this area difficult. Attempts at suture ligation or electrocoagulation usually result in increased bleeding.
  - The first measure should be direct finger pressure or pressure with a cotton pledget to allow anesthesia to "catch up" with resuscitation.
  - One method of permanent hemostasis is to use sterile thumbtacks or specially designed "occluder pins." These are driven into the sacrum at right angles to occlude the site of bleeding.
  - Another method is to suture a rotated flap of rectus abdominis muscle (based on the inferior epigastric pedicle) on either side of the bleeding site to tamponade the opening.
  - Alternatively a 2×2 cm^2 of rectus muscle can be sutured over the bleeding site and electrocoagulated to form a secure coagulum on the surface of the bleeding plexus.
  - If all these measures fail or the patient is unstable, the pelvis can be tightly packed with several laparotomy sponges. The ends of the sponges are brought out through the lower portion of the abdominal incision. The remaining incision is closed and the patient resuscitated in the intensive care. After 24–48 h the patient is returned to the operating room for pelvic pack removal.

Wound Infection and Intra-abdominal Abscess

Wound Infection

- Currently, the wound infection rate is 5–10 %.
- Risk factors for wound infection include malnutrition, diabetes mellitus, immunosuppression, age >60 years, American Society of Anesthesiologists

score >2, fecal contamination, length of hospitalization before surgery, and extent of surgery.
- Mechanical bowel preparation does not decrease the incidence of wound infection.
- Wound infections usually present around the fifth postoperative day.
- Wound infections are characterized by erythema, warmth, tenderness, fever, and purulent drainage.
- Initial treatment is opening the wound and debridement if necrotic tissue is present. A packing regimen is started after adequate drainage and the wound allowed to heal by secondary intention.
- Antibiotics are not typically needed unless there is cellulitis.
- For larger wounds, after several days of wet to dry dressings, a vacuum-assisted wound closure device may be applied. This device will only need to be changed every 3–5 days and wounds typically close within several weeks.
- Deep infections of the rectus muscle and fascia may result in dehiscence that requires operative debridement and repair.
- Infections from *Clostridium perfringens* or beta-hemolytic *Streptococcus* can lead to invasive wound infections.
  - A high level of suspicion is important for a timely diagnosis. These infections occur within 1–2 days of surgery and may be associated with minimal skin changes.
  - Fever and unusually severe wound pain in the early postoperative period should prompt opening the wound. The drainage is typically thin gray fluid.
  - Thorough wound exploration in the operating room along with debridement of all devitalized tissue back to healthy bleeding edges is required.
  - Broad-spectrum antibiotics which include high-dose penicillin are also needed.

Intra-abdominal Abscess

- Intra-abdominal abscesses can result from anastomotic leaks, enterotomies, or spillage of bowel contents at the time of surgery.
- Patients present with fever, leukocytosis, and abdominal or pelvic pain 5–7 days after surgery.
- The diagnostic modality of choice is CT scan of the abdomen and pelvis with IV and oral contrast. Rectal contrast is included in patients with a colorectal anastomosis.
- The characteristic findings on CT scan are a fluid collection with a thickened, enhancing rim, surrounding inflammatory stranding, and possible air bubbles.
- A collection proximal to a staple line and the presence of contrast material in the abscess are both suggestive of an anastomotic leak.

- Radiological percutaneous drainage can be accomplished to adequately drain the abscess 65–90 % of the time. Success depends on size, complexity, etiology, and microbial flora.
- IV antibiotics are usually administered.
- Once the cavity has collapsed and no fistula to the bowel is identified, the catheter can be removed.
- Some abscesses cannot be drained percutaneously due to the lack of a safe "radiographic window" for drainage.

Perineal Wound Infection

- Eleven to fifty percent of perineal wounds can have delayed healing due to a perineal wound infection.
- The rigidity of the boney pelvis combined with a wide resection of perineal soft tissue and levator muscles will result in dead space cephalad to the skin closure that can easily become infected.
- Technical factors to reduce perineal wound infections include reapproximation of subcutaneous tissues, suction drainage of the pelvis (to prevent hematoma and resultant fibrosis), and filling the dead space with an omental pedicle graft.
- For benign disease, a cuff of levator muscle can be left just outside the external sphincter muscle. This will allow closure of the levators and reduction in dead space.
- Neoadjuvant radiation therapy increases the incidence of perineal wound infections that can lead to a nonhealed perineal wound at 30 days.
- Intraoperative radiation further increases the rate of perineal wound complications.
- Factors associated with perineal wound problems include long operative time (>300 min), intraoperative hypothermia, and fecal contamination during perineal dissection.
- In patients with inflammatory bowel disease, an intersphincteric dissection may lead to improved perineal wound healing due to preservation of the external anal sphincter. Figure 10.4a–c illustrates the technique of an intersphincteric dissection.
- For a perineal wound infection, the skin is opened and wet to dry packing begun. When the wound is clean, a vacuum-assisted closure device can be applied.
- For a chronic perineal sinus, closure may require wound debridement and myocutaneous flap reconstruction with the gracilis, inferior gluteus, or rectus abdominis muscle.

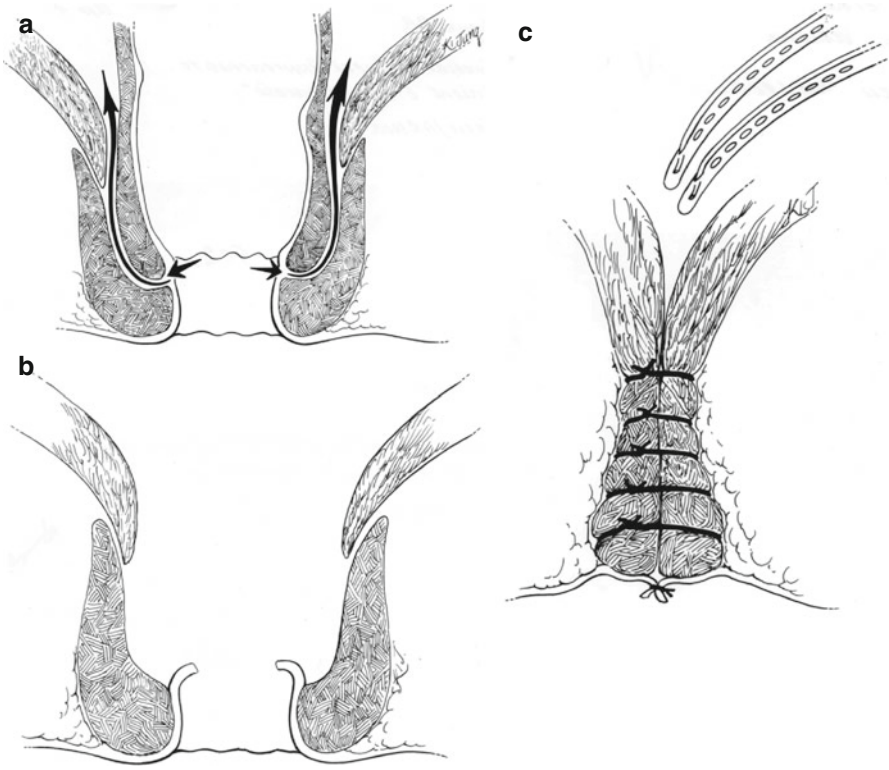

Fig. 10.4 (**a**) Technique of intersphincteric proctectomy. (**b**) The mucosa overlying the intersphincteric groove is incised near the dentate line, and the dissection is carried cephalad between the internal and external sphincters. (**c**) This results in retention of the external sphincters and levators, which are then closed in the midline

- After proctectomy, the small bowel may adhere to the raw surfaces in the pelvis which could lead to a small bowel obstruction.
  - Methods to exclude small bowel from the pelvis include closure of the pelvic peritoneum, posteriorly retroverting the uterus, rotating the cecum into the pelvis, or the excluding the pelvis using absorbable mesh. Absorbable mesh has been associated with obstruction and fistulization.

11. Hemorrhoids

Marc A. Singer

Anatomy

- Hemorrhoids are normal components of anorectal anatomy.
- Hemorrhoids are vascular cushions in the submucosal space of the anal canal.
- Hemorrhoids are classically described as occurring in the left lateral, right anterior, and right posterior position. However, this finding was identified in less 20 % of cadavers.
- They are composed of blood vessels, connective tissue, and smooth muscles.
- The smooth muscle is known as Treitz's muscle and originates from conjoined longitudinal muscle and internal sphincter.
- Histologically, hemorrhoids lack a muscular wall and are therefore sinusoids (not veins or arteries).
- Blood inflow to hemorrhoids is from the superior hemorrhoidal artery with some contribution from middle hemorrhoidal artery, and most distally from inferior hemorrhoidal artery. pH analysis of hemorrhoidal bleeding confirms that it is arterial blood.
- Venous drainage distal to dentate line (external hemorrhoids) is to the inferior hemorrhoidal veins which flow into the pudendal and ultimately the internal iliac veins. Internal hemorrhoids (proximal to the dentate line) drain into the middle hemorrhoidal veins which also drain into the iliac veins.
- Innervation proximal to dentate line is from sympathetic and parasympathetic nerves (noncholinergic/nonadrenergic mediators). Distal to dentate line is from somatic nerves (sensitivity to touch, pain, temperature, and stretch).

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- Exact function of hemorrhoids is unknown. Theories include maintaining closure of anal canal which could contribute to continence and protecting the sphincters from trauma related to passing stool.
- Internal hemorrhoids are covered by columnar epithelium. Near the dentate line, there is transitional epithelium which is viscerally innervated.
- External hemorrhoids are covered by anoderm which is a specialized squamous epithelium devoid of hair follicles or sweat glands. The most distal aspect is covered by normal skin. Anoderm and perianal skin are somatically innervated.

Etiology

- The etiology of hemorrhoidal symptoms is poorly understood but most likely multifactorial. Contributors include the following:
- *Venous congestion* with hypertrophy of internal hemorrhoids due to straining, constipation, pregnancy, chronic cough, pelvic mass, pelvic floor dysfunction, and ascites.
- *Conditions that promote prolapse of vascular cushions* with secondary attenuation of fibers in Treitz's muscle and the elastic tissue in the submucosa.
- *Dietary* patterns such as low fiber which leads to hard stool and excessive straining. Hard stools may cause local tissue trauma.
- *Behavior features* such as prolonged time sitting on the commode.
- *Diarrhea and frequent bowel movements* have the same effect as *constipation*.
- *Advanced age* which leads to less supportive tissue (Treitz's muscle).
- *Elevated sphincter pressures* which may impair venous drainage.

Epidemiology

- The true incidence is difficult to assess as patients may not seek medical attention, self-medicate themselves, seek care from a diverse group of specialists, or self-diagnose other anal problems as hemorrhoids.
- Prevalence in the USA is estimated to be 4.4 % (8.5 million patients) with 1.9–3.5 million doctor visits and 168,000 hospitalizations annually.
- Two million prescriptions are written annually for hemorrhoid therapies (over $43,000,000 which does not include over-the-counter, herbal, or homeopathic treatments).

Classification

- Internal hemorrhoids originate proximal to dentate line and are lined by columnar epithelium.

- External hemorrhoids are located distal to the dentate line and are lined by anoderm and most distally by skin.
- Mixed hemorrhoids have both internal and external components.
- Internal hemorrhoids are classified based on prolapse:
  - Grade I—internal bulge into the anus without prolapse
  - Grade II—internal hemorrhoids that prolapse during defecation and spontaneously reduce
  - Grade III—internal hemorrhoids that prolapse and require manual reduction
  - Grade IV—hemorrhoids that prolapse and are irreducible

Clinical Presentation

Internal Hemorrhoid Symptoms

- *Bleeding* is typically bright red blood with bowel movements, or seen on the toilet paper, dripping in the toilet, or squirting into the toilet at the completion of a bowel movement. Anemia due to hemorrhoids is rare and patients with anemia should be considered for a full GI tract assessment.
- *Itching and burning* which may be caused from *mucous* related to prolapse.
- *Sensation of fullness*, *urge to defecate*, *or feeling of incomplete evacuation* can be from internal *prolapse*.
- *Difficulty with perineal hygiene*.
- Sense of *anal wetness* or *soiling of undergarments* or *sense of a lump* if internal hemorrhoid prolapses through the anal canal.
- Even though not somatically innervated, patients still may report *pain*. Severe pain may be from thrombosis or strangulation.
- Internal hemorrhoids may spontaneously reduce, or may require manual reduction.

External Hemorrhoid Symptoms

- *Pain* (mild to excruciating) can result from acute thrombosis. This is often associated with a firm anal lump. As the thrombus erodes through the skin, patients may see *bleeding*. After the external hemorrhoid resolves, a skin tag (*redundant skin*) may remain. This could lead to *difficulty maintaining hygiene or itching*.

Differential Diagnosis Based on Anal Symptoms

- Presented in Table 11.1.

Table 11.1 Differential diagnosis based on anal symptoms

Symptom	Differential diagnoses
Pain	Thrombosed hemorrhoids, fissure, abscess, fistula, pruritus, anorectal Crohn's disease, anismus, abscess
Bleeding	Internal or external hemorrhoids, fissure, fistula, hypertrophic papilla, polyps, anal or colorectal cancer, ulcerative colitis, Crohn's disease, infectious colitis, draining thrombosed hemorrhoids, rectal prolapse
Pruritis	Prolapsing hemorrhoids, fistula, incontinence, anal condylomata, rectal prolapse, pruritus ani, anal papilla, dermatitis, dietary causes
Mass	Thrombosed or prolapsed hemorrhoids, abscess, anal cancer, prolapsing polyp or papilla, skin tags, prolapsing tumor, rectal prolapse, condylomata

Evaluation

History

- Document the patient's bowel habits, including constipation, diarrhea, urgency, frequency, and changes in bowel habits. A prospectively maintained bowel diary may be helpful.
- History can help differentiate hemorrhoids from other anal pathology. It can also elicit "red flag" symptoms such as bleeding or change in bowel habits that may be indicative of malignancy.
- Dietary history is included particularly focusing on fiber and fluid intake with attention to foods that cause diarrhea or constipation.
- Changes in bowel and diet habits due to an acute illness or travel should be noted.

Physical Examination

- Includes a general exam that focuses on liver disease, COPD, or coagulopathy.
- The abdominal exam will focus on signs of constipation.
- An anal exam may be embarrassing and same gender chaperone should be offered to be in the room to help relax the patient. Also reassure your patient and communicate what you will be doing.
- The prone jackknife position allows for maximal anal exposure. If impractical (too obese, pregnant, or orthopedic issues), then left lateral or lithotomy position is chosen.
- Describe anatomy and pathology in anatomical terms (left, right, anterior, posterior), and avoid using the position of the clock (patient's position may change).
- Inspect the anoderm and sacrococcygeal region. Identify external hemorrhoids, skin tags, prolapsing internal hemorrhoids, rectal prolapse, excoriated skin, fissures, fistulas, abscesses, anal cancer, thrombosed external hemorrhoids, rashes, or dermatitis.
- Palpate the area to assess induration, tenderness, masses, or thrombus in external hemorrhoids.

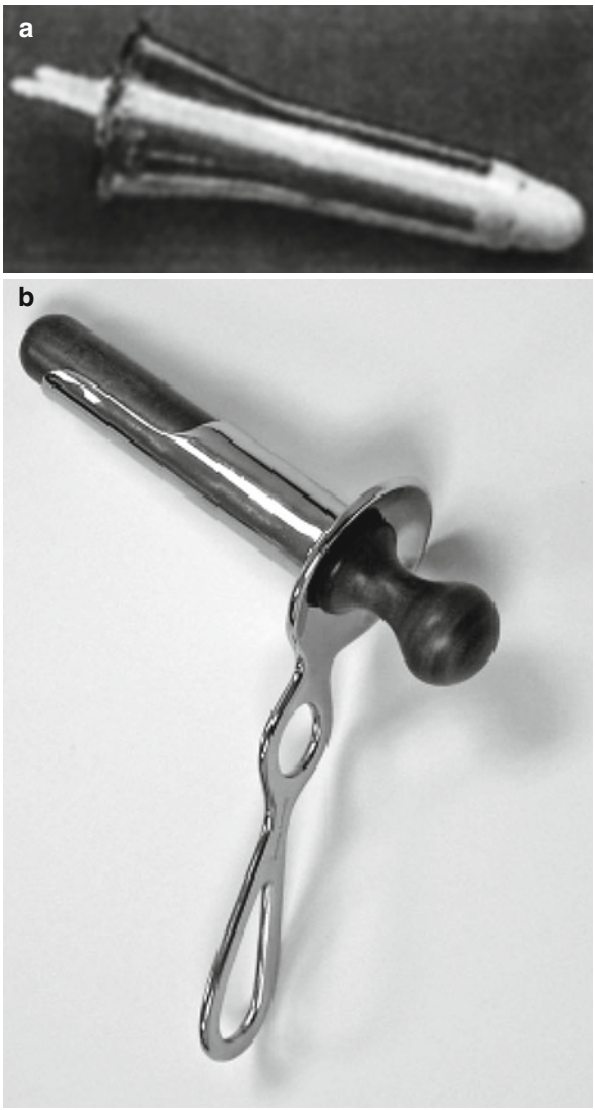

Fig. 11.1 (**a**) a clear plastic anoscope and (**b**) Ives-Fansler anoscope

- Use the digital exam to assess sphincter tone (both rest and squeeze), and identify masses, abscesses, and localized pain.
- The degree of prolapse is examined by asking the patient to strain. If there is any concern, an evaluation with the patient on a commode (which is a more physiologic situation) may be required.
- Anoscopy is performed using one of the several types of anoscopes available (Fig. 11.1).
- Rigid or flexible proctoscopy evaluates the rectum for inflammation.

- Colonoscopy or barium enema is ordered if red flag symptoms are present. These are considered in the context of the patient's age, personal and family history of colorectal pathology, duration of symptoms, and nature of bleeding. Due to concerns of inflaming hemorrhoids with a bowel preparation, treatment of the hemorrhoids for several weeks to months may be reasonable prior to a more in-depth colonic evaluation.

Treatment

- Control of symptoms is the primary treatment goal.
- Reassure patient that hemorrhoids are normal components of human anatomy and removal of all hemorrhoid tissue is not necessary.
- Treatment is categorized into three groups:

Medical Management (Dietary and Behavioral Therapies)

- Modify stool through increased dietary fiber (25 g/day for women and 38 g/day for men) and increased water intake (64 oz daily).
- Encourage regular sleep/wake cycle and exercise to maintain regular bowel habits.
- Add bulk-forming agents such as psyllium to modify quality of stool (Table 11.2). Taken with oral fluid, the goal is to add moisture and soften stools. Optimally, patients should ingest supplements in the morning so fluid can be consumed throughout the day to hydrate the supplements. If needed (inadequate stool mixing), divide doses throughout the day. Long-term compliance may be difficult due to poor palatability, bloating, excessive flatus, or crampy abdominal pain. Start at a low dose and titrate up for the desired effect to minimize side effects.
- Stool softeners (docusate), lubricants (mineral oil), and laxatives (hyperosmolar [polyethylene glycol], saline [magnesium citrate], or stimulant [senna or bisacodyl]) are used to treat constipation. Transition to fiber and stool softeners as quickly as feasible. Goal is a bulky but soft stool that is easy to pass.

Table 11.2 Fiber supplements

Fiber supplement	Brand name products
Psyllium	Metamucil, Konsyl, Fiberall, Hydrocil, Perdiem, Serutan
Methylcellulose	Citrucel
Calcium polycarbophil	FiberCon, Fiber-Lax, Equalactin, Mitrolan
Wheat dextrin	Benefiber
Inulin	FiberChoice

- Diarrhea may require additional evaluation including diet recommendations to increase fiber and reduce fat consumption, along with assessment of caffeine intake, alcohol intake, and irregular sleep/wake cycle which can all contribute to diarrhea. Profound or bloody diarrhea needs further evaluation with stool cultures, fecal fat analysis, and endoscopy. Loose stools can be treated with fiber supplementation that is titrated according to the patient's symptoms.
- The trial of increased fiber should be from 4 to 6 weeks followed by reevaluation of symptoms. The goal of medical management is symptom control. The appearance of the hemorrhoids may not change.

Toileting Behavior

- Patients should spend only 3–5 min on toilet. Do not read on toilet.
- Patients that cannot avoid excessive straining or require >30 min on the commode to evacuate stool should be evaluated for a pelvic floor disorder.
- Avoid compulsive wiping which can lead to local trauma, contribute to inflammation from internal hemorrhoids, increase bleeding from external skin, and worsen pruritus. Use premoistened wipes, i.e. witch hazel, but avoid those with alcohol.

Sitz Baths

- Use warm, approximately 40 °C water (without additives such as salt or oils), in a bathtub or portable device.
- Limit duration to 15 min.
- This treatment can provide relief of pain, itching, and burning and may aid hygiene (particularly after bowel movements).
- May alleviate sphincter and pelvic floor muscle spasms.
- Limited objective evidence regarding the use of sitz baths, but low cost and low risk, makes this an attractive treatment.

Medications

- Topical medications have little objective evidence to support firm recommendations, but since they are so commonly used by patients to self-medicate themselves, surgeons need to be familiar with them. Many employ a combination of agents.
- Local anesthetics may provide temporary relief of pain, itching, and burning. The medication delivery mechanism may cause local irritation. Some contain vasoconstricting agents in an effort to reduce swelling.
- Barrier protectants prevent skin irritation by eliminating contact of mucous and stool with the skin.
- Astringents clean and dry skin.

- Analgesics sooth the skin.
- Corticosteroids relieve perianal inflammation. Prolonged use may thin the skin.
- Suppositories do not typically remain localized in the anal canal. However, they may provide indirect relief by delivering the medication to the rectum and anal skin. Suppositories frequently contain a combination of medicating agents.

Phlebotonics

- These are a heterogeneous collection of substances used to treat many vascular conditions including hemorrhoids purportedly by improving venous flow, improving venous tone, stabilizing capillary permeability, and increasing lymphatic drainage.
- Safety concerns with some phlebotonics include flavonoids that can cause GI side effects and calcium dobesilate which can cause agranulocytosis.
- Citrus bioflavonoids are used in Europe. Commercially available nutritional supplements can contain diosmin and patients can obtain these.
- Calcium dobesilate is a synthetic product which can stabilize capillary permeability, decrease platelet aggregation, and improve lymphatic transport. In a randomized trial comparing this to fiber, patients significantly improved after 2 weeks using calcium dobesilate.
- Meta-analysis of 14 trials showed that flavonoids appear to give a beneficial effect.

Office-Based Procedures

- Many office-based treatments are available and choice depends on surgeon experience, patient preference, availability of equipment, and the medical status of patient.
- All techniques are directed at internal hemorrhoids that lack somatic innervation allowing these treatments to be applied proximal to the dentate line.

Rubber Band Ligation

- Most common office procedure to treat internal hemorrhoids due to its efficiency, safety, and cost-effectiveness.
- A small rubber band is applied at the apex and fixes the pedicle into its normal anatomical position. Ischemia causes hemorrhoids to shrink which corrects prolapse and improves venous drainage.
- No bowel prep is needed, but an enema may improve visualization. Ideally, the patient is positioned in prone jackknife position, but can be in left lateral position. Rarely, if the patient cannot tolerate a full anoscopic exam, sedation in a monitored setting may be needed. Additionally, a bright light for viewing the anal canal and an assistant are usually required.

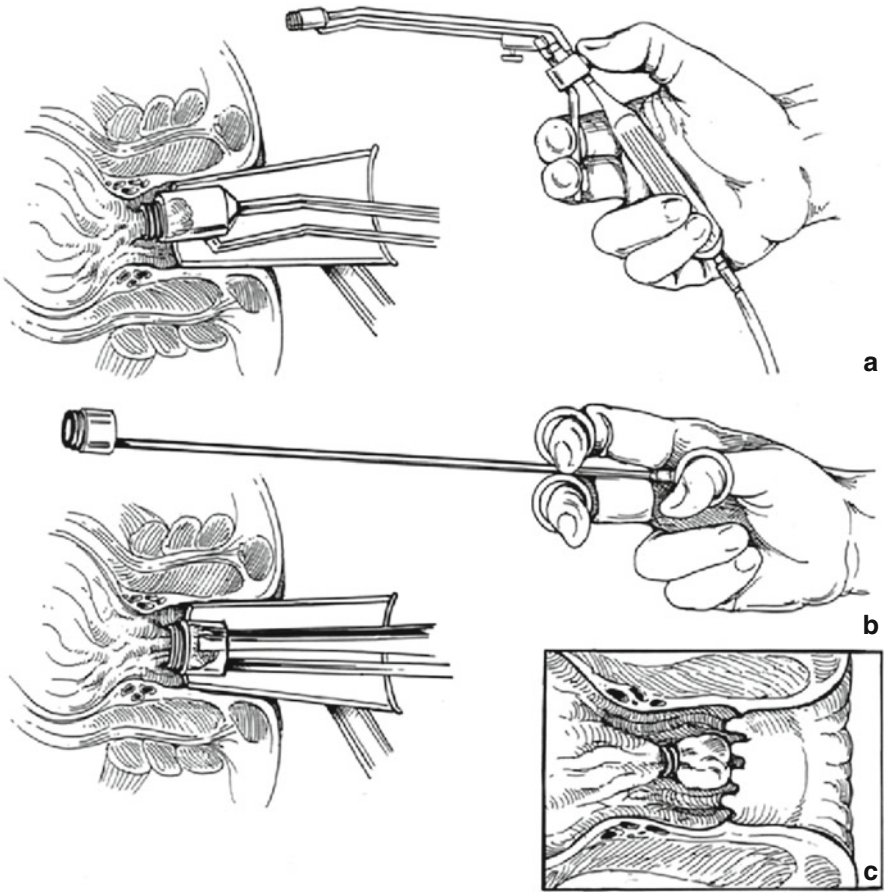

Fig. 11.2 Rubber banding an internal hemorrhoid. (**a**) The internal hemorrhoid is teased into the barrel of the ligating gun with a McGown suction ligator or (**b**) a McGivney-type ligator. (**c**) The apex of the banded hemorrhoid is well above the dentate line in order to minimize pain (Reprinted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

- Using a grasping instrument (McGivney-type ligator or a variation), the apex of the tissue, approximately 2 cm proximal to the dentate line, is grasped and brought into the barrel (Fig. 11.2). The band can then be deployed from the end of the barrel. The band causes ischemia of the tissue it contains which will slough in 5–7 days. This creates an ulcer and inflammatory response. As this heals, fibrosis develops to secure the rectal mucosa to the sphincter.
- Another type of ligator uses suction to draw the tissue into the barrel (McGown-type suction ligator). Since the ligator can be positioned and activated with the same hand, it leaves the other available to position the anoscope (versus the grasping ligator that requires two hands to deploy).

Fig. 11.3 A ShortShot® Saeed Hemorrhoidal Multi-Band Ligator (Cook Medical)

- The endoscopic variceal ligator (used by gastroenterologists for bleeding esophageal varices) can be used with a flexible endoscope to band internal hemorrhoids.
- Two disposable instruments have been developed for rubber band ligation. One is a suction device with four preloaded rubber bands (ShortShot®) (Fig. 11.3). The other disposable ligator (O'Regan ligating system, Fig. 11.4) uses a syringe type of device, which creates negative pressure to draw tissue into the device, and the band is deployed with a thumb trigger.
- Banding is appropriate for first-, second-, and third-degree hemorrhoids. Patients with bulky hemorrhoids may require multiple treatments.
- The largest or most symptomatic is treated first. If there is pain, the procedure is aborted.
- Post-op instructions include normal activities, patients may see some blood per rectum, refrain from meds that promote bleeding (such as aspirin and NSAID) if possible for 10 days, and avoid constipation.

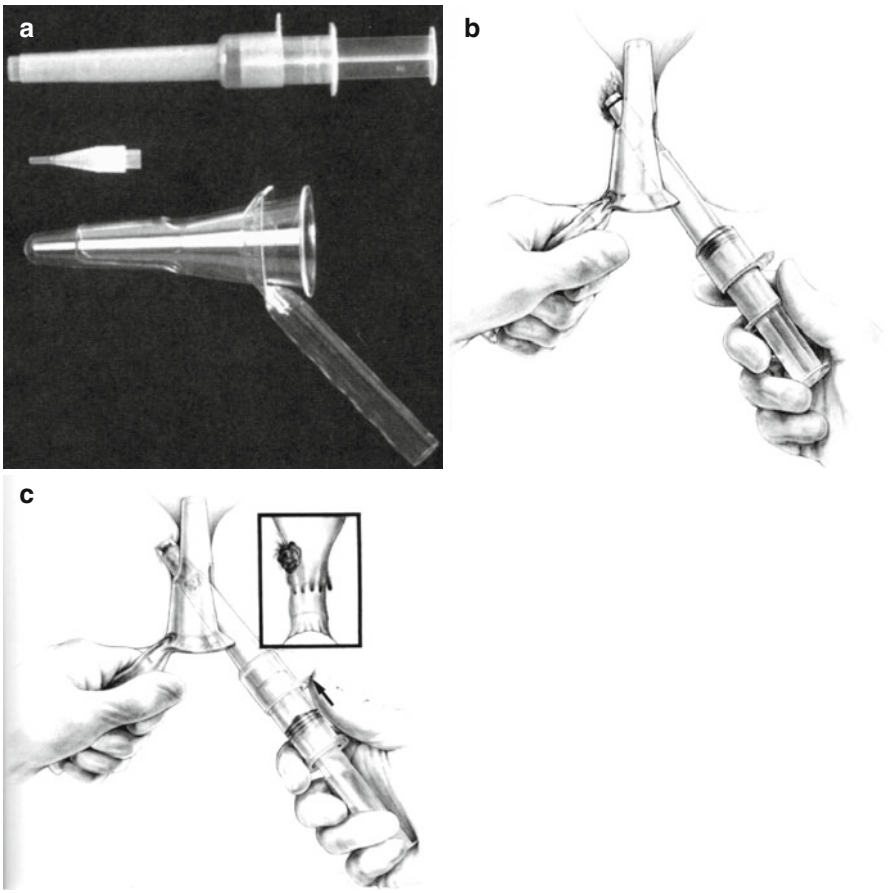

Fig. 11.4 (**a**) O'Regan disposable banding system (Medsurge Medical Products Corp., Vancouver, Canada). (**b**, **c**) Technique of internal hemorrhoidal ligation using the O'Regan ligating system

- This procedure is relatively contraindicated in patients requiring systemic anticoagulation or antiplatelet therapy as there can be massive bleeding when the tissue sloughs off at about 1 week.
- Multiple bandings at the same setting are safe, but may lead to increased pain, vago-vagal symptoms, and urinary retention.
- Complications are rare with the most common being pain, thrombosis, bleeding, and urinary retention or hesitation.
- The most concerning rare complication is pelvic sepsis which can be fatal. The patient will have worsening pain, fever, and/or urinary retention, and these symptoms may mandate immediate evaluation typically with an exam under anesthesia.
- Most bands are made from latex and latex-free bands must be obtained if a patient truly has a latex allergy.
- Long-term studies show this is a durable procedure that can be easily and safely repeated if necessary.

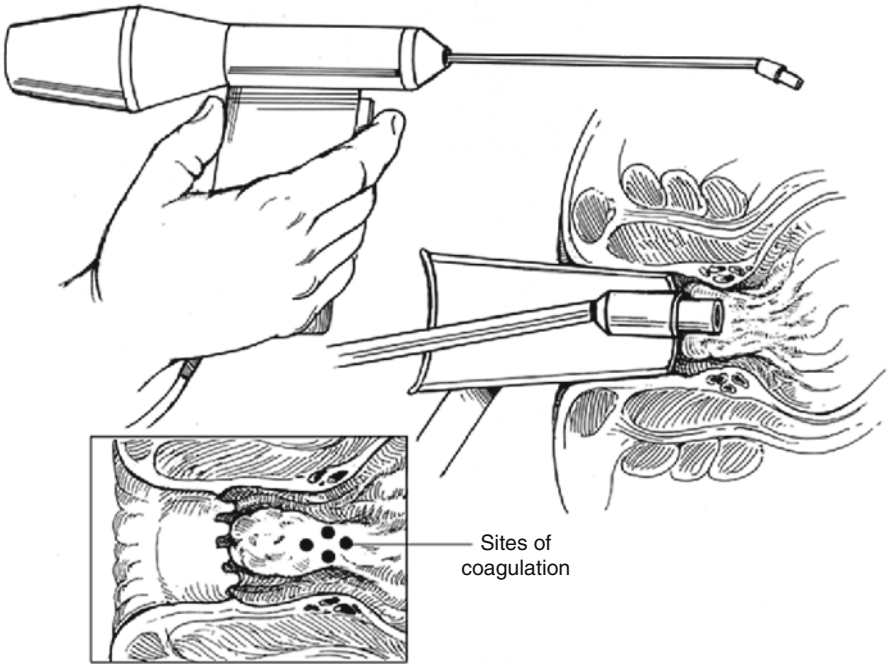

Fig. 11.5 Infrared photocoagulation. The infrared photocoagulator creates a small thermal injury. Thus, several applications are required for each hemorrhoidal column (Reprinted from Beck D. Hemorrhoids. Handbook of Colorectal Surgery. 2nd ed. Copyright 2003 by Taylor & Francis Group LLC)

Infrared Photocoagulation, Bipolar Diathermy, and Direct-Current Electrotherapy

- All of these treatments are performed much less frequently than rubber band ligation. Patient preparation, positioning, and anticoagulation management are similar as for rubber band ligation.
- All these treatments are different techniques of hemorrhoid fixation.

Infrared Photocoagulation

- Infrared radiation generates heat which coagulates proteins and creates an inflammatory bed. The resultant eschar and scarring leads to fixation of the internal hemorrhoid. The applicator tip is placed at the apex of the internal hemorrhoid, with 3–4 applications per hemorrhoid for a 1–1.5 pulse of energy (Fig. 11.5). Up to three hemorrhoids can be treated per session.
- Complications are rare and include pain if the application is too close to the dentate line and bleeding from excessive application of energy.
- This can be used for first- and second-degree hemorrhoids.
- The device is more costly than the rubber band ligation equipment.

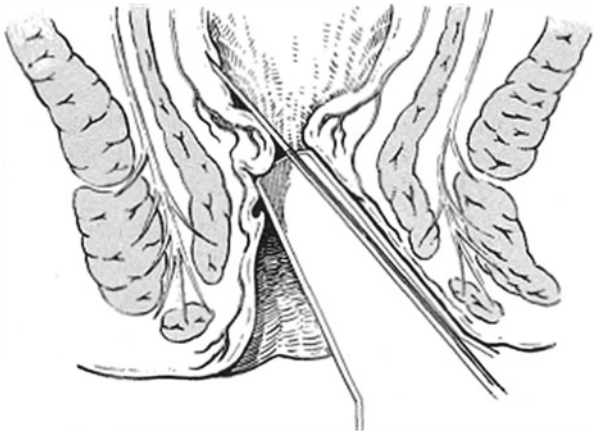

Fig. 11.6 Injection sclerotherapy. The needle is placed proximal to the apex of the internal hemorrhoids into the submucosal space

Bipolar Diathermy

- Bipolar radiofrequency is applied to the apex of the hemorrhoid and this treatment does not penetrate as deeply as monopolar electrocautery. While success rates are reported to be 80–100 %, up to 20 % may require excisional hemorrhoidectomy due to prolapse.

Direct-Current Electrotherapy

- A 110 V direct current is delivered at the apex of the hemorrhoid with increasing amperage until just tolerable for a total of 10 min. This treatment has not gained popularity due to the time needed for a treatment session.

Sclerotherapy

- This is another method of fixation, but employs chemical agents to create fibrosis, obliterates vascularity of the internal hemorrhoids, and reduces the size of the hemorrhoid.
- A spinal needle injects 2–3 cc of the agent, 1–2 cm proximal to the dentate line near the base of the hemorrhoid in the submucosal space (Fig. 11.6). Agents used are 5 % phenol in oil base or 5 % quinine and urea, or hypertonic saline. It is important to avoid injecting into the mucosa or intramuscular space as this can lead to sloughing and a large ulcer.
- This treatment can be used with patients on anticoagulation as it does not use sloughing to induce fibrosis. Repeated treatments should be avoided as this can lead to stricture.
- Complications of this treatment are related to injection into the incorrect space and can be abscess, urinary retention, and impotence.

- This treatment is indicated for first- and second-degree hemorrhoids.
- The degree and amount of successful results are conflicting in the literature but this treatment should be considered in anticoagulated patients.

Anal Dilatation

- Unpopular treatment in the USA due to creating an uncontrolled stretch injury to the sphincter that can lead to incontinence.

Cryotherapy

- Using a specialized cooled (−70 to 196 °C) probe, tissue is destroyed at the hemorrhoid apex to induce fixation.
- The procedure is time-consuming and patients may have pain and foul-smelling rectal drainage afterwards. Due to probe unavailability and possible complications (anal stenosis and sphincter damage with fecal incontinence), this procedure is rarely used.

Operative Procedures

- Only 5–10 % of patients will require operative hemorrhoidectomy. An operative approach is considered for patients that fail lesser techniques, have advanced disease, or have significant external hemorrhoids that require excision.
- Some patients with other anal pathology (fissures or fistula disease) may elect for an operative hemorrhoidectomy to address all anal pathology at the same setting.
- Patients intolerable of an office procedure or if coagulopathic may require operative hemorrhoidectomy for definitive treatment.
- Surgical treatment is divided into three categories: excisional hemorrhoidectomy, stapled hemorrhoidopexy, and Doppler-guided transanal devascularization.
- Excisional hemorrhoidectomy is the gold standard with the main drawback being pain. There are three types: open, closed, and circumferential.

Closed Hemorrhoidectomy (Ferguson Hemorrhoidectomy)

- This treatment is the most commonly practiced operative treatment of hemorrhoids in the USA. Enemas are given as the only needed bowel preparation.
- Patients are positioned in prone position, but left lateral is acceptable. Anesthesia can be general, regional, or local with IV sedation.
- An absorbable anchoring suture is placed deeply into the submucosa to incorporate the feeding artery at the apex of the internal hemorrhoid. A diamond- or figure-of-8 (hourglasss)-shaped incision is made to outline the area of resection starting just distal to the suture and then onto the anal skin (Fig. 11.7). The key is to preserve as much anoderm as possible to avoid stricture. Starting at the distal aspect, the skin and subcutaneous tissue of the external hemorrhoid are dissected off the external sphincter using cautery, scalpel, scissors, or an advanced energy device. Great care is taken to avoid

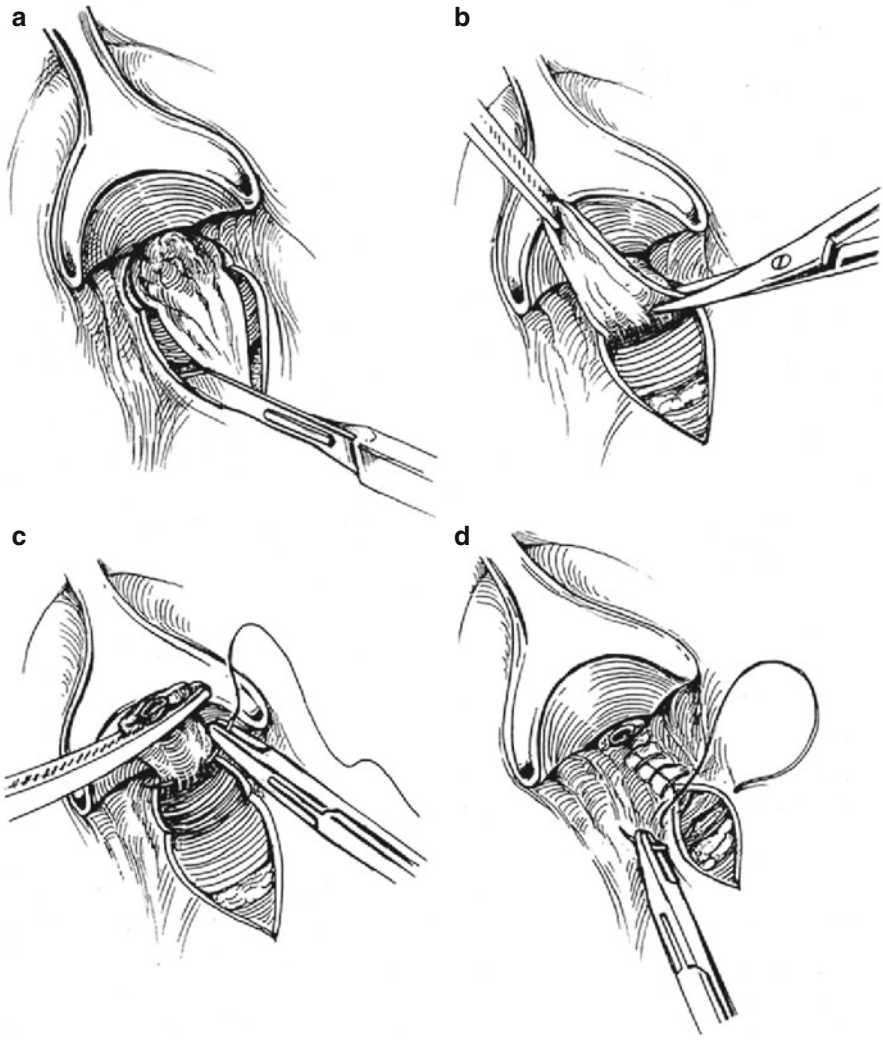

Fig. 11.7 Ferguson closed hemorrhoidectomy. (**a**) An incision is made in the mucosa and anoderm around the hemorrhoid bundle. (**b**) The hemorrhoid dissection is carefully continued cephalad by dissecting the sphincter away from the hemorrhoid. (**c**) After dissection of the hemorrhoid to its pedicle, it is 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

damage to the external sphincter or the internal sphincter more cephalad when the internal hemorrhoid is mobilized for resection. The specimen is amputated and the anchor suture used to close the wound. If there is bleeding from the edges, the suture can be applied as a running locked suture. Care is taken to match the anal verge from both sides when closing. The distal 5 mm is left open for drainage. If there is significant dead space, a three-point stitch incorporating a small portion of the internal sphincter is used.

- One, two, or three quadrants can be excised. It is important to maintain a bridge of viable skin and mucosa between excision sites to prevent stenosis.
- A nonadherent dressing is used which is held in place with mesh panties to avoid tape on the anal skin.
- Most patients can be discharged home on the same day.
- Routine pathologic examination is not always required if the clinical exam is normal.
- A new liposomal bupivacaine (Exparel®) lasts 72 h and can significantly reduce the pain associated with hemorrhoidectomy.

Open Hemorrhoidectomy (Milligan-Morgan)

- The open technique is more commonly used in the UK and Europe.
- A V-shaped incision is used extending from the distal anoderm (incorporating the external component) to the mucocutaneous junction. The tissue is carefully dissected off the underlying sphincter muscle (Fig. 11.8).
- The apex is suture ligated and the tissue amputated.
- The wounds are left open and one, two, or three columns can be excised at one setting.

Circumferential Technique (Whitehead Hemorrhoidectomy)

- This technique has never been a popular treatment in the USA and is used more commonly in Europe.
- A circumferential hemorrhoidectomy involves total excision of the hemorrhoids and mucosa starting from the dentate line and excising the rim of tissue circumferentially and proximally (Fig. 11.9).
- The rectal mucosa is sutured to the anal skin and the site of the old dentate line. Too distal, an anastomosis can lead to a mucosal ectropion (so-called Whitehead deformity). Additionally, high rates of stenosis and incontinence have led to rare use of this technique.

Results of Hemorrhoidectomy

- There is limited long-term data, but it appears that the recurrence of symptoms or need for subsequent treatment is low.
- Randomized trials comparing the open and closed technique revealed similar postoperative pain, analgesic requirements, length of stay, and complications.
- Neither procedure produced definitive superior wound healing.
- Postoperative pain has been the greatest concern of patients, and even with modern postoperative analgesia, patients frequently still require narcotics and have a delayed return to normal activities. Recent multimodality regimens as described previously may improve this.
- Alternative energy devices have been studied looking at the question of whether they can give less thermal injury and tissue destruction and hence less postoperative pain. The use of the Harmonic® scalpel, LigaSure™, or EnSeal® may shorten the operation by approximately 10 min compared to

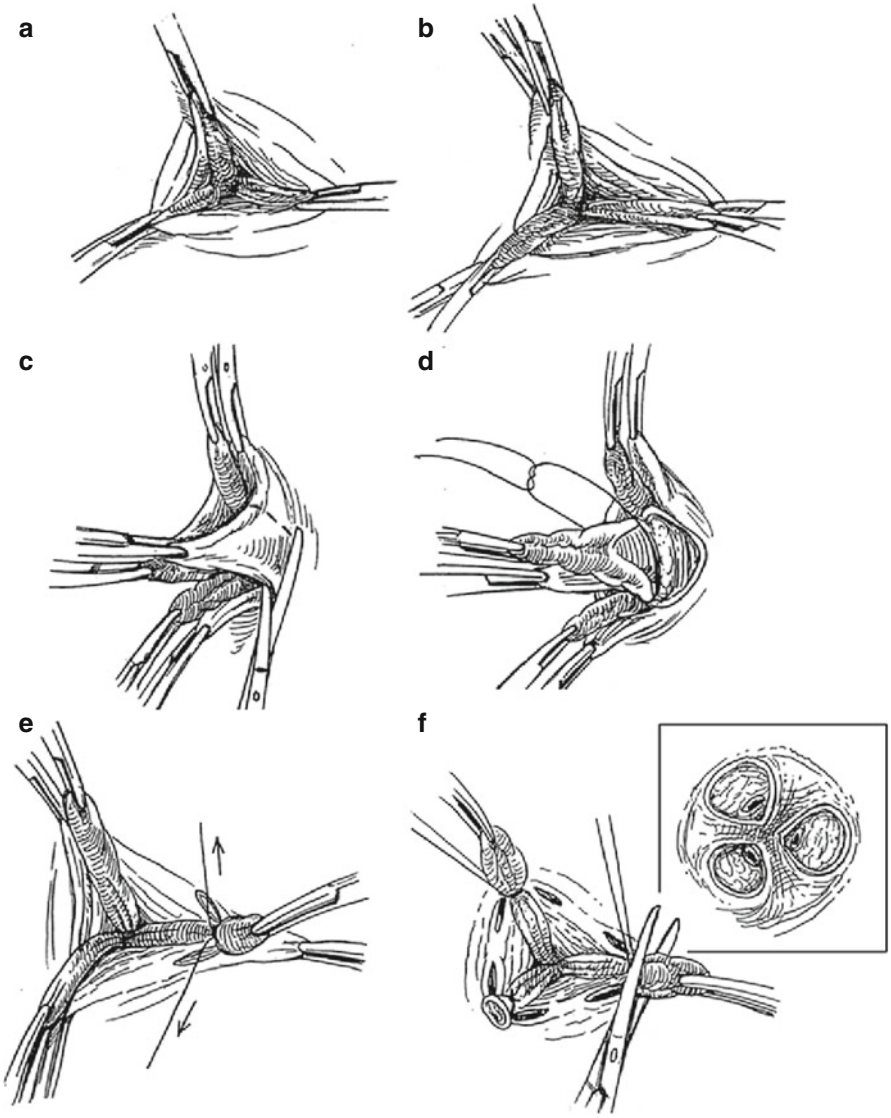

Fig. 11.8 Open (Milligan-Morgan) hemorrhoidectomy. (**a**) External hemorrhoids grasped with forceps and retracted outward. (**b**) Internal hemorrhoids grasped with forceps and retracted outward with external hemorrhoids. (**c**) External skin and hemorrhoid excised with scissors. (**d**) Suture placed through proximal internal hemorrhoid and vascular bundle. (**e**) Ligature tied. (**f**) Tissue distal to ligature is excised. *Insert* depicts completed three-bundle hemorrhoidectomy

the traditional excision methods, and their use may lead to less postoperative pain. However, the cost-efficiency versus standard procedures must be considered. Also, long-term follow-up using these energy devices has not been published.

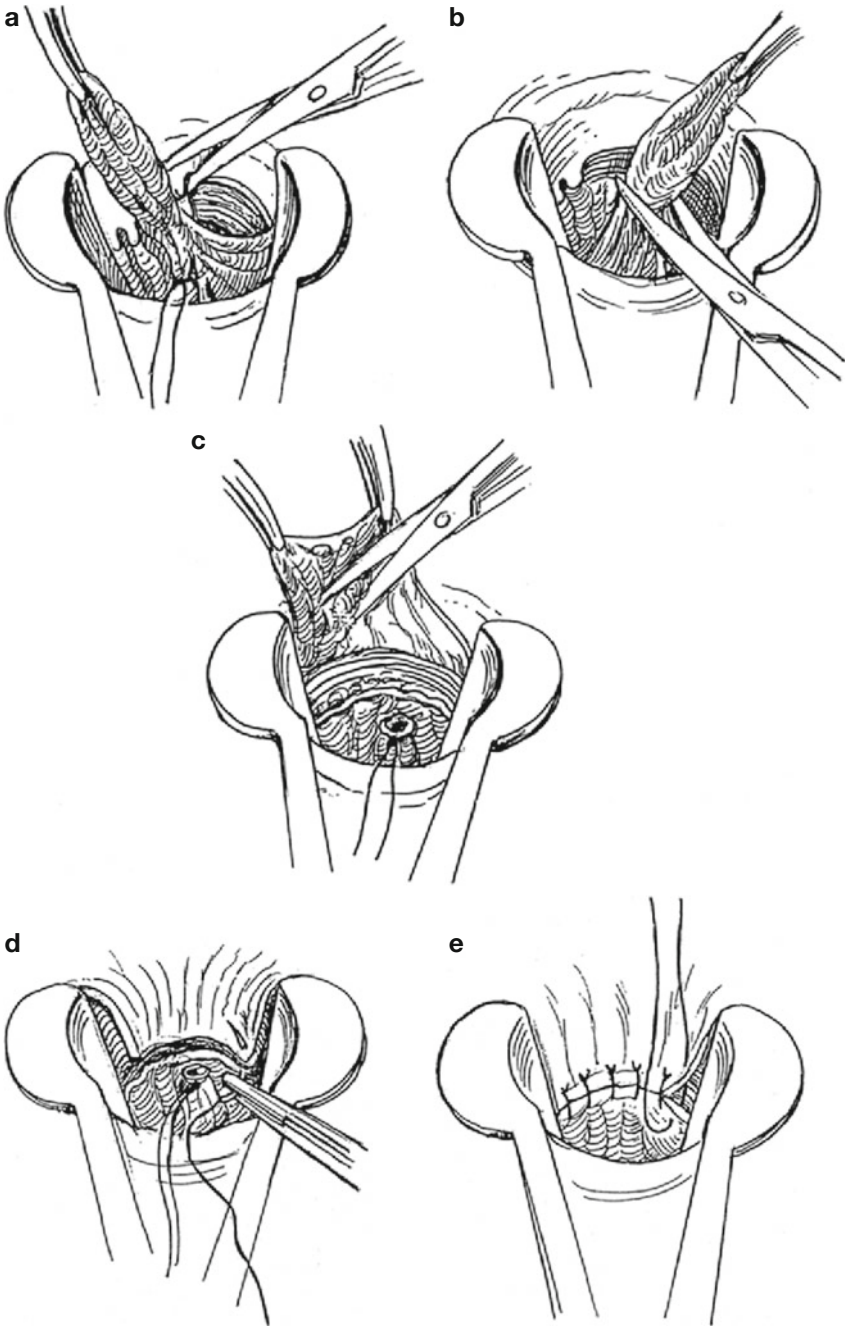

Fig. 11.9 Whitehead hemorrhoidectomy. (**a**) Suture placed through proximal internal hemorrhoid for orientation. Excision started at dentate line and continued to proximal bundle. (**b**) Internal hemorrhoidal tissue excised above ligated bundle. (**c**) Vascular tissue excised from underside of elevated anoderm. (**d**) End of anoderm reapproximated with sutures to original location of dentate line. (**e**) Completed procedure

- There is no difference between scissor and diathermy hemorrhoidectomy.
- NdYAG laser hemorrhoidectomy offers no significant clinical advantage and is costly.
- Lateral internal sphincterotomy at the time of surgery may reduce postoperative pain presumably due to reduction in sphincter spasm after hemorrhoidectomy.
- Oral or 10 % topical metronidazole has been shown to reduce postoperative pain for unclear reasons.

Complications of Hemorrhoidectomy

- Postoperative bleeding, most likely as a result of technical factors, is a more common complication.
- Massive postoperative bleeding can be controlled with anal canal packing or inflation of a balloon-tipped catheter into the rectum and then pulled back against the anorectal junction. If these maneuvers are unsuccessful, an exam under anesthesia is appropriate.
- Other complications include urinary retention, infection, fecal incontinence, fecal impaction, and anal stenosis.

Stapled Hemorrhoidopexy

- Using a modified circular end-to-end stapler, transanally, circumferential sections of mucosa and submucosa are excised well proximal to the dentate line. This will pexy the hemorrhoid pedicles and secures the internal hemorrhoids into a normal anatomical position. This will improve venous outflow.
- The staple line may divide arterial inflow in the submucosal space, thus devascularizing the hemorrhoid.
- This treatment is advantageous as a single setting procedure without painful incisions.
- Multiple synonyms exist for this procedure: stapled anopexy, stapled prolapsectomy, stapled mucosectomy, and procedure for prolapse and hemorrhoids (PPH).
- This is an alternative to excisional hemorrhoidectomy; therefore, the indications are similar (for first-, second-, and third-degree hemorrhoids). Patient preparation, anesthesia, positioning, and management are similar.
- This treatment is not indicated for thrombosed internal or external hemorrhoids or fourth-degree hemorrhoids.
- Using a company-manufactured kit, via a translucent anoscope, a circumferential purse-string suture (2-0 polypropylene) is placed into the submucosa 2 cm proximal to the apex of the internal hemorrhoids. With the head maximally extended, the stapler is inserted into the anus and the purse string is tied down. With gentle traction on the purse-string suture, the redundant tissue is drawn into the stapler, and it is closed and fired. A circular partial-thickness anastomosis proximal to the dentate line is created while excising a 1–3 cm wide ring of mucosa/submucosa (Fig. 11.10).

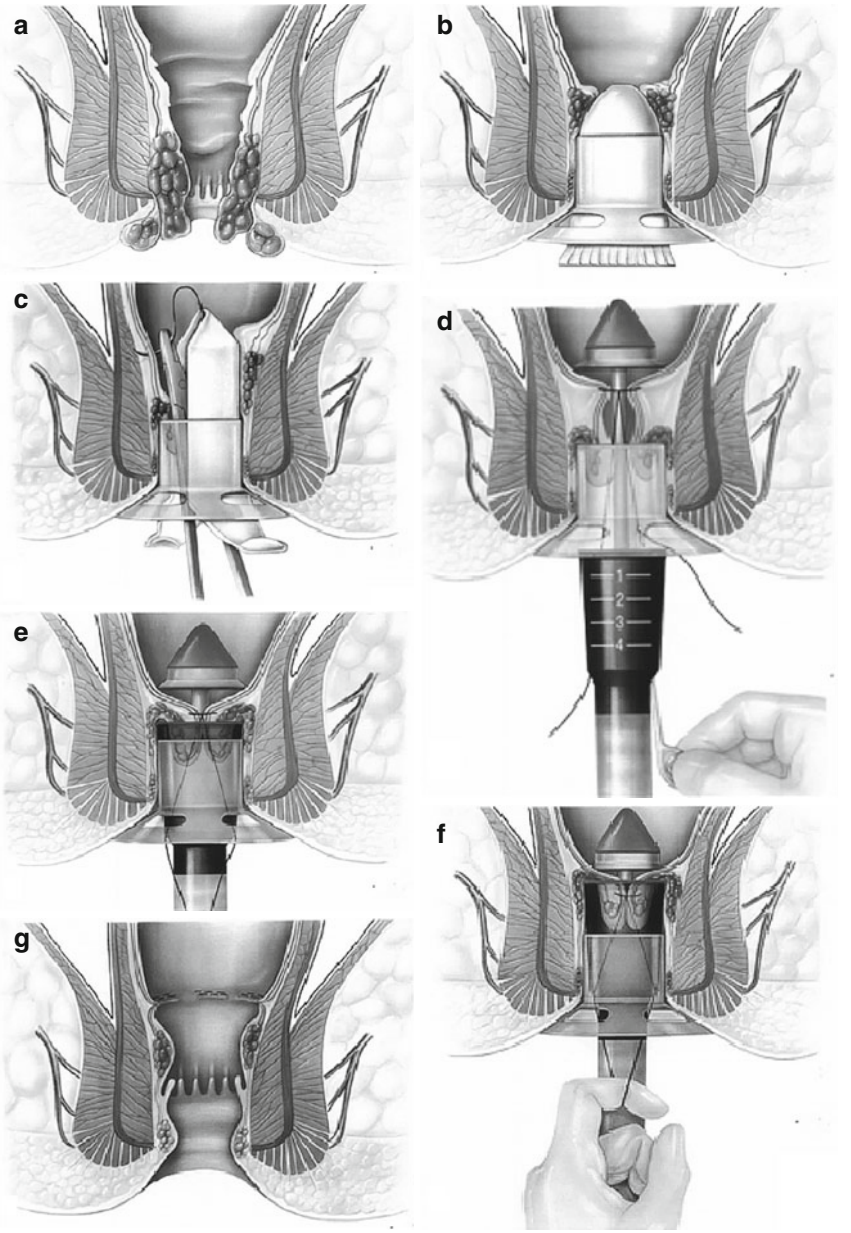

Fig. 11.10 Stapled hemorrhoidopexy. (**a**) Prolapsing internal hemorrhoids and external hemorrhoids. (**b**) Circular anoscope is inserted. (**c**) Purse-string anoscope is inserted and circumferential purse-string suture is placed proximal to hemorrhoids. (**d**) The purse strings are drawn through the stapler. (**e**) Traction on the purse string draws the redundant mucosa into the head of the stapler. (**f**) The stapler is closed onto the mucosa and fired. (**g**) The final staple line draws the hemorrhoids into the anatomical positions

- The staple line should be carefully inspected for bleeding.
- Placement of the purse-string suture is the critical element of the operation. Placement too proximal will lead to inadequate retraction of the hemorrhoids and recurrent prolapse. Placement too distal will lead to pain from impingement at the dentate line. Placement too deep will give a full-thickness anastomosis that carries the risk of pelvic abscess, fistula, or stapled rectovaginal septum (rectovaginal fistula).
- This procedure indirectly addresses external hemorrhoids by devascularization. Significant tags or thrombosed external hemorrhoids can be excised at the same setting if needed.
- Many comparisons of this technique to excisional hemorrhoidectomy have been published. Most concluded that hemorrhoidopexy is safe and has a shorter operative time, less postoperative pain, and shorter recovery. Most also seem to imply that recurrent prolapse is more common after hemorrhoidopexy but the further need for operative intervention may be similar between both procedures.
- Specific complications that are important to note include rectal obstruction, rectal perforation, retroperitoneal sepsis, pelvic sepsis, the potential for sphincter injury (if muscle is incorporated into stapler), and rectovaginal fistula.

Transanal Hemorrhoidal Dearterialization

- This is the newest technique to address hemorrhoids.
- This is a nonexcisional operative technique that utilizes a Doppler-guided ligation of arterial inflow from branches of the superior hemorrhoidal arteries to hemorrhoids. Suture rectopexy can also be done at the same setting if needed.
- Two available US products: transanal hemorrhoidal dearterialization (THD) and hemorrhoidal artery ligation and rectoanal repair (HAL/RAR).
- This procedure is done in the operating room and requires anesthesia similar to the hemorrhoidectomy. Feeding arteries are precisely identified using a Doppler ultrasound attached to a special anoscope. A slot in the anoscope allows a figure-of-8 suture to be placed just proximal to the artery (Fig. 11.11). The adequacy of ligation can immediately be confirmed by a change in the Doppler signal. At a setting, four to six arteries are typically ligated.
- After artery ligation, a hemorrhoidopexy or mucopexy is performed through the anoscope. The suture is anchored at the apex of the internal hemorrhoid and a running suture is performed from proximal to distal. Tension is progressively applied to draw more of the redundant tissue up inside the anoscope and the suture line is terminated proximal to the dentate line to minimize pain. The distal tail of the suture is tied to the proximal tail to further lift the tissue and fix it within the anal canal. Typically two to four pexies are performed.

Fig. 11.11 Specialized anoscope for the transanal hemorrhoidal dearterialization (AMI Surgical). From www.THDAmerica.com

- Benefits are similar to the stapled hemorrhoidopexy with less postoperative pain.
- Complications are mostly related to operative issues such as anesthesia risks, operating room costs, bleeding, infection, urinary retention, and postoperative pain.
- The anoscope and Doppler ultrasound probe are disposable which adds significant cost when compared to excisional hemorrhoidectomy, but device is cheaper than the equipment for the stapled procedure.
- This can be used for grade II and III hemorrhoids and has the advantage over traditional hemorrhoidectomy due to reduced pain and shorter recovery in the limited studies published. Long-term results are unclear and unknown. The addition of the mucopexy seems to reduce recurrence.

External Hemorrhoids

- External hemorrhoids are innervated by somatic nerves making office-based procedures less attractive.
- This treatment is for elective hemorrhoidectomy or treatment of an acute thrombosed external hemorrhoid.

Acute Thrombosis of External Hemorrhoids

- Acute thrombosis results form an episode of constipation, diarrhea, excessive straining (weight lifting), coughing (COPD exacerbation), or even no precipitating factor.

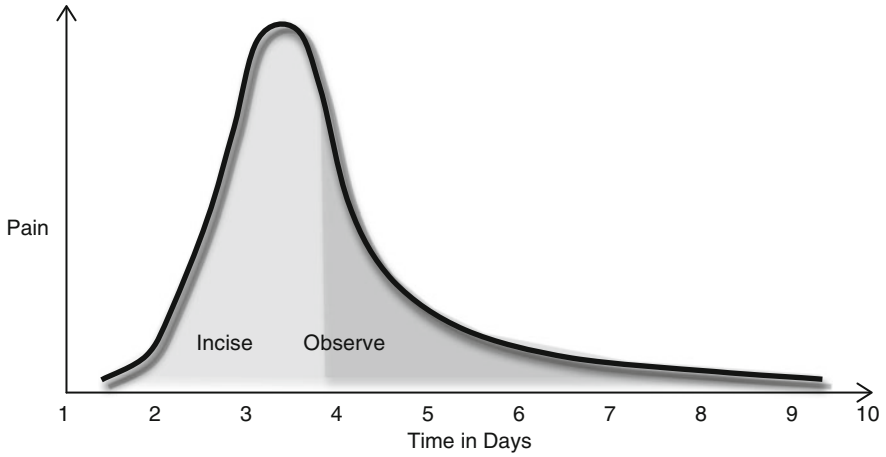

Fig. 11.12 Thrombosed hemorrhoid management. Timing of excision of a thrombosed external hemorrhoid

- The symptoms are characterized by the acute onset of anal pain with a firm/hard lump appreciated by the anus. The pain peaks at 48 h and diminishes by day 4 (Fig. 11.12).
- The skin over the thrombosis may have pressure necrosis or ulceration with spontaneous clot evacuation, which may decrease the pain and pressure.
- Management is directed at pain control.
- The operative treatment is evacuation of the clot in the office or operating room. The entire thrombus should ideally be removed. The skin edges may be left open or closed. Postoperative care includes analgesics, frequent sitz baths, bowel regimen of bulk-forming agents, and a stool softener or lubricant.
- If at presentation the patient has minimal pain, then fiber, stool softener, sitz baths, and analgesics are the treatment.
- After resolution, the anus and rectum should be evaluated.

Special Clinical Scenarios

Strangulated Hemorrhoids

- Prolapsed hemorrhoids that become incarcerated may lead to acute pain and urinary retention.
- Depending on the time course, the tissue may become ulcerated and necrotic or have gangrene.
- Treatment is urgent excisional hemorrhoidectomy in the operating room.
- All devitalized tissue is debrided and if an abscess is present, consideration should be given to leaving the skin wounds open.

- Another treatment option may be the use of a perianal block and to then reduce the internal hemorrhoids. Rubber band ligation is performed and thrombectomies of any external hemorrhoids are done. This is not an option if there is devitalized tissue.

Hemorrhoids, Varices, and Portal Hypertension

- Rectal varices are NOT the same as hemorrhoids.
- Rectal varices provide collateral circulation from the portal to the systemic system and are common in patients with portal hypertension. They may appear to exacerbate hemorrhoid symptoms, but they are not hemorrhoids. These varices rarely bleed.
- Treatment ranges from medical management of the portal pressures, sclerotherapy, suture ligation, stapled anopexy, TIPS, and portosystemic shunts.

Hemorrhoids in Pregnancy

- Hemorrhoids are common in pregnancy due to increased circulating blood volume, impaired venous return, straining secondary to constipation, and prolonged straining during labor.
- Most symptomatic hemorrhoids resolve in the postpartum period.
- Surgical treatment is reserved for strangulated hemorrhoids and acute external thrombosis.
- Use of local anesthesia in the left lateral position is preferred.

Hemorrhoids in Crohn's Disease

- Diarrhea may lead to symptomatic exacerbation of hemorrhoids.
- Prolonged wound healing and ulceration is a consideration when contemplating surgical options. If there is well-controlled anorectal disease and little active inflammation, Crohn's disease is not an absolute contraindication to operative therapy.
- With modern medications and well-controlled disease, 90 % healing rate can be achieved in selected patients after hemorrhoidectomy.

Hemorrhoids and the Immunocompromised Patient

- The immunocompromised patient experiences difficulty healing anorectal surgical wounds and is at an increased risk for infectious complications. Therefore, nonoperative methods should be exhausted prior to surgical treatment considerations.
- Before surgery, optimization of the medical condition should be done.
- Patients with thrombocytopenia should have a hemorrhoidectomy to provide definitive control versus rubber band ligation which may lead to delayed bleeding.

12. Anal Fissure

Rocco Ricciardi, Sharon L. Dykes, and Robert D. Madoff

Introduction

- An anal fissure is a linear or oval tear distal to the dentate line that can be extremely painful with bowel movements and may lead to bright red blood per rectum.
- The estimated prevalence is inaccurate as many people with an anal fissure never seek medical treatment.
- Anal fissures occur equally in men and women and tend to occur in younger patients (mean age 40 years).
- Seventy-five percent are located in the posterior midline, but anal fissures can be seen anteriorly in 25 % of women and 8 % of men. Three percent can have both anterior and posterior fissures.
- If the fissure is in an atypical location or there are multiple fissures, other complicated diseases such as Crohn's disease, trauma, tuberculosis, syphilis, HIV/AIDS, or anal carcinoma should be investigated.
- Acute fissures appear as a simple tear. Symptoms lasting longer than 8–12 weeks are considered chronic and the fissure may demonstrate evidence of chronic inflammation such as sentinel piles/skin tags at the distal fissure margin and a hypertrophied anal papilla proximal to the fissure in the anal canal. Also in chronic fissures, fibers of the internal anal sphincter may be visible.

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Etiology

- The etiology of an anal fissure is debatable, but typically anal trauma after either a hard or loose stool is reported prior to symptoms.
- Sustained anal resting hypertonia is found in patients with anal fissures.
- Since many patients may experience constipation or diarrhea and never develop a fissure, other contributing factors were investigated. The concept of ischemia of the area is supported by cadaver studies, which showed a paucity of blood vessels in the posterior midline in 85 % studied. Also by Doppler laser flowmetry, the posterior midline had the lowest perfusion compared to other quadrants of the anal canal.

Symptoms

- Patients with symptomatic fissures report pain during and after defecation. With chronic fissures, this can last hours to all day.
- Due to this severe pain, patients can have fear of defecation.
- Many patients report limited bright red rectal bleeding seen on the toilet tissue.
- Anal fissure is the most common cause of painful bright red rectal bleeding.

Diagnosis

- The diagnosis of a symptomatic anal fissure is suggested by the characteristic pain description.
- With gentle spreading of the buttocks, the fissure can usually be seen (as demonstrated in Fig. 12.1). Anal exam with a finger or scope should be avoided due to the exquisite tenderness of the fissure and the limited additional information obtained from the digital exam.
- The differential diagnosis includes perianal abscess, anal fistula, inflammatory bowel disease, a sexually transmitted disease, and anal carcinoma.
- Atypical fissures (off the midline, multiple, painless, and nonhealing fissures) warrant further evaluation with an exam under anesthesia, possible biopsy, and culture. Figure 12.2 illustrates the location of the anal fissure correlated with possible etiologies of the fissure.

Management

- Fifty percent of acute fissures heal with sitz baths, psyllium, and topical anesthetics or anti-inflammatory ointments. Eighteen to twenty-seven percent recur within 5 years.

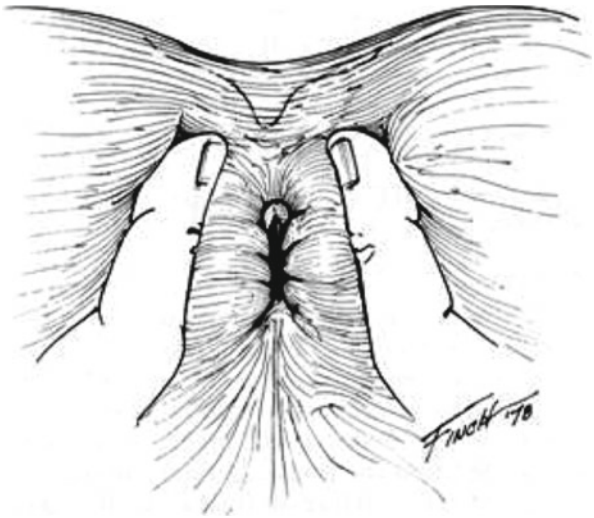

Fig. 12.1 Examination revealing an anal fissure

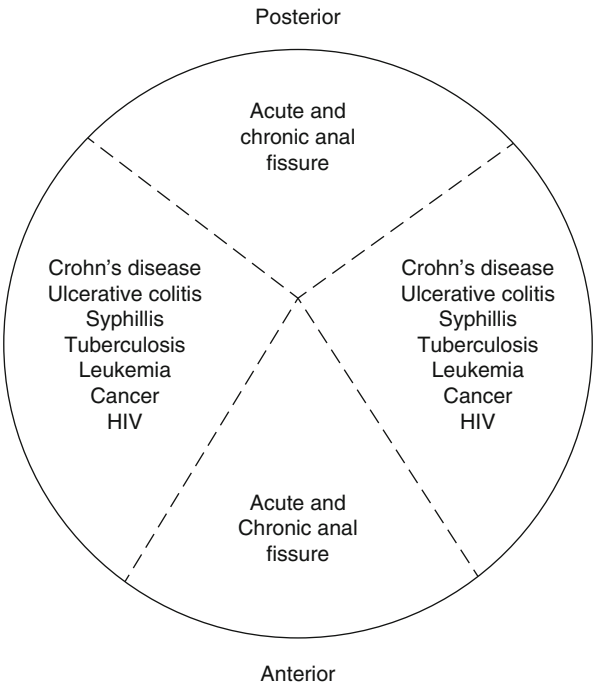

Fig. 12.2 The location of anal fissure suggests etiology

Sphincter Relaxants

- Many agents to reduce mean and maximum anal resting pressure have been tested.
- Many of the topical preparations are only available through compounding pharmacies. Clinicians should be familiar with their available pharmaceutical resources before recommending a medical treatment that requires compounding.

Topical Nitrates

- The internal sphincter is a smooth muscle and topical nitrates relax smooth muscle to theoretically improve blood flow to the fissure and promote healing.
- Initial healing rates were encouraging with the use of topical 0.2 % nitrates (nitroglycerin cream). Headaches and problems with patient compliance following the planned treatment regiment were a problem with this therapy.
- Sustained healing of anal fissures has not been optimal, and combined with adverse reactions such as headaches (and some reports of orthostatic hypotension) has limited the use of topical nitrates.

Calcium Channel Blockers

- Calcium channel blockers can be administered in an oral form (as 20 mg oral or sublingual nifedipine) or topically (2 % diltiazem gel) to treat anal fissures. There have not been sufficient studies with large enough numbers comparing oral versus topical therapy to give a definitive conclusion as to superiority of one delivery method over the other.
- From several randomized studies, it appears that topical calcium channel blockers have at least similar healing potential compared to topical nitroglycerin with fewer side effects. This has led some authors to conclude that calcium channel blockers should be the first line of treatment.
- Topical calcium channel blockers compared to lateral internal sphincterotomy showed fewer relapses with surgery. Studies comparing these two types of treatment for initial fissure healing, pain relief, and compliance show conflicting results.
- There are few long-term studies looking at sustained healing rates for calcium channel blockers. Therefore, definitive assessment of long-term healing is not possible.

Adrenergic Antagonists

- Despite reduction of anal sphincter resting pressures, (limited) studies have failed to demonstrate that oral administration of alpha-1 adrenergic blockers will heal fissures.

Cholinergic Agonists

- 0.1 % bethanechol gel reduces maximal anal resting pressures and has been shown to heal anal fissures in one limited study.

Phosphodiesterase Inhibitors

- Topical administration of a phosphodiesterase-5 inhibitor (sildenafil) was shown to significantly reduce anal sphincter pressures in one study. Whether this effect will lead to sustained healing of anal fissures has yet to be demonstrated.

Botulinum Toxin

- Botulinum toxin is an exotoxin that, when locally injected, binds to presynaptic nerve terminals of the neuromuscular junction preventing release of acetylcholine and temporarily paralyzing the muscle. Studies have shown that the predominant effect on the internal sphincter is through sympathetic blockade.
- Authors report that this treatment can be easily injected/administered in the outpatient setting and is well tolerated.
- After evaluation of multiple studies focusing on the optimal dose and injection site of botulinum toxin, it appears that 20 units injected on either side of the anterior midline in the intersphincteric groove provides the best results.
- Comparative studies of botulinum toxin versus topical nitroglycerin showed conflicting results as to healing.
- Studies comparing lateral internal sphincterotomy with botulinum toxin injection showed superior long-term healing in the surgical group. One study showed that flatal incontinence was a side effect in 16 % of patients that underwent surgery versus no side effects in the botulinum group.
- Late recurrences may be seen in up to 40 % of patients who initially healed after injection of botulinum toxin. A higher risk of recurrences was associated with fissures that had an anterior location, disease longer than 12 months, and those requiring multiple injections of botulinum toxin.
- Some authors advocate repeat injection(s) if a patient experiences a recurrent fissure. They also cite improvement of symptoms and possibility of healing with repeated injections.
- The Food and Drug Administration (FDA) has issued a warning based on a small number of patients who had adverse reactions after injection of botulinum toxin including respiratory failure and death. It is speculated that this may be related to overdosing.

Operative Treatment

- The goal of anal fissure treatment is to decrease elevated anal resting tone. Operative procedures produce permanent reduction in maximum resting anal pressures.

Anal Dilatation

- Anal dilatation can reduce anal resting pressures. This treatment was standardized to mean dilatation by means of opening a Parks' anal retractor to 4.8 cm or a pneumatic balloon inflated to 40 mm. Performing dilatation with one of these measures found fissure healing in 94 %.
- Widespread criticism toward the use of this technique focuses on fecal incontinence due to diffuse sphincter damage.
- Comparison of sphincterotomy with dilatation showed conflicting results as far as which surgical treatment is superior for healing of fissures and which leads to fewer problems with fecal incontinence.
- While dilatation is still performed in some centers, this procedure is not commonly used across North America as a primary treatment for anal fissures.

Fissurectomy

- While excision of the anal fissure has been proposed as a therapeutic option, given the accepted etiology of a fissure being secondary to inadequate blood flow and spasm, the benefit of fissurectomy is questioned.

Lateral Internal Sphincterotomy

- Lateral internal sphincterotomy is recommended in the American Society of Colon and Rectal Surgeons practice parameters as the surgical procedure of choice for refractory anal fissures.
- Division of the internal anal sphincter is done on the lateral sides of the anus. Initially, it was proposed to divide the muscle posteriorly over the fissure bed. However, posterior muscle division could result in a scarred groove (so-called keyhole deformity), which may lead to leakage through this groove and incontinence of gas and/or stool.
- The procedure can be performed with an open technique where an incision is made over the intersphincteric groove and the internal muscle is identified and divided under direct vision (Fig. 12.3). Alternatively, the closed technique uses a small scalpel such as a beaver blade that is inserted through a very small incision into the intersphincteric groove and carefully divides the intersphincteric groove (Fig. 12.4).
- Long-term complications are higher with the open technique versus the closed technique. Also, continence is reported to be better using the closed technique versus the open technique.
- Persistent incontinence to gas and stool is a major concern after sphincterotomy and this rate varies greatly between studies, mostly due to differences in definition and intensity of follow-up. Etiology of incontinence is related to type and extent of sphincter division.
- Care is needed when dividing the internal sphincter in women due to an inherent shorter anal canal versus men. Additionally, external anal sphincter defects in women should be recognized before the sphincterotomy procedure.

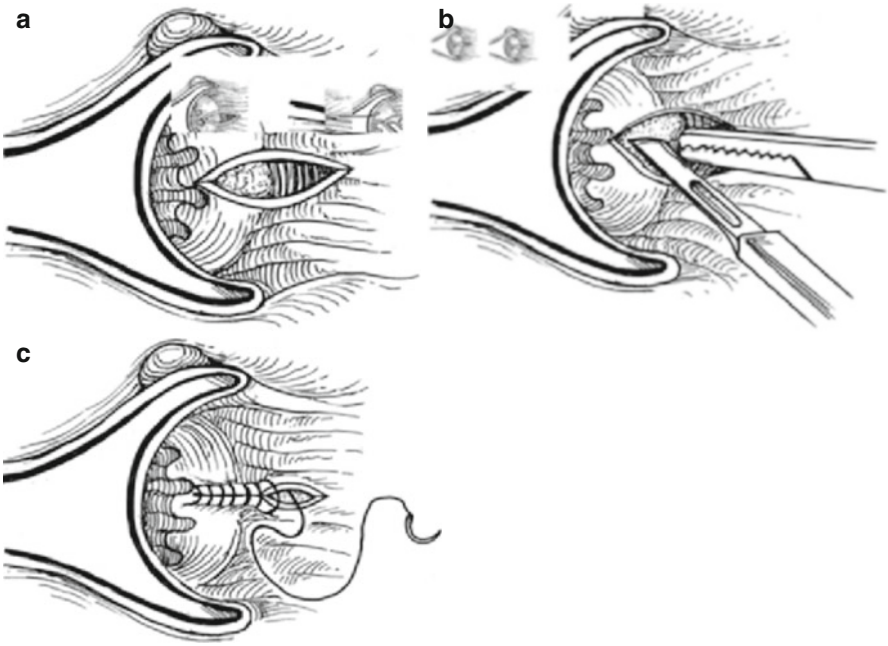

Fig. 12.3 Open lateral internal sphincterotomy. (**a**) Radial skin incision distal to the dentate line exposing the intersphincteric groove. (**b**) Elevation and division of the internal sphincter. (**c**) Primary wound closure

- Overall troublesome fecal incontinence is uncommon if the extent of internal muscle division is limited to the length of the fissure rather than division of the internal sphincter from the intersphincteric groove to the dentate line.
- Consideration should be given to excision of the hypertrophied anal papillae and fibrous anal polyp to improve patient satisfaction when performing the sphincterotomy.
- Earlier wound healing may be achieved with primary closure of the open sphincterotomy (technique) wound versus allowing this to heal by secondary intention.
- For patients with recurrent or persistent fissures, inadequate division of the internal sphincter must be considered.

Advancement Flaps

- Advancement flaps are an alternative surgical treatment for anal fissures. Healing has been reported using this technique.
- For patients with low-pressure fissures, the advancement flap is a reasonable consideration for surgical closure of the fissure.
- However, data is limited regarding using this technique for traditional spasm-related anal fissures.

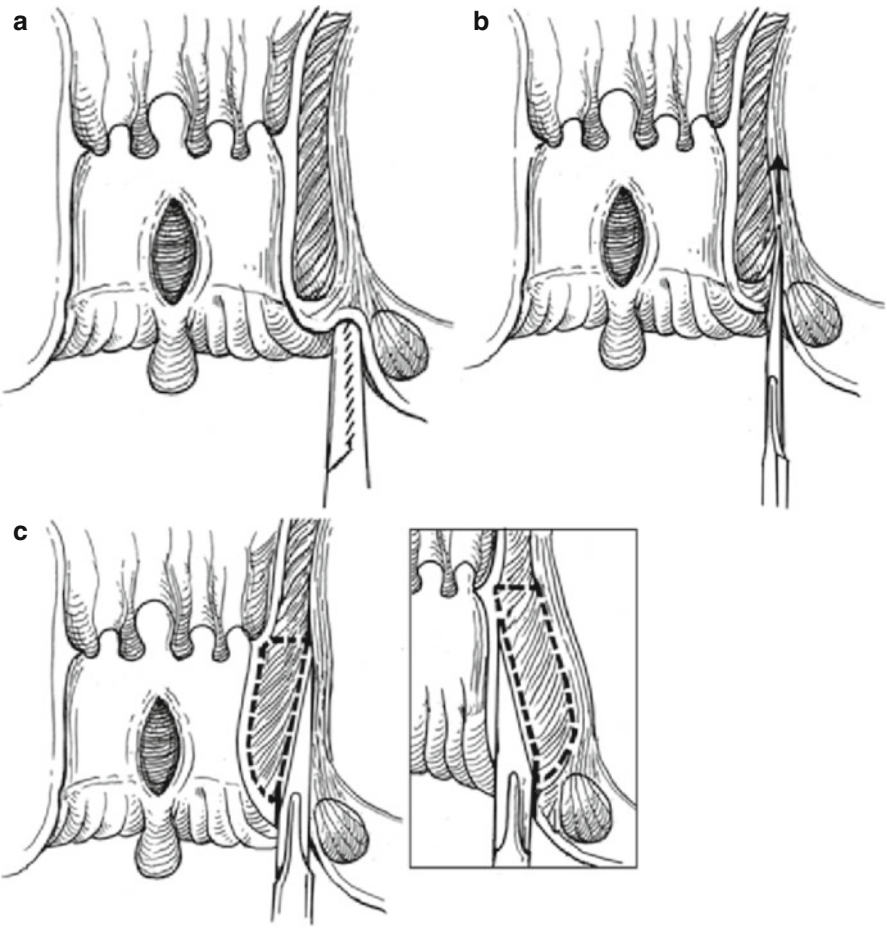

Fig. 12.4 Closed lateral internal sphincterotomy. (**a**) Location of the intersphincteric groove. (**b**) Insertion of the knife blade in the intersphincteric plane. (**c**) Lateral to medial division of the internal anal sphincter (*inset:* medial to lateral division of the muscle)

Summary of Treatment Options

All recommendations and statements are based on systematic reviews designed to compare specific treatments:

- Nitroglycerin is better than placebo at healing fissures, but late recurrences are common.
- Botulinum toxin and calcium channel blockers were equivalent in efficacy to nitroglycerin at healing fissures but had fewer adverse events.
- No medical therapy was as efficacious as surgical sphincterotomy for healing anal fissures.
- Open and closed lateral internal sphincterotomy were felt to be equally efficacious. Anal dilatation and posterior sphincterotomy should be abandoned.

- For women who have had children or are planning on children, it is suggested to maximize nonsurgical therapy prior to resorting to surgical sphincterotomy.

Atypical Fissures

- Fissures seen in patients with incontinence are identified as low-pressure fissures and often seen postpartum. It is recommended that surgical interference with the sphincter mechanism should be avoided in patients with low-pressure fissures.
- Management of low-pressure fissures should begin with a trial of conservative management.
- An island or sliding flap or endoanal advancement flap has been suggested as the preferred treatment for low-pressure fissures that do not heal with conservative management. One study is published to support this treatment approach.

Crohn's Disease

- Multiple, nonhealing, or asymptomatic fissures should raise the possibility of Crohn's disease. If the suspicion of Crohn's disease is entertained, a thorough evaluation with endoscopy and imaging should be considered.
- Persistent nonhealing deep fissures in Crohn's disease can evolve into fistulae or perianal abscesses.
- Concerns regarding incontinence, nonhealing wounds, and progression to proctectomy have led clinicians to advocate medical management as the preferred treatment of anal fissures in Crohn's disease. This treatment includes efforts to reduce diarrhea, bulk stools, and improve comfort. If the fissure does not heal, an exam under anesthesia may be indicated to rule out other pathology.
- Some authors have reported successful healing and avoidance of proctectomy after surgical treatment of anal fissures in patients with Crohn's disease. It is prudent with Crohn's fissures to control underlying disease with medical management prior to permanent surgical therapy.

Human Immunodeficiency Virus (HIV)

- In HIV-positive patients, it is important to recognize the difference between ulcers and fissures as they are not the same. Ulcers are deep and boring with a broad base and located anywhere in the anus.
- HIV patients with true anal fissures can be treated with the same algorithm as non-HIV patients.

Conclusions

- The diagnosis of an anal fissure can usually be made based on the history and classic appearance of the fissure. An invasive anal exam should be avoided due to exacerbation of pain without appreciable benefit.
- Trauma is felt to be the predisposing factor leading to a fissure. Additionally, elevated sphincter pressures and reduced blood flow likely play a role.
- Initial therapy for an anal fissure is typically oral fiber, sitz baths, and analgesics.
- A recent Cochrane review found that medical therapy is only marginally better than placebo for treating anal fissures and far less effective versus surgery for treating chronic fissures.
- Despite these findings, a trial of medical management is still recommended before permanent sphincter division is done unless patients are extremely uncomfortable.

13. Anorectal Abscess and Fistula

Carol-Ann Vasilevsky

Abscess

- Anorectal abscess and fistula-in-ano represent different stages of anorectal suppuration.
- The abscess is the acute inflammatory event.

Anatomy

- Ducts from anal glands empty into the anal crypts at the level of the dentate line.
- Anal glands penetrate into deeper tissue: 80 % submucosal, 8 % internal sphincter, 8 % conjoined longitudinal muscle, 2 % intersphincteric space, and 1 % penetrate the internal sphincter.
- Understanding the potential anorectal spaces (Table 13.1) is essential for successful treatment of anorectal suppuration.

Pathophysiology

Etiology

- Table 13.2 lists the etiologies of anorectal abscesses. 90 % are from nonspecific cryptoglandular suppuration.
- Abscesses result from obstruction of the anal glands (Park's cryptoglandular theory published in 1961).
- Persistence of anal gland epithelium in the tract between the crypt and the blocked duct results in fistula formation.

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Table 13.1 The potential spaces of the anorectum and their boundaries

Potential space	Superior border	Anterior border	Inferior border	Posterior border	Lateral border	Medial border	Other features
Perianal space			Anal verge		Becomes continuous with the ischioanal fat	Lower portion of anal canal	Continuous with the intersphincteric space and forms the most common abscess
Ischioanal space		Transverse perineal muscles		Lower border of the gluteus maximus and sacrotuberous ligament	Obturator internus	Levator ani and external sphincter muscle	Extends from the levator ani to the perineum. If the deep postanal space becomes infected, pus can spread circumferentially via the ischioanal space and this could form a horseshoe abscess
Intersphincteric space	Rectal wall		Continuous with perianal space				Lies between the internal and external sphincters. If infected, pus can spread circumferentially
Supralevator space	Peritoneum		Levator ani muscle		Pelvic wall	Rectal wall	The rarest abscesses form from this space. If infected, pus can spread circumferentially
Deep postanal space	Levator ani muscle		Anococcygeal ligament	Tip of the coccyx			Pus can spread circumferentially via the ischioanal space and form a horseshoe abscess

Table 13.2 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

- Predisposing factors for abscess formation are diarrhea and trauma from hard stool.
- Associated factors may be anal fissures, infection of a hematoma, or Crohn's disease.

Classification

- Abscesses are classified by their location within the potential anorectal spaces (Figs. 13.1 and 13.2).

Evaluation

Symptoms

- Anorectal pain, swelling, and fever.
- Gluteal pain may accompany a supralevator abscess.
- An intersphincteric or supralevator abscess may produce severe rectal pain with urinary symptoms (dysuria, retention, inability to void).

Physical Exam

- On inspection, erythema, swelling, and possible fluctuation may be seen.
- Digital exam may not be possible due to extreme pain.

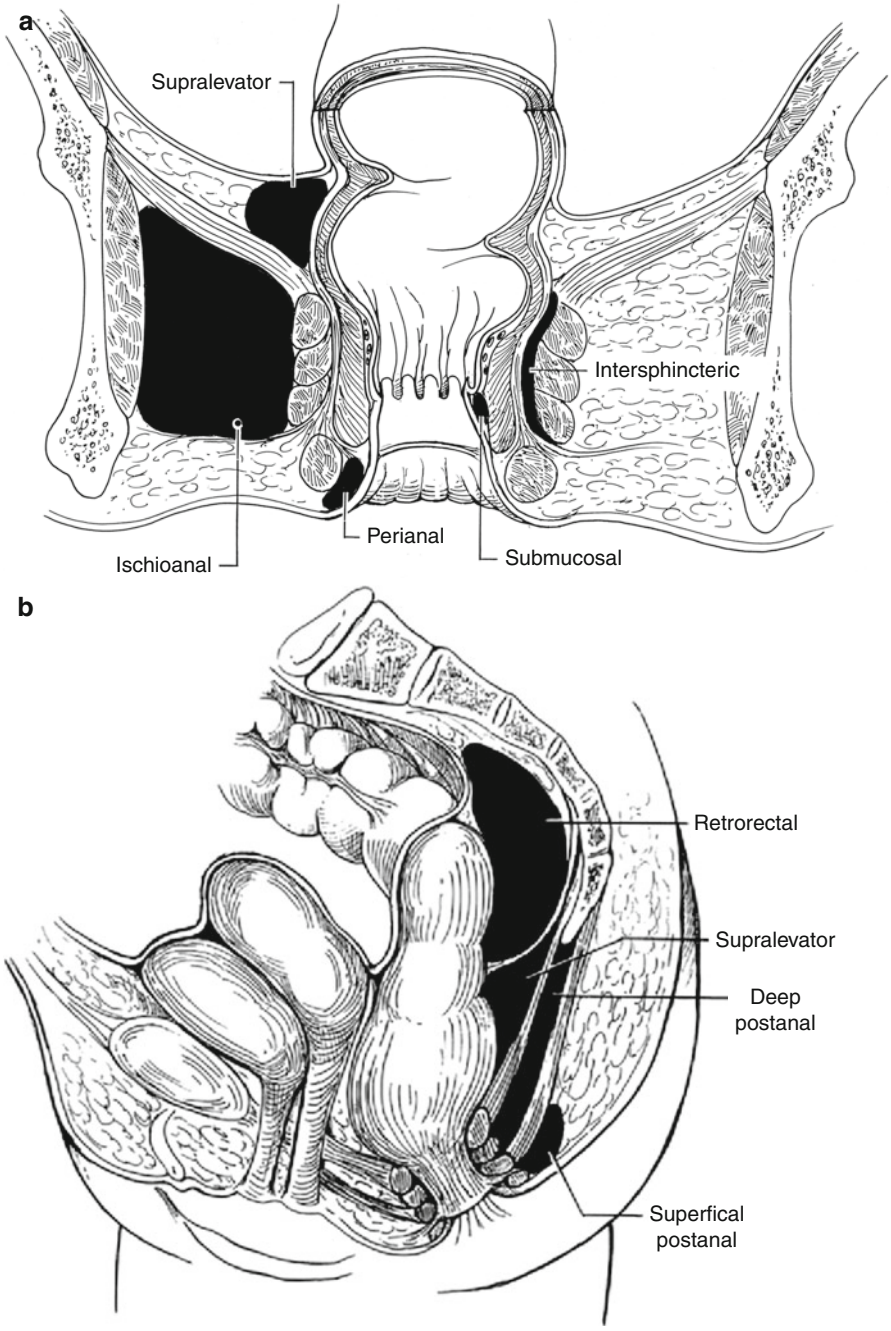

Fig. 13.1 Anorectal spaces: (**a**) Coronal section. (**b**) Sagittal section

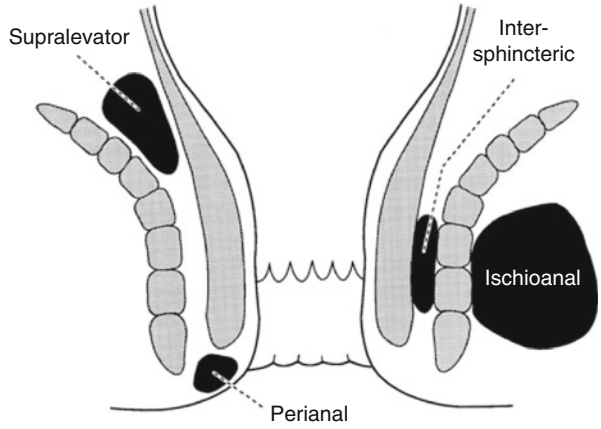

Fig. 13.2 Classification of anorectal abscess

- Anoscopy and proctoscopy are avoided in the acute setting.
- There may be no visible external manifestations despite severe rectal pain with an intersphincteric or supralevator abscess. If palpation is possible, a mass may be appreciated.
- With a supralevator abscess, a tender mass may be palpated on rectal or vaginal exam.

Treatment

General Principles

- The treatment of an anorectal abscess is prompt incision and drainage.
- Watchful waiting with antibiotics is ineffective and may lead to a more complicated abscess with sphincter mechanism damage.
- Delay in treatment may lead to a life-threatening necrotizing infection and death.

Operative Management

Incision and Drainage

- A *perianal abscess* may be drained with local anesthesia. A cruciate or elliptical incision is made over the point of maximal tenderness and the edges trimmed to prevent premature closing (which could lead to recurrence). No packing is required.
- Most *ischioanal abscesses* can be drained similarly to a perianal abscess, but the location of the incision should be shifted medial toward the anal side of the abscess but lateral to the external sphincter muscle (this minimizes the complexity if a fistula develops). Large abscesses or horseshoe

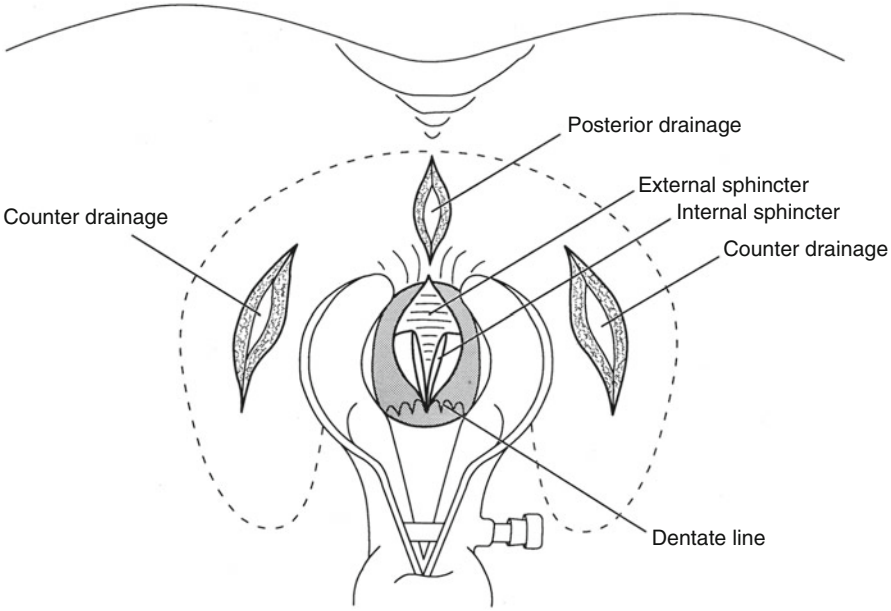

Fig. 13.3 Drainage of a horseshoe abscess

abscesses (with the infection usually originating from the deep postanal space) often require drainage with regional or general anesthesia in the prone or left lateral position.

- For a *horseshoe abscess*, a midline incision between the anus and coccyx is made and the superficial external sphincter muscle fibers are spread to enter the deep postanal space. Counter-incisions are made over each ischioanal fossa to allow drainage of the anterior extensions (Hanley procedure). The distal half of the internal sphincter may be divided to drain the gland where the infection originated (Fig. 13.3).
- For pain out of proportion to physical findings, an exam under anesthesia is mandatory. An *intersphincteric abscess* may be established by palpation of a mass or aspiration of pus in the operating room. The treatment is division of the internal anal sphincter along the length of the abscess. The wound may be marsupialized for adequate drainage.
- A *supralevator abscess* may result from an upward extension of an intersphincteric or ischioanal abscess or downward extension of a pelvic abscess. If the origin is from an intersphincteric abscess, drainage is accomplished through the rectum by dividing the internal sphincter (not through the ischioanal fossa as that would result in a suprasphincteric fistula). If the origin is an ischioanal abscess, this is drained through the perianal skin (not through the rectum as that would lead to an extrasphincteric fistula) (Fig. 13.4). If the abscess is of pelvic origin, it can be drained via the area it is pointing: through the rectum, ischioanal fossa, or percutaneously via the abdominal wall.

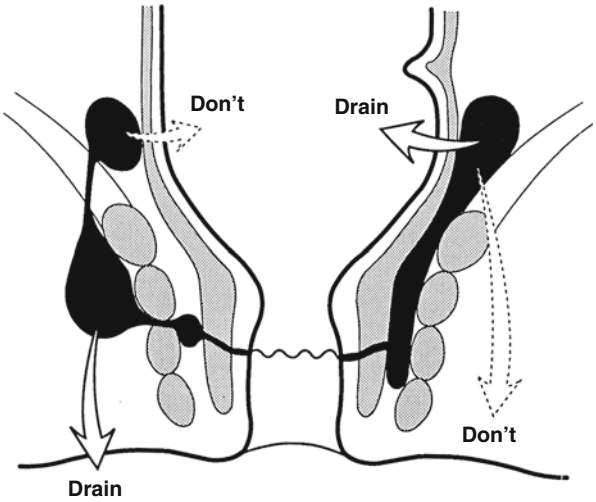

Fig. 13.4 Drainage of a supralevator abscess

Catheter Drainage

- The area of maximal tenderness is prepped and the skin around it is infiltrated with local anesthesia (injecting at the maximal point of fluctuation may preclude the local anesthesia working in that acid environment).
- A stab incision is made as close to the external sphincter muscle as possible so the tract is as short as possible in case a fistula develops.
- A 10–16 French soft mushroom catheter is inserted over a probe into the cavity. It typically does not need to be sutured in place.
- The catheter is shortened to 2–3 cm outside the skin with the tip in the depth of the abscess (Fig. 13.5a, b).
- The length of time that the catheter is left to drain the abscess cavity depends on the size of the abscess cavity, amount of granulation tissue around the catheter, and character and amount of drainage. If in doubt, it is better to leave it longer.

Primary Fistulotomy

- Primary fistulotomy at the time of abscess drainage is controversial.
- A meta-analysis showed that when the fistula is identified, drainage plus primary fistulotomy decreased the rate of subsequent fistula formation (by 83 %) with no increase in incontinence.
- Against primary fistulotomy:
  - Difficulty in finding the internal opening (as high as 66 % of the time of abscess drainage) can lead to creation of a false passage and neglect to find the main source of infection.

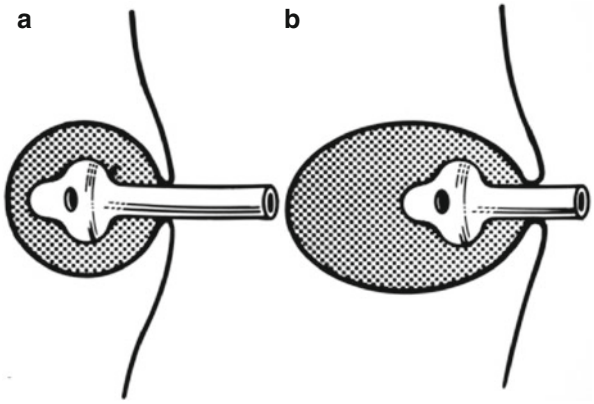

Fig. 13.5 Catheter in an abscess cavity: (**a**) The correct size and length of catheter. The size of the catheter should correspond to the size of the cavity. (**b**) When a catheter is too short. A catheter that is too short or too small could fall into the wound

  - Thirty-four to fifty percent of patients with first time abscess formation will not develop a fistula after drainage.
  - The search for an internal opening converts a procedure that can be done under local anesthesia (drainage) to one that requires regional or general anesthesia.
- Those younger than 40 years old have a significantly higher risk of developing a fistula or recurrent abscess after initial drainage of a perianal abscess.
- Abscess recurrence is more often observed after drainage of an ischioanal abscess.
- If the internal opening of a low transsphincteric fistula is readily apparent at the time of abscess drainage, primary fistulotomy is feasible EXCEPT in patients with Crohn's disease, acquired immune deficiency syndrome (AIDS), advanced age, high transsphincteric fistula, and an anterior fistula (in women).

Antibiotics

- Antibiotics are only used as an adjunct for patients with valvular heart disease, prosthetic heart valves, extensive soft tissue cellulitis, prosthetic devices, diabetes, immunosuppression, or systemic sepsis.

Postoperative Care

- Postoperatively, patients are instructed to take a regular diet, bulk-forming agents, the prescribed analgesia, and sitz baths.
- Follow-up for patients is generally 2–4 weeks after the procedure, but those with an intersphincteric or supralevator abscess may be seen sooner at about 2 weeks.

- If catheter drainage has been done, these patients are seen about 7–10 days after catheter placement. If the cavity has closed around the catheter and the drainage ceased, the catheter is removed. Otherwise, the catheter is left in place or a smaller catheter placed.
- In all cases, patients are observed until complete healing occurs.

Complications

Recurrence

- Up to 89 % of patients after drainage of an ischioanal or intersphincteric abscess will develop a recurrent abscess or fistula.
- Recurrence is higher in those who had a previous abscess drained.
- Recurrence of anorectal infections may be due to missed infections in adjacent anatomic spaces, presence of an undiagnosed fistula or abscess at the initial drainage, or failure to completely drain the initial abscess.

Extra-anal Causes

- Extra-anal etiologies that can lead to abscess recurrence include hidradenitis suppurativa, pilonidal abscess (with downward extension), Crohn's disease, tuberculosis, human immunodeficiency virus (HIV) infection, perianal actinomycosis, rectal duplication, lymphogranuloma venereum, trauma, foreign bodies, and perforated rectal carcinoma.

Incontinence

- Iatrogenic injury can lead to incontinence, which occurs with division of external sphincter muscle during drainage of a perianal or deep postanal space abscess (in a patient with borderline continence) or division of puborectalis muscle in a patient with a supralevator abscess.
- Prolonged packing of an abscess cavity may impair continence by leading to excessive scar formation.
- Primary fistulotomy at the time of initial abscess drainage may lead to continence disturbances while unnecessarily dividing sphincter muscle.

Special Considerations

Necrotizing Anorectal Infections

- Rarely, necrotizing anorectal infections may occur and could result in death.
- Factors associated with this are delay in diagnosis and management, virulence of the organism, bacteremia, metastatic infections, underlying medical disorders (diabetes, blood dyscrasias, heart disease, chronic renal failure, hemorrhoids, previous abscess, or fistula), obesity, and cigarette smoking.

Symptoms and Signs

There are two types of presentation.

- Group one: This group demonstrates superficial infection of the surrounding tissue including necrosis of the skin, subcutaneous tissue, fascia, and/or muscle. A black spot on the skin may occur early. Perianal crepitation, erythema, skin induration, blistering, or gangrene may be present.
- Group two: This group presents with sepsis that involves the preperitoneal or retroperitoneal spaces. The signs may be subtle such as abdominal wall induration, tenderness, or a vague mass. Fever, tachycardia, and vascular volume depletion may precede appearance of an overt infection. CT scan is an excellent diagnostic tool (it will demonstrate origin and extent of infection).

Treatment

- Early recognition, aggressive surgical debridement, and appropriate antibiotic administration are the most important factors to improve outcome and reduce mortality.
- Vigorous resuscitation with invasive monitoring and respiratory and renal support is aggressively carried out (and treated).
- Antibiotics effective against Staphylococci, Streptococci, gram-negative coliforms, Pseudomonas, Bacteroides, and Clostridium are administered intravenously. If a gram stain shows gram-positive rods, penicillin G (24–30 million units per day) and an aminoglycoside are given.
    - Tetanus toxoid is administered.
    - The goals of surgical debridement are to radically remove all nonviable tissue back to healthy tissue, halt infection progression, and alleviate systemic toxicity.
    - The skin changes may not reflect the severity of the liquefactive necrosis of the subcutaneous tissue and extensive necrosis of the underlying fascia. Reexamination under anesthesia is usually necessary to fully evaluate wounds for further debridement.
    - Vacuum-assisted closure may be helpful for healing these wounds, which may be quite extensive.
    - Colostomy is controversial, but should be considered if the sphincter muscle is grossly infected, the patient is incontinent, there is colonic or rectal perforation, or the patient is immunocompromised. A “medical colostomy” using enteral or parenteral nutrition has also been used.
    - Suprapubic urinary diversion is controversial and considered in the presence of a known urethral stricture or urinary extravasation with phlegmon.

- Hyperbaric oxygen therapy (with 100 % oxygen via mask or endotracheal tube at 3ATM for 2 h over 1–2 treatments in patients *without* chronic obstructive pulmonary disease) has been advocated for patients with diffuse spreading infections and then also to promote wound healing. This does not eliminate the mandate for wide debridement of ischemic tissue.
- High rates of mortality due to anorectal sepsis are related to extent of disease and the patient's metabolic status at presentation. Mortality is two to three times higher in diabetics, the elderly, and patients with delayed treatment.

Anal Infection and Hematologic Diseases

- There is a relationship between the number of circulating granulocytes and the incidence of perianal infections in patients with hematologic diseases (most occurred with fewer than 500 neutrophils per cubic millimeter).
- The risk of developing anorectal infections is related to severity and duration of neutropenia.
- The most important prognostic factor is the number of neutropenic days during the infectious episode.
- Presenting symptoms commonly are fever preceding pain and urinary retention. Early signs are point anal tenderness and poorly demarcated induration. External swelling and fluctuation often appear late.
- A neutropenic patient with perianal pain is assumed to have an acute anorectal infection and started on precautionary measures (no digital exams, suppositories, or enemas), sitz baths, stool softeners, bulk agents, analgesia, and antibiotics.
- The most common bacteria are *Escherichia coli* and group D streptococcus. Appropriate antibiotic coverage could be a third-generation cephalosporin with an additional drug for anaerobic coverage or extended spectrum penicillin, an aminoglycoside, and an antianaerobic covering drug.
- Surgical intervention is controversial. Incision and drainage may produce scant or no pus and may lead to hemorrhage, poor wound healing, or an expanding soft tissue infection.
- Surgery has been recommended if there is obvious fluctuation, progression of the soft tissue infection, or persistent sepsis after a trial of antibiotic therapy.
- With fewer than 500 neutrophils per cubic millimeter, low-dose radiation therapy (300–400 rads for 1–2 days) has been suggested. Conflicting successful results have been published with this approach.

Anorectal Sepsis in the HIV-Positive Patient

- With incision or catheter drainage of an anal abscess in an HIV-positive patient, due to being immunocompromised, adjunctive antibiotics should also be given.

- Attempts should be directed at keeping the wounds small due to the potential to have poor wound healing.
- Serious septic complications are rare and may be associated with in situ neoplasia.

Fistula-in-Ano

Pathophysiology

Etiology

- A fistula-in-ano is an abnormal tract or cavity communicating with the rectum or anal canal by an identifiable internal opening. Most fistulas arise from a cryptoglandular infection.

Classification

- Table 13.3 and Fig. 13.6 describe the classification of fistula-in-ano.

Intersphincteric Fistula-in-Ano

- An intersphincteric fistula results from a perianal abscess and the tract passes in the intersphincteric space.
- This is the most common fistula type (70 %).

Table 13.3 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

Adapted from Parks (1961)

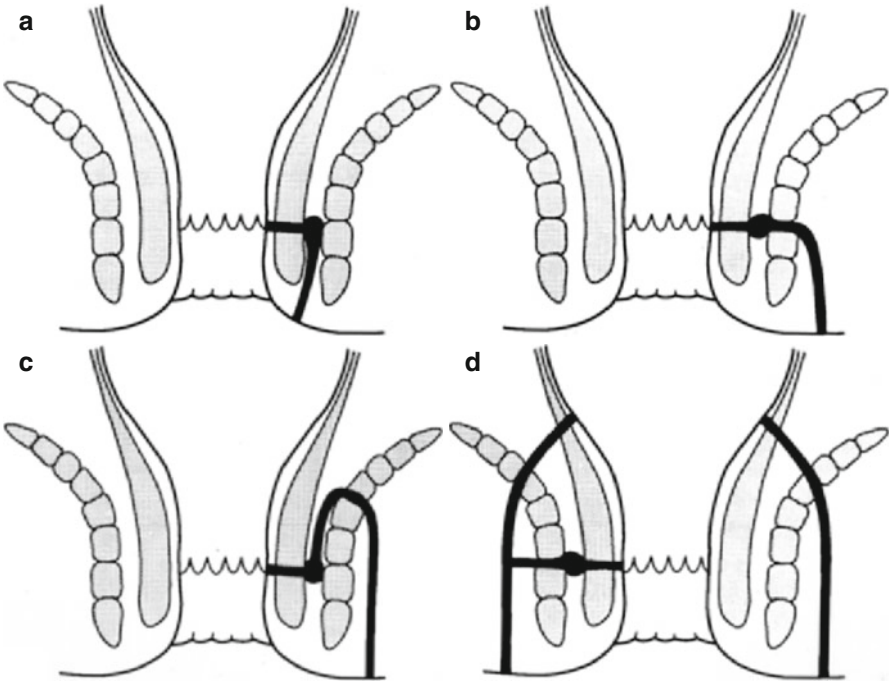

Fig. 13.6 Classification of fistula-in-ano: (**a**) intersphincteric, (**b**) transsphincteric, (**c**) suprasphincteric, and (**d**) extrasphincteric

- A tract can end blindly in the intersphincteric space, pass cephalad and end blindly, or pass cephalad into the lower rectum.
- There is no downward extension to the anal margin.
- Rarely, an intersphincteric infection can tract cephalad into the pelvic cavity (above the levator muscle) or may originate as a pelvic abscess and manifest itself distally into the perianal area.

Transsphincteric Fistula-in-Ano

- Twenty-three percent are transsphincteric fistula associated with an ischioanal abscess where an infection from the internal opening passes through the internal and external sphincter into the ischioanal fossa.
- This type of fistula could have a high blind tract that passes through the levator ani muscle into the pelvis.
- A rectovaginal fistula (discussed in Chap. 14) is a form of transsphincteric fistula.

Suprasphincteric Fistula-in-Ano

- Five percent of suprasphincteric fistula-in-ano are from a supralevator abscess.

- The tract starts as an intersphincteric abscess and passes above the puborectalis and then curves downward and lateral to the external sphincter in the ischioanal space and ends at the perianal skin.
- A high blind tract may result in a horseshoe extension.

Extrasphincteric Fistula-in-Ano

- The rarest form of fistula (2 %).
- The tract originates in the rectum and passes above and through the levators, then through the ischioanal space, and exits at the perianal skin.
- The etiology of this fistula may be from a foreign body penetrating the rectum, a penetrating injury to the perineum, Crohn's disease, or carcinoma (or its treatment).
- Another common cause is an iatrogenic injury from vigorous probing during fistula surgery.

Evaluation

Symptoms

- Most patients with a fistula-in-ano recall an abscess (that was incised or drained spontaneously). They may also have continual drainage, pain with defecation, bleeding (if there is granulation tissue at the internal opening), or a decrease in their swelling/pain when spontaneous drainage occurs.
- Bowel symptoms may be present if the fistula results from Crohn's disease, actinomycosis, or anorectal carcinoma.
- Systemic diseases like HIV, carcinoma, or lymphoma should also be considered.

Physical Examination

- The number and location of external openings may be helpful to locate the primary opening (Goodsall's rule, Fig. 13.7). This rule is highly accurate for posterior fistulas and less accurate with anterior fistula (especially in women).
- On digital exam, the internal opening may feel like a nodule or pit. An indurated cord-like structure may be palpable beneath the skin oriented toward the direction of the internal opening.
- Posterior or lateral induration may reflect a deep postanal space or horseshoe fistula.
- Digital exam also should note any relation of the tract to the sphincter muscle, along with the bulk, tone, and voluntary squeeze of the anal sphincter muscle.

Investigations

- Prior to operative intervention, anoscopy may identify an internal opening. Proctoscopy can exclude underlying proctitis or neoplasia.

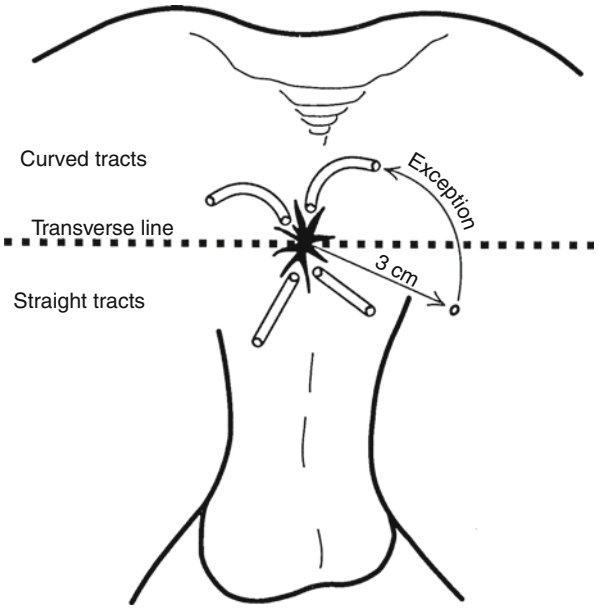

Fig. 13.7 Goodsall's rule: An opening seen posterior to a line drawn transversely across the perineum originates from an internal opening in the posterior midline. An anterior external opening typically originates in the nearby crypt. Generally, the greater the distance from the anal margin, the greater the probability of a complicated upward extension

- Colonoscopy (or barium enema) and small bowel evaluation (as a small bowel series, CT enterography, or MRI enterography) are indicated if there are multiple fistulas, recurrent fistula, or bowel symptoms suggestive of inflammatory bowel disease.
- Anal manometry may be useful in planning the operative approach in a patient with a history of obstetrical trauma (in women), advanced age, Crohn's disease, AIDS, or recurrent fistula.
- Preoperative imaging is strategically used to decrease recurrence rates after fistula surgery by demonstrating clinically undetected sepsis, guide surgery, and determine the relationship of the fistula to the sphincters.

Fistulography

- Cannulation of the external opening and injection of a water-soluble contrast into the fistula tract are considered when the anatomy may be altered such as in recurrent fistulas or in Crohn's disease.
- Accuracy is variable and reported to be between 16 and 96 %. This test may not demonstrate secondary tracts, distinguish an abscess located in the high ischioanal fossa versus supralevator space, or fail to precisely show the internal opening.
- One study found that fistulography altered surgical management or revealed other pathology 48 % of the time.

Computed Tomography Scan

- A CT scan performed with IV and rectal contrast may distinguish an abscess from cellulitis. It may assess the degree of rectal inflammation in inflammatory bowel disease. It may not visualize fistula tracts in relation to the levators.

Endoanal Ultrasound

- Establishes the relation of the primary tract to the anal sphincters, determines simple from complex fistula, determines the primary internal opening, and assesses the adequacy of drainage.
- An enhancing agent such as hydrogen peroxide injected into the tract at the time of endosonography improves accuracy.
- This study is operator dependant and scars or defects from previous sepsis or surgery impede ultrasonographic interpretation.

Magnetic Resonance Imaging

- MRI is valued to assess complex fistulas particularly in patients with anatomic distortion from previous surgery.
- An MRI is felt by some to be the most accurate technique to delineate the internal opening along with showing the course of primary and secondary extensions.

Treatment

General Principles

- The surgical principles are to eliminate the fistula, prevent recurrence, and preserve sphincter function. This is done by finding the internal opening and dividing the least amount of sphincter muscle.
- Steps to identify the internal opening are:
  - Passage of a probe from the external to the internal opening (or vice versa).
  - Injection of dye (dilute methylene blue, milk, or hydrogen peroxide) in the external opening and noting its presence at the dentate line.
  - Following the granulation tissue in the fistula tract while incising over the extrasphincteric component of the tract.
  - Placing traction on the tract and noting puckering in the anal crypt associated with its internal opening. This maneuver is less successful for complicated fistula.

Operative Management

Lay-Open Technique

- For a simple intersphincteric or low transsphincteric fistula (while typically in the prone position), gently passing a probe from the external opening through the internal opening and incising the overlying tissue can be done (Fig. 13.8).
- No packing is required if adequate unroofing is accomplished.

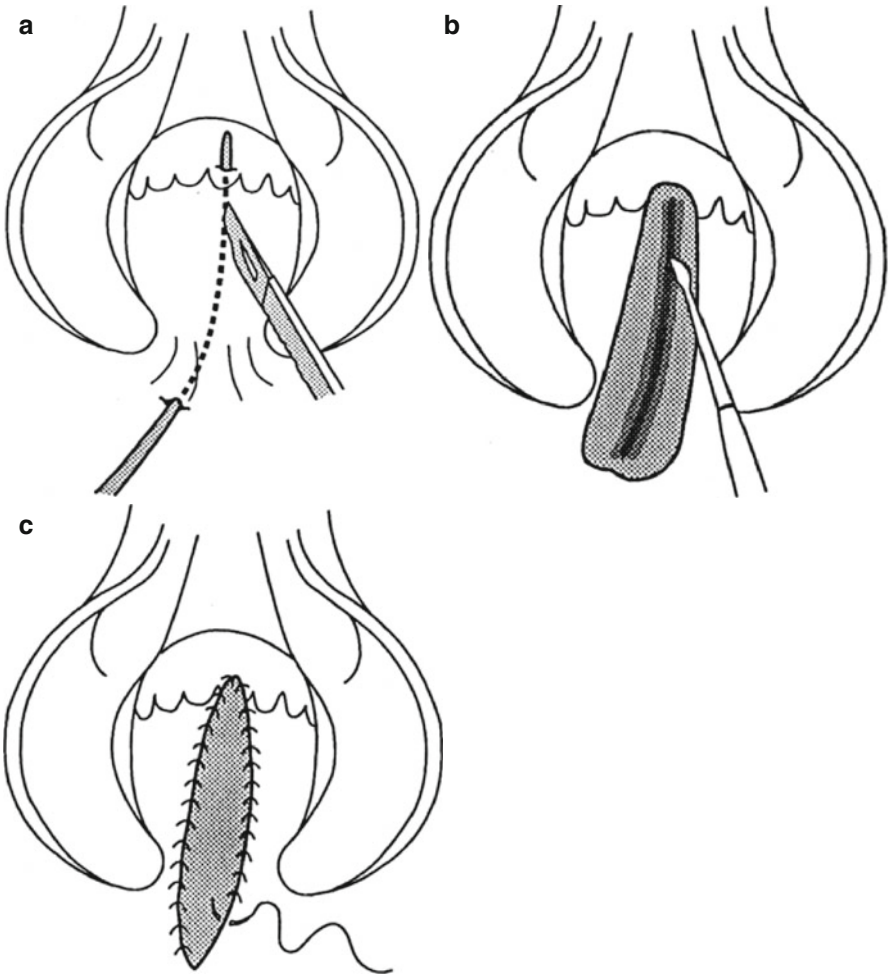

Fig. 13.8 Technique of laying-open: (**a**) The insertion of probe from the external opening to the internal opening at the dentate line. The tissue over the probe is then incised. (**b**) Curettage of granulation tissue which may be sent to pathology. (**c**) Marsupialization of wound edges

Seton

- When the tract transverses a high and significant amount of sphincter muscle, a combination of the lay-open technique with a seton insertion may be chosen in an effort to preserve anal incontinence.
- The seton may be from silk or other nonabsorbable sutures, a Penrose drain, rubber bands, vessel loops, or Silastic catheters.
- The distal internal sphincter along with the skin leading up to the external opening is incised (Fig. 13.9).
- For a cutting seton, the seton is threaded through the tract and tied with multiple knots to create a handle. At regular intervals, the seton is tightened. The seton slowly cuts through the muscle and the proximal sphincter that it cuts through heals with fibrosis. This, in theory, prevents separation and retraction of the sphincter muscle. If it does not totally cut through the external sphincter, the seton allows delineation of the remaining external sphincter muscle, so at a second procedure 8 weeks later, the remaining external sphincter muscle may be divided.
- A cutting seton is preferred for treatment of low transsphincteric fistula, but its use in higher transsphincteric fistula risks fecal incontinence.
- The seton may also be tied loosely and left as a draining seton.
- Indications for placement of a loose seton include to:
    1. Identify and promote fibrosis around a complex anal fistula that encircles most or all of the sphincter mechanism.
    2. Mark the site of a transsphincteric fistula where massive anorectal sepsis has distorted anatomic landmarks.

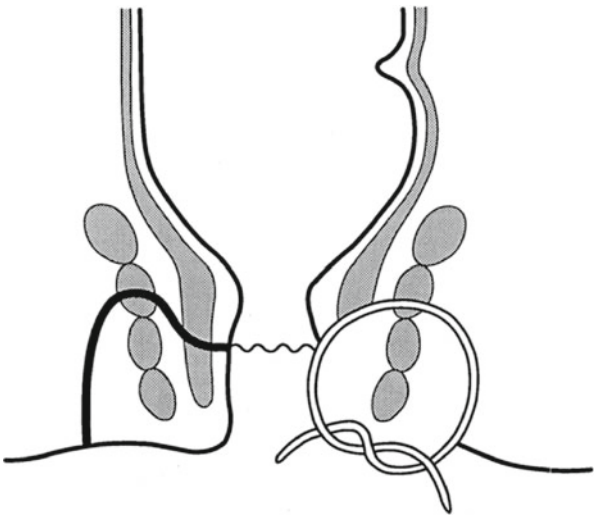

Fig. 13.9 Technique of seton placement

3. Drain an anterior high transsphincteric fistula in a woman (anteriorly, the puborectalis is absent and this leads to a tenuous external sphincter where a fistulotomy may result in incontinence).
4. Drain a high transsphincteric fistula in a patient with AIDS where healing may be poor.
5. Avoid premature skin closure, prevent recurrent abscess, and promote long-term drainage in a patient with Crohn's disease.
6. Provide drainage when there is concern that primary fistulotomy may result in incontinence (i.e., patients with multiple simultaneous fistulas, multiple prior sphincter operations, and the elderly with a weakened sphincter).

- Suprasphincteric fistulas involve the entire sphincter and puborectalis muscle. To avoid laying-open the entire sphincter, one proposed method of seton treatment involves division of the distal internal sphincter muscle and the superficial portion of the external sphincter muscle up to the external opening. A seton is placed around the remaining external sphincter muscle. The wound is allowed to heal and the seton is removed. A variation of this technique is to divide the internal sphincter and perform a partial fistulotomy, unroofing only the skin from the external opening to the level of the external sphincter without dividing any of the external sphincter. The external sphincter is encircled with a seton to promote fibrosis and drainage and removed when the wound is healed. Compete healing with the latter technique has been reported in about two third of patients.
- Treatment of a deep postanal space suprasphincteric fistula starts with adequate draining of the postanal space as previously discussed and outlined in Fig. 13.3. The horseshoe extensions are enlarged for counter drainage and granulation tissue is curetted. The seton is placed around the posterior muscle for drainage. Since the initial drainage involves division of a portion of the internal sphincter muscle, when all wounds are healed, the seton may be removed.
- The treatment of an extrasphincteric fistula depends on its etiology.
  - If the internal opening is at the anal crypt, the fistula is felt to be iatrogenic from extensive probing of a transsphincteric fistula. The lower portion of the internal sphincter is divided and the rectal opening is closed with nonabsorbable sutures. A temporary colostomy (or a "medical colostomy") may be needed for healing.
  - If the cause of the fistula was due to a foreign body, this must be removed and drainage established. The internal opening is closed and a temporary colostomy established.
  - If this type of fistula results from Crohn's disease, drainage may be aided by a seton placement. Addressing the anorectal mucosa with medical treatment may be needed.
  - Another etiology of an extrasphincteric fistula is downward tracking of a pelvic abscess, which requires drainage for the fistula to heal.

Flaps

- *Dermal island flaps* have been advocated for fistula treatment as they do not divide muscle. There is a 23 % failure rate typically in males, patients with previous treatments for their fistula, large fistula requiring combined flaps, and those where simultaneous fibrin glue was used with the flap.
- *Anorectal advancement flaps* are considered for anterior fistula in women, select patients with inflammatory bowel disease, a high transsphincteric fistula, suprasphincteric fistula, patients with previous multiple sphincter operations, and complex fistula.
- Advantages of this technique include reduced healing time, reduced discomfort, lack of deformity to the anal canal, and reduced potential for additional sphincter damage (Fig. 13.10a–d).
- Factors associated with poor healing include Crohn's disease, steroid use, and cigarette smoking.

Fistulectomy

- Not recommended as it creates large wounds and has a greater risk of injuring the anal sphincter muscle.

Fibrin Glue

- Associated with a low incontinence rate as well as a disappointing low long-term cure rate.

Anal Fistula Plug

- A bioprosthetic plug made from lyophilized porcine intestinal submucosa or synthetic scaffold has been used to treat complex anal fistula.
- The implant is colonized by host tissue cells and blood vessels to provide a scaffold for infiltration of a patient's own connective tissue.
- Indications for an anal fistula plug are:
  1. A transsphincteric fistula
  2. An intersphincteric fistula if there is concern that fistulotomy will lead to incontinence
  3. An extrasphincteric fistula
- Contraindications for plug use include:
  1. Fistula with a persistent abscess cavity
  2. Fistula with ongoing infection
  3. An allergy to porcine products
  4. An inability to identify internal and external openings
- Technique for placement of an anal fistula plug.
  1. Following a full bowel preparation or enema and a single dose of IV antibiotics, the patient is placed in the prone position.
  2. The internal and external opening must be clearly delineated. The tract is neither debrided nor curetted out.

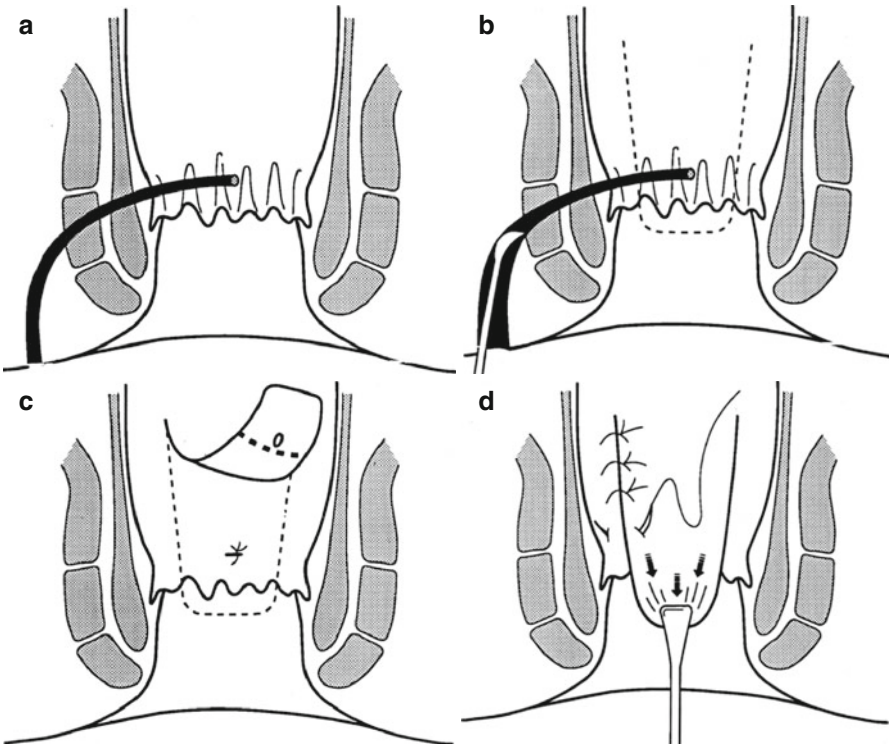

Fig. 13.10 Technique of the anorectal advancement flap: (**a**) After a full mechanical bowel preparation, antibiotics are administered and a Foley is placed. The surgery is done in the prone or left lateral position under regional or general anesthesia. The fistula tract is identified with a probe and curetted or cored out. (**b**) The external opening is enlarged to allow drainage. (**c**) A full-thickness flap of rectal mucosa, submucosa, and part of the internal sphincter muscle is raised. The base of the flap should be twice the width of the apex to maintain adequate blood flow. (A full thickness of the rectal wall may improve successful closure.) The residual internal opening is closed with absorbable suture. The flap is advanced 1 cm below the internal opening. The tip of the flap with the fistula opening is excised. (**d**) The flap is sewn in place with absorbable suture

3. The plug is immersed in sterile saline for 2 min for rehydration.
4. A fistula probe is placed through the tract and this allows a suture to be then threaded through the tract. The tapered end of the plug is secured to the suture and pulled from the internal opening out the external opening until wrinkling of the external layer of the plug is detected.
5. The excess plug is transected at the primary opening. Using a 2-0 absorbable suture in a figure-of-8 fashion, a generous portion of the sphincter mechanism is sutured to the plug. Any plug protruding at the external opening is trimmed. The external opening is left open for drainage.

6. The patient is advised to avoid vigorous activity for 2 weeks to avoid displacement of the plug.
7. There are no dietary restrictions.
8. Topical antibiotics are not recommended.

- Despite its simplicity and avoidance of sphincter muscle division, this procedure has tempered enthusiasm due to variable success rates (14–87 %).
- Dislodgement and sepsis requiring drainage are possible complications of treatment with the fistula plug.

Ligation of the Intersphincteric Fistula Tract Procedure (LIFT)

- This treatment relies on closure of the internal opening and removal of the intersphincteric tract. A patient with an early abscess is not appropriate until an intersphincteric tract is well formed.
  - Technique of LIFT (patients have a mechanical bowel preparation and are placed in the prone or left lateral position).
    1. The internal opening is identified.
    2. A 1.5–2.0 cm curvilinear incision is made at the intersphincteric groove overlying the fistula tract.
    3. Cautery is used to dissect in the intersphincteric plane while avoiding cutting internal sphincter or breaching the anal mucosa.
    4. The intersphincteric tract is ligated next to the internal opening with 2-0 or 3-0 absorbable suture and the tract next to the suture is ligated.
    5. Probing or injecting the external opening confirms tract division.
    6. The granulation tissue is curetted.
    7. Via the intersphincteric wound, the part of the tract leading to the external opening is sutured.
    8. The incision is closed with 3-0 absorbable suture.
- Postoperatively, wounds are cleaned with tap water twice daily and following defecation.
- Patients are given two weeks of oral ciprofloxacillin and metronidazole.
- Problems with the LIFT procedure include difficulty exposing a high fistula tract (especially with a horseshoe tract) and potential damage to the internal sphincter during dissection.
- Success rates are reported to be 58–94 %.

New Biologic Injectables

- Use of human acellular dermal matrix (as a plug of dermis without cellular components) and a suspension of Permacol™ (a cross-linked porcine dermal collagen matrix) have been trialed by injecting them into the fistula tract. These remain to be evaluated in large trials.

Postoperative Care

- Following the lay-open technique, patients eat a regular diet, use bulk agents, and are given analgesic medication.
- Frequent sitz baths ensure perianal hygiene.
- Patients are seen at 2-week intervals to ensure healing is from the bottom up. Silver nitrate sticks may be used to cauterize granulation tissue and assess the depth of the wound.
- One strategy of care after the advancement flap is to remove the Foley on postoperative day 1 and discharge when a diet is tolerated.

Complications

Incontinence

- Continence problems after fistulotomy are related to the complexity of the fistula, the location of the internal opening, preexisting sphincter damage, and the amount of muscle divided.
- Patients with complicated fistulas, high openings, posterior openings, and fistula extensions are at a higher risk of incontinence.
- If the edges of the fistulotomy wound do not precisely approximate, the anus may be unable to properly close and result in intermittent leakage of gas and stool.
- Impaired incontinence after fistula treatment has been associated with increasing age and female gender.
- After treatment with a seton, minor incontinence was reported in 39–73 %. Placing a seton and later removing it without dividing any muscle reduced this to 17 % in one series.
- Major fecal incontinence using the seton approach was reported in 6.7 %.
- Decreased resting and squeeze pressures have been noted in some patients after a fistulotomy.
- Nine to thirty-five percent have disturbed continence with an advancement flap. This has been attributed to overstretching the anal sphincter by retractor placement and disruption of internal fibers with flap development. Decreased resting pressures have been noted in some patients after an advancement flap.
  It is important to recognize preexisting sphincter defects prior to embarking on fistula surgery.

Recurrence

- A 0–18 % recurrence rate is found after fistulotomy. Recurrence has been associated with failure to identify the primary internal opening (due to a circuitous tract, spontaneous closure of the internal opening, or a microscopic internal opening) or to recognize lateral or upward fistula extensions.

- Diligent postoperative care is needed to avoid premature closure of the external component of the fistulotomy wound which can lead to recurrence.
- Long-term recurrence after an advancement flap is about 40 % typically associated with necrosis and flap retraction. A full-thickness rectal flap may assist in preventing ischemic necrosis of the flap.
- Early postoperative complications after fistula surgery include urinary retention, hemorrhage, fecal impaction, and thrombosed external hemorrhoids.
- Late complications include pain, bleeding, pruritus, and poor wound healing.
- Anal stenosis and mucosal prolapse have also been reported.

Special Considerations

Crohn's Disease

- Anal fistula may be the most challenging Crohn's disease manifestation to manage.
- The location of Crohn's disease in the bowel affects frequency of fistula occurrence. Those with rectal disease have the highest fistula incidence.
- A full evaluation of the small and large bowel is done to determine the extent of disease.
- Since many Crohn's-related fistulas are complex, delineation of the fistula tract is important.
- Endoanal ultrasound and MRI have been helpful for evaluation. MRI may detect unsuspected abscesses and determine the relationship of the fistula tract to the sphincter muscles.
- Surgical management of Crohn's fistula may lead to poor and delayed wound healing along with possible sphincter injury.
- A conservative approach has been advocated with antibiotics (metronidazole and ciprofloxacillin) and immunomodulators (corticosteroids, 6-mercaptopurine [MP], azathioprine, and infliximab [or other anti-TNF alpha medications]).
- Treatment with 6-MP and infliximab may prolong the effect of infliximab for fistula closure. Seton placement with infusion of infliximab and then maintenance with azathioprine or methotrexate has been reported to result in complete healing in 67 %. Initial therapy should be aimed at addressing rectal inflammation with topical or oral treatment.
- Primary fistulotomy at the time of abscess drainage is not advocated.
- Asymptomatic fistula requires no treatment.
- For low fistula with simple tracts and no active proctitis, the lay-open technique has been successfully used. However, delayed healing may be seen.
- Factors associated with delayed healing are rectal involvement, anorectal complications (like stricture), and the presence or absence of an internal opening.

- Fecal incontinence has been reported even in patients after drainage of an abscess and with no division of sphincter muscle. This is speculated to be from a noncompliant rectum or diarrhea. Caution at division of any sphincter muscle in these patients is advised.
- For complex high fistula, (prolonged) seton drainage to limit suppuration and preserve anal sphincter function has been advocated.
- Rectal advancement flaps have successfully been used in patients without severe rectal disease. A covering stoma may be considered in these patients, particularly if they have undergone multiple unsuccessful repairs, but does not guarantee success.
- Quiescent intestinal disease has been suggested to improve outcome for Crohn's fistula surgery but has not been conclusively proven.
- Fecal diversion provides temporary improvement in anal fistula disease, but restoration of the fecal stream leads to reactivation of the fistula.
- Fibrin glue and the fistula plug have been variably successful to close Crohn's anal fistula.
- Mesenchymal adipose stem cells have been successfully used to stimulate fistula closure.
- For severe intractable disease, an intersphincteric proctectomy may ultimately become necessary.

Fistula-in-Ano in the HIV-Positive Patient

- Anoreceptive HIV-positive individuals have frequent anal fistula which may begin at the dentate line but end in a blind sinus tract.
- Concern for wound healing has led to caution with surgical intervention.
- Asymptomatic fistulas require no treatment.
- A low CD4+ count may be associated with poor wound healing.
- A 5-day course of preoperative antibiotics has been advocated due to a high risk of infectious complications.
- Care is taken to avoid creation of a large wound and to avoid division of significant sphincter muscle.
- For low fistula in patients who are good operative risks, fistulotomy may be appropriate. An indwelling seton should be considered for patients who are poor operative risks or have a high or complex fistula.
- Metastatic abscesses have been reported in patients with asymptomatic perianal fistula.

Mucinous Adenocarcinoma Arising from a Fistula-in-Ano

- Long-standing fistula-in-ano with chronic inflammatory changes has been associated with the development of carcinoma arising in the fistula tract. This is extremely rare.
- Diagnostic criteria include that the fistula antedates the carcinoma by 10 years, the only tumor should be directly from the carcinoma in the fistula

tract, and the internal opening should be in the anal canal and not into the tumor itself.
- Early diagnosis is difficult.
- MRI is helpful and may show pools of extracellular mucin lined by columns of malignant cells, cords, and vessels which produce a mesh-like structure and the presence of a fistula between the mass and the anus.
- Treatment is abdominoperineal resection, but recent successful treatment with chemoradiation with abdominoperineal resection reserved as a salvage procedure has been reported.

Rectourethral Fistulas

Pathophysiology

- The prostatic urethra is the most common site of rectourethral fistula.
- These may occur following open, laparoscopic, or robotic prostatectomy; radiation treatment for prostate cancer; trauma; perineal abscess from cryptoglandular origin or Crohn's disease; or following radiofrequency treatment for benign prostatic hypertrophy.

Evaluation

Symptoms

- The most common symptoms are urine leakage via the rectum, pneumaturia, fecaluria, or recurrent urinary tract infections resistant to antibiotics.

Investigations

- For patients with a history of prostate cancer, a PSA should be done and recurrence ruled out.
- A digital exam and proctoscopy can visualize the rectal opening and rule out rectal pathology as the source.
- Cystoscopy and retrograde urethral cystography are performed to rule out a urethral stricture.
- Assessment of urinary continence is also done prior to repair.

Operative Treatment

- Operative repair is difficult due to the limited exposure and the first attempt at repair is felt to be the best as subsequent repairs are more difficult.
- Small fistulas, due to rectal injury during laparoscopic or robotic surgery, should be repaired at the time of injury, but persistent fistula may be managed with an indwelling Foley catheter.

- Urethral defects from radiation that are felt to be too large to repair may be treated with a colostomy or ileostomy and urinary diversion (such as suprapubic catheterization). This type of treatment has been associated with recurrent sepsis and persistent symptoms.

Transabdominal Approach

- A transabdominal repair combines a pull-through of bowel with an omental interposition. Closure of the urethral defect may be difficult in the male pelvis.
- A fenestrated splinting catheter covered with omentum has been used when the prostatic defect must be left open.
- Complications associated with this approach include impotence and urethral stricture.

Perineal Approach

- Interposition using the gracilis muscle, dartos, or Martius flap has been described. A rotational flap using the gracilis is the most popular.
- Important principles for this repair include excision of the fistula, development of layers on the urinary and rectal sides of the fistula, and closure or nonoverlapping suture lines with interposition of the levators (when possible).
- The gracilis provides a well-vascularized interface between the urethra and rectum.
- Ninety-seven to hundred percent successful rates of closure have been reported.
- Complications include urinary retention, stricture, and complications associated with the muscle harvest.

Anterior Transanorectal Approach

- Making a midline perineal incision and dividing all structures superficial to the prostatic capsule allow better access to repair the membranoprostatic fistula. This approach is reported to preserve continence and erectile function.

Paranal Approach

- Advancement of full-thickness anterior rectal wall with a diverting colostomy has been reported to successfully close the fistula in 83 % of cases.
- This approach provides limited exposure, but also has minimal scarring and fewer wound infections. Also, future interventions are not compromised if they are needed.
- This approach works best for rectourethral fistula from iatrogenic causes or trauma as opposed to Crohn's disease.

Kraske Laterosacral Approach

- The disadvantages of this approach including excising two to three sacral segments, with nerves, muscles, and ligaments, make this treatment unattractive.

York Mason (Transsphincteric) Approach

- This approach affords excellent exposure and allows complete separation of the urinary and fecal openings. It avoids damage to neurovascular bundles and pelvic floor structures that maintain continence and sexual function.
- It may be performed with a diverting or "medical" colostomy.
- This approach is associated with longer operative times and more postoperative pain.

Transanal Endoscopic Microsurgery

- This specialized technique allows meticulous two-layer closure of the rectal wall.
- Limited experience has been reported using this approach.

Cystectomy and Ileal Conduit

- For patients with a low probability of successful fistula closure or known urinary continence issues, cystectomy and ileal conduit may be the best therapeutic choice.

Reference

Parks AG. Pathogenesis and treatment of fistula-in-ano. Br Med J. 1961;1(1):763–769.

14. Benign Anovaginal and Rectovaginal Fistulas

David A. Etzioni and Ann C. Lowry

Introduction

- Although not life threatening, passing stool and flatus through the vagina is distressing for the patient.
- The lack of a uniformly successful surgical repair for rectovaginal fistula (RVF) is frustrating for the surgeon.

Etiology

- RVF can be acquired or congenital. Acquired is the focus of this outline.
- An obstetrical injury is the most common cause of an acquired RVF. An inadequate repair, breakdown of the repair, or an infection may result in fistula formation commonly 7–10 days after delivery.
- In developed countries, RVF occurs after 0.06–0.1 % of vaginal deliveries.
- In developing nations, the incidence of RVF is three times higher than developed countries, and over half of the fistulas are >4 cm in diameter. These large fistulas are due to prolonged labor with necrosis of the rectovaginal septum.
- Cryptoglandular abscesses that spontaneously drain into the vagina.
- Inflammatory bowel disease (IBD), most commonly Crohn's disease.

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- Operative and nonoperative trauma. Low fistula may result from rectal or vaginal surgery, while high fistulas typically are due to complications of a stapled anastomosis. Other examples: a stapled transanal rectal resection, an ileopouch anal anastomosis, dilatation of a radiated vaginal cuff, fecal impaction, infection in patients with human immunodeficiency virus, and sexual assault.
- Anorectal and gynecologic malignancies either by direct extension, after radiotherapy, with shrinkage of the tissue from chemotherapy, or the use of antiangiogenic chemotherapy.

Evaluation

- Initially confirm the fistula, and then evaluate the anatomy to plan treatment.

History

- A history of anorectal or gynecologic malignancy should prompt a thorough evaluation including prior treatment with radiation therapy. Recurrence will need to be investigated and ruled out.
- Continence should be documented since up to 48 % of patients with RVF can have fecal incontinence preoperatively. If the etiology of an RVF is childbirth, the patient is at a significant risk of having a sphincter defect.
- Bowel function should be documented.
- IBD or concerns that IBD may have caused the RVF should prompt evaluation of the intestinal tract with colonoscopy and radiological studies to allow for preoperative medical optimization and planning.

Physical Examination

- Fluctuance, cellulitis, or any other issues pointing to active infection should prompt an exam under anesthesia with drainage (with or without a seton).
- A mass palpated on exam should prompt a biopsy especially when there has been a history of pelvic malignancy. For patients who have had pelvic radiation, an exam under anesthesia with biopsy may be required if a thorough evaluation is not possible in the clinic.
- On digital exam, a palpable dimple in the anterior midline may represent the rectal opening of the RVF.
- Multiple perineal fistulas suggest Crohn's disease.
- If the rectal opening cannot be appreciated on digital exam or seen with anoscopy, a methylene blue test may be helpful. In the prone position, a tampon is placed in the vagina, and 20–30 cc of dilute methylene blue is instilled in the rectum. Staining on the tampon is diagnostic of RVF.

- Alternatively, in the lithotomy position, saline is instilled in the vagina and air injected per rectum. The vagina is observed for bubbles.
- The sphincter function should also be assessed.

Radiography

- There is no clear "best" radiologic test to detect an elusive fistula.
- Vaginography is most helpful in identifying a colovaginal or enterovaginal fistula. A balloon-tipped catheter is placed in the vagina and the balloon inflated to occlude the vagina. Contrast is instilled in the vagina. This test may not demonstrate a low RVF as the vaginal opening may be covered and occluded by the balloon.
- Computed tomography (CT) performed using oral and rectal contrast may delineate the fistula and characterize the surrounding tissue. Fluid or air in the vagina is suggestive of an RVF.
- Magnetic resonance imaging (MRI) and endorectal ultrasound may also be useful to identify the fistula. Additionally they have a role in evaluation of the anal sphincter muscles particularly in patients with an obstetric-related RVF.
- CT, MRI, and endosonography also can be used to rule out ongoing sepsis.

Classification

Fistula Height

- Low fistulas have their rectal opening at the dentate line and the vaginal opening just inside the vaginal fourchette. Typically, surgical repair can be performed via a perineal approach.
- Middle RVFs are located between high and low RVF.
- High RVFs have a vaginal opening near the cervix, and repair typically requires an abdominal approach.
- True RVFs have their bowel opening at or above the dentate line.
- Anovaginal fistulas have a rectal opening distal to the dentate line.
- Most fistulas involving a communication from the bowel to the vagina or perineum are referred to as RVF perhaps incorrectly. For simplicity in this outline, all fistulas will be cited as RVF (RVF).

Simple vs. Complex Fistulas

- *Simple fistulas* are <2.5 cm in size, located distally along the rectovaginal septum and secondary to trauma or infection.
- *Complex fistulas* are large in size, located high along the rectovaginal septum, caused by IBD, radiation or malignancy, or persistent after failed repair(s).
- *Simple fistulas* may be amendable to local repairs, while complex fistula may require resection or interposition possibly with fecal diversion.

Surgical Management

General Considerations

- The patient preoperatively performs mechanical bowel preparation, and antibiotics are administered just before the surgical incision.
- Usually the repair is done with general anesthesia although regional may be appropriate.
- A Foley catheter is placed. For transanal and perineal approaches, the prone position is chosen. For vaginal approaches, the lithotomy approach is chosen.
- Appropriate lighting (may require a headlight) and retractors (Lone Star, Pratt bivalve, Fansler, Wylie renal vein retractor, narrow Deaver, and malleable retractor) should be available.

Fistulotomy

- In very select and very low fistula involving no sphincter muscle, a simple fistulotomy may be appropriate.
- Fistulotomy is avoided if there is any concern this unroofing the fistula could lead to fecal incontinence.

Fibrin Sealant

- Success has been reported in small studies by instilling fibrin glue in the fistula tract or under a mucosal advancement flap.
- The risk to surrounding structures and success rates are low.

Mucosal Advancement Flaps

- Can be done from the transanal or vaginal approach. The anal approach is intuitively preferable since that repair is on the high-pressure side of the fistula (Fig. 14.1).
- Postoperatively patients are given a normal diet and fiber supplements. Constipation and diarrhea should both be avoided using medical management. Patients should abstain from intercourse and using tampons for 6 weeks.
- The transvaginal repair—technique:
  - A vaginal flap is raised starting near the introitus.
  - The flap is developed laterally to the ischial tuberosities for adequate mobility.
  - The rectal defect is closed with absorbable sutures.
  - The levator ani muscle is approximated in the midline. This maneuver is felt to be critical for success.
  - The vaginal flap is secured with absorbable sutures.
- Another variation for a flap repair is a retrograde anocutaneous flap, used for very low fistula. A flap of anoderm and perineal skin is raised, advanced into the anal canal, and sutured in place.

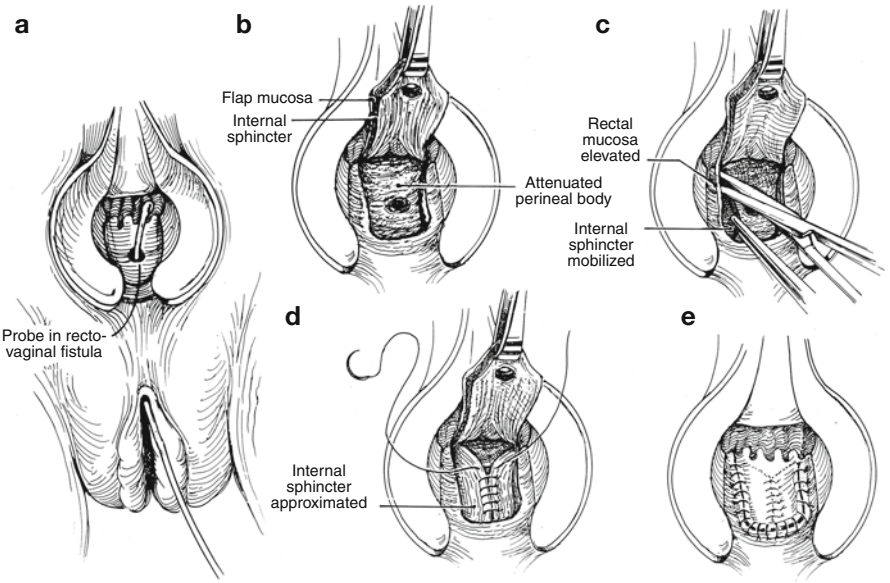

Fig. 14.1 Endorectal advancement flap. (**a**) The patient is placed in the prone position. (**b**) A U-shaped flap of mucosa, submucosa, and internal sphincter is raised. (**c**) The dissection is usually 4–5 cm cephalad to allow a tension-free repair. The base should be two to three times wider than the apex to prevent ischemia. (**d**) The fistula tract is debrided (not excised) and the muscles reapproximated with one to two layers of long-acting absorbable sutures. (**e**) The distal end of the flap with the fistula is excised, and the flap is sutured in place. The vaginal side is left open for drainage

- In the literature, success rates for advancement rectal flaps range from 29 to 100 %. Disturbances in continence range from 21 to 40 %.
- In an effort to improve success, transposition of labial fat beneath an endorectal advancement flap was done. However, no improvement in successful fistula closure was found.
- Transanal endoscopic microsurgery (TEM) has been used to facilitate repair with success in small studies.
- Smoking has been linked to unsuccessful closure of fistula when using advancement flaps.

Fistulectomy with Layered Closure

- Excision of the fistula and closure of the tract in layers can be done via the rectum, vagina, or perineum.
- Transanally, an elliptical excision is made to core out the fistula, and 2–3 cm mucosal flaps are raised. Vaginal mucosa, rectovaginal septum, rectal muscle, and rectal mucosa are closed in successive layers. Plication of the levator muscles can be added.
- For a perineal approach, a transverse incision is made between the anus and vagina. The incision is deepened until the tract is encountered.

The tract along with the openings in the rectal and vaginal walls is excised. The wound is closed in layers.

- In a small series, success with these approaches has been reported in 88–100 %.

Rectal Sleeve Advancement

- Circumferential mobilization of the distal rectum with advancement to cover the anorectal side of the fistula is reserved for fistula associated with an anal stricture or disease in the proximal anal canal/distal rectum.

Technique

- The patient is prepared as for the endorectal advancement flap.
- Starting at the dentate line, a circumferential incision is created that deepens through mucosa and submucosa but not through the internal sphincter. The dissection is continued cephalad becoming full thickness above the anorectal ring.
- Dissection is continued until healthy nonscarred tissue can be pulled down to the dentate line without tension.
- The diseased distal end is trimmed, and the healthy tissue is sutured to the anoderm.
- One reported variation in treating recurrent RVF is to perform this repair using the Kraske approach.
- Another variation is the Noble-Mengert-Fish technique. A 180° full-thickness anterior rectal wall flap is mobilized cephalad to the vaginal vault. The lateral margins are the full width of the rectovaginal space. The flap must reach the external sphincter muscle without tension. Success rates have been documented between 86 and 100 % with minor incontinence in 25 %.

Sphincteroplasty and Perineo-proctotomy

Sphincteroplasty

- For this procedure, a probe is inserted through the fistula, and it is unroofed converting the anatomy to a fourth-degree laceration. Then a layered anatomical repair is done.
- If there is a defect in the external sphincter muscle, this repair obliterates the fistula while repairing the muscle.
- Successful closure is reported for 65–100 % of patients.

Perineo-proctotomy

- When there is an intact sphincter muscle, this repair is termed a perineo-proctotomy. When the fistula is unroofed, the sphincter is divided. Figure 14.2 describes and illustrates the procedure.

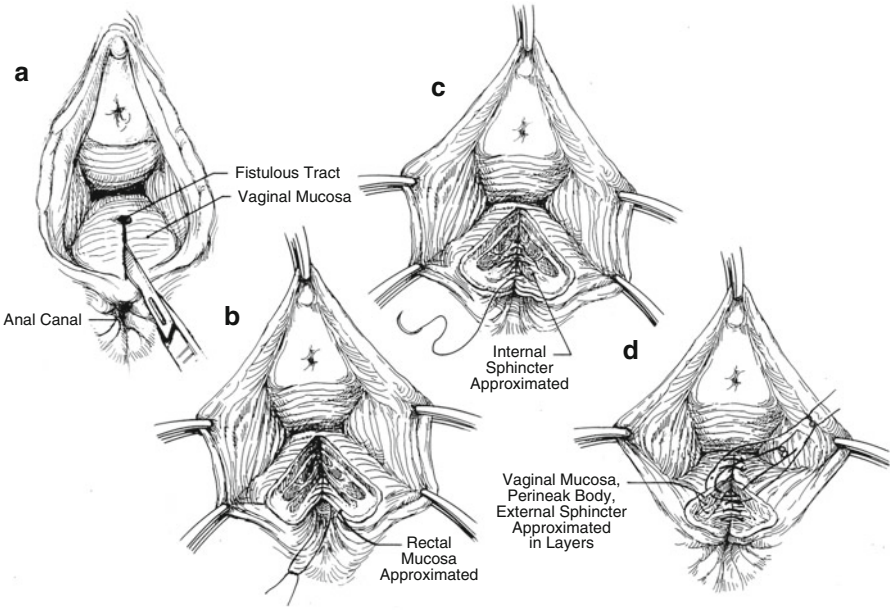

Fig. 14.2 Perineo-proctotomy. (**a**) For a perineo-proctotomy, there is intact sphincter muscle. The fistula is still unroofed to create a defect like a fourth-degree obstetrical laceration. (**b**) The tract is excised, and the vaginal and rectal walls are dissected away from the sphincter muscle. The rectal mucosa is approximated. (**c**) The internal sphincter muscle is sutured together. (**d**)The external sphincter muscle and then the vaginal mucosa are reapproximated. The perineal body is reconstructed and the skin closed

- The deliberate division of an intact sphincter muscle should be approached with caution (the perineo-proctotomy) as the impact on continence has not been well studied. Success rates have been reported from 87 to 100 %.

Inversion of Fistula

- Usually performed through the vagina, the vaginal mucosa around the fistula is mobilized and the tract is excised. A purse-string suture is used to invert the fistula into the rectum. The vaginal wall is closed over this inverted tissue.
- Ligation of the intersphincteric fistula tract (LIFT) uses a similar technique. An intersphincteric dissection is carried out, and the fistula tract is identified and divided. The openings on the rectal and vagina side are ligated and the wound closed. Success rates of 60–94 % have been reported.
- Patients with a complex transsphincteric fistula and an intact sphincter may be the best candidate for the LIFT.

Tissue Interposition

General Considerations

- Tissue interposition allows well-vascularized tissue to be placed between the vagina and rectum. Sources include rectus, bulbocavernous, gracilis, gluteus, and sartorius muscle.
- The perineal dissection is similar for all types of interposition. Dissection in the rectovaginal septum allows separation of the posterior vaginal wall from the anal sphincter and distal rectum. This dissection is carried cephalad until soft pliable tissue is reached. Dense scarring can make the dissection difficult. Injection of saline in the rectovaginal septum may help facilitate the separation and avoid inadvertent entry into the rectum.
- The rectal and vaginal openings are closed with absorbable sutures. Trimming the openings is generally not needed and only makes the hole larger.
- The mobilized muscle is rotated and inserted between the rectum and vagina and secured in place. The incision is closed loosely over a (closed) suction drain.

Labial Fat Pad or Bulbocavernous Muscle

- The mobilized labial fat pad is known as the Martius flap. In the lithotomy position after the above perineal dissection is performed, a longitudinal incision is made over the labia majora, and skin flaps are generously raised laterally.
- The fat beneath the flaps is encompassed and freed from the periosteum of the pubis posteriorly working superiorly to the pubic symphysis.
- When the entire fat pad with the bulbocavernous muscle is mobilized, to provide maximal length, the anterior end is divided as close to the pubic symphysis as possible. This preserves the posterior pedicle (with the perineal branch of the pudendal artery).
- A generous tunnel is made from the base of the pedicle to the perineal incision, and the flap is rotated through the tunnel into the perineum.
- The flap is sutured to the posterior wall of the vagina ensuring that it reaches cephalad to the closed fistula site. The labial and perineal incisions are closed (Fig. 14.3).
- If vaginal stenosis is a concern, inclusion of an island of inner thigh skin with the pedicle can be added.
- Success for this technique is reported to be 78–84 %.

Bioprosthetics

- Placement of a bioprosthetic sheet composed of porcine intestinal submucosa has been laid transperineally to separate a rectal and vaginal fistula repair. Also this material has been rolled as a “plug” inserted into the RVF tract.

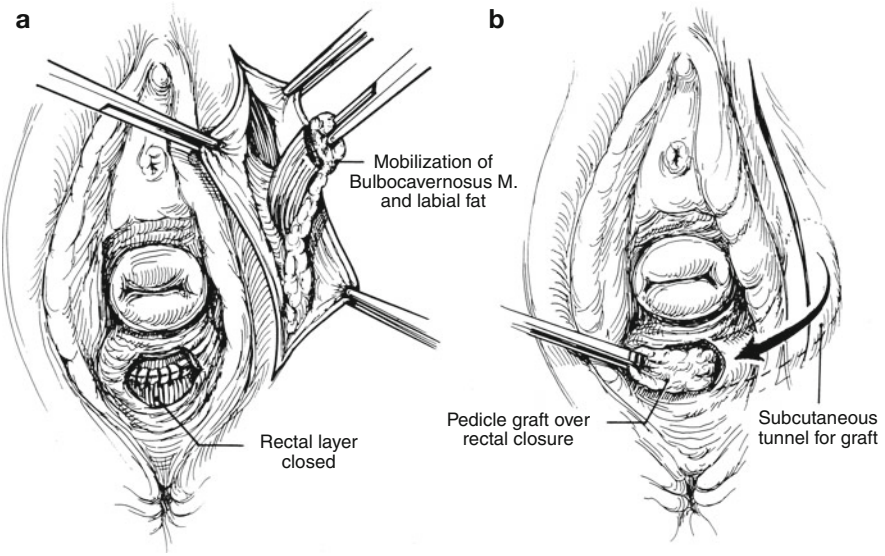

Fig. 14.3 (**a**) Martius graft: perineal dissection and mobilization of the graft. (**b**) Martius graft: interposition of the labial graft

- Use of this material is technically straightforward and avoids injury to the sphincter mechanism. Additionally the plug avoids dissection in the perineum.
- Success using either of these approaches is uncertain.
- A specially designed bioprosthetic plug specifically constructed for RVF has been used with a success rate of perhaps 30–50 %.

Muscle

- The gracilis muscle is the most commonly used muscle for interposition to obliterate a RVF.
- Success rates of 75–83 % have been reported using the gracilis, with healing less likely to occur in Crohn's disease.
- Rectus, sartorius, and gluteal muscles have been successfully used and reported in small series.
- Fecal diversion is routinely performed for muscle interposition.
- Drawbacks of this procedure are the morbidity associated with the mobilization of the pedicled muscle flap and that a more extensive perineal dissection in the rectovaginal septum is required to accommodate placement of the bulky muscle.

Bowel

- The Bricker procedure is an onlay patch of sigmoid colon.
- Through an abdominal incision, the fistula is divided and the sigmoid colon is mobilized and divided proximally.

- The distal end is looped back into the pelvis and sutured as an end of colon to side of rectum (over the fistula in the rectum) anastomosis. The proximal colon is anastomosed to the looped area in the mid-sigmoid to restore intestinal continuity. Fecal diversion is used until healing is verified with a contrast enema.

Resection

- In some instances, resection of the rectum with repair of the vagina and a low colorectal or coloanal anastomosis can be done. When possible, omentum is used to separate the vaginal defect from the new anastomosis.
- One variation described by Parks involves a sleeve coloanal technique. The rectum is mobilized and divided below the fistula. A transanal mucosectomy is done. The vagina is repaired. The healthy colon is pulled through the anus covering the fistula repair. Then a hand-sewn coloanal anastomosis is constructed along with proximal diversion.
- Technical success is reported in 78–100 % with complete continence at l year reported in one study to be 75 %.

Choice of Treatment

- Not all RVF require surgical treatment. Small fistula with minimal symptoms may only require medical management.
- Obstetrical-related fistula may spontaneously close during 6–9 months following delivery. Optimization of bowel function, most importantly controlling diarrhea may improve success.
- If the symptoms are intolerable, surgical treatment is required.
- Fibrin glue or a fistula plug are reasonable choices in low, small fistula. While their success rates are unproven, these procedures are well tolerated, carry minimal risk, and do not impede future efforts at repair.

Rectovaginal Fistulas Secondary to Obstetrical Injury

- If an obstetrical RVF does not close within 6–9 months, surgical repair is considered.
- Surrounding tissue must be soft and free of sepsis before attempting surgical repair. This may require debridement with or without a draining seton.
- Symptomatic women do not need to delay repair until after completing their childbearing, although a subsequent pregnancy after successful closure should be delivered by C section.
- An important consideration is assessment of the anal sphincters looking for a defect. In some series, 100 % of patients had a sphincter defect associated with the RVF.

- A sphincteroplasty addresses the defect and repairs the fistula simultaneously. Additionally, this technique provides excellent exposure.
- For women with an intact sphincter and obstetric-related RVF, an advancement flap or layered fistulectomy is recommended as the initial approach.
- The next step if the flap fails would be an interposition perhaps utilizing a Martius flap.
- Perineo-proctotomy or a sleeve advancement flap is considered after multiple failed repairs. Preoperative fecal diversion should be strongly considered in these complex recurrent cases.

Rectovaginal Fistulas Secondary to Cryptoglandular Disease

- These fistulas are rare.
- Local sepsis must be controlled and the patient evaluated for an occult sphincter defect.
- In the absence of a sphincter defect, an endorectal advancement flap, fibrin glue, or a fistula plug are reasonable treatments.

Rectovaginal Fistulas Secondary to Crohn's Disease

- In patients with Crohn's RVFs, control of symptoms is the primary goal vs. elimination of the fistula.
- The initial treatment is to control sepsis followed by medical management with antibiotics and immunosuppressive medication.
- Infliximab (antitumor necrosis alpha) has demonstrated efficacy in healing Crohn's RVF.
- With infliximab treatment, radiologic healing is lower than clinical healing, and long-term healing is unknown. Drainage of local sepsis and placement of a seton before starting medical treatment improves results. The seton must be removed before the completion of the infliximab course if the goal is complete healing.
- When proctitis has been controlled with medical management, surgical intervention and repair follows the same guidelines as considered for obstetrical RVF except division of sphincter muscle (perineo-proctotomy) is typically avoided. Fecal diversion in this group is controversial, but generally used.
- Most reports of healing with an advancement flap predate the introduction of infliximab and range from 30 to 92 %.
- For patients with refractory rectal disease, long-term use of a draining seton can be considered. If symptoms are still troublesome, a proctectomy and permanent stoma may be the best option.
- In a few patients with a long-term RVF, anal stricture, and active colitis, malignancy has been reported.

Rectovaginal Fistula Secondary to Malignancy

- Treatment of RVF secondary to malignancy is dictated by the treatment for the primary malignancy.
- Fecal diversion may be indicated prior to treatment for patient comfort.
- When resection with anastomosis is performed, interposition with tissue such as omentum or rectus muscle between the vagina and anastomosis may prevent postoperative fistula (especially in the face of a pelvic abscess or anastomotic leak).
- A RVF associated with squamous cell carcinoma may require diversion for symptom control during chemoradiation treatment.
- After complete resolution of the tumor if the fistula persists, repair with interposition of bulbocavernous or gracilis muscle can be considered. It is important to delay repair to allow the acute radiation effects to subside. Local repair is typically not successful in the irradiated field.

Rectovaginal Fistulas Secondary to Radiation Therapy

- A thorough evaluation for recurrent tumor is done for RVF due to radiation therapy. This may need to be carried out in the operating room with multiple biopsies.
- Fecal diversion is strongly considered to allow inflammation in the surrounding tissue to resolve.
- Decisions regarding surgical repair center on the patient's overall medical condition, the degree of symptoms from the fistula, associated abnormalities, and the risk of the proposed surgery to repair the RVF.
- Sometimes a permanent colostomy is the best choice particularly if the patient has significant fecal incontinence.
- Without interposition of healthy nonirradiated tissue into the fistula tract (gracilis muscle, Martius flap, rectus muscle, or Bricker procedure), the likelihood of successful fistula closure is low.
- Stricture or severe radiation proctitis may require proctectomy with nonirradiated colon introduced as a neorectum.

Iatrogenic Rectovaginal Fistula

- RVF after a proctectomy nearly always arise at the anastomosis. These can occur after both hand-sewn and stapled anastomosis.
- It is important to ensure that no posterior vaginal wall is trapped in the EEA stapler before firing it to perform the anastomosis.
- The first step in treatment of an RVF is to control local sepsis which may require fecal diversion and/or drainage.
- Repair depends on the location. Low fistula may be suitable for rectal or vaginal advancement flaps or a transperineal repair with interposed bioprosthetic material or muscle.

- High fistulas require repeat resection with anastomosis or interposition of omentum or muscle.
- Large fistula or those failing previous repair usually require tissue interposition.

Persistent Rectovaginal Fistula

- After an unsuccessful attempt at a repair, a repeat repair is reasonable but the success rates appear to be reduced. Therefore, subsequent options should be carefully chosen.
- It is important to tailor the surgical approach to the patient and the tissue.
- Transperineal placement of bioprosthetic material (porcine intestinal submucosal biologic mesh) in recurrent RVF has been reported to have over a 70 % success rate.
- From data available, a reasonable approach for recurrent RVF involves initial conservative treatment ensuring all sepsis is drained and assessing the integrity of the anal sphincter muscles.
- For low recurrent RVF with an intact sphincter muscle and one to two previous repairs, an advancement flap or rectal sleeve advancement would be appropriate.
- Fibrin glue is a safe alternative treatment, but little data exists regarding the chance of a successful outcome in this situation.
- If there is a defect in the sphincter muscle, sphincteroplasty or perineoproctotomy is appropriate.
- If the sphincter is intact, but there have been >2 failed repairs, interposition should be considered. The choice of technique depends on the surgeon's experience, but bulbocavernous muscle is the least morbid muscle interposition technique. There is no comparative data regarding outcomes of various interposition methods.
- Fecal diversion is not mandatory but likely increases the chance of a successful repair, especially in patients with Crohn's disease.
- Recurrent RVF located in the mid-vagina nearly always requires tissue interposition. The choice of muscle to interpose depends on the fistula level and the patient's body habitus.
- The bulbocavernous muscle may not reach a fistula in the upper/mid-vagina in an obese woman, and the gracilis is a good alternative.
- High fistulas require a transabdominal approach with resection or tissue interposition.

Conclusion

- The literature regarding RVF lacks uniform terminology, standard evaluations, and comparative studies.
- Since RVFs are diverse with multiple etiologies and varying anatomy, improving the quality of research will be challenging.

15. Pilonidal Disease and Hidradenitis Suppurativa

Harry T. Papaconstantinou and Thomas E. Read

Pilonidal Disease

Background and Incidence

- Pilonidal disease is a subcutaneous infection in the upper half of the gluteal cleft.
- The acute form is an abscess.
- The chronic form is a sinus that is an indolent wound resistant to healing.
- Pilonidal disease is most commonly found in young adults, with increased body hair, in their 20's.
- Men outnumber women 3–4 to 1.
- Occupations associated with the development of pilonidal disease include those in the military, hairdressers, and sheepshearers.
- Possible predisposing factors include obesity, being a vehicle driver, a sedentary occupation, a history of a furuncle at another site on the body, a deep natal cleft, and a positive family history.
- The actual incidence is unknown but reported to be 0.7 % in adolescents and 26 per 100,000 in all ages.
- Pilonidal is not really a "cyst" as no epithelialized wall exits in the cavities this disease creates.

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Pathogenesis

- Experience suggests this is not a congenital disease but rather acquired since it occurs in young, hirsute men, and more frequently in certain occupations such as the hands of barbers and sheep shearers.
- However, no current theory has been accepted or refuted.
- Common features in pilonidal disease:
  - There are midline pits in the natal cleft referred to as primary openings.
  - The pit may extend into subcutaneous fibrous tracts called a pilonidal sinus. The pilonidal sinus may connect to a secondary opening.
  - The secondary opening is located off the midline and characterized by drainage of purulent and serosanguineous fluid with granulation tissue and hypertrophy of epithelium surrounding the opening.
  - Hair is often seen extruding from the primary opening.
  - The pilonidal sinus may be single, multiple, short, or long. Over 90 % extend cephalad.
  - If a pilonidal sinus extends caudad, the secondary opening may resemble a fistula-in-ano.

Clinical Presentation and Diagnosis

- *Acute pilonidal abscess* is a tender fluctuant subcutaneous mass with surrounding cellulitis located off the midline of the natal cleft. The onset is rapid and may be associated with severe pain.
- *Chronic pilonidal sinus* has primary pits in the midline natal cleft 4–5 cm cephalad to the anus. There may be a secondary opening cephalad and off the midline. The openings may have hair extruding from them.
- *Complicated pilonidal sinus* is found in patients with long-standing disease and multiple sinus tracts. There may be partially drained abscesses. Occasionally this process can extend laterally into the gluteal region.
- *Recurrent pilonidal disease* occurs in patients who have undergone different surgical procedures and have a persistent wound from the surgical procedure which has failed due to technical issues or recurrent disease.
- The differential diagnosis of pilonidal disease includes hidradenitis suppurativa, fistula-in-ano, actinomycosis, and syphilitic or tuberculous granulomas.
- Patients with chronic draining sinus wounds and/or failed surgical procedures may have osteomyelitis.

Treatment

- No treatment is universally satisfactory and is determined by the initial presentation of the disease.

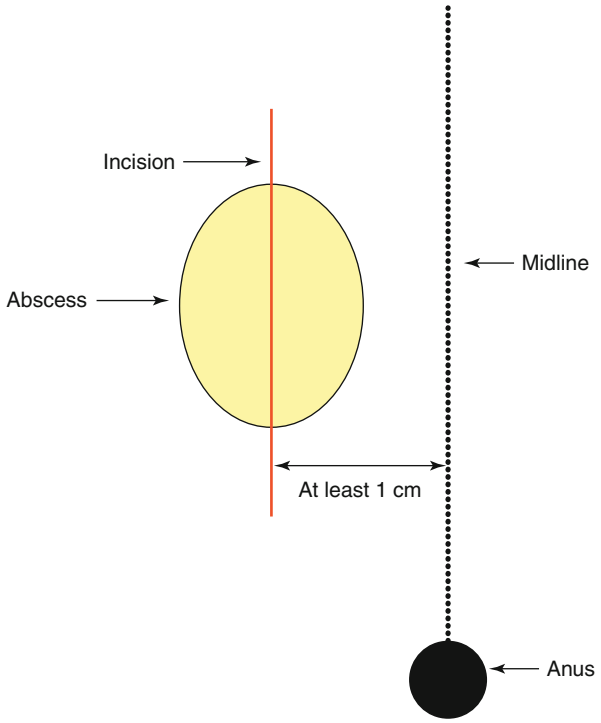

Fig. 15.1 Incision and drainage of an acute pilonidal abscess. An incision is made parallel to the midline at least 1 cm laterally. A small ellipse of skin is removed to prevent the wound edges from sealing and the abscess reforming. Packing is avoided

- Goals of treatment are complete resolution of pilonidal disease with low recurrence and low morbidity. Additionally the ideal treatment would have a short or limited hospital stay, allow fast return to normal activity, and be cost-effective.

Acute Pilonidal Abscess

- All abscesses must be incised and drained either in the office or emergency room. This can be done under local anesthesia (Fig. 15.1).
- Packing the wound is avoided as it interferes with drainage and healing.
- Sitz baths or a handheld shower is used two to three times daily to clean the wound.
- Antibiotics are only necessary in patients with diabetes, prosthetic implants, diseases leading to the patient being immunocompromised, and significant cellulitis.
- Wound checks are done every 1–2 weeks and include shaving all hair within 2 in. of the entire gluteal cleft (on both sides of the gluteal cleft for 2 in.).

- After healing, recurrence occurs in 50 % and presents as another abscess or a chronic pilonidal sinus.

Chronic Pilonidal Sinus

- Chronic pilonidal sinuses have no acute inflammation and may have primary and secondary visualized openings. The sinus tract connects the openings.
- Treatment is nonoperative or operative depending on the patient's preference and extent of disease.

Nonsurgical Approach

Hair Removal

- Shaving alone has been advocated as an alternative to surgery. Though studies looking at shaving have demonstrated healing, but flaws exist in these studies. Shaving can improve rates of pilonidal sinus healing.
- Hair removal may be an effective therapy in chronic pilonidal sinus disease, but the duration of shaving to prevent recurrence is unknown. Shaving should be continued at least until complete healing has occurred.
- Laser depilation of the natal cleft may also aid in healing a pilonidal sinus.

Surgical Approaches

- Many approaches have been advocated when performing surgery for pilonidal disease including incisional and excisional, with or without primary closure of the resultant wound.
- Wide excisional techniques have fallen out of favor, and minimal surgical procedures are preferred.

Midline Excision

- The most common operation is midline en bloc excision with or without primary closure of the entire sinus.
- Studies suggest that excision with primary closure decreases healing time; however, closing the wound may lead to increased wound complications and recurrence of the pilonidal disease. Prophylactic antibiotics are not necessary.
- Compared to past recommendations, limited excision is currently favored as it creates smaller wounds.

Unroofing and Secondary Healing

- Unroofing the sinus and curettage leaves a smaller wound. Unroofing is associated with half the healing time of wound excision, but still requires dressing changes and wound care.

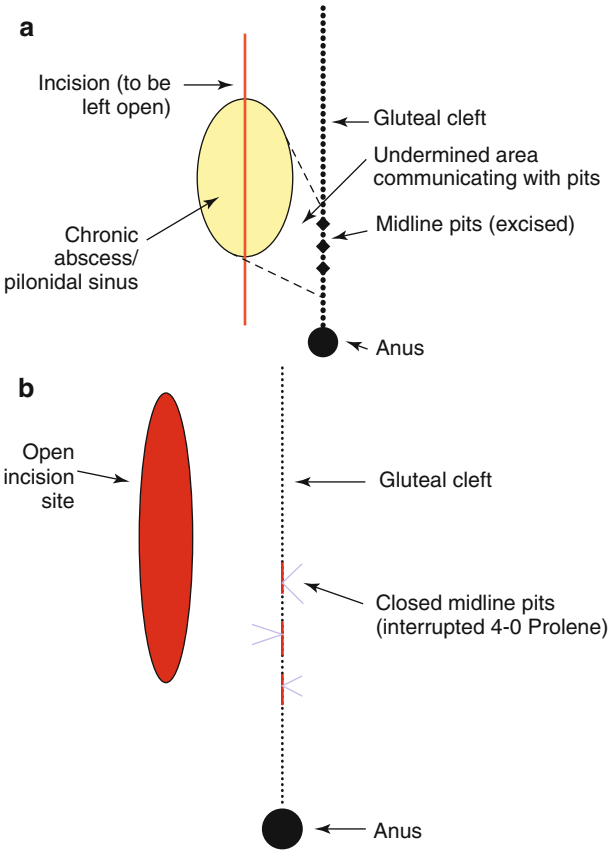

Fig. 15.2 The Bascom procedure: (**a**) A generous vertically oriented incision is made through the abscess cavity 1 cm off the midline. The wound is curettaged to remove the hair and debris. The fibrous sinus tract or abscess wall is left in place. The connecting tracts to the midline pits are identified, and the overlying skin is undermined so that they drain to the site of the incision. The midline pits are excised using a small diamond-shaped incision to remove each of them. (**b**) The undermined flap of skin is tacked down and the pit excision sites closed

- Marsupialization of the skin edges to the fibrous tract may decrease the wound surface.
- Hair removal is an important adjunct for healing.

Bascom's Chronic Abscess Curettage and Midline Pit Excision (Bascom I)

- The Bascom technique focuses on changing the conditions of the gluteal cleft versus excising a large amount of normal tissue in the diseased area (Fig. 15.2a–b).
- Meticulous shaving is performed weekly either at the doctor's office or by a trained family member or friend until the wound is healed.

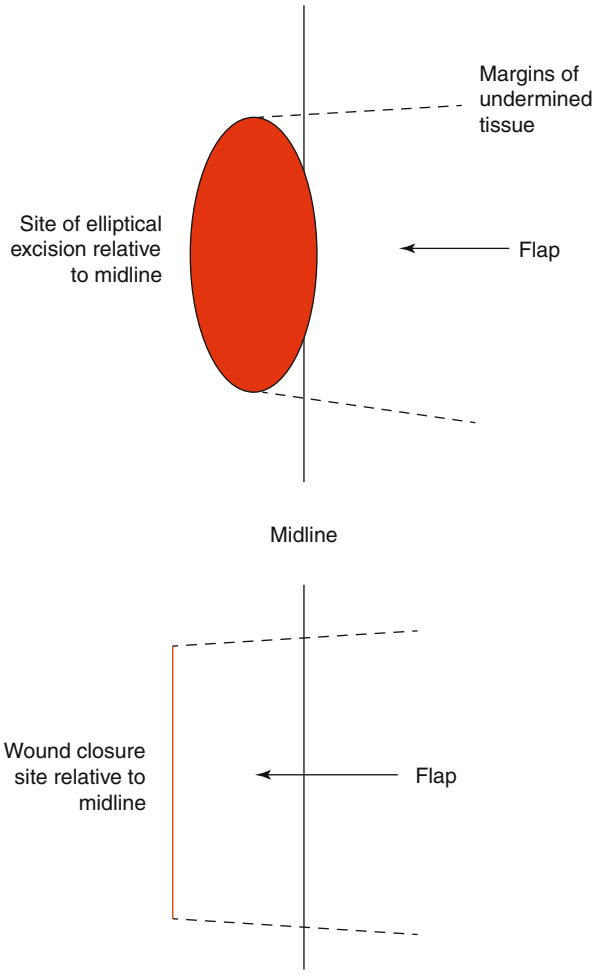

Fig. 15.3 The Karydakis procedure. The upper portion of the figure illustrates the elliptical incision that is parallel and 1 cm from the midline. The skin and gluteal fat containing the pilonidal sinus is excised down to the sacral fascia. The lower portion of the figure shows that the subcutaneous flap which is mobilized such that it can be advanced across the midline to the opposite side. The flap is sutured to the sacral fascia and the skin is closed. The incision will be lateral to the cleft

Karydakis Procedure (Advancing Flap; Fig. 15.3)

- A drain is always placed at the upper end of the wound for 2–3 days. Antibiotics are not routinely used.
- The goals as shown in Fig. 15.3 involve eccentrically excising the diseased midline tissue. The surgical wound is laterally displaced out of the midline gluteal cleft.

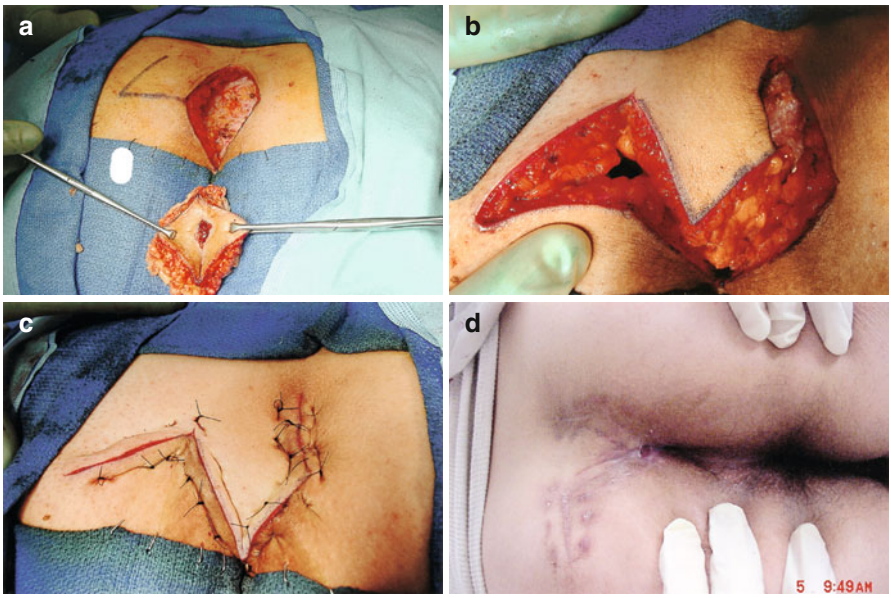

Fig. 15.4 The Rhomboid flap technique for recurrent pilonidal disease. (**a**) Initial excision of the sinus cavity. Counter incisions are created as shown. (**b**) Flaps are raised and maneuvered as shown to close the defect. (**c**) Final surgical result. (**d**) Result 1 month postoperatively

- Studies show that this procedure is successful with a low complication and recurrence rate. This procedure should be considered for recurrent or complex cases.

Recurrent or Complex Pilonidal Sinus

- Patients who have failed conservative measures or standard surgical procedures may require excision of the pilonidal sinus combined with a flap closure and modification of the midline natal cleft.

Surgical Approaches

Rhomboid Flap

- The rhomboid flap (also called Limberg) is a cutaneous rotational flap used to fill the soft tissue defect (Fig. 15.4a–d).
- Drains have been used to prevent a seroma or deep wound space infection, but one study showed that drains did not improve outcome and hence not routinely used.
- Collectively studies show that this technique is reliable, can be quickly performed in the operating room, and is associated with low

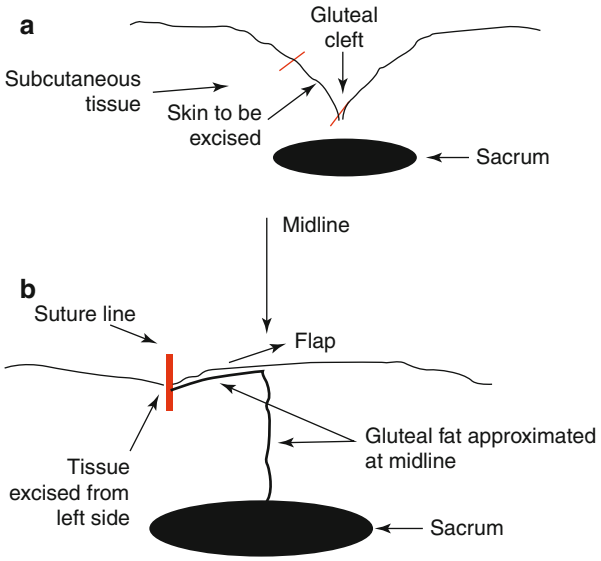

Fig. 15.5 The Bascom Cleft Lift. (**a**) The skin of the gluteal cleft is detached from the underlying subcutaneous tissue as a flap. A portion of the flap containing the diseased skin and pits is excised from the side of the buttock with which the flap will be sutured. (**b**) The flap is pulled across the midline, and the subcutaneous tissue is approximated underneath the flap obliterating the gluteal cleft. Any open chronic wounds or sinus cavities are curetted out but not excised. The raised skin flaps cover the prior wound sites in addition to coapting the normal gluteal flap. The final suture line lies parallel to but well away from the midline and is tension-free

complications and recurrence. This technique may also be superior to midline excision with primary closure.

- Flap coverage should be considered for wounds in the gluteal cleft that have failed to heal over a prolonged period of time.
- Disadvantages are that it excises a large amount of normal tissue and creates a large scar at the flap site.
- If abscesses are located far laterally or cephalad to midline pits, the size of the flap required to cover the area may be very large and an alternative surgical treatment may be considered.

Bascom Cleft Lift (Bascom II)

- This is the most technically challenging technique.
- The only tissue that is excised is a portion of the skin, i.e., normal subcutaneous tissue is not excised.
- The goal of the procedure is to undermine and completely obliterate the gluteal cleft in the diseased area (Fig. 15.5).

- Dr. Bascom reports spectacular results for this procedure; however, it remains for others to duplicate the results.

V-Y Flap

- Flaps slide along their long axis to provide healthy tissue to wounds. The size of the flap and volume depend on the arterial input and venous drainage, not length-to-breadth ratio.
- The V-Y advancement flap maintains blood supply from the fascia (so division of these vessels should be avoided).
- This method has been reported to provide satisfactory results but is a demanding procedure. Therefore simpler procedures should be considered first and this technique reserved for failure (such as failure of the rhomboid flap).

Z-Plasty

- The diseased tissue is excised, and the natal cleft can be then obliterated with a Z-plasty reconstruction.
- The limbs are fashioned at 30–45° angles to the wound axis. Full-thickness subcutaneous skin flaps are raised transported and the skin edges sutured.
- Studies show that this technique may be superior to the midline excision technique.

Myocutaneous Flaps

- This technique is reserved for the most severe cases, usually after failure of multiple simpler techniques. This technique creates a large, extensive defect at the harvest site for the flap used to perform the reconstruction.
- This technique can also lead to significant debilitation when the harvested area is from the gluteal muscle.

Skin Grafting

- Excision and split-thickness skin grafting after excision is infrequently used for recurrent pilonidal disease.
- This technique requires prolonged hospital stay for wound care.

Summary

- Pilonidal disease can present with a spectrum of problems, symptoms, and physical findings anywhere along the continuum of this disease.
- The cornerstone of all treatment is wide meticulous shaving and hygiene.
- Ritualistic weekly shaving is mandatory until healing is complete.
- Figure 15.6 provides an overview of the algorithm presented.

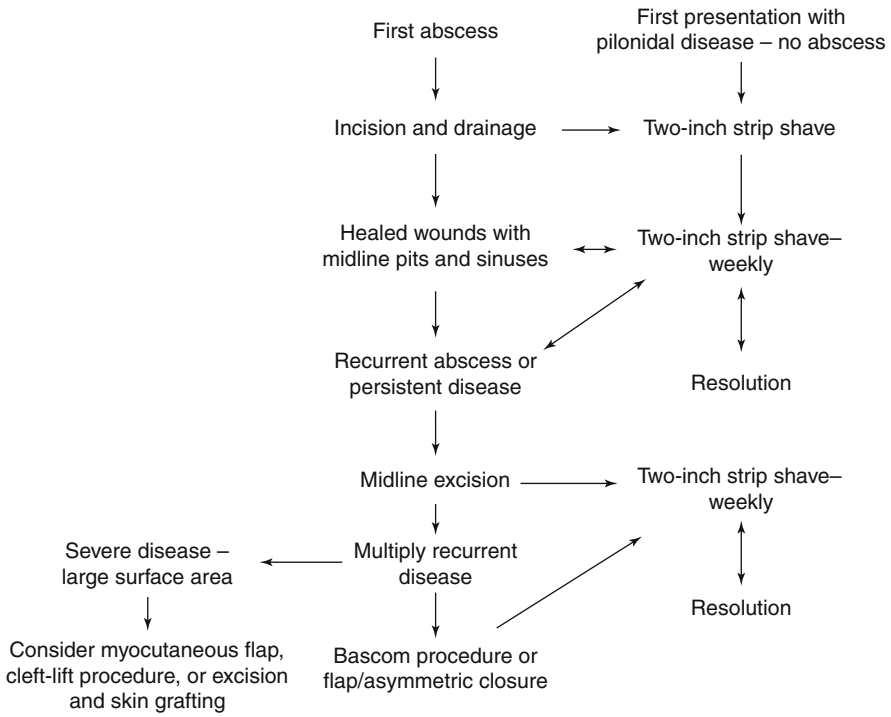

Fig. 15.6 Pilonidal disease algorithm

Hidradenitis Suppurativa

Background

- Hidradenitis suppurativa is a cutaneous condition typically seen in young people, with cyclic periods of flares and quiescence.
- There can be a spectrum of problems including abscess, severe contracted scarring, disability, and even malignancy.
- Apocrine glands may play a role in this disease.
- Commonly located in the perineum, axilla, and groin, this disease can also be found in the inguinal and mammary regions.

Incidence and Etiology

- Perhaps 1/300 people are affected in some way with hidradenitis suppurativa.
- African-Americans are affected more often than Caucasians.
- Perianal disease is twice as common in males. Perianal disease appears to recur less frequently after surgical treatment.
- Hidradenitis in all locations occurs more commonly in females and African-Americans.

- Nearly all patients present after puberty in their 20 and 30's.
- Androgen excess and decreased progesterone levels have been found in affected people suggesting the influence of hormones in this disease.
- Predisposing factors seem to be obesity, tobacco use, acne, stress, poor skin hygiene, excessive sweat, hyperhidrosis, and chemical depilatories.

Bacteriology

- While wound cultures have grown a variety of organisms, *S. epidermidis* and *Staphylococcus aureus* are the most commonly isolated organisms.

Pathophysiology

- Occlusion of hair follicles typically in skin that contains apocrine sweat glands appears to result in hidradenitis suppurativa. However, the involvement of the apocrine glands appears to be secondary.
- Dilation and rupture of the hair follicles into the dermis leads to dermal infiltration by inflammatory cells, giant cells, and formation of sinus tracts and fibrosis.
- The apocrine glands secrete fluid into the hair follicle and have an unknown function.
- Obstruction of the apocrine gland leads to secondary bacterial infection, with rupture of the gland into the dermis and subcutaneous tissue. This causes cellulitis, abscesses, and draining sinuses.
- Chronic fibrosis of the destroyed glandular unit can lead to "pitlike" scars.
- Microscopically there are pathognomonic serpentine epithelialized sinus tracks with giant cells and granulomas.

Clinical Presentation and Diagnosis

- There can be a spectrum of disease presentations from indurated, painful, subcutaneous nodules, to subcutaneous abscesses, and/or draining sinuses with malodorous discharge.
- Sinuses may be simple or a complex network of subcutaneous cavities and tracts with extensive fibrosis.
- Diagnosis is usually by clinical findings and biopsy is rarely required.
- Differential diagnosis includes perianal Crohn's disease, cryptoglandular fistula-in-ano, cancer, other inflammatory conditions of the perianal skin, and cutaneous infections (furuncles, carbuncles, lymphogranuloma venereum, erysipelas, epidermoid or dermoid cysts, and tuberculosis).
- Hidradenitis does not affect the rectum or involve the dentate line nor penetrate the sphincter complex.
- No definitive link with Crohn's disease has been proven in the literature.
- Squamous cell carcinoma can arise in chronic long-standing hidradenitis wounds.

Treatment

- There is a wide spectrum of severity, and this disease is persistent and recurring, so an individualized treatment program is needed.
- It is imperative to educate the patient regarding the relapsing nature of this disease and that it is not contagious or routinely due to poor hygiene.

Nonsurgical Treatment

- Antibiotic therapy both topical and systematic for 1–2 weeks is the cornerstone of nonsurgical treatment.
- The antibiotics must cover skin flora (particularly *Staphylococcus* species).
- Prophylactic long-term antibiotics after resolution of an acute process have not demonstrated an advantage, and no data supports this as it alters the course of the disease.
- Other medications that have been used include retinoids, antiandrogen therapy, immunomodulators, and anti-inflammatory (etanercept, infliximab, adalimumab) drugs. Meaningful conclusions about their use and recommendations are not possible using the current limited literature.
- Radiotherapy has been successfully used, but wound problems are significant.

Surgical Treatment

Surgery to Control Local Infection

- Incision and drainage of abscesses and sinus tracts can control the local infection.
- This leaves diseased skin and hence recurrence is high.
- Once the local inflammation has been controlled, further surgery is offered with a curative intent.

Surgery for Curative Intent

- Surgery with a curative intent requires the complete excision of diseased tissue (skin and subcutaneous tissue).
- Excision with primary closure is acceptable if the wound can be closed without tension. This results in decreased morbidity, decreased length of stay, and decreased postoperative disability.
- Wide excision of all apocrine-bearing skin utilizing wide margins and allowing healing by secondary intention has proven beneficial.
- In the perianal region, wide excision may involve full-thickness excision to the uninvolved gluteal fat. This does not require fecal diversion, but may require a staged excision if the area is large.
- If excision is required in the anal area, all attempts should be made to remain outside the anal verge. If excision is required near the anal canal,

consideration of performing this in a staged manner should be entertained to prevent anal stricture.

- Wide excision leads to prolonged wound healing (greater than 1 month) and requires daily wound care. Physical therapy may be required to prevent contractures.
- Negative pressure dressings (which have been used both on open wounds and skin grafts) appear to promote healing and shorten time to wound closure. Negative pressure dressings have increased costs, and it can be technically difficult to obtain a seal near the anal verge and perineum.
- If the patient has chronic extensive scarring and sinus tracts, the gold standard is wide excision of all involved skin-bearing apocrine glands and reconstruction.
- Reconstruction can be accomplished with cutaneous flap closure, myocutaneous flap closure, immediate or delayed split-thickness skin grafting, or excision with healing by secondary intent. Cutaneous or myocutaneous flaps are analogous to those previously discussed for pilonidal disease.
- Flap procedures after wide excision are typically reserved for patients with extensive scarring and tissue damage that involves large areas of perianal skin around the anus extending out to the buttocks.
- The need for diversion is rare and is considered in those who cannot care for their wounds or in patients with simultaneous symptomatic Crohn's disease.

Summary

- A treatment algorithm is presented in Fig. 15.7.

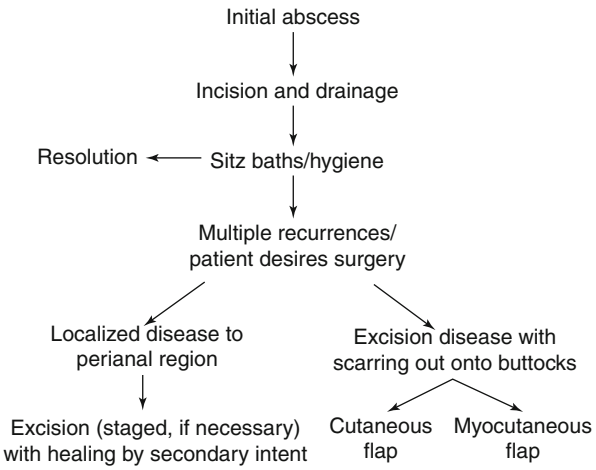

Fig. 15.7 Hidradenitis suppurativa algorithm

16. Dermatology and Pruritus Ani

Charles O. Finne III and John R. Fenyk Jr.

Introduction

- Table 16.1 provides the varied diagnoses of anal dermatoses.

Definitions

- Accurate description of the morphology of skin lesions aids in diagnosis and follow-up of patients with pruritic complaints.
- *Macules* are flat spots.
- *Papules* are elevated circumscribed solid lesions.
- *Vesicles* are separations of the epidermis from the dermis filled with serum.
- *Bullae* are larger vesicles or blisters ≥10 mm.
- *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 and fungal infections – associated with moisture, obesity, and poor hygiene.
- *Pruritus or itch* is the unpleasant sensation that provokes the desire to scratch.
- *Primary pruritus ani* is the classic syndrome of idiopathic pruritus ani.
- *Secondary pruritus ani* has an identifiable cause or a specific diagnosis.

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Table 16.1 Differential diagnosis of anal dermatoses

Inflammatory diseases	*Nonsexual infectious disease*
Pruritus ani	Pilonidal disease
Psoriasis	Hidradenitis suppurativa
Lichen planus	Beta-hemolytic streptococcus
Lichen sclerosus et atrophicus	Fistula-in-ano
Atrophoderma	Crohn's disease
Contact (allergic) dermatitis	Tuberculosis
Contact (irritant) 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
Darier's disease	Schistosomiasis cutis
Familial chronic pemphigus	Bilharziasis
Hailey-Hailey disease	Oxyuriasis (pinworm)
Pemphigus vulgaris	Creeping eruption (larva migrans)
Cicatricial pemphigoid	Larva currens
Bullous pemphigoid	Cimicosis (bed bugs)
Dermatitis herpetiformis	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

Physiologic Considerations

- There are three different modalities of itch: (1) pruritoceptive (C mediated), (2) neuropathic (post-zoster), and (3) central or neurogenic.
- Pruritoceptive fibers that mediate itch are usually unmyelinated C fibers in the epidermis and subepidermis.
- These fibers may be more superficial than pain fibers and have a lower threshold for stimulation than pain fibers.
- Because itch fibers are more superficial, minor mechanical stimuli (like wearing wool) may induce itch.

- Although histamine (and kallikrein, bradykinin, papain, trypsin) can produce itch, topical antihistamines are not always effective to block itch.
- Gastrin-releasing peptide receptors may mediate itch; thus, some H_2 blockers may have an impact on itch.
- Minimal stimulation may induce itching and scratching. If there is not an adequate inhibitory feedback, a self-defeating loop may occur. Substitution of heat, cold, painful, or stinging stimulus for itch by applying alcohol or pepper extract may provide an inhibitory feedback not supplied by scratching alone.
- Antidepressant medication (i.e., paroxetine) and anticonvulsant medication (i.e., gabapentin) have antipruritic effects mediated at the central nervous system level.
- Itching from wound healing is associated with histamine release, release of other kinins and prostaglandins, and regeneration of nerves. Release of histamine, kinins, and prostaglandins occurs during the inflammatory phase of healing.
- Antihistamines, topical anti-inflammatory agents (steroids), topical anesthetics, moisturization, petrolatum, and aloe preparations (prostaglandin inhibitors) all have beneficial effects on itching from wound healing.

Etiology of Pruritus

- Table 16.2 outlines various causes of idiopathic pruritus ani.
- There are few rigorous studies of anal pruritus.

Localized Itch Syndromes

- *Notalgia paresthetica* is associated with itching or pain of the upper to mid-back to either side of the scapula presumed due to spinal nerve damage or entrapment. There may also be an inherited form.
- Skin biopsy demonstrates increased sensory innervation.
- Treatment is with topical pepper cream (capsaicin 0.025 %) which may exacerbate the symptoms during the first week of treatment, but this subsides.
- Topical EMLA (2.5 % lignocaine plus 2.5 % prilocaine) may also be effective.
- *Dermatographism* may cause anogenital pruritus.

Fecal Contamination

- Regarding fecal contamination leading to pruritus, some rigorous studies have been published.
- One study supports the notion that skin in different body locations reacts differently to having feces sitting upon it. Feces is probably an irritant rather than producing an allergic effect.

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, lichen sclerosis, dermographism
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, IV steroids
Gynecologic conditions	Pruritus vulvae, vaginal discharge of infection
Idiopathic	
Infection	Viruses: herpes simplex, cytomegalovirus, papillomavirus; bacteria: *Staphylococcus aureus*, beta-hemolytic strep, mixed infections; fungi: dermatophytes, *Candida* 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 due to radiation proctitis
Systemic disease	Jaundice, diabetes mellitus, chronic renal failure, iron deficiency, thyroid disorders, lymphoma, polycythemia vera

- Anal seepage of liquid and mucous may be an important factor in pruritus symptoms.
- Coffee consumption reduces the resting anal pressure in some people and may increase the chance of anal leakage.
- Patients with pruritus ani have lower leak point pressures than controls. Additionally the anal inhibitory reflex seems to be more pronounced in patients with pruritus which implies that rectal distension may lead to a greater fall in anal resting pressures.

Viral Infection

- Condylomata acuminata commonly cause itching.
- Lesions due to herpes typically cause pain or burning versus itching.
- HIV-associated lesions typically do not itch unless there is a secondary fungal infection.

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

Fungal Infection

- Conflicting studies regarding the association of fungal infections and pruritus have been published.
- If dermatophytes are cultured from the skin, there is some evidence that this may be associated with itching. Topical steroids may facilitate hyphae growth.

Bacterial Infection

- Beta-hemolytic streptococci have been associated with pruritus (when cultured from the anal area).
- Erythrasma (*Corynebacterium minutissimum*), which is probably normal skin flora, may lead to pruritus after moisture, diabetes, or obesity, allowing it to become pathogenic. This usually develops in body folds.

Contact Dermatitis

- Contact dermatitis may have an irritant or allergic basis, but is recognized by being an eczematous inflammation characterized by erythema, scale, and vesicles.
- The cause is often obscure, and a detailed history may be beneficial to resolve the cause.
- Common sensitizing agents are listed in Table 16.3.

Psoriasis

- Psoriasis (which affects 1–3 % of the population) may present as an isolated anal lesion that can lead to itch. The appearance may not be classic due to maceration.
- Biopsy is rarely diagnostic.

- Initial treatment is with daily low to mid-potency topical steroids for 4 weeks to induce remission. This is followed by topical calcipotriene, pimecrolimus, or tacrolimus for maintenance to avoid long-term steroid side effects. A combination of these agents may be needed.

Atopic Dermatitis

- Atopic dermatitis or eczema (found in 15–20 % of the population) may be the most common hereditary cause of pruritus ani.
- With atopic dermatitis, there is disruption of the epidermal barrier function.
- There appears to be no expression of filaggrin (keratin filament-aggregating protein which is the cement of the epidermis) in atopic dermatitis.
- Biopsies are not diagnostic and show mixed inflammatory infiltrates with eosinophils.
- Recognizing associated findings assists in making the correct diagnosis. These associated findings include:
    1. Keratosis pilaris (rough sandpaper-like texture over the posterior biceps and thighs)
    2. Morgan's folds or Dennie-Morgan lines (redundant creases beneath the eyes)
    3. "Sniffers" or "snuffers" lines (a transverse often subtle crease across the mid-nose)
    4. Urticaria
    5. White dermatographism
- Treatment of atopic dermatitis is application of a barrier, such as Vaseline®, the use of aggressive moisturization techniques, the use of anti-inflammatory agents, and the use of antipruritic agents both topic and systemic.
- Development of allergies to any topical treatments may be seen with long-term use.

Lichen Sclerosus

- Lichen sclerosus (formerly known as lichen sclerosus et atrophicus) is a chronic disease of unknown cause seen more frequently in women (10:1).
- In females, this has a predilection for the vulva and perianal area.
- When it occurs on the penis, it is termed balanitis xerotica obliterans.
- The characteristic appearance is gradual progression from erythema to white atrophic and wrinkled skin. The end stage is loss of normal perineal and perianal architecture.
- These patients need periodic long-term follow-up as they have an increased risk of squamous cell carcinoma which is independent of human papillomavirus. Treatment does not modify the risk of cancer.
- Topical testosterone probably is not beneficial.

- Potent topical steroids (clobetasol propionate 0.05 %) for 6–8 weeks are often successful in normalizing skin.
- Tacrolimus ointment may be an alternative as it avoids the skin atrophy associated with steroids.

Food Factors

- No controlled trials have been done to examine food or diet as a cause of itching.
- Six common foods implicated to cause itching are coffee, tea, beer, chocolate, and tomatoes (ketchup).
- One recommendation is to eliminate all of these foods from the diet and after 2 weeks slowly reintroduce them one at a time. The amount ingested is slowly increased to determine the threshold that will cause itching.
- Typical reported thresholds are 3 cups coffee, 4 cups tea, or less than 2 cans of beer.
- Coffee has been shown to lower the anal resting pressure.
- Other foods implicated to lead to itching are alcohol, peanuts, milk products, and citrus.

Coexisting Anal Disease

- Hemorrhoids, fissures, idiopathic proctitis, condyloma, ulcerative proctitis, abscess, fistula, fissures, and anal tags have been implicated to lead to itching.
- Pruritus may be the only symptom of these anal conditions.
- Fecal soiling or leakage of mucous may be associated with the condition, and contact with the anal skin may secondarily result in itching.
- Another theory is that coexisting anal disease may result in fungal infections and consequent pruritus. Therefore, correction of the anal disease eliminates the fungal infection.

Psychological Factors

- In isolated cases, psychological factors such as anxiety, stress, fatigue, personality traits, coping skills, and obsessive compulsive disorders may play a role in exacerbations of pruritus ani.
- Because of this, psychotropic drugs such as doxepin HCL, amitriptyline, nortriptyline, and gabapentin may be considered in the management of pruritus.

Steroid-Induced Itching

- Anogenital itching has been reported after IV bolus steroid infusions.

- More commonly itching occurs as a rebound phenomenon after steroids are withdrawn. This is termed "steroid addiction" and leads to reinstitution and chronic use.
- Allergic contact dermatitis to topically applied steroids has been well described and is chemical class specific. Switching to a less commonly used agent in a steroid class may eliminate the allergic reaction, but discontinuing the topical steroid is the ideal solution.
- The goal should be to eliminate steroid use or use the least dose and fewest treatments possible.
- Topical macrolide anti-inflammatories, tacrolimus, and pimecrolimus offer excellent anti-inflammatory effects without the side effects produced by topical steroids.

Skin Trauma

- Anal skin trauma associated with frequent wiping (i.e., from diarrhea) can lead to maceration.
- Scratching then may occur consciously or subconsciously at night.
- Inadequate anal hygiene or over vigorous cleaning can also lead to trauma.
- Wet wipes should be advised with caution as these can induce irritation or allergic contact dermatitis. Additionally, water may break down the barrier function in the anal skin. Therefore, a smooth dry article with olive oil may work best.
- Contact dermatitis from over-the-counter preparations and perfumed or scented products (including toilet paper) may contribute to perianal irritation.
- To avoid anal trauma, possible cleaning products to recommend include bland emollients, Acid Mantle creams, waterless cleansing agents, or dilute white vinegar (1 tablespoon in 8 oz of water) with Burow's solution (Domeboro®). These can be applied with tissue paper or cotton balls.

Neoplasms

- Perianal Paget's disease, Bowen's disease (intraepithelial squamous cell carcinoma in situ), AIN, lichen sclerosus associated with carcinoma, and non-LS-associated vulvar cancer may have itching as a complaint.
- Melanoma and squamous cell carcinoma usually are not associated with pruritus.

Diagnosis of Perianal Disease

- Table 16.4 lists morphological characteristics of various perianal skin lesions.
- Some diseases may have several different appearances.

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	
Behcet'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 Exam

- Table 16.5 lists points to be addressed during the history and physical exam to aid in diagnosis.
- Hyperpigmentation in the buttock cleft or other intertriginous regions suggests a chronic inflammatory condition. There also may be chronic infection or chronic secretions associated with hyperpigmentation.
- Broad areas of erythema with indistinct borders and findings suggestive of excoriation or chronic rubbing should lead to consideration of eczema or atopic dermatitis.
- A sharply defined border with scales may be tinea.
- Psoriasis may have a sharply defined border and the lesion may be scaly. However, in the cleft which is not exposed to air, the lesion may lack scale and could be macerated.
- Neoplastic changes may appear to have sharply delineated margins.
- Infiltrative processes such as Paget's disease may have less well-defined margins.

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

Table 16.6 Differential diagnosis of groin (inguinal) adenopathy

Benign reactive (shoeless walking)
Lymphoma
Carcinoma (penis, vulva, anal canal)
Sarcoidosis
Syphilis (nontender)
Leishmaniasis
Chancroid (tender)
Herpes genitalis (tender)
Lymphogranuloma venereum

- Inflammatory changes due to an idiopathic etiology often have borders that are indistinct and nondescript.
- Brilliant red erythema is often seen with perianal yeast. There may be "satellite" pustules outside of the main area of involvement.
- Erythema may be seen with chronic steroid use.
- Table 16.6 lists the differential diagnosis for groin adenopathy

Laboratory Examination

- Infected material ideally is aspirated and placed in a sterile container for culture. A swab of exudate from the deep portion of the wound is also an option.
- Bacterial and fungal cultures should be placed on appropriate transport medium and refrigerated if there will be a delay in transport to the laboratory.

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 showerhead, 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 (esp. 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

- Anaerobic cultures require a special anaerobic transport medium and should not be refrigerated.
- Viral cultures require a viral transport medium and should be kept on ice.
- Vesicular lesions should be unroofed and a culture taken of the base. Fluid or exudate from the lesion may be placed on a viral culture medium.
- Ulcerated lesions should have the base vigorously swabbed.
- The conventional water-soluble lubricant typically used to lubricate a scope for anal insertion is bactericidal for some organisms such as Neisseria gonorrhoeae.
- Arrangements with a lab to supply current updated culture swabs and transport media (aerobic, anaerobic, fungal, and viral) should be in place.
- A skin biopsy should be done so that it includes a representative lesion and adjacent normal skin.
- Skin scrapings may be submitted for fungal culture.

Treatment of Pruritus Ani

- Table 16.7 presents the general strategy for treatment of pruritus ani.
- Since diet may contribute to itching, a list of potential foods implicated in itching may be reviewed with the patient.
- Diarrhea should be controlled.
- To eliminate moisture in the cleft, application of athlete's foot powder or barrier cream may lubricate and prevent maceration.
- Cornstarch is avoided as this promotes the growth of yeast.
- Diluting white vinegar on a cotton ball (1 tablespoon in 8 oz of water) is an effective cleanser.
- Burow's solution (Domeboro®) is a nonirritating cleanser. It can also be used as an antibacterial soak for 5–15 min, and then the skin can be allowed to dry.

- Balneol® is a commercially available mineral oil-based preparation that can be kept in a pocket and squeezed onto toilet paper and used as a soothing cleaning agent when using public facilities.
- Topical anesthetics, menthol, phenol, or camphor may control symptoms that result from scratching or vigorous cleaning. These may be used in combination with topical steroids, topical antifungal, and topical antibacterial agents.
- Topical doxepin is an effective antihistamine.
- Oral diphenhydramine and doxepin (which is 1,000 times stronger) may eliminate itching and could be useful at bedtime to avoid nocturnal scratching.
- Cimetidine (1 g/day) has been reported to eliminate itching induced by lymphoma and polycythemia vera.
- Nocturnal scratching may be a contributing factor to idiopathic pruritus ani. When a patient is awakened with an urge to scratch, they should apply either a barrier or steroid cream and resist the urge to scratch.
- Topical capsaicin may break the overwhelming urge to scratch by substituting the itch sensation with a temporary powerful burning stimulus.
- Oral gabapentin and paroxetine have been reported to have a centrally acting antipruritic effect.
- Regarding clothing, loose underwear to allow circulation promotes dryness. Clothes should be laundered with soaps that do not have perfume. A small amount of chlorine bleach used in the laundry lowers bacterial counts and may be a consideration.
- An office-based treatment for acute moderate to severe skin changes is application of Berwick's dye. This is a combination of gentian violet and brilliant green. There is alcohol in this product and when applied it will sting. After dried, benzoin tincture is applied over the area and allowed to dry. If only water is used to clean the area, this preparation will stay in place for several days and allow skin reepithelialization.
- For patients with mild to moderate symptoms and minimal skin changes, topical 1 % hydrocortisone cream can be applied. This can be combined with menthol (0.5–1.0 %), topical antibiotics (gentamicin, clindamycin, or bacitracin), or antifungals (clotrimazole, nystatin). This preparation is applied twice daily and after bathing with the number of applications tapered off after the symptoms subside. Then the topical treatment is changed to a barrier cream such as Calmoseptine®.
- For patients with moderate or severe skin changes that may appear thickened or chronic, a higher-intensity therapy with a higher potency steroid is used initially for a defined period of time (4–8 weeks). Table 16.8 lists the relative potency of topical steroids.
- Patients treated with high-potency steroids are switched to a milder form of topical steroids after skin normalization occurs. This is accompanied by a gradual reduction in the frequency of application until all topical steroids are totally eliminated.

Table 16.8 Relative potency of topical steroids (descending order)

Group 1 (*most potent*)	*Group 4*
Betamethasone dipropionate 0.05 % (Diprolene®)	Desoximetasone 0.05 % (Topicort LP®)
Clobetasol propionate 0.05 % (Temovate®)	Flurandrenolide 0.05 % (Cordran®)
Group 2	*Group 5*
Desoximetasone 0.25 % (Topicort®)	Betamethasone valerate cream 0.1 % (Valisone®)
Fluocinonide 0.05 % (Lidex®)	Hydrocortisone butyrate 0.1 % (Locoid®)
	Triamcinolone acetonide 0.1 % (Kenalog®)
Group 3	*Group 6* (*least potent*)
Betamethasone valerate ointment 0.1 % (Valisone®)	Alclometasone dipropionate 0.05 % (Aclovate®)
Triamcinolone acetonide 0.5 % (Aristocort®)	Hydrocortisone 1 %

Table 16.9 Adverse reactions to topical steroids

Skin atrophy with telangiectasia, pseudoscars, purpura, striae, spontaneous bleeding
Ulceration
Tinea, impetigo, scabies incognito
Allergic contact dermatitis
Systemic absorption with adrenal suppression
Burning, itching, dryness from vehicle
Rebound worsening after withdrawal

- Eroded or denuded skin may benefit from topical antibiotics such as silver sulfadiazine cream. Hydrocortisone or triamcinolone and menthol may be added for soothing relief and to promote regrowth of the dermis.
- Skin atrophy is a serious problem with prolonged use of steroids with cream causing greater atrophy than ointments.
- Newer double-ester, nonfluorinated steroids may be less atrophogenic, but prednicarbate and mometasone furoate may still have 6–8 % incidence of mild skin atrophy.
- Table 16.9 lists the potential complications of topical steroid use. An important point regarding these complications is that they are all preventable and the result of treatment and not a complication of the primary problem.
- Macrolide topical immunomodulators (tacrolimus and pimecrolimus) do not appear to cause skin atrophy, but these are only FDA approved for atopic dermatitis, and hence, any use is off label for pruritus ani. There is no published literature on their use with pruritus. These compounds may give a burning sensation when applied that is reported to subside. These compounds have a good clinical safety record, but carry a warning (from the FDA) of a risk of lymphoma or skin cancer, that does not seem be supported in the literature. Due to the treatment risks with topical steroids, these may be an alternative but require further study.
- Table 16.10 lists the topical nonsteroidal therapies for itching.

Table 16.10 Nonsteroidal topical therapy for itching

Berwick's dye (crystal violet 1 % + brilliant green 1 % + 95 % ethanol)
50 % + distilled H_2O q.s.ad. 100 % with benzoin barrier
Burow's solution 1:40
Calmoseptine®
Camphor (0.1–3 %)
Calcipotriene (Dovonex®)
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"

Anal Tattooing

- Some patients continue to experience severe symptoms of itching that interferes with their quality of life despite exhaustive use of conventional treatments. For this subset of patients, anal tattooing may be beneficial.
- This procedure is done in the prone position with intravenous sedation using a 30 or 27 gauge needle. 30 ml consisting of 10 ml of 1 % methylene blue + 5 ml normal saline + 7.5 ml 0.25 % bupivacaine with 1/200,000 epinephrine + 7.5 ml 0.5 % lidocaine is injected into the skin over the involved perianal region up to the dentate line. The depth of the injection is similar to that for cutaneous anesthesia.
- Patients experience hypalgesia and numbness of the perianal skin that can be disagreeable for some patients, and they must be warned regarding this possible side effect prior to the procedure.
- Rapid resolution of itching typically occurs.

Conclusion

- Skin problems in the anal region are quite common and often poorly diagnosed.
- The appearance of the lesion is rarely pathognomonic, so a systematic approach to evaluation with a full physical exam and extensive past history is key.
- Reevaluation to review ongoing prescriptions and assess symptom improvement should be carried out. This is done to avoid long-term use of medication in the anal area that itself could cause harm.
- Additionally reevaluation provides the opportunity to make a correct diagnosis in the event that the initial diagnosis was not correct.

17. Sexually Transmitted Diseases

Charles R. Whitlow, Lester Gottesman, and Mitchell A. Bernstein

Introduction

- There are over 25 diseases primarily spread by sexual means with an annual incidence of approximately 15 million cases in the USA.
- Site and route of infection determine the symptoms caused by 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 infections are typically the result of anal receptive intercourse.
- Proctitis from sexually transmitted organisms is almost always acquired from anal intercourse.
- Current estimates are that less than 2 % of adult males regularly practice anal receptive intercourse while between 2 and 10 % participate in homosexual activity at some point in their life. Between 5 and 10 % of females engage in anal receptive intercourse "with some degree of regularity," and females appear to be more likely than men to have unprotected anal intercourse.
- Difficulty in correct diagnosis and appropriate treatment of STD of the anorectum is caused by several factors. (1) 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.

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(2) The presence of more than one organism is common, especially with anogenital ulcerations. (3) Determining a true pathogen from colonizing organisms may be difficult. (4) Lastly, there is a lack of rapid sensitive diagnostic tests for many STDs so that empiric treatment is frequently required.

Overview of Anorectal Immunology

- The optimal state of health of the anus requires the integrity of the skin, which acts as the primary protection against invasive pathogens. The mucosa shed from the rectum contains IgA, which traps foreign antigens and expels them with stool, preventing them from reaching the rectal 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.
- Although study of anal immunology is still in its infancy, it appears that certain pathogens may alter the balance of cellular elements. It is known that while human papillomavirus (HPV) increases Langerhans cells, human immunodeficiency virus (HIV) may damage their effectiveness.
- HIV is known to impair cell-mediated immunity by depletion of T cells and destruction of Langerhans cells. This process allows propagation of oncogenic processes such as HPV to become dysplastic. Although both exact switches and the mechanism(s) have not yet been elucidated, they appear to be related to the coexistence of perhaps HSV and the highly active antiretroviral therapy (HAART) drugs.
- Failure of the mucous complex to protect the rectum is seen in various diseases contracted through anal intercourse.
- Latex allergies may also cause severe invasive and erosive proctitis and should be in the differential of a caustic burn to the rectum after protected sexual anoreceptive intercourse.

Diagnosis and Management of Bacterial Pathogens

Gonorrhea

- *Neisseria gonorrhoeae,* the Gram-negative diplococcus (Fig. 17.1) 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 do 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.

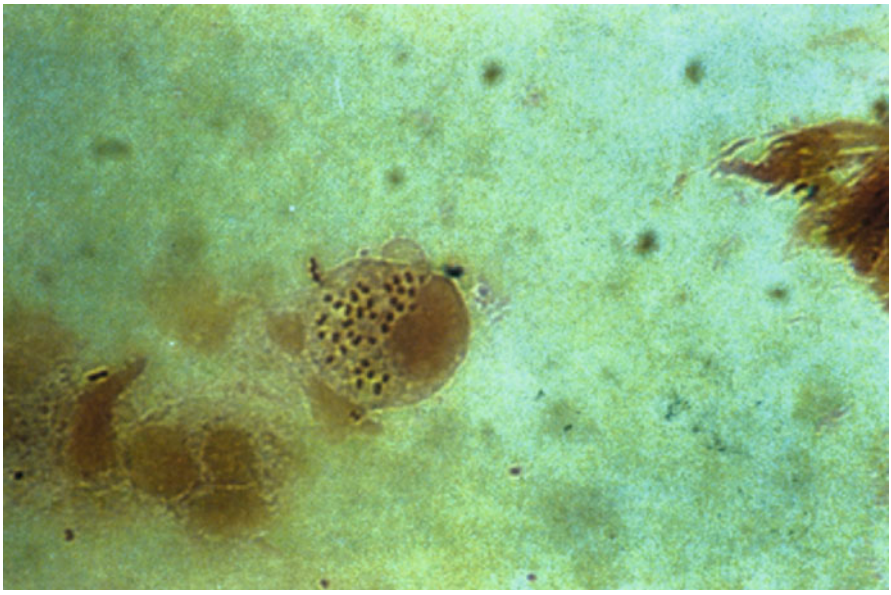

Fig. 17.1 Gram-negative intracellular diplococcus

- Untreated infection may lead to disseminated gonococcal infection with transient bacteremia, arthritis, and dermatitis. Rare but severe sequelae include endocarditis and meningitis.
- Anorectal transmission in homosexual males and in some females is by anoreceptive intercourse with an infected partner.
- 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, or severe pain (Fig. 17.2).
- 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 CO_2-rich environment and Gram stain of directly visualized discharge. The use of lubricants other than water may introduce antibacterial agents during anoscopy and decrease diagnostic yield.

Fig. 17.2 Anorectal gonorrhea

Table 17.1 Treatment of anorectal gonococcal infection

One of the following as a single dose
Ceftriaxone – 125 mg IM
Ciprofloxacin – 500 mg orally
Ofloxacin – 400 mg orally
Levofloxacin – 250 mg orally
Cefixime – 400 mg orally

- Nonculture detection of gonorrhea is being used more frequently especially in urethral and cervical infections but is not currently licensed for the detection of rectal gonorrhea.
- The most current recommended treatment regimen from the Centers for Disease Control (CDC) is 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 exclude chlamydial infection should be taken.
- Routine follow-up at 3 months is no longer necessary since 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 (LGV)

- *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 commonly reported STD in the USA with an annual incidence of about three million cases per year.
- Anorectal transmission of chlamydia is through anoreceptive intercourse although secondary involvement can occur as a late manifestation of genital infection.
- Different serovars of *C. trachomatis* produce differing clinical illness. Serovars D through K (non-LGV) are responsible for proctitis and common genital infections.
  - Lymphogranuloma venereum is caused by LGV serovars L1–L3. The incubation period for *Chlamydia* is 5 days to 2 weeks.
  - Non-LGV serovars are less invasive and cause mild proctitis (manifest by tenesmus, pain, and discharge), but asymptomatic infection is common.
  - LGV serovars produce a much more aggressive infection with perianal, anal, and rectal ulceration. The proctitis produced can be difficult to distinguish from Crohn's disease (including microscopic findings of granulomas) with resulting rectal pain and discharge.
- Anoscopy and sigmoidoscopy demonstrate friable rectal mucosa, which is more severe in appearance (and extends above the rectum in some cases) in LGV strains. Perianal abscesses, fistulas, and strictures may also occur. Lymphadenopathy develops in draining nodal basins, including the iliac, perirectal, inguinal, and femoral regions, several weeks after initial infection. Large indurated matted nodes and overlying erythema may produce a clinical picture similar to syphilis (Fig. 17.3).
- 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). Specimen for tissue culture should be transported on specific medium and kept refrigerated or on ice until inoculated onto culture plates. Specimens that are to be tested by a nonculture technique are transported and stored in accordance with the test manufacturers guidelines. In patients with a clinical presentation consistent with chlamydia proctitis, rectal Gram stain showing polymorphonuclear leukocytes without visible gonococci is presumptive for a diagnosis of chlamydia.
  - 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. A trained microscopist is needed for interpretation.

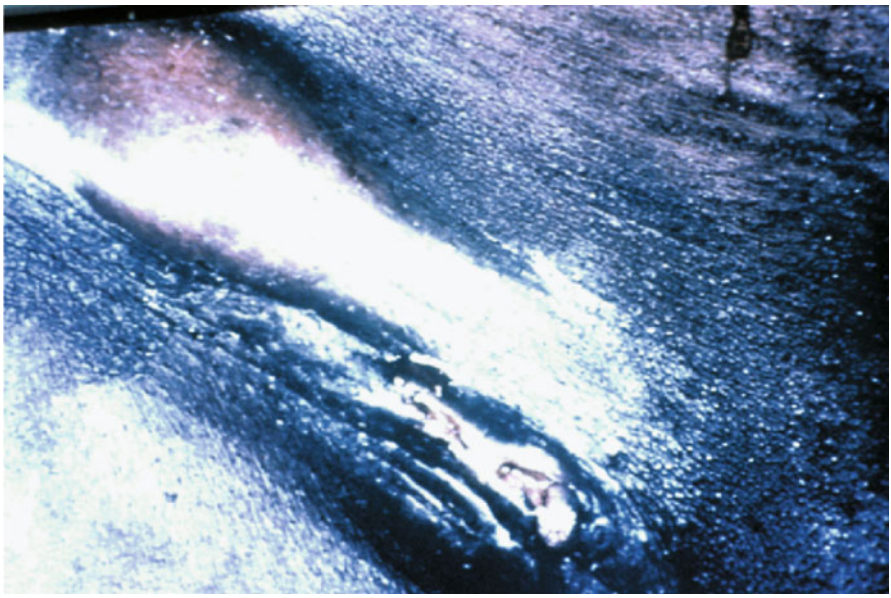

Fig. 17.3 Inguinal adenopathy of LGV; *LGV* lymphogranuloma venereum

- 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. Management of sexual contacts is the same as for gonorrhea. 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 (Figs. 17.4 and 17.5) 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. Proctitis from syphilis may occur with or without chancres. Untreated lesions in this stage 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,

Fig. 17.4 Solitary anal chancre

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, wartlike 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 have a relapse of symptoms in the first year, a stage known as early latent syphilis.
- Diagnosis in the primary or secondary stage is made by visualization of spirochetes on dark-field microscopic exam of scrapings from chancres (Fig. 17.6).
- 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

Fig. 17.5 Multiple anal chancres

Fig. 17.6 Spirochetes demonstrated on dark-field microscopy

for 14 days) or tetracycline (500 mg orally, four times a day for 14 days). Follow-up serology (VDRL or RPR) should be checked at 6 months after therapy for HIV-negative patients and every 3 months for HIV-positive patients.

- Partner notification, testing, and treatment depend 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.*
- Transmission of *H. ducreyi* is strictly via sexual contacts through breaks in the skin during intercourse and results in genital ulcers.
- The initial manifestation (hour to days after exposure) is an infected tender papules with erythema that subsequently develop into pustules and then (days to weeks) become ulcerated and eroded. Multiple ulcers are common and are generally painful, especially in males.
- Painful inguinal adenopathy accompanies half of cases in males and is usually unilateral. Females are less likely to develop adenopathy from *H. ducreyi* infection.
- Abscess formation may result, necessitating drainage.
- Besides causing genital ulcers, *H. ducreyi* facilitates transmission of HIV and vice versa.
- Diagnosis of chancroid is made by Gram stain and culture of *H. ducreyi* (on selective medium agar) from the base of ulcers. *H. ducreyi* is difficult to culture, and many labs in the USA are not equipped to perform this test. PCR is more sensitive than culture for detecting *H. ducreyi* but is not commercially available at this time.
- Treatment for *H. ducreyi* is single-dose treatment with azithromycin (1 g, orally) or ceftriaxone (250 mg, intramuscularly). Alternatively, regimens include ciprofloxacin, 500 mg orally twice a day for 3 days, or erythromycin 500 mg three times a day for 1 week.

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 nonsexual contact.

- It is rarely seen in the USA but is common in parts of Africa, South America, and Australia.
- Morphologic manifestations include an ulcerogranulomatous form (non-tender, fleshy, beefy red ulcers), hypertrophic or verrucous lesions, necrotic ulcers, or cicatricial. Genital involvement is most common, but contiguous involvement of the anorectum occurs. Development of sclerotic lesions causes anal stenosis.
- *C. granulomatis* cannot be cultured by routine techniques. Diagnosis can be made by tissue smear or biopsy that reveals Donovan bodies (small inclusions) within macrophages.
- Several antibiotic regimens have been recommended, although the most recent CDC guidelines is 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).

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 (CMV).
- Herpes is the most prevalent STD in the USA with current the 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 commonly presents as labial oral or ocular lesions but accounts for about 30 % of genital infections.
- 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. Productive infection causes viral replication within cells and cell death. Clinical infection presents first with systemic symptoms, such as fever, headache, and myalgias, followed by local symptoms, including pain and pruritus. Vesicles appear over the anogenital area, increase in number and size, and eventually ulcerate and coalesce (Figs. 17.7 and 17.8). These vesicles and ulcerations generally 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, dysuria, 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

Figs. 17.7 and 17.8 Perianal herpes

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. For HSV, the site of latent infection is the sensory ganglia of nerves innervating the site of infection. Reactivation of latent virus results in recurrent infection, but the stimuli for this process are poorly understood. Recurrent attacks are generally milder, shorter in duration, and without the constitutional symptoms that occur with initial infection.
- Diagnosis is frequently made by clinical evidence although cultures taken from ulcerations, rectal swabs, or biopsies confirm the diagnosis. Multinucleated giant cells with intranuclear inclusion bodies (ground-glass appearance) on Pap smear or Tzanck prep are less sensitive than viral culture. Direct immunofluorescence has also been used for diagnosing 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. Topical acyclovir has limited efficacy and is not recommended. Treatment of initial episodes of HSV does not prevent latency, asymptomatic viral shedding, or the course of subsequent episodes.

- Recurrent episodes may be treated with oral antiviral agents. Valacyclovir (500 mg twice a day) and acyclovir (200 mg five times a day) have demonstrated equal efficacy in treating genitourinary HSV recurrences. Prompt initiation of treatment at the onset of symptoms of HSV recurrence reduces the duration of symptoms and healing times. Patients who experience more than five recurrences per year are considered for suppressive treatment. Valacyclovir, acyclovir, and famciclovir have all demonstrated 70 % or greater reduction compared to placebo.
- As with all STDs, counseling of patients with HSV is an important part of treatment and prevention. Specific items that should be addressed are (1) infectivity is not isolated to symptomatic outbreaks; most sexual HSV transmission occurs during asymptomatic periods; (2) latent infection and the risk of recurrence; suppressive therapy does not eliminate latent infection or viral shedding; (3) abstinence is recommended while lesions are present. Condoms are advised for all other times although they most 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 Papillomavirus

- HPV is a DNA papovavirus. It is the most common STD in the USA with an estimated incidence of over five million cases per year. There are over 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, while subtypes 16 and 18 have the greatest associated risk of anal dysplasia and anal cancer. Transmission is via sexual contact. Perianal involvement can occur in the absence of receptive anal intercourse.
- Presenting complaints of perianal or anal condyloma acuminata include the 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 (Fig. 17.9). In the anal canal, the lesions tend to be small papules, and involvement above the dentate line is rare. Examination should focus on the genitalia, including vaginal speculum exam and Pap smear, as well as evaluation of the perineum and groin folds.

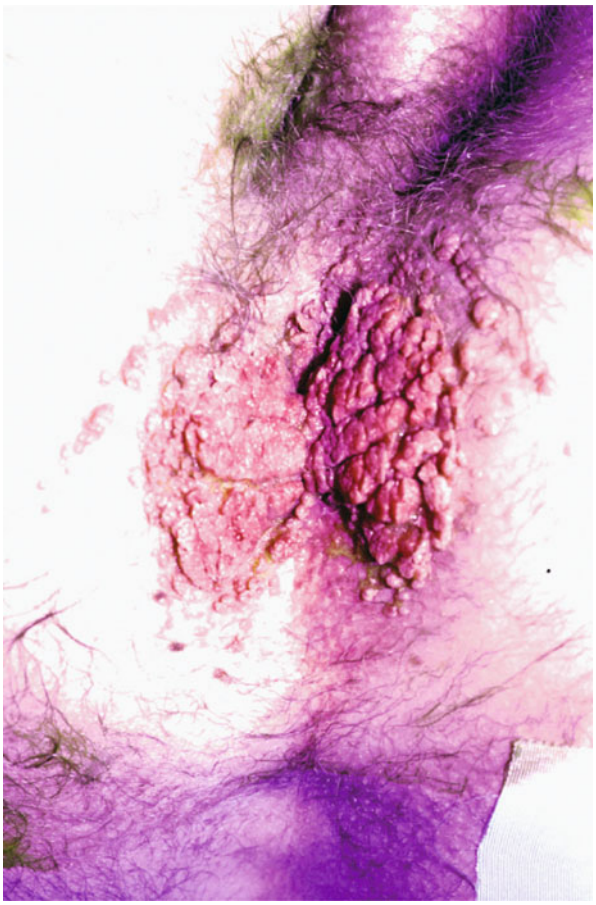

Fig. 17.9 Perianal condyloma

- The goal of treatment of condyloma acuminata is destruction or removal of all obvious disease while minimizing morbidity, although this process 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, causing little discomfort or inconvenience to the patient. Larger lesions are treated by electrodessication. Tissue from HIV+ patients, recurrent lesions, flat lesions, or those suspicious lesions which may be ulcerated, friable, or hypervascular should be sent for histopathologic evaluation. 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 post-operative care in most patients. Silver sulfadiazine or mupirocin is 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 %.

- The patient can apply topical agents like podofilox and imiquimod although neither agent is approved for use in the anal canal.
- Podofilox is the purified active component of the antimitotic plant resin podophyllin and is available as a 0.5 % gel or solution. A treatment cycle consists of twice daily application for 3 days followed by no treatment for 4 days utilized for up to 1 month. Toxicity concerns are less than those issues with podophyllin while clearance rates for condyloma of 35–80 % have been reported. Recurrence rates in patients treated with podofilox are 10–20 %.
- Imiquimod is an immune response modifier that increases local production of interferon. A 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 electrodessication reserved for those who have incomplete response or (2) following destructive treatment and epithelial healing to treat remaining disease or decrease recurrence (no randomized data to support this use). Currently, imiquimod is not approved for anal canal use, but this application is being investigated. Trichloroacetic acid is applied topically and is useful for treating small lesions in the anal canal. Topical and intralesional interferon have been used to treat condyloma acuminata with mixed results. Other agents that have been used to treat anogenital condyloma but are not in widespread use include 5-FU cream, cidofovir, and autologous vaccine.
- 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 has lead 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.
- Abdominal–perineal resection has been used for GCA involving the anal sphincters.
- 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.

Fig. 17.10 Anal cancer in HIV-positive patient; *HIV* human immunodeficiency virus

HPV, Anal Intraepithelial Dysplasia, and Anal Cancer

- While it is clear that HPV plays a significant role in the development of cervical cancer, its significance in the development of anal cancer (Fig. 17.10) and its presumed precursor, anal intraepithelial dysplasia, is not as well defined. Parallels can be drawn between the anal canal and the cervical canal as they share embryologic and histologic features.
- Epidemiologic parallels can be drawn as well. Studies prior to the HIV infection epidemic showed the incidence of anal cancer in homosexual males to be 12.5–37 per 100,000 in the USA. This incidence is similar to the incidence of cervical cancer prior routine Pap testing.
- 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 to 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).
- The benefit and best timing of this screening is undetermined. Evaluation and treatment algorithms as well as recommended testing schedules have been reported.

- Subsequent treatment is based on histologic findings which are typically reported as normal or anal epithelial neoplasia (AIN) I, II, or III. Options for treatment include local destruction (with topical agents, cryotherapy, or fulguration), excision, or observation.
- However, there are limitations of our understanding of the relationship between HPV, AIN, and anal cancer that prevent the dogmatic recommendation and widespread acceptance of such an approach.
  - First, the incidence and predictability of the progression of AIN to invasive cancer is unclear.
  - Second, data demonstrating efficacy, which is defined as long-term removal of AIN and prevention of anal cancer of treatment, is lacking.
- The absence of established benefit combined with the morbidity of treatment leads us and others to the recommendation that AIN, regardless of grade, be observed unless there are gross visual or palpable lesions or ulcerations present.
- Two additional comments with regard to the association of HPV, HIV, and AIN should be made.
  - First, the use of HAART (discussed further 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 the development of 2–6 mm flesh-colored, umbilicated papules.
- Symptoms are uncommon though pruritus or tenderness may occur. Immunocompromised hosts, such as those with HIV, are more prone to infection with *Molluscum contagiosum* (compared to HIV negative) and may have a more severe form of the disease with hundreds of lesions.
- Diagnosis is usually made on clinical grounds, but excisional biopsy demonstrates enlarged epithelial cell with intracytoplasmic molluscum bodies.
- Treatment is generally through eradication with curettage, electrodessication, or cryotherapy. Podophyllotoxin (0.5 %) and imiquimod (5 %) have both been used as self-applied topical preparations with success, although neither compound is FDA approved for this use.

Table 17.2 Revised classification system for HIV and AIDS

CD4+ T-lymphocyte categories

Category 1: greater than or equal to 500 cells/μL

Category 2: 200–499 cells/μL

Category 3: less than 200 cells/μL

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 (greater 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, coccidioidomycosis, 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

Bold italic groups are defined as AIDS

HIV and the Acquired Immunodeficiency Syndrome

- Infection from the HIV (originally called human T-lymphotropic virus) related to acquired immunodeficiency syndrome (AIDS) was first described in 1983.
- While the incidence of HIV infection has apparently stabilized, the numbers of new AIDS cases and deaths have decreased, mainly due to HAART therapy, potent anti-HIV drugs that are nucleoside analogs, non-nucleoside reverse transcriptase inhibitors, or protease inhibitors. Table 17.2 shows the current classification system for HIV and AIDS.
- Surgery for anorectal diseases is the most common indication for surgery in HIV infected patients and in 5 % of patients; their anorectal complaint is 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.
- There is a lack of data describing wound healing in anorectal surgery since the widespread use of HAART; however, the observation of the

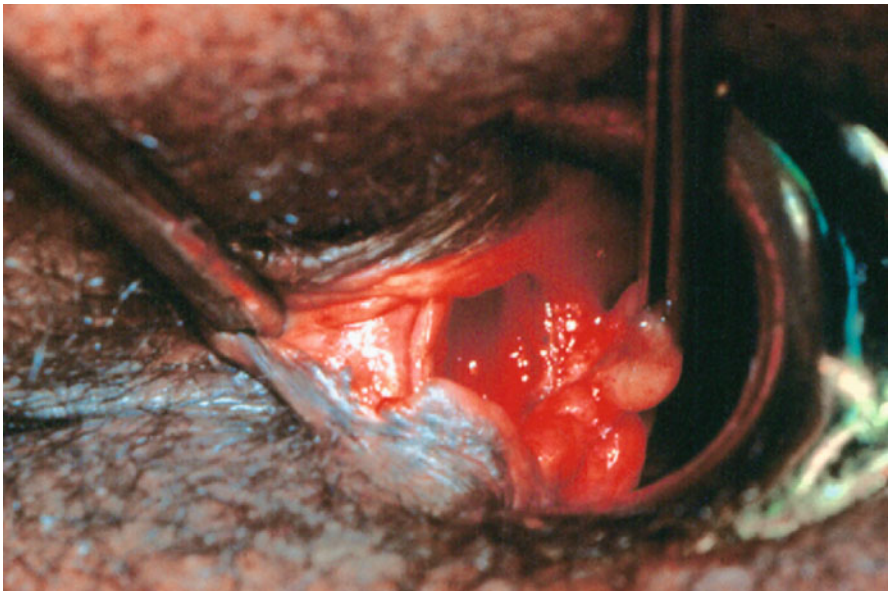

Fig. 17.11 AIDS and ulcer

authors is that compensated HIV+ patients are at no significant risk of increased complications from anorectal surgery. 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 (Fig. 17.11) and ulcerating STDs, such as HSV or syphilis. Treatment of fissures in HIV+ patients is modified by the factors described previously and includes controlling diarrhea when possible and encouraging abstinence from anoreceptive intercourse.
- While data on the incidence of AIDS-related anal ulcers is lacking, it appears 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 the destruction of sphincter planes, and may demonstrate mucosal bridging.
- Debilitating pain is a common presenting symptom of these ulcers. Surgical debridement allows for adequate drainage of feculent or purulent material trapped in the ulcer and removal of necrotic debris.
- Biopsy and culture identifies potentially treatable causes for ulceration – malignancy, acid-fast bacilli, HSV, *H. ducreyi,* and *T. pallidum.* CMV has been cultured from these ulcers by some authors but is apparently not

causal and therefore does not require treatment. Intralesional injection with steroids (methylprednisolone 80–160 mg, in 1 cc 0.25 % bupivacaine) provides relief in the majority of patients but not healing. Patients who have persistent pain are reinjected at their ulcer sites.

- Perianal suppurative diseases are common conditions in AIDS patients. Abscesses should be drained using small incisions and the placement of a mushroom catheter lessens recurrent sepsis. Broad spectrum antibiotics should be given in immune compromised especially if cellulitis is present. Culture (to include *Mycobacterium*) and histopathologic evaluation identifies infection from atypical organisms and malignancy.
- Draining setons are placed liberally with selective use of fistulotomy for low uncomplicated fistulas in patients with low CD4+ counts and absolute leukocyte counts of less than 3,000/mm. 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.
- 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. Other nonoperative techniques, such as bipolar coagulation, cryotherapy, or injection sclerotherapy, are acceptable.
- There are conflicting recommendations for operative treatment of hemorrhoids published within the last decade.

18. Fecal Incontinence

Dana Reiver Sands and Mari A. Madsen

Introduction

- Fecal incontinence is a socially devastating condition, affecting between 1.4 and 18 % of the population and up to 50 % of all nursing home residents.
- It has been defined as "recurrent uncontrolled passage of fecal material for at least 1 month," while partial incontinence is typically described as inability to control the passage of flatus and fecal soiling.
- Populations at risk for fecal incontinence include: parous females, patients with cognitive impairment, neurologic disorders, and nursing home residents.
- Fecal incontinence is the second leading reason for admission to nursing homes.

Etiology

- It is important to realize that fecal incontinence is not a diagnosis, but a symptom of which there are multiple causes.
- Normal bowel continence requires a complex integration of function between the anal sphincters, pelvic floor, stool volume/consistency, rectal compliance, and neurologic function.

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- It is first necessary to determine if the patient is having true fecal incontinence.
  - Pseudo-incontinence can be caused by a variety of anorectal conditions including hemorrhoidal prolapse, incomplete evacuation, poor hygiene, fistula-in-ano, dermatologic conditions, anorectal sexually transmitted diseases (STDs), and anorectal neoplasms.
- Fecal urgency from a noncompliant rectum can also cause incontinence. Consideration should be given to other disease states such as inflammatory bowel disease and radiation proctitis.
- The diagnosis of overflow incontinence from incomplete rectal evacuation should also be entertained in patients whose history indicates this condition.
- Various systemic disease states can affect continence. In the appropriate patient, central nervous system pathology including spinal cord injury and neoplasm should be part of the differential diagnosis.
- Autonomic neuropathies such as diabetes can also cause derangements in continence.
- Perhaps the more common etiologies of incontinence treated by the colorectal surgeon are those that pertain to abnormal pelvic floor function.
  - Anal sphincter injury can be the result of obstetric injury, direct trauma, neoplasm, or rectal prolapse.
  - Obstetric injury is a common occurrence with occult tears of the anal sphincter reported in 25–35 % of women after vaginal delivery.
  - Factors that affect the risk for developing obstetric tears are use of forceps, mediolateral episiotomy, and primiparity.
- Denervation injuries to the pelvic floor are also common sequelae of childbirth; 60 % of patients with an obstetric tear also have evidence of pudendal nerve damage.
  - The mechanism of pelvic floor denervation appears to be a result of compression or traction injury to the pudendal nerves during vaginal delivery, particularly when it is prolonged or requires forceps assistance.
  - High birth weight is also a risk factor for compression injury. The end stage of denervation injury is pelvic floor failure and descending perineum syndrome.
- Iatrogenic injury to the anal sphincter musculature is also a cause of fecal incontinence. Incontinence after surgery for fissure with lateral internal sphincterotomy is not uncommon.
- Fistulotomy is also associated with seepage and soiling and incontinence rates reported as high as 35–45 %.
- Patients who have suffered from congenital malformations including spina bifida, imperforate anus, and myelomeningocele often have severe alterations of continence and evacuatory function. The difficulty is related not only to the function of the pelvic floor musculature but also to the proprioceptive response of the rectum.
- Radiation therapy can result in fecal incontinence from both a direct damage to the anal sphincter and through its effect on the compliance of the rectum.

Diagnosis

History

- A thorough patient history is the first step. Patients with fecal incontinence are often embarrassed and reluctant to provide details of the problem unless specifically asked. It is important to create a comfortable environment for the patient during the history and physical examination. The onset of the symptoms can provide useful insight into the etiology of the problem. Changes in bowel consistency are a common cause of fecal incontinence, which can be overlooked by many physicians. Any cause of diarrhea should be explored as a potential etiology of the patients' symptoms especially if there is a temporal relationship.
- After appropriate questioning, the physician will often be able to determine if the patient has active or passive incontinence.
  - Active (urge) incontinence, or the loss of stool despite the patients' best efforts to control it, will lead the physician to consider etiologies which involve an intact sensory mechanism with a derangement in the external anal sphincter function.
  - Passive incontinence, or the loss of stool without the patient's awareness, will lead the examiner to consider internal anal sphincter pathology or neurologic etiologies.
    - It is helpful to quantify the degree of the fecal incontinence. Numerous scoring systems have been used to evaluate incontinence. The Cleveland Clinic Florida Fecal Incontinence Score (CCF-FIS) is an independently validated tool, which has the benefit of ease of use combined with incorporation of a quality of life component (Table 18.1).
    - An often overlooked component of the history of the patient suffering from fecal incontinence is the presence of other pelvic floor complaints. Physicians should be sure to inquire about the presence of any form of rectal prolapse as well as the presence of urinary incontinence or genital organ prolapse. There is significant overlap of symptoms in this complex patient population.

Table 18.1 Cleveland Clinic Florida Fecal Incontinence Score (CCF-FIS)

			Frequency		
Type of incontinence	Never	Rarely	Sometimes	Usually	Always
Solid	0	1	2	3	4
Liquid	0	1	2	3	4
Gas	0	1	2	3	4
Pad usage	0	1	2	3	4
Lifestyle impact	0	1	2	3	4

0 = perfect continence, 20 = complete incontinence, never = 0, rarely = <1/month, sometimes = >1/month, <1/week, usually = >1/week, <1/day, always = >1/day

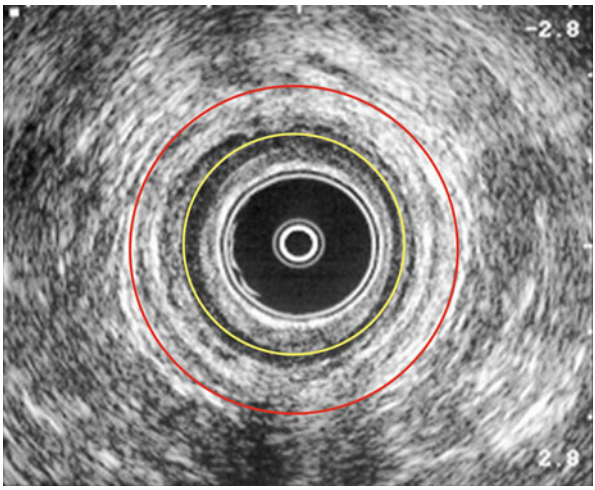

Fig. 18.1 Normal endoanal ultrasound. The *red line* illustrates the lateral border of the external anal sphincter (hyperechoic) while the *yellow depicts* the lateral border of the internal anal sphincter (hypoechoic)

Physical Examination

- A complete physical examination will include inspection of the perianal skin for scars from prior surgeries, trauma or birthing injuries, fistulae, excoriation from chronic soiling, or large prolapsing hemorrhoids.
- A specific evaluation of the perineal body in parous females should include palpation to determine if it is thinned.
- At rest, the anal canal should be well approximated, not patulous. A patulous anus suggests a possible rectal prolapse, which is best reproduced by asking the patient to Valsalva while sitting on a toilet or squatting. Checking the perianal sensation to pinprick as well as the anocutaneous "wink" reflex will serve as a simple assessment of neurologic function.
- Digital rectal examination can reveal masses or a fecal impaction. It also provides a gross assessment of both resting tone and voluntary squeeze.
- Lastly, anoscopy or potentially a rigid vs. flexible proctosigmoidoscopy may reveal inflammatory bowel disease, infectious proctitis, or neoplastic process if suspected.

Diagnostic Studies

Endoanal Ultrasound

- Endosonography has become the diagnostic cornerstone of the anorectal physiologic evaluation of fecal incontinence.
  - The ultrasound provides excellent imaging of the internal anal sphincter, which appears hypoechoic (Fig. 18.1).
  - The external sphincter is hyperechoic, and scar tissue often has a mixed echogenicity appearance.

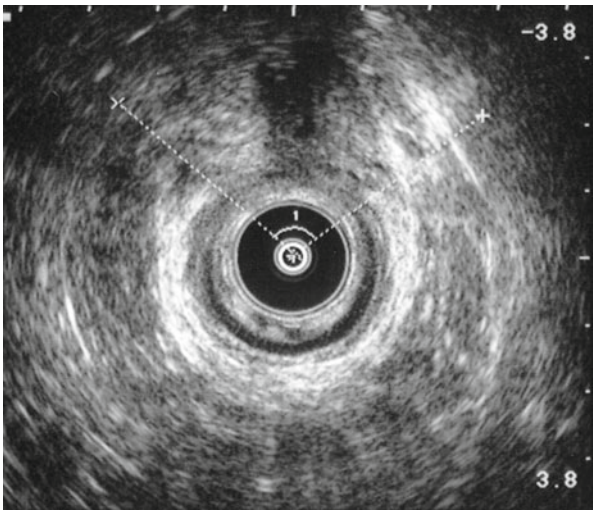

Fig. 18.2 Endoanal ultrasound with anterior sphincter defect (internal and external)

- The most important parameter is to determine if the musculature is intact or if there are traumatic defects present. When present, defects in the musculature should be measured.
- Additionally, the perineal body thickness (PBT) should be measured. PBT less than 10 mm is considered abnormal, and those patients with PBT greater than 12 mm are considered unlikely to have a sphincter defect in the absence of prior reconstructive surgery (Fig. 18.2).

Anorectal Manometry

- Anorectal manometry provides important information about the functional status of the anal sphincters and distal rectum. There is no standardized method of manometric evaluation. Several methods have been described.
  - Microtransducers can be used in the anal canal and are well tolerated by patients. Multichannel water-perfused catheters are perhaps the most common tool used to perform anal manometry.
- The resistance of flow of fluid from the catheter determines pressure measurements.
- Measurements can be taken in a continuous fashion (continuous pull-through) or at set levels within the anal canal (station pull-through).

Measurements

- *Resting Pressure*. The mean resting pressure in healthy volunteers ranges from 40 to 70 mmHg. The internal anal sphincter generates the majority of the resting pressure. This smooth muscle is in a continuous state of maximal contraction accounting for 55–60 % of resting tone.

- *Squeeze Pressure*. The maximal squeeze pressure in healthy individuals is two to three times the baseline resting value. The external anal sphincter is the main contributor to the generation of these pressures. Traumatic defects of the external anal sphincter, whether from obstetric or surgery, often result in decreased squeeze pressures.
- *High-Pressure Zone*. The high-pressure zone is defined as the length of the internal anal sphincter, through which pressures are greater than half of the maximal resting pressure. The high-pressure zone is approximately 2–3 cm in women and 2.5–3.5 cm in men.
- *Rectoanal Inhibitory Reflex.* The rectoanal inhibitory reflex (RAIR) is thought to play a role in the fine adjustments of continence. Rectal distension, usually with small volumes (10–30 mL), causes a contraction of the external anal sphincter followed by a pronounced internal anal sphincter relaxation. This reflex enables the sensory mucosa of the anal canal to "sample" the contents of the distal rectum and the patient to distinguish between gas, liquid, and solid stool. This reflex is absent or abnormal in patients with Hirschsprung's disease, Chagas' disease, dermatomyositis, and scleroderma.
- *Rectal Sensation.* Alterations in rectal sensation can lead to decreased fecal continence. Rectal sensation is measured with an intrarectal balloon and incremental instillation of known volumes of air. Sensation is generally achieved with 40 mL air. Overflow incontinence can result from a decrease in rectal sensation and subsequent fecal impaction.
- *Rectal Compliance*. Compliance is determined by the change in pressure associated with a change in volume ($C = V/P$). This is calculated by subtracting the volume of first sensation from the maximum tolerable volume and dividing by the change in pressure at these two points. A non-compliant rectum can contribute to fecal incontinence as the patient is not able to accommodate the amount of stool presented to the rectum. This is common in conditions, which cause proctitis.

Pudendal Nerve Terminal Motor Latency (PNTML)

- Pudendal neuropathy has been implicated in the etiology of fecal and urinary incontinence. Assessment of the PNTML is an important component to the evaluation of the patient with fecal incontinence. A disposable electrode is attached to the examiner's finger, which is then directed toward the ischial spine, and electrical impulses are delivered to the pudendal nerve. The time for response at the level of the external anal sphincter is measured. Normal response is within 2.0 ± 0.2 ms.

Electromyography

- Anal electromyography (EMG) relies on the use of a concentric needle electrode to record electrical activity generated by the anal sphincter muscle fibers. Sequential recordings of the motor unit potentials are taken circumferentially around the anal canal.

Defecography

- Defecography is the radiological visualization of the act of defecation. It provides a picture of the successive phases of defecation and gives a dynamic 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.

Colonoscopy

- Endoscopic evaluation of the colon and rectum should be considered in the evaluation of patients with fecal incontinence to exclude a mucosal lesion or inflammatory condition, which could cause a change in the stool consistency or rectal compliance.

Treatment

Nonoperative Management

Medical Therapies

- There are a variety of pharmacotherapies available for the medical management of fecal incontinence, but ultimately the number of randomized, placebo-controlled trials is limited. In fact, the Cochrane Database systemic review on the subject stated "there is little evidence with which to assess the use of drug therapies for the management of fecal incontinence."
- Medical management therapies are broadly broken down into the following categories: bulking agents, constipating agents, and laxative regimen with scheduled disimpactions.

Bulking Agents

- Fiber, both natural and synthetic, has long been a staple in treatment of minor fecal incontinence. It has the benefit of adding bulk and has the ability to absorb additional fluid, providing a more solid stool in the face of mild chronic diarrhea.

Constipating Agents

- In patients with diarrhea-predominant irritable bowel syndrome, it is estimated that 20 % have associated fecal incontinence.
  - It therefore stands to reason that use of constipation-inducing drugs, such as loperamide, codeine, diphenoxylate plus atropine, difenoxin plus atropine, and amitriptyline, is of utility for this group of patients. Loperamide is a synthetic opioid, which inhibits small and large intestinal peristalsis via the m (Mu) receptors in the gut. It has also been shown to increase anal resting sphincter pressure, improve

rectal sensation, and retention of fluid load, as well as increase the RAIR. Amitriptyline has also been suggested as therapy based on its anticholinergic properties leading to a reduction in the frequency and amplitude of rectal motor complexes.

Laxative Regimen with Scheduled Disimpactions

- In contrast to patients with diarrhea, patients with constipation and fecal impaction experience fecal incontinence secondary to overflow incontinence. Chassagne et al. compared a regimen of 30 g lactulose daily to 30 g of lactulose daily with the addition of a daily glycerin suppository and a weekly tap water enema in 206 institutionalized elderly patients with a history of prior fecal impaction and at least weekly episodes of fecal incontinence. The patients receiving the suppositories and weekly enemas in addition to the lactulose had a 35 % reduction in fecal incontinence episodes and a 42 % reduction in soiled laundry.

Biofeedback

- The goal of biofeedback is to use visual, auditory, or other forms of sensory information to improve a patient's ability to sense rectal distention and reinforce appropriate sphincter contraction.
- Published studies typically demonstrate improvement in continence for both adults and children as a result of biofeedback in over 70 % of the patients.
- Current described methods are widely variable and include weekly or biweekly sessions of 30 or 60 min, use of home practice machines, EMG, manometry, and even ultrasound. Long-term, the benefits of biofeedback are less clear, with many authorities suggesting an attenuation of results and the need for "refresher" training sessions. Regardless, a trial of biofeedback is considered an important noninvasive, first-line therapeutic option for highly motivated patients who have failed medical management.

Secca® Procedure

- The Secca® procedure involves the use of radiofrequency delivered as an alternating current at high frequency leading to frictional movement of ions and generation of heat or thermal energy. As a result of the delivered thermal energy, there is immediate contraction of collagen fibers, which are then permanently shortened via remodeling resulting in a tightening of the muscle.
- In Secca®, the radiofrequency is delivered to the anal sphincter under constant monitoring of the temperature and tissue impedance while simultaneously cooling the probes at the surface to minimize mucosal damage.
- The Secca® procedure is typically performed in an outpatient, ambulatory setting under intravenous sedation with local anesthetic. Prophylactic

antibiotics are given. The patient is positioned in either prone jackknife or lithotomy, following which, the handpiece is inserted into the anal canal and lined up, so the four needle electrodes will be deployed at the level of the dentate line.

- The patients selected are generally those with mild to moderate complaints of fecal incontinence who have failed conservative measures including dietary modification, pharmacotherapy and biofeedback, and do not have a demonstrable sphincter defect.
- To date, the studies have been limited by either small sample size or length of follow-up.

Injectables

- Injection of a biocompatible bulking agent has been adapted from its initial reported successful application in the treatment of urinary incontinence. Its chief application is for the treatment of minor fecal incontinence due to internal anal sphincter dysfunction.
- This option gains significance because surgical repair of the internal anal sphincter has not been shown to be effective, whereas more aggressive operations and their attendant complications are typically out of proportion to the complaints of this specific patient population. Proponents of this therapy cite the fact that it is a safe, minimally invasive therapy, typically administered on an outpatient basis, in some instances in an office setting with minimal complications under local anesthetic alone or with intravenous sedation.
- The technique involves injection of a bulking agent either into the anal submucosal or intersphincteric space.
- Currently the two most studied materials are silicone biomaterial and carbon-coated microbeads.
  - The mechanism of action is not fully understood, but Davis et al. suggested an increase in anal resting pressure secondary to augmentation of the anal cushions and restoration of anal canal symmetry. Other proposed mechanisms include bulking of the anal canal providing increased resistance to the passage of stool, allowing for improved sensation and that fibrosis over time contributes to increased sphincter muscle volume.
- Typically, the maximal improvement in fecal continence is observed within the first 1–6 months and appears durable up to 1–2 years later.
- Because of concerns of absorption and migration of the bulking agent, further long-term data are still needed.
- Additionally, the ideal number and location of injections, utility of ultrasound guidance for said localization, and which materials and volume are most suitable for injection have yet to be definitively determined.
- Table 18.2 summarizes the results of the use of injectables for the treatment of fecal incontinence.

Table 18.2 Injectable anal sphincter bulking agents for treatment of minor fecal incontinence

Author (year)	*N*	Bulking agent	Significant improvement of fecal incontinence	Mean follow-up (months)
Shafik (1995)	14	Autologous fat	Yes[a]	18.6
Kumar et al. (1998)	17	GAX collagen	*P* value not reported	8
Kenefick et al. (2002)	6	Silicone	Yes $P=0.04$	18
Weiss et al. (2002)	10	Carbon-coated microbeads	Yes ($P=0.012$) FIS 13–10	6
Davis (2003)	18	Carbon-coated microbeads	Yes ($P=0.003$) FIS 11.89–8.07	28.5
Tjiandra et al. (2004)	82	Silicone	Yes ($P<0.001$)	6
Van der Hagen (2007)		Silicone	Yes ($P<0.001$)	12
Altomare (2008)	33	Carbon-coated microbeads	Yes ($P<0.001$) FIS 12–8	20.8
Aigner (2009)	11	Carbon-coated microbeads	Yes ($P=0.003$) FIS 12.27 ± 0.97–4.91 ± 0.87	26.1
Tjiandra (2009)	20	Silicone	Yes $P<0.0001$ at 6 months	12
	20	Carbon-coated microbeads	Yes $P<0.0001$ at 6 months	12
Danielson (2009)		Hyaluronic acid	Yes ($P=0.004$)	

[a]All patients had complete continence at 2–3 months – following which all but three had deterioration of their results

Table 18.3 Long-term results of anterior overlapping sphincteroplasty

Year	Author	*N*	Months follow-up	Results
2000	Karoui et al.	74	40	45 % continent to solid and liquid
2002	Halverson and Hull	49	69	4 stomas 46 % continent to solid and liquid
2006	Barisic et al.	65	60	48 % "good or excellent"
2009	Oom et al.	120	69	37 % "good or excellent"

Operative Procedures

Anterior Overlapping Sphincteroplasty

- Anterior overlapping sphincteroplasty is the mainstay surgical treatment for patients suffering from severe fecal incontinence in conjunction with an external sphincter defect (Table 18.3 and Fig. 18.3).
- The details of the procedure are described in the ASCRS textbook.
  - Lateral dissection allows for identification of the normal ends of the external anal sphincter musculature.
  - Care should be taken not to proceed too far posterior due to the potential for injury to the nerves entering in this location.
  - Preservation of the scar tissue in this location is important for the ensuing repair as it is helpful in holding the sutures.

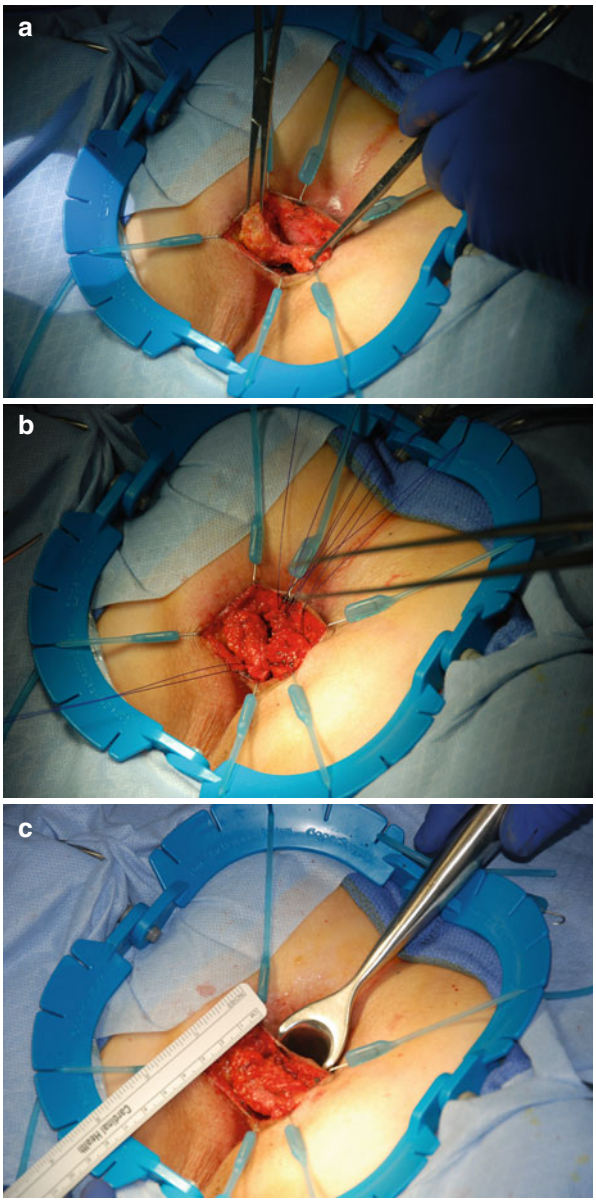

Fig. 18.3 (**a**) Anterior overlapping sphincteroplasty. Overlapping and suturing of the external anal sphincter in the *midline*; (**b**) anterior overlapping sphincteroplasty. (**c**) Final repair with recreation of the perineal body

- There has been suggestion that the presence of overlapped scar tissue correlates with improved short-term outcome as well.
- Outcome after end-to-end repair is somewhat inferior to overlapping repair, whereas overlapping repair might be associated with more evacuation difficulties.

  - The initial results of anterior sphincteroplasty are promising; however, numerous authors have noted diminishing efficacy over time with disappointing long-term continence.

Parks Posterior Anal Repair

- The Parks posterior anal repair has been described for the treatment of neurogenic fecal incontinence in those patients without a sphincter defect.
- The initial premise was that it lengthened the anal canal and corrected the anorectal angle.
- This operation is rarely performed and has not gained widespread support in the USA, possibly because of the published poor long-term results with continence rates of only 33 % at 5 years. Details of the procedure are in the ASCRS Textbook.

Sacral Nerve Stimulation

- Sacral nerve stimulation (SNS) or neuromodulation was initially developed for the management of urinary incontinence. It was subsequently noted that in patients with fecal incontinence treated with SNS for urinary incontinence the fecal incontinence also improved.
- This procedure has the most promising results for selected patients with fecal incontinence.
- Unlike other therapeutic modalities, SNS is a staged procedure.
  - The first stage is the percutaneous nerve evaluation (PNE), which serves as feasibility trial period lasting 2 weeks.
  - Patients who experience an improvement of 50 % or greater decrease in the number of incontinence episodes progress to the final stage and are offered placement of a permanent stimulator.
- The electrode placement is performed under sterile conditions with fluoroscopic guidance. Stimulation of the S2, S3, and S4 nerve roots via their sacral foramina is tested. The goal is to elicit contraction of the levator ani and external anal sphincter with plantar flexion of the first two toes, seen with stimulation of S3. The purpose of direct stimulation of the sacral nerves is to recruit additional inactive motor units to improve muscle strength, resulting in an increase in resting anal pressure. Additionally, SNS has been shown to improve the rectal sensory threshold and balloon expulsion time.
- Both the initial PNE and subsequent placement of the permanent stimulator are performed on an outpatient basis. Complications are rare and have all been minor with lead migration being most typical.
- The obvious benefit of sacral nerve stimulation is that it avoids creation of an incision around or near the anal canal, which decreases the risk of infection.
- Recently, the results of the largest prospective randomized trial of the use of sacral nerve stimulation have been published.

  - Sixteen centers in North America and Australia participated in the trial, which included 129 patients who underwent the subchronic stimulation phase. Of the 129 patients, 120 qualified for permanent implantation by achieving a decrease in the incontinent episodes by at least 50 % during the test phase. The mean follow-up period was 28 months. Persistent benefits of a 50 % decrease in the weekly incontinence episodes, incontinent days, and urgent incontinent episodes were noted in over 75 % of the patients at all follow-up periods up to 36 months, with most of interval measurements over 80 % success. There was also a consistent improvement in quality of life throughout the study period.
- This device is currently Food and Drug Administration (FDA) approved and shows promising results in the treatment of fecal incontinence.
- Promising short- and long-term success has been reported with significant and sustained decreases in the CCF-FIS. The results of sacral nerve stimulation and summarized in Table 18.4.

Artificial Bowel Sphincter

- The artificial bowel sphincter was first reported in 1987. The procedure involves creating a subcutaneous tunnel around the anus, typically through a transverse perineal incision. The cuff is situated around the anus. The pump is tunneled through a pfannenstiel incision down to either the labia or scrotum, while the reservoir is placed in the space of Retzius (Fig. 18.4a, b). All of the tubing is tunneled subcutaneously. The device provides continence by keeping the perianal cuff full in the resting state. When the patient needs to evacuate, he/she needs to actively pump fluid from the cuff to the reservoir. The cuff will then passively refill. When considering a patient for artificial bowel sphincter, it is important to ensure that there is not a significant soft tissue loss on the perineum, which could preclude adequate coverage and guarantee erosion. It is also imperative to ensure that the patient will have the manual dexterity to activate the device.
- Infection and erosion of the artificial sphincter with the subsequent need for explantation and revisional surgery have been the greatest challenge for patients and surgeons utilizing the artificial bowel sphincter.
  - The results of a multicenter trial were published by Wong et al. in 2002; 112 patients were implanted. There were 384 device-related adverse events in 99 patients. Two hundred and forty-six required either no or noninvasive intervention. Seventy-three revisional operations were performed in 51 (46 %) patients. Twenty-five percent of patients developed infection requiring surgical revision, and 41(37 %) patients had devices completely explanted. While the intention to treat success rate was low at 53 %, 85 % of patients with a functional device had a successful outcome.
  - Recent reports of the long-term outcome for patients with the artificial bowel sphincter have been published.

Table 18.4 Results of sacral neuromodulation

Author (year)	Patients (*N*)	Patients with permanent implant (*N*)	Fecal incontinence episodes/week		Cleveland Clinic Fecal Incontinence Score			
			Baseline	Follow-up	Baseline	Follow-up	*P* value	Follow-up (months)
Leroi (2001)	11	6	3	0.5				6
Rosen (2001)	20	16	2	0.67				15
Uludağ (2002)	44	34	8.66	0.67				11
Matzel (2003)	16	16	40 % of movements	0 % of movements	17	5	0.003	32.5
Jarrett (2004)	59	46	7.5	1	14	6	<0.0001	12
Hetzer (2007)	44	37			16	5	<0.001	13
Holzer (2007)	36	29	2.33	0.67				
Tjandra (2008)	60	53	9.5	3.1	16	1.2	<0.0001	12
Altomare (2009)	94	60	3.5	0.7	15	5	<0.001	74
Wexner (2010)	129	120	87 % of patients decreased incontinent episodes per week by 50 %					28

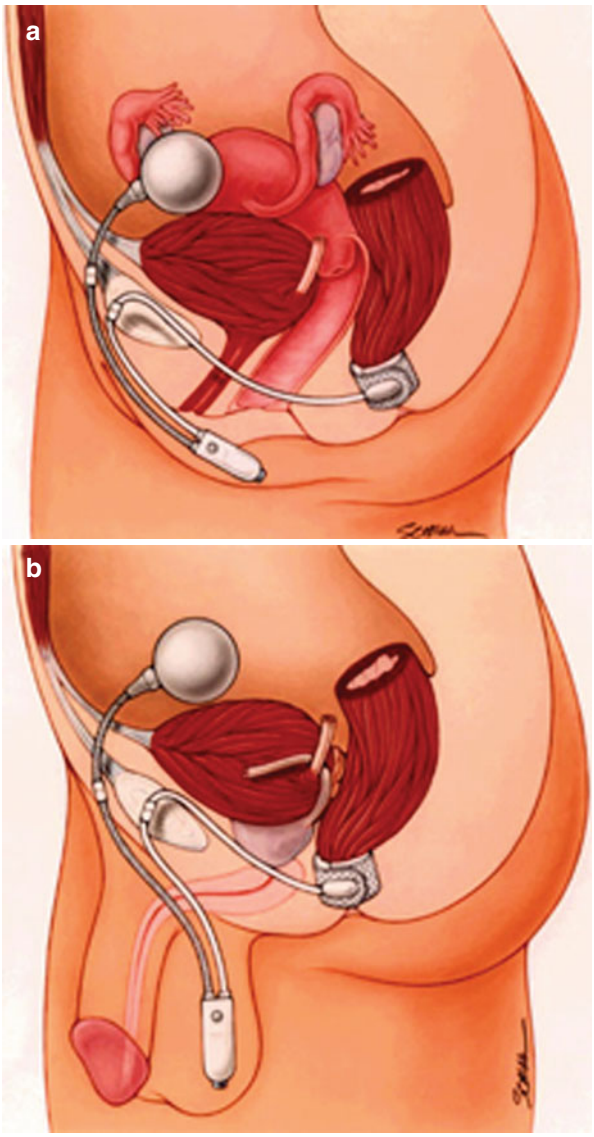

Fig. 18.4 Artificial bowel sphincter. Artificial bowel sphincter implanted in the (**a**) female and (**b**) male patient (With permission from Acticon®, American Medical Systems®, Inc., Minnetonka, MN, http://www.AmericanMedicalSystems.com)

All of the patients had some complication and 65 % required at least one reoperation. There was a 41 % infection rate noted in the series of 51 implantations, of these, 35 % were early and 6 % late.

- The major challenge of this treatment for fecal incontinence continues to be infection followed by late device-related complications.

Muscle Transposition

- The concept of substituting the anal sphincter was first reported by Chetwood in 1902 using the gluteus maximus. The ideal muscle for substitution of the sphincter complex should have a negligible role in movement and posture, yet it should be able to provide sufficient bulk. The muscle itself must have a reliable neurovascular bundle, so that it will not be damaged in the process of dissection.
- The advantages of the gluteus maximus muscle are that it has a location in close proximity to the anal canal and provides excellent strength and bulk to the anal canal; however, its use poses significant functional impairment to the patient while standing or climbing stairs.
- The majority of data are case series.
- The procedure is rarely performed today. The major technical difficulty of this procedure is obtaining sufficient length to adequately encircle the anal canal.

Gracilis Muscle Transposition

- Gracilis muscle transposition was first reported by Pickrell in 1952 for the treatment of children with fecal incontinence due to neurologic and congenital anomalies.
- It is generally a treatment option best for those patients whose incontinence results from either trauma or congenital anomaly, where the additional muscle bulk can supplement deficient native tissue.
- The essence of the operation is mobilization of the gracilis muscle followed by transposition of the muscle around the anus and fixation to the contralateral ischial tuberosity. Details about the procedure are in the ASCRS textbook.
- A randomized, controlled trial comparing unstimulated to stimulated graciloplasty has not been done.
- With the use of sacral nerve stimulation and the lack of FDA approval for gracilis stimulated myoplasty in the United States, the procedure is rarely performed. It remains a viable option for a highly selected group of patients in other countries.

Fecal Diversion

- Creation of a colostomy or ileostomy is typically the therapeutic option of last resort, when all other reasonable options have been exhausted.
- The majority of patients will be best served with an end sigmoid colostomy, but some patients with chronic constipation and slow transit may be best served with an ileostomy.
- Predictably, strong resistance even in the face of severe and debilitating incontinence is common. Patient education in the form of a visit with an enterostomal therapist and perhaps a patient already living with an ostomy can greatly ease anxiety.
- It is important to emphasize that there is no time limit for the decision to convert an uncontrolled perineal stoma to a more easily managed abdominal one.

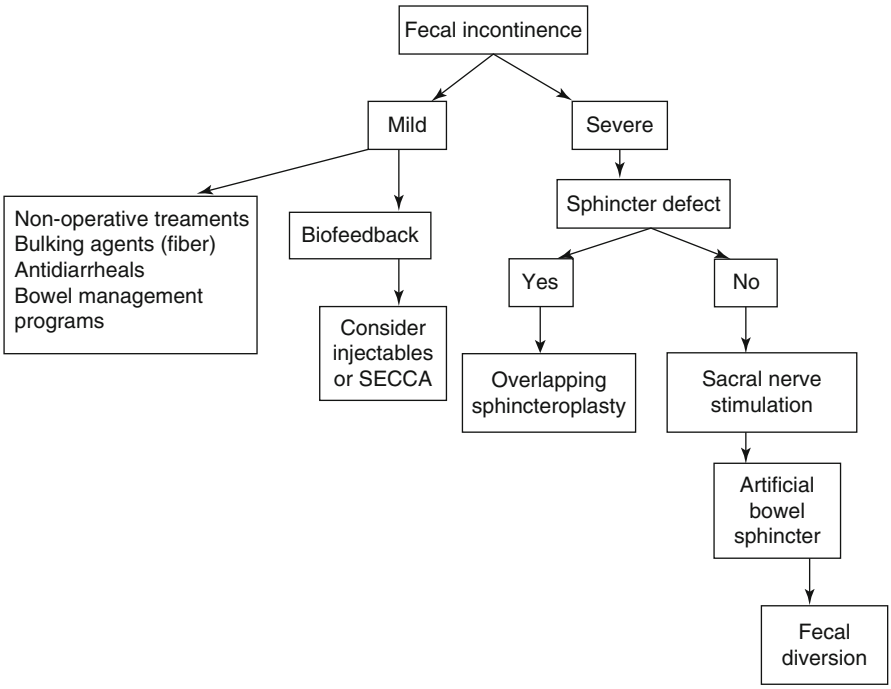

Fig. 18.5 Algorithm for the management of fecal incontinence

Conclusion

- Fecal incontinence is a socially devastating condition, which is extremely common and under reported.
- There are many options available for patients who can treat or significantly improve their symptoms.
  - The first step for the physician is to diagnose the problem. This will often not take place until the examiner specifically asks the patients as they will often not offer the information. Through a detailed history, the physician can formulate a differential diagnosis.
  - Anorectal physiologic testing can add specific information with regard to the functional status to the sphincter musculature. Many patients quality of life can be improved with noninvasive modalities focused on improving stool consistency and strengthening of the musculature with biofeedback.
- If there is a significant impact on quality of life and the patient is a candidate for invasive therapy, surgical intervention should be considered.
  - The overlapping sphincteroplasty remains the mainstay of surgical treatment when a sphincter defect is present. Sacral nerve stimulation has an increasing role in the treatment of fecal incontinence. For less severe forms of incontinence, injectables and SECCA may be of benefit. Figure 18.5 provides a generalized algorithm for the management of fecal incontinence.

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19. Pelvic Floor Disorders

Patrick Y.H. Lee and Guillaume Meurette

- Pelvic floor disorders are a continuum of a disease processes resulting from the loss of pelvic floor support.
- Although these diseases are commonly believed to afflict primarily women, the ease of examination of the pelvic floor in women makes the identification of pelvic floor disorders easier in women than in men.
- Anatomical differences in the size of the genital hiatus between the sexes also make women more prone to pelvic floor prolapse.
- Epidemiologic studies on pelvic floor prolapse suggest that it is a disease that will become more prevalent as the population ages.
- Despite the incomplete knowledge on the etiology of pelvic floor laxity and prolapse, surgical management is one of the most important modalities in the repair of the pelvic floor in women.
- Hence, successful repair of the pelvic floor requires a good understanding not only of the pelvic floor anatomy but also of the dynamic interaction between pelvic floor muscles and organs.
- The levator ani complex and the supporting or endopelvic fascia are the two most important dynamic structures of the pelvis (Fig. 19.1a, b).
- The endopelvic fascia is found between the visceral peritoneum and parietal fascia of the levator ani and is a fibroareolar tissue containing neurovascular bundles, smooth muscles, collagen, and elastin (Fig. 19.2).
- Equally important to the understanding of pelvic anatomy is an understanding of the dynamic changes of the pelvic organs. Kelvin and associates popularized the use of four-contrast study to outline the small bowel,

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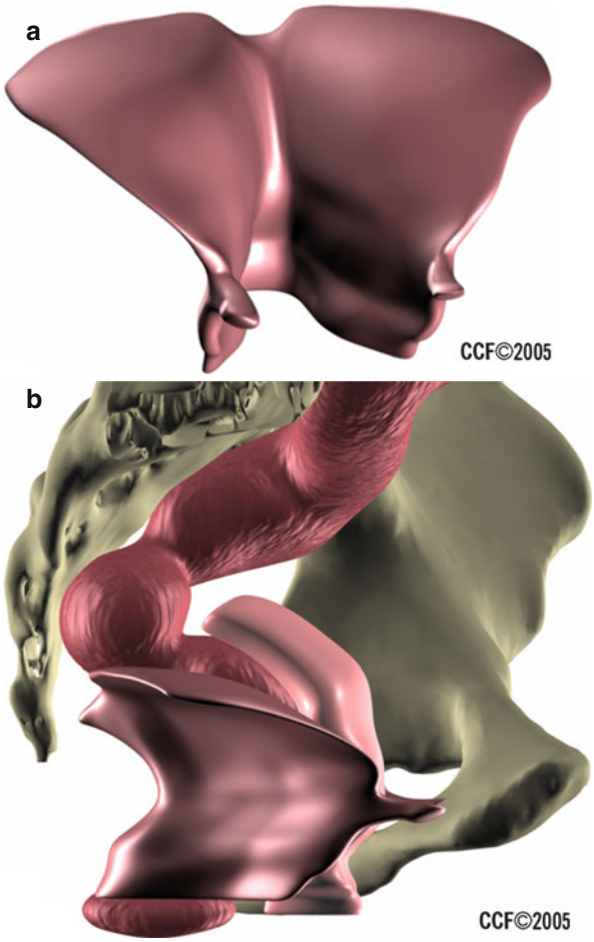

Fig. 19.1 (**a**, **b**) Digitally enhanced MRI reconstruction of the levator ani at rest in a 23-year-old nulliparous woman. The levator ani gives a biconcave shape posteriorly and the puborectalis show as a sling imbedded in the muscle of the pelvic floor (Reprinted with permission from Cleveland Clinic Center for Medical Art and Photography© 2004–2009 and Matthew Barber, MD)

bladder, vagina, and rectum. The dynamic evaluation of the pelvic floor before, during, and after evacuation of the contrasts in the rectum and bladder not only yields a tremendous amount of information about the function of the pelvic organs and the surrounding structures which support them, but it also complements physical examination for enterocele, one of the findings in advanced pelvic floor prolapse.

- Kelvin et al., using their four-contrast study to evaluate 74 women with pelvic floor prolapse, found 14 (19 %) to have enteroceles, 50 % of which were missed on physical exam.

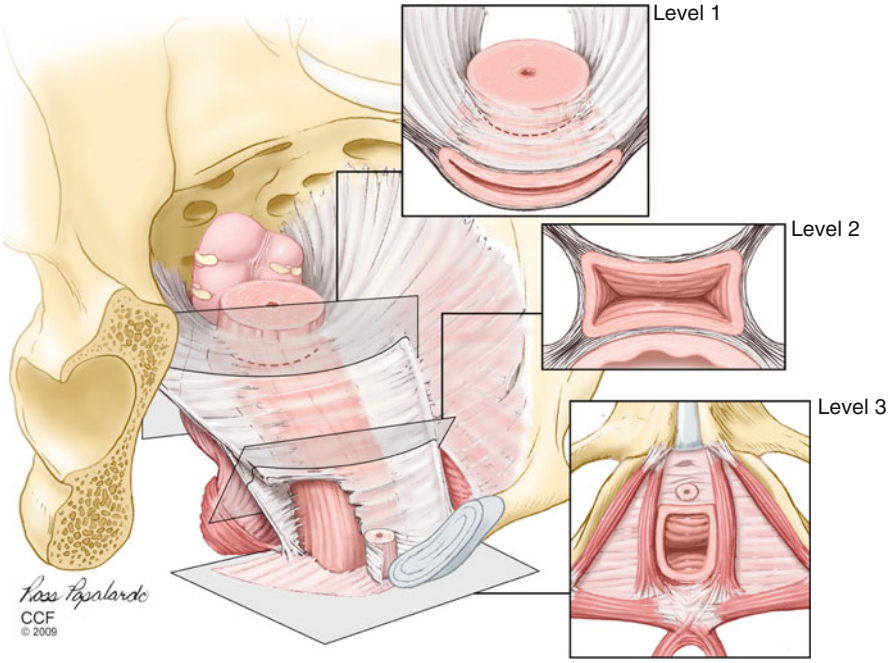

Fig. 19.2 Illustration of the endopelvic fascia as it fans out to cover the pelvic floor and provide support to the surrounding organs. The *levels 1*, *2*, and *3* depict the vaginal support (Reprinted with permission from Cleveland Clinic Center for Medical Art and Photography© 2004–2009 and Matthew Barber, MD)

- These dynamic studies also helped to identify other pelvic organ dysfunctions. In a study of 100 women referred for evaluation of pelvic floor prolapse, dynamic cystoproctography or cystodefecography found that of the 20 patients with anterior compartment systems (urinary), 45 % had middle compartment findings of vaginal vault prolapse; of posterior compartment findings, 90 % had rectocele, 40 % had enterocele, and 35 % had rectal intussusception.
- Similarly, of the 45 patients with symptoms of middle compartment defects (genital), 91 % had anterior compartment findings of cystocele and 56 % of hypermobile bladder neck; of posterior compartment findings, 82 % had findings of rectocele and 58 % of enterocele.
- Of the 17 patients with posterior compartment symptoms (anorectal), 71 % had cystocele, 65 % had hypermobile bladder neck, and 35 % had vaginal prolapse. Their study concluded that 95 % of the women with pelvic floor dysfunction had abnormalities of all three compartments.
- This study underscores the global nature of pelvic floor disorders and the need to understand the pelvic floor as a unit rather than as compartments.

Enterocele

- The loss of pelvic organ alignment as seen on cystodefecography of the bladder, vagina, uterus, and rectum is obvious, but the significance of an enterocele remains controversial.
- Kinzel described an enterocele as a "true" hernia because it contains a hernia sac (the pouch of Douglas), neck, and contents.
- Delancey postulates that enterocele sac develops as a result of the loss of suspension of the upper vagina and muscle integrity of the levator ani muscles that leads to the herniation of the cul-de-sac between the rectum and vagina.
- Enteroceles are often classified as congenital, pulsion, traction, and iatrogenic.
  - A congenital enterocele is a result of the failure of the fusion of the anterior and posterior peritoneum during fetal development, resulting in a deep pouch of Douglas.
  - Pulsion type is caused by chronic increase of abdominal pressure.
  - While traction type is caused by the loss of pelvic floor support and resulting in the pulling or traction of the pelvic organ on the surrounding structures out of the pelvis such as the vagina.
  - Iatrogenic is caused by surgical injury.
- The clinical presentations of an enterocele are dependent on the extent of the herniation and may present from no physical findings to bulging of the perineum or posterior vagina during strain.
- Clinical examination of the vagina or bidigital exam of the rectum and vagina during maximum strain can help detect the spreading of the rectovaginal plane between the fingers as the enterocele enters into the rectovaginal plane; however, physical examination is unreliable in detecting enterocele.
- Kelvin et al. reported their findings on 170 patients with symptoms of pelvic floor dysfunction who were evaluated by urogynecologist and found 47 patients (28 %) with an enterocele; only 24 (51 %) of these patients were found by physical exam.
- There are, however, controversies about the significance of enterocele containing small bowel versus sigmoid colon.
- Some contend that enteroceles containing sigmoid colon result in defecatory dysfunction, whereas enteroceles containing small bowel are more reflective of pelvic floor prolapse.
- MRI has been reported to be useful in the detection of enteroceles (Fig. 19.3).
- It is also helpful in evaluating not only the size of the levator hiatus in prolapse but also the changes in the anatomy of the levator ani muscle.

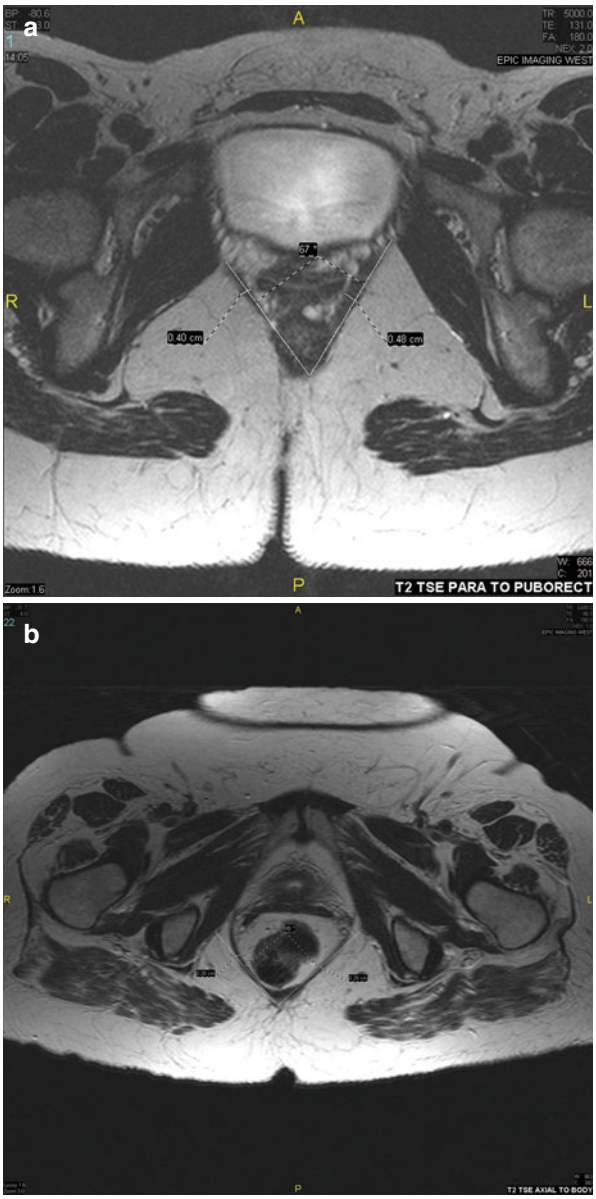

Fig. 19.3 MRI of the levator hiatus, normal on the *top* (**a**) and enlarged on the *bottom* (**b**). The angle between the *two lines* drawn along the puborectalis muscle and bisecting in the posterior midline of the levator ani defines the levator hiatus angle. This angle can also be measured by endorectal ultrasound and is found to correlate with findings of enterocele and pelvic floor prolapse findings on MRI and cystodefecography

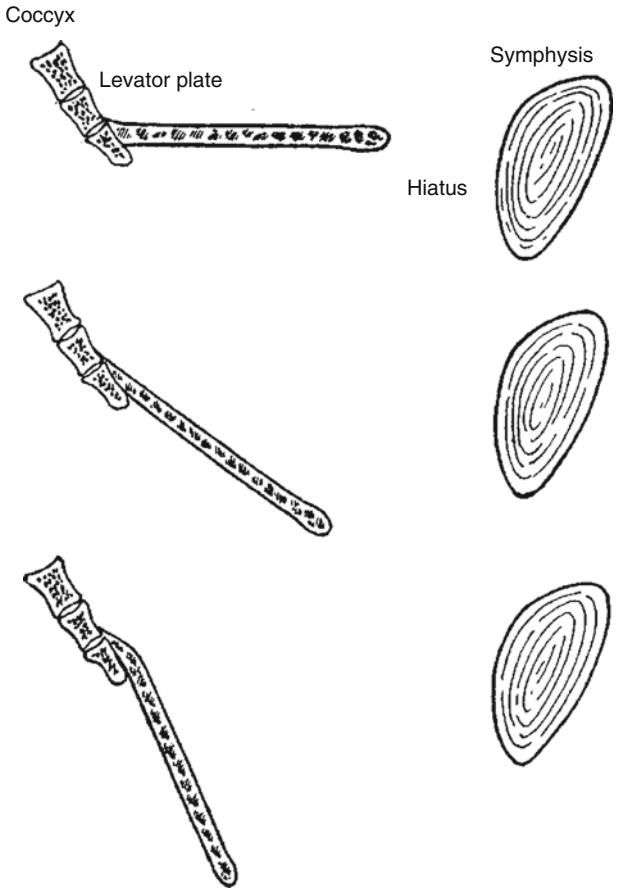

Fig. 19.4 Illustration of the incline of the levator plate and enlargement of the levator hiatus resulting in pelvic organ prolapse (With permission from Berglas B, Rubin IC. Study of the supportive structures of the uterus by levator myography. Surg Gynecol Obstet 1953;97:677–92)

- Singh et al. used a three-dimensional MRI reconstruction to assess the size of the levator hiatus and morphology of the levator ani muscle.
- They found that increasing stage of prolapse correlated with increasing size of the levator hiatus, but not with the morphology of the levator ani (Fig. 19.4).
- They proposed that patients who have pelvic organ prolapse with normal levator ani morphology may only need fascial repair compared to those who show morphologic changes of muscle injury.
- Currently, the MRI remains the best imaging technique in looking at the anatomy of the pelvic floor, while cystodefecography provides for dynamic images of the pelvic organs during defecation and urination.
- The increasing use of open-configuration MRI to allow the patient to assume a sitting position has shown this to be equivalent to the supine

MRI in the evaluation of pelvic floor laxity. In the future, the open-configuration MRI may offer superior imaging findings compared to cystodefecography.

- The MRI and cystodefecography studies have helped confirm what is already clinically known about the enlargement of the levator hiatus in pelvic organ prolapse. What is not known is at what point in the levator hiatus enlargement does pelvic organ dysfunction or prolapse occur, and why.
- The true incidence or prevalence of colorectal diseases associated with pelvic floor disorder is unknown.
- This is in part due to our failure to recognize the early signs of pelvic floor laxity and in part due to the poor correlation between the degree of pelvic organ prolapse and symptoms.
- In an attempt to identify patients with pelvic organ prolapse by history, Barber et al. found that when patients with high probability of prolapse were asked, "Do you usually have a bulge or something falling out that you can see or feel in your vagina?" an affirmative answer had a 96 % sensitivity (95 % CI 92–100) and 79 % specificity (95 % CI 77–92) for stage III and IV vaginal prolapse defined by the Pelvic Organ Prolapse Quantification (POP-Q).
- Interestingly, the degree of colorectal symptoms associated with vagina and bladder prolapse seems to be higher in early stages than in late.
- The progression of enlargement of the levator hiatus appears to be in a ventral-caudal direction.
- This view is supported not only by cystodefecography and MRI studies but also by numerous clinical studies showing the higher incidence of urinary and vaginal prolapse over rectal prolapse in women with pelvic floor prolapse.
- Furthermore, patients with rectal prolapse have on average of 1.5–3.3 operations related to bladder and vaginal prolapse prior to their presentation with anorectal symptoms. Peters et al. studied 55 women with rectal prolapse; 95 % had other pelvic floor defects. The five most common complaints were vaginal prolapse/pressure (92 %), rectal prolapse/pressure (69 %), constipation (71 %), fecal incontinence (40 %), and obstructive defecation (38 %). Their study underscores the importance of colorectal evaluation in patients with vaginal prolapse/pressure.
- Although there are no longitudinal studies to validate the progression of pelvic floor prolapse resulting in rectal symptoms, the clinical studies along with the cystodefecography and MRI support the postulate that as the rectum descends and loses its anatomical alignment in the pelvis, a spectrum of colorectal symptoms will emerge.
- In the early phase, the symptoms of worsening "hemorrhoids" and mucous discharge may be related to rectal mucosal prolapse.
- As the rectum descends further from the pelvic floor, symptoms of incomplete evacuation of stool and needing to splint or use fingers to extract the stool are often associated with rectocele and internal rectal prolapse.

Fig. 19.5 Extreme form of multiorgan prolapse with rectum, uterus, vagina, and bladder prolapsed out of the levator hiatus

- In the advanced phase of rectal prolapse, symptoms of tissue protrusion out of the anus or vagina, along with pressure and pain in the local and regional areas of the pelvis, may represent the rectal and vaginal prolapse with enterocele.
- In the extreme form of pelvic floor prolapse, the rectum, vagina, uterus, and bladder are prolapsed out, as shown in Fig. 19.5. Sullivan et al. described this condition as the tetralogy of Fallot.
- The continuum of pelvic floor laxity leading to anorectal symptoms makes it difficult to evaluate the effectiveness of medical versus surgical management, but medical management becomes less effective than surgery when the patient's complaints and physical findings of rectal and other pelvic organ prolapse become evident.

Rectocele

- The presence of rectocele and multi-pelvic organ prolapse is specific to pelvic floor disorders and manifests as complaints of rectal pressure, defecation difficulty, incomplete emptying, fecal seepage, low back and pelvic pain, "hemorrhoids," and tissue "falling out" of the rectum and vagina.
- The evaluation and determination of when a rectocele becomes significant for surgical intervention are hampered by the lack of a unified agreement on the pathogenesis and diagnostic evaluation of rectoceles.

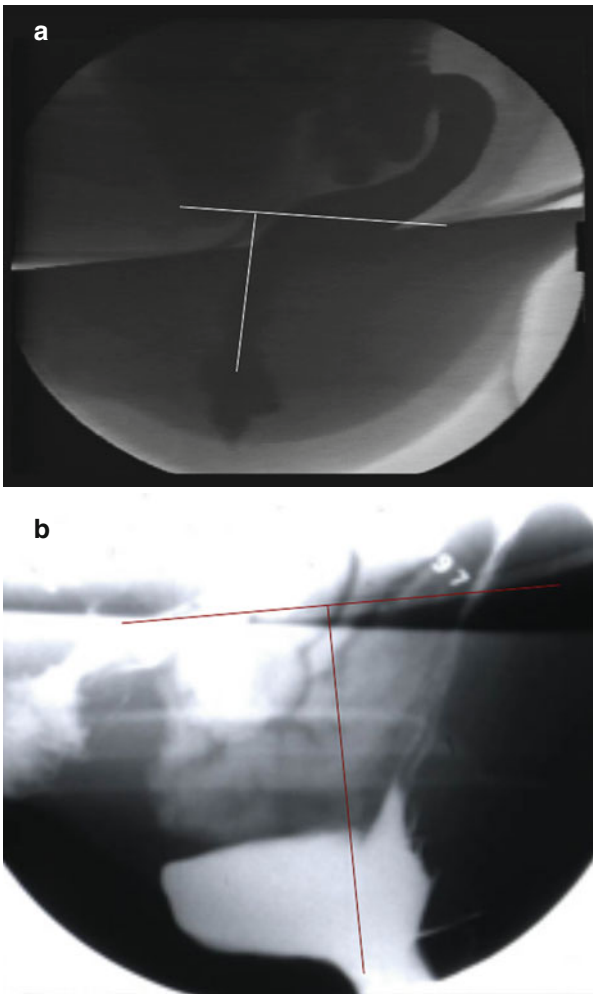

Fig. 19.6 Cystodefecographies show the widening of the distance between the pubis and anal opening in patients on the *top* (**a**) compared to the normal on the *bottom* (**b**). Measurement of the distance can be made by drawing a perpendicular line from the pubococcygeal line to the anal opening during the defecation phase

- They are usually described as herniation or defect of the rectovaginal septum, but clinical findings of perineal laxity and cystodefecography findings of increased length between the pubis and anus during strain, as shown in Fig. 19.6a, b suggest that rectoceles also have a component of rectal descent in addition to rectovaginal defect.
- The evidence of rectal descent is even more compelling in men with rectocele.
- Chen et al. evaluated 234 men with defecation complaints and found 40 men (17 %) with rectocele; 40 % had prostatectomies. Rectoceles were

anterior in 48 % and posterior in 52 %, nonrelaxing or partially relaxing puborectalis muscle 66 %, perineal descent 65 %, intussusception 23 %, and sigmoidocele 15 %.

- Their findings support the view that rectoceles rarely occur in isolation. Furthermore, rectoceles are not all equal in their effect on defecation dysfunction.
- Pucciani et al. described two types of rectocele in women, type I (distension) and type II (displacement), and found that type II was associated with higher incidence of vaginal prolapse, more frequent manual evacuation, lower anal pressure, and greater mucosal intussusception than type I.
- The displacement type of rectocele is likely a result of the descent of the rectum. Brubaker described the displacement of the rectum as the "rectal width" and correlated this to stool entrapment. The loss of rectal alignment in the pelvis means that intraabdominal pressure is ineffectively transferred during defecation, leading to obstructive defecation complaints. Halligan et al. showed that patients who were able to expel a 10 cc pressure transduced balloon had higher intrarectal pressure than those who did not (median 208 versus 143 cmH_2O). Evacuation ability of the rectal balloon correlated with defecography findings of prolonged and incomplete evacuation.
- Interestingly, they found eight patients who had prolonged evacuation time, low intrarectal pressure, and very little change in pelvic floor descent, and concluded that these patients lacked the ability to generate intraabdominal pressure. It is unclear if these eight patients had extreme pelvic descent such that they could not have any further excursion of their pelvic floor during the evacuation phase of their defecography.
- Karlbom et al. showed that successful improvement of rectal emptying after rectocele repair is associated with elevation of the pelvic floor.
- Surgical repairs of rectoceles are generally divided into transanal and transvaginal approaches.
- Transabdominal approaches for rectocele are usually done in conjunction with other more severe pelvic organ prolapse findings.
- The most common transanal approach to rectocele repair is the modified Delorme procedure popularized by Sullivan et al. in which the anterior rectal wall was plicated after the mucosa was lifted up from the muscularis propria.
- The recognition that up to 70 % of rectal mucosal intussusceptions or internal rectal mucosal prolapses were associated with rectocele led to the return of Delorme's original description of the repair, which involved the circumferential stripping of the rectal mucosa and plication of the rectal musculature.
- The technique is described in the ASCRS textbook.
- Long-term outcomes of transanal rectocele repair are associated with 50 % recurrence at 5.5 years. It is unclear if recurrence means return of symptoms of obstructive defecation or anatomical recurrence of rectocele, or both.

- Other techniques using a stapler to obliterate the rectocele and reduce intussusception, such as the single-stapled transanal prolapsectomy with perineal levatorplasty (STAPL) and double-stapled transanal rectal resection (STARR), had 76 and 88 % improvement of obstructive defecation symptoms at 20 months, respectively.
- Again, the lack of postsurgical defecography or MRI studies makes it difficult to explain why reduction of the rectocele results in improvement of symptoms.
- Van Laarhoven et al. showed that there is no correlation between patients' symptoms and size of rectocele reduction, suggesting that other factors may be at play for patients' improved symptoms.
- Transvaginal techniques of rectocele repair or posterior colporrhaphy are primarily performed by gynecologists using one of the four techniques:
  1. Levator ani (puborectalis) or rectovaginal muscularis reapproximation
  2. Site-specific repair of the rectovaginal septum
  3. Reapproximation of the rectovaginal septum to the levator ani fascia
  4. Posterior repair of the rectovaginal defect with grafts or mesh
- All these techniques involve an incision in the posterior wall of the vagina and separating the plane between the rectum and vaginal wall.
- Once the exposure is complete, then various techniques of reinforcement of the septum are performed. In general, the approximation of the levator ani results in up to 50 % incidence of dyspareunia.
- This technique has been mostly abandoned and replaced with rectovaginal septal repair by reapproximating it either longitudinally or transversally, with or without grafts or mesh.
- The concept of site-specific repair of the rectovaginal septum is best described by Richardson, who described "breaks" in the rectovaginal septum resulting in rectocele formation. Depending on the location and extent of the breaks, various types of rectocele emerge, and with higher "breaks," enteroceles may enter into the rectovaginal plane. The use of biologic grafts and synthetic mesh in rectocele repair is reserved for large rectoceles (with >4 cm depth), presence of vaginal prolapse, poor native tissue, and associated vagina and bladder prolapse. In general, the use of grafts or mesh in the repair of rectocele is safe, but its superiority and efficacy over established repair remains inconclusive.
- The best study on the benefits of transvaginal repair of rectocele was done by Mellgren et al. who reported on 25 patients prospectively for a mean period of 1 year.
- Constipation was present in 88 % preoperatively and relieved in 84 % postoperatively.
- Paraiso et al. reported their randomized trial evaluating three surgical techniques of posterior colporrhaphy (rectovaginal muscularis reapproximation, site-specific repair, and site-specific repair with a xenograft) and found all three methods had similar improvement in symptoms, quality of

life, and sexual function. Interestingly, they found a 46 % anatomical failure rate with the xenograft, but without any difference in outcome compared to the other two techniques.

- No cystodefecography studies were performed before or after the repairs to document the effects of the surgical intervention, which makes it difficult to explain the unexpected outcomes of any pelvic floor repair.
- Progression of pelvic floor laxity leads to complex, multi-pelvic organ prolapse similar to what Sullivan et al. described as the tetralogy of Fallot.
- Central to the successful restoration of the pelvic organs to their anatomic position is stabilization of the perineal body and reinforcement of the rectovaginal septum or posterior vaginal fascia.
- In men, this septum or fascia is known as Denonvilliers' fascia.
- In 1933, Sears published anatomic findings of the rectovaginal septum and described it as a double-layer sheet of fascia arising from the levator ani and uterosacral ligament. One of the layers (lateral) forms the urogenital diaphragm, and the other (medial) fuses to the fibers of the posterior vagina and perineal body (Fig. 19.7).
- Milley and Nichols provided further evidence of the relationship between the rectovaginal septum and perineal body in 143 specimens, whose ages ranged from 8 weeks fetus to 100 years.
- Lane in 1962 was the first to use mesh in the pelvis to reinforce the rectovaginal septum in the repair of vaginal vault prolapsed. Although there has been a plethora of mesh development, Lane's technique of the transabdominal sacrocolpopexy has undergone very little modification.
- Nygaard et al. summarized the published data on abdominal sacrocolpopexy from 1966 to 2004 and reported that the range of success rates for apical prolapse was 78–100 %, organ prolapse 58–100 %, reoperation for prolapse median 4.4 % (range 0–18.2 %), and mesh erosion 3.4 %.
- They concluded that sacrocolpopexy with mesh is an effective technique for vaginal apical prolapse, but reported an increase in constipation complaints from 29 to 52 %.
- Pilsgaard and Mouritsen reported their experience with 35 patients who underwent sacrocolpopexy with mesh with a mean follow-up period of 2 years (6 months to 4.5 years) and reported a 30 % increase in the symptoms of defecation difficulty. The exact etiology of the increased defecation dysfunction or constipation is unclear.
- Addison et al. reported on three cases of sacrocolpopexy with mesh failure and suggested mesh avulsion from the apex of the vagina or herniation below the mesh repair as a cause of recurrent symptoms of prolapse. They advocated placement of the mesh throughout the length of the vagina.
- Sullivan et al. in 2001 published the largest long-term result on pelvic floor prolapse repair with their technique called total pelvic mesh repair (TPMR).

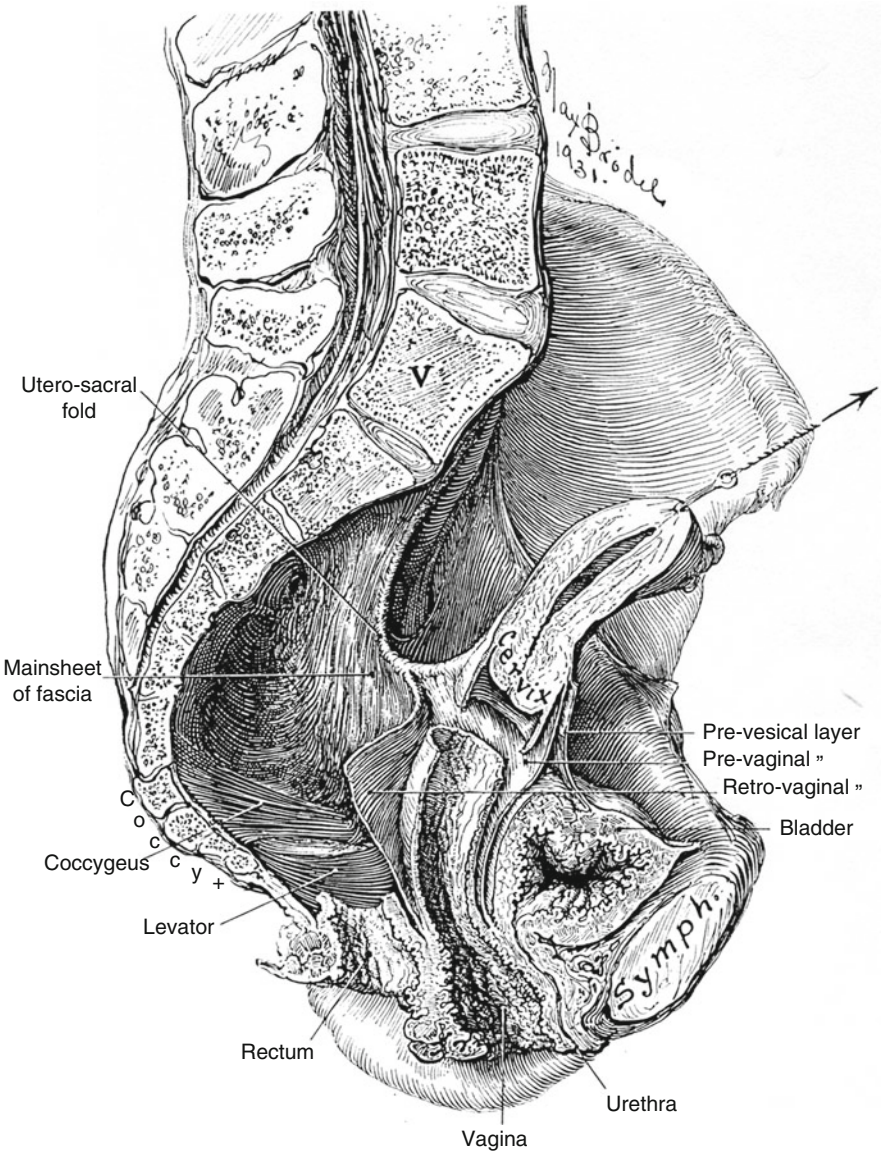

Fig. 19.7 The endopelvic layer arising from the pelvic sidewall and fanning out between the rectum and vagina to form the rectovaginal septum and anchoring to the perineal body (With permission from Sears NP. The fascia surrounding the vagina, its origin and arrangement. Am J Obstet Gynecol 1933;25:484–92)

Fig. 19.8 In the total pelvic mesh repair (TPMR), a Cobb-Ragde needle (V. Mueller, Deerfield, IL) is placed in back of the rectovaginal sulcus and pushed through into the introitus to secure the perineal body. A polypropylene suture is placed through the eye of the Cobb-Ragde needle and pulled into the pelvis to secure the mesh between the sacrum and the perineal body. Two additional strips of mesh are then placed on each side of the sacroperineal mesh, tunneled deep to the peritoneum, and secured lateral to the vagina and bladder to Cooper's ligament in the space of Retzius

  - Over a 10-year period, 236 women had TPMR, and 205 were available for a median follow-up of 5.3 years. They reported resolution of defecation difficulty in 76 % and of fecal incontinence in 85 %, and patient satisfaction of 74 % at 6 years or greater. Their procedure incorporates the current understanding of perineal stabilization and reinforcement of the rectovaginal septum by placing a mesh for the full length of the vagina and anchoring it to the perineal body. The procedure is outlined in Fig. 19.8). This study highlights the importance of perineal body stabilization and rectovaginal septum reinforcement with mesh in the support of pelvic floor prolapse.
- The use of mesh slings have proliferated beyond the initial use for urinary incontinence and have been advocated for the treatment of fecal incontinence and rectal prolapse.
- Although mesh placement, regardless of whether it is a transabdominal, transvaginal, or transperineal approach, seems to offer a better outcome than non-mesh repairs, there are no conclusive evidence to suggest that patients with early symptoms and findings of pelvic floor laxity will require more advance repairs with mesh than those patients reported by Sullivan et al., Cundiff et al., and others.

- The current techniques of local repair of the bladder, vagina, and rectum may be adequate, provided that clinical and radiologic findings show them to be truly isolated pelvic organ prolapse, but as discussed earlier such isolated prolapse is uncommon, and the failure to recognize and repair multiorgan prolapse is a primary source of patient dissatisfaction.
- Unlike diseases, which are surgically addressed with one technique such as appendicitis, the pathogenesis of pelvic floor prolapse is chronic and results in progressive constellation of symptoms and findings.
- The global transformation of the pelvic floor may result in surgical treatments that are successful for a limited period of time and fail not because of the technique but because of the progression of the pelvic floor prolapse.
- The exact etiology of pelvic floor prolapse remains unknown, and it is for this reason that dynamic imaging with cystodefecography, MRI, and other modalities are so important in documenting the disease process of pelvic floor disorders.
- Undoubtedly there will be new technologies and techniques that will evolve to replace the old, but as Moschcowitz most elegantly put it in his axiom, or generally accepted truth, about treatments of rectal prolapse, "the more remedies there are suggested for the cure of a malady, the less the likelihood of the efficacy of any particular one."
- A corollary to this axiom would be, "the more remedies there are for a disease, the more reflective of our lack of understanding of its pathogenesis."

20. Anal Cancer

Mark Lane Welton and Nalini Raju

New Anatomic Considerations

- In 2013, the American Cancer Society estimates that there will be 7,060 new cases of anal cancer in the United States.
- New terminology based on landmarks that all healthcare providers can easily visualize and understand has been developed and adopted in the latest version of the American Joint Committee on Cancer (AJCC) Staging Manual. The new terminology is necessary because true anal canal lesions may have a more aggressive biology requiring chemoradiotherapy while 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 classification system divides the region into three easily identifiable regions: anal canal, perianal, and skin (Fig. 20.1a, b).
  - *Anal canal* lesions are lesions that cannot be visualized at all, or are incompletely visualized, with gentle traction placed on the buttocks.
  - *Perianal lesions* are completely visible and fall within a 5 cm radius of the anal opening when gentle traction is placed on the buttocks.
  - *Skin lesions* fall outside of the 5 cm radius of the anal opening.

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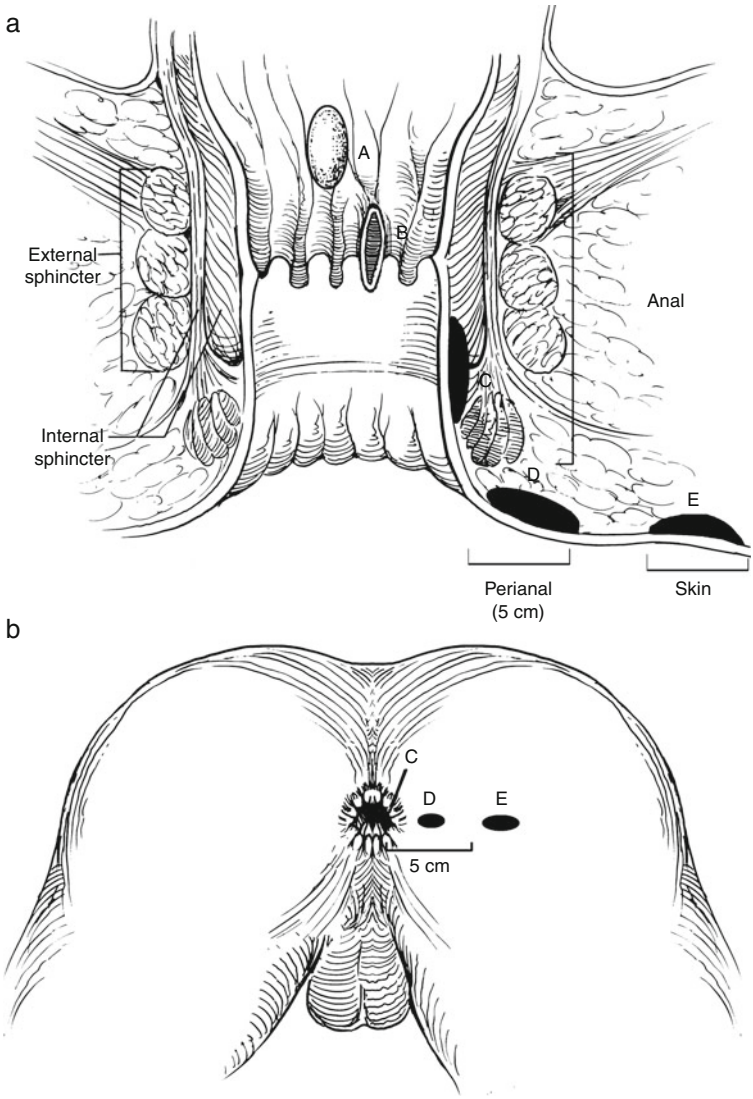

Fig. 20.1 (**a**, **b**) Terminology for location of anal and perianal lesions. Tumors *A*, *B*, and *C* represent *ANAL* lesions that are not visible or are incompletely visible while gentle traction is placed on the buttocks. Tumor *D* is a perianal tumor because it is completely visible with gentle traction on the buttocks and lesion *E* is a skin cancer

- 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 exam in their offices without the aid of an anoscope or a clear understanding of the anatomic landmarks (dentate line and anal verge) of the region.

- Identification of a new zone, the *transformation zone*, was also proposed to help clinicians and pathologists understand how anal squamous cell carcinomas (SCC) 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.
- The *transformation zone* of the rectum is a region in which squamous metaplasia may be found overlying the normal columnar mucosa. This immature metaplastic tissue may extend up to the rectum in a fluid and dynamic fashion 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.

Terminology

- The terminology used by pathologists when reporting premalignant lesions of the anus and perineum is often confusing to the treating clinicians.
- The terms squamous cell carcinoma 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 (a cytologic diagnosis) and dysplasia have both historically been broken into AIN I, II, and III and low-, moderate-, and high-grade dysplasia. However, as with other pathological staging systems, the intra- and interobserver variability is too high with this many categories. Therefore, when referring to anal canal, perianal, and skin lesions of the buttock, the tissue should be classified histologically, as either normal, low-grade squamous intraepithelial lesions (LSIL), high-grade squamous intraepithelial lesions (HSIL), or invasive cancer as is done in the AJCC Staging Manual.

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.

Etiology and Pathogenesis of Anal Dysplasia and Anal Squamous Cell Carcinoma

- The HPV is a necessary but not sufficient cause for the development of anal SCC and SIL. HPV is a DNA papovavirus with an 8 kb genome and is the most common viral sexually transmitted infection.
- 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 develop subclinical infections that may harbor malignant potential (HPV serotypes 16, 18, 31, 33, 35).
- Transmission is not prevented by condoms as 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 intra-anal disease, but the presence of condylomata or dysplasia within the anus does not indicate that anoreceptive intercourse has occurred.
- Fortunately, the angiogenic changes associated with the development of anal HSIL are also visible with the aid of acetic acid and Lugol's solution in the perianal skin, anus, and distal rectum through an operative microscope, colposcope, or loupes in the office or operating room (Fig. 20.2a–d). 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 were introduced for cervical disease.
- The cost-effectiveness of 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 MSM 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. Initial studies accumulating anal cancer rates from the pre-HAART (highly active antiretroviral therapy) era failed to show a correlation presumably because patients succumbed to complications of the HIV.
- HPV is an indolent infection that leads to cancer in a minority of patients who generally suffer from a long-term infection. 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. Supporting this association is the observed rise in anal cancer and dysplasia rates seen in HIV-positive MSM and HIV-positive heterosexual men and women who do not report anoreceptive intercourse.

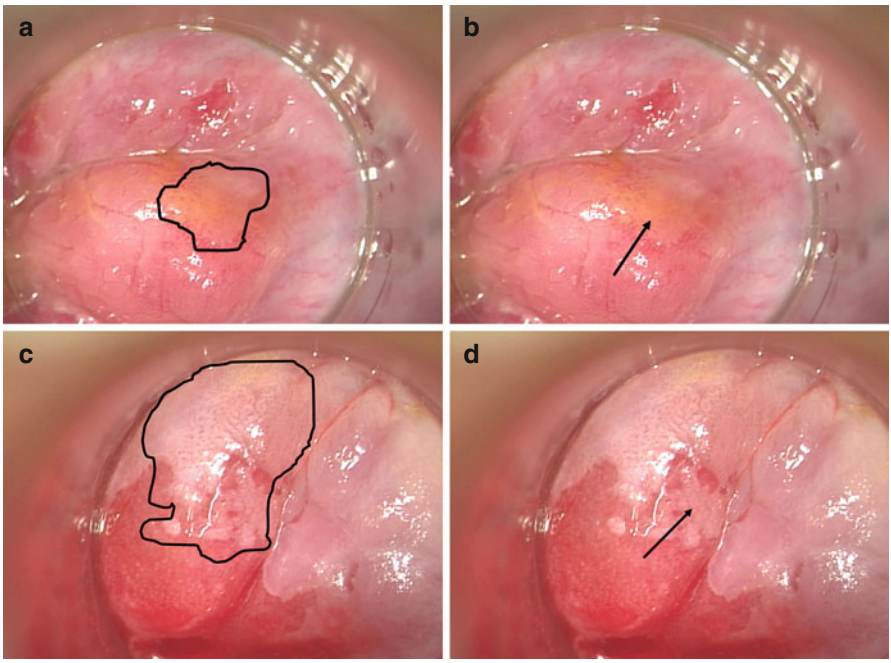

Fig. 20.2 LSIL and HSIL visualized in the office with a colposcope after the application of acetic acid. The *arrows* in both images depict where the biopsy of the lesion was taken. (**a**, **b**) Anal LSIL in the distal rectal mucosa with subtle punctate vessel changes. The geography of the lesion in highlighted in the *left frame*. (**c**, **d**) Anal HSIL in the distal rectal mucosa with the *left image* highlighting serpiginous, cerebriform vessels and the outline of the entire lesion and the *right image* highlighting the mosaic pattern created by the vessels in the acetowhite background

  - Further, HIV-positive patients are more likely to have HSIL and are more likely to progress from LSIL to HSIL over a 2-year time period, and both of these findings are increased in the patients with a lower CD4 count (<200 cells/mm).
  - Low CD4 counts are a surrogate measure for immunosuppression from the HIV infection, and it is therefore suggested that HIV infection is associated with an increased risk of progression of anal disease.
- Data is accumulating that suggests that as men and women live longer in the HAART era, the indolent HPV infection results in an increased risk for the development of anal cancer, and this effect is the most significant in the most immunocompromised patients.

Epidemiology

- The incidence of anal SCC has been increasing in frequency in over the last 30 years in the United States, Europe, and South America.

Anal Canal and Perianal High-Grade Squamous Intraepithelial Lesions (Formerly Bowen's Disease)

- The distinction between Bowen's disease and HSIL is unclear and appears to have more to do with the pathologist's training and histopathologic versus cytopathologic terminology, than any biologic difference.
- Bowen's disease is anal SCC in situ, AIN II and III, and HSIL.
- The term Bowen's disease is applied to SCC in situ in both keratinizing and nonkeratinizing tissues. Thus, we feel the term is archaic and confusing, and should be abandoned in favor of HSIL. Throughout this chapter, we use the term HSIL to refer to what has previously been termed Bowen's disease.
- HSIL is commonly 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 HSIL (Fig. 20.3). Alternatively, patients may present with complaints of perianal burning, pruritus, or pain. Physical examination may reveal scaly, discrete, erythematous, or pigmented lesions (Fig. 20.4).
- The natural history of HSIL is poorly defined.
  - In the immunocompetent, fewer than 10 % progress to cancer.
  - However, in immunocompromised patients, the progression rate appears greater as evidenced by the higher rates of anal cancers observed in the HIV (+) and immunosuppressed transplant patients.
- As we are as yet unable to identify those patients that progress, the authors favor treatment of HSIL.
  - An exception to this recommendation would be patients with advanced AIDS with poor performance statuses despite maximal medical therapy. The other exception might be the elderly patient with an asymptomatic lesion and a short life expectancy.
- The preferred treatment is controversial and should be tailored to the given patient. An older 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 clocklike fashion.
  - Frozen sections establish the presence of HSIL and these areas are widely locally excised with 1 cm margins. Large defects are covered with flaps of gluteal and perianal skin. Although this technique has been shown to provide excellent local control, it does not prevent recurrences. Recurrence rates in one series were as high as 23 % despite this radical approach. Although no cancers developed in this group, HIV status was not noted and complications, including incontinence, stenosis, and sexual function, were not reported. In another study of wide local excision, the authors noted a 63 % persistence rate at 1 year and a 13 % recurrence rate at 3 years. Eleven percent of the patients developed incontinence or stenosis. The unknown risk of disease progression, high recurrence rate, and

Fig. 20.3 Perianal HSIL (With permission from Beck DE, Wexner SD. Anal neoplasms. In: Beck DE, Wexner SD, editors. Fundamentals of anorectal surgery. London: W.B. Saunders; 1998. p. 261–277)

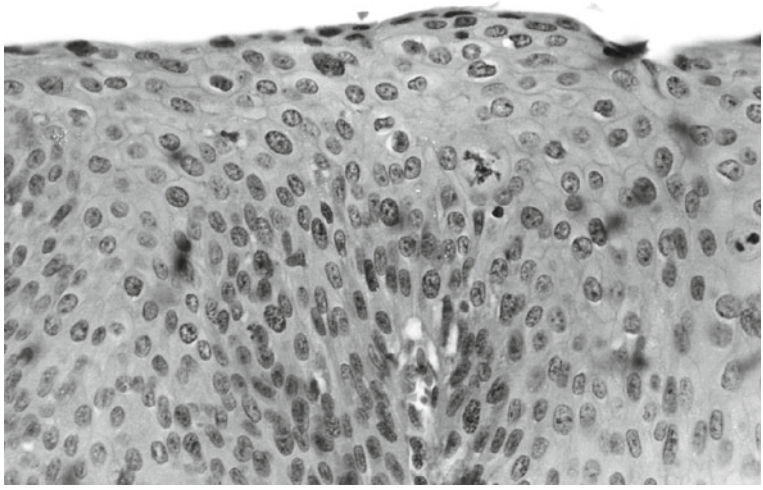

Fig. 20.4 Perianal HSIL (Photomicrograph hematoxylin and eosin ×400) (With permission from Beck DE, Wexner SD. Anal neoplasms. In: Beck DE, Wexner SD, editors. Fundamentals of anorectal surgery. London: W. B. Saunders; 1998. p. 261–277)

the significant morbidity associated with extensive wide excisions have led many authorities (including the authors and a few editors) to rarely use or recommend this option.

- A less radical approach involves taking patients to the operating room to perform high resolution anoscopy (HRA) with the aid of an operating microscope, acetic acid, and Lugol's solution. The lesions are visualized and targeted for electrocautery destruction. Like cervical disease, the HSIL is visible because of its characteristic vascular pattern identifying the at-risk tissue for selective destruction (Fig. 20.2). 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 significant as with any perianal procedure. HSIL identified with HRA may also simply be locally excised taking care to stay close to the lesion margin directly visualized with the operative microscope. The deep margin is kept equally close as 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 anoreceptive intercourse should be followed with Pap smears at yearly and 3 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.

Perianal Squamous Cell Carcinoma (Formerly Anal Margin)

- SCC arises from both the perianal skin and the anal canal.
- The distinction between the two locations has become more important as they are increasingly considered different entities with separate treatments and prognosis. Immunohistochemical studies of squamous cell tumors from the anal margin and anal canal demonstrate differences in expression of cadherin, cytokeratins, and p53 confirming that these tumors are of distinct histogenetic origin.
- Perianal lesions are completely visible and fall within a 5 cm radius of the anal opening when gentle traction is placed on the buttocks.

Clinical Characteristics

- Perianal tumors resemble SCC of other areas of skin and are therefore staged and often treated in a similar fashion.
- 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, perianal tumors are characterized by a delay in diagnosis due to their location and indistinct features, and SCC is no exception.

Staging

- The staging of perianal SCC is based on the size of the tumor and lymph node involvement, both of which correlate with prognosis.
- Lymphatic drainage of the perianal skin extends to the femoral and inguinal nodes and then to the external and common iliac nodes. Venous drainage occurs through the inferior rectal vein. Lymph node involvement is associated with the size and differentiation of the tumor.
- Distant visceral metastasis at presentation is rare but should be evaluated with a CT scan of the abdomen and pelvis to assess for liver metastases, as well as the presence of nodal disease. A chest X-ray or CT may be performed to evaluate for lung metastases. These tumors are generally slow growing and histologically are well differentiated with well-developed patterns of keratinization. The AJCC staging system is described in Table 20.1.

Treatment Options

- Treatment of perianal 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 20.2) and should be reserved for those lesions that can be excised with a 1 cm margin, are T*is* or T1, and do not involve enough sphincter to compromise function. A series of 27 patients with T*is* and T1 lesions treated with wide local excision had a 100 % 5-year survival, and in another study, all patients with small or superficial tumors locally excised had a survival of 100 %, whereas those with deep invasion did not survive 5 years.
- 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 perianal tumors 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 utilized as the first line therapy using perineal 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 %; and T3, 37–100 % (Table 20.3).

Table 20.1 American Joint Committee on Cancer (AJCC) staging of squamous cell carcinoma (SCC)

Primary tumor (*T*)				
Tx	Primary tumor cannot be assessed			
T0	No evidence of primary tumor			
T*is*	Carcinoma in situ (Bowen's disease, high-grade squamous intraepithelial lesion (HSIL), anal intraepithelial neoplasia II–III (AIN II–III)			
T1	Tumor ≤2 cm in greatest dimension			
T2	Tumor 2–5 cm in greatest dimension			
T3	Tumor ≥5 cm in greatest dimension			
T4	Tumor of any size invades adjacent organ(s), e.g., vagina, urethra, bladder[a]			
Nodal status (*N*)				
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			
Distant metastasis (*M*)				
M0	No distant metastasis			
M1	Distant metastasis present			
Stage grouping				
Stage 0	T*is*	N0	M0	
Stage I	T1	N0	M0	
Stage II	T2,3	N0	M0	
Stage IIIA	T1,2,3	N1	M0	Or T4 N0 M0
Stage IIIB	Any T	N2,3	M0	Or T4 N1 M0
Stage IV	Any T	Any N	M1	

[a]Direct invasion of the rectal wall, perirectal skin, subcutaneous tissue, or the sphincter muscle(s) is not classified as T4

Table 20.2 Results of local excision of perianal 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

- The use of chemoradiation specifically pertaining to perianal SCC 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

Table 20.3 Radiation therapy for perianal tumors by T stage

Author	Year	*N*	Local control (%)			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

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 sphincter function, radiation provides similar local control and survival.
- Larger T2 tumors should be treated with radiation therapy to the primary lesion and inguinal fields due to 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.

Squamous Cell Carcinoma of the Anal Canal

- SCC incorporates all large-cell keratinizing, large-cell nonkeratinizing (transitional), and basaloid histologies. The terms epidermoid, cloacogenic, and mucoepidermoid carcinoma are all encompassed in the squamous cell carcinoma group. SCC of the anal canal is five times more common than perianal SCC, but its incidence is one-tenth that of rectal cancer.

Clinical Characteristics

- The most common presenting symptom is bleeding, which occurs in over 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.
- Unfortunately, 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 exam; anoscopy; proctoscopy, when necessary; and examination of inguinal nodes.
- 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 may include 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 although this may be limited by pain. Ultrasound has been found to be superior to physical exam in assessing the involvement of internal and external anal sphincter muscle and perirectal lymph nodes.
- Inguinal nodal involvement at the time of presentation can be difficult to determine. The sensitivity of radiologic imaging and clinical exam are poor.
- Enlarged lymph nodes can be reactive to secondary inflammation in some cases and therefore should be biopsied with direct fine-needle aspiration (FNA) or ultrasound-guided FNA if detected by imaging. Excisional lymph node biopsy is rarely required but may be done if FNA is inconclusive.
- Studies of sentinel lymph node biopsy have demonstrated that the technique is safe and may result in more accurate staging, but the actual impact on initial and subsequent management remains unclear as long as inguinal fields are included during radiation therapy.
- CT scan or MRI of the abdomen and pelvis can add to locoregional staging as well as evaluating for liver metastasis. A chest CT or chest X-ray is used as a screening tool for lung lesions.
- PET scans are primarily useful for assessing persistent or residual disease after treatment. Sigmoidoscopy 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 staging is listed in Table 20.1.
- The risk of nodal metastasis correlates with the size, depth of invasion, and the histologic grade of the tumor.

- 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 to invasion of the internal sphincter.
- At the dentate line, the drainage basin includes the internal pudendal, internal iliac, and obturator nodes. Below the dentate line, the lymphatic drainage is through the inguinal, femoral, and external iliac lymph nodes.
- Mesenteric lymph nodes are more common in tumors of the proximal anal canal (50 %) than the distal anal canal (14 %).
- Distant visceral metastasis occurs in 10–17 % of patients at presentation and can be found in the liver, lung, bone, and subcutaneous tissues. Subsequent metastasis is more common and was the cause of 40 % of cancer-specific deaths in one series.

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 below 20 %.

Radiation Therapy

- Primary radiation therapy is quite effective in treating SCC as 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 20.4). However, when tumors are larger than 5 cm or lymph nodes are involved, the cure rate decreases to 50 %.
- Better results with higher doses of radiation must be contrasted to 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 bowel control due to anal complications can lead to the placement of a colostomy.
- Studies have found a dose-dependent effect on morbidity with the requirement of a colostomy in 6–12 % of patients. However, one study examining risk factors predictive of requiring a colostomy for management of anal cancers found that tumor size was the only risk factor.

Table 20.4 Response to radiation based on dosage

		Local control (%)	
Author	Year	<54 Gy	>54 Gy
Hughes et al.	1989	50	90
Constantinou et al.	1997	61	77

- Brachytherapy used alone or in conjunction with external beam radiation is also effective with local control rates of 75–79 % and 5-year survival of 61–65 %, but 3–6 % of patients had serious complications that required surgery.
- The high rate of anal necrosis seen when both modalities are used has dampened the enthusiasm for this approach. At this time, radiation therapy alone is not commonly utilized but may have a role in treating T1 tumors.

Chemoradiation Therapy

- The introduction of chemoradiation therapy by Nigro in 1974 revolutionized the treatment of anal canal SCC by demonstrating equivalent local control and survival rates with the preservation of sphincter function and thus avoidance of a colostomy.
- Since that time, multiple studies have confirmed these results and chemoradiation is the standard therapy for SCC of the anal canal. Nigro described using 30 Gy external beam radiation with 5-FU and mitomycin C and demonstrated a complete pathological response in 21 of 26 patients treated (81 %).
- Since that time 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 20.5).
- As a result, operative treatment for anal canal SCC was largely abandoned and reserved for those patients with persistent or recurrent disease after chemoradiation. Although much controversy existed as to the benefit of chemoradiation therapy compared to primary radiation therapy, two randomized controlled studies have demonstrated the superiority of chemoradiation therapy with 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 20.6) but no significant difference in survival (51 %).
- Although the use of mitomycin C has provided excellent results, cisplatin has gained favor as 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.
- The US Gastrointestinal Intergroup trial RTOG 98–11 was a randomized controlled trial conducted between October 1998 and June 2005 that compared treatment with cisplatin, 5-FU, and radiotherapy to mitomycin C, 5-FU, and radiotherapy. A total of 682 patients with anal canal carcinoma

Table 20.5 SCC of the anal canal: results of combination of radiation and 5-FU plus mitomycin C

Author(s)[a]	No. of patients	Dose (Gy)	Complete regression (%)	Follow-up (month)	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*97 T2*80	46 % > 36	72
Beck and Karulf (1994)	35	30–45	97	4–155	87
Smith et al. (1994)	42	30	T1*90 T2*87	31 31	90 87
Bartelink et al. (1997)	51	30–45	80	Med. 42	Overall survival 58 % $P = 0.17$
UKCCCR (1996)	292	45	Not specifically reported	Med. 42	3-year survival – 65 %
Ajani et al. (2008)	324	45–59	Not specifically reported	Med. 30	75

[a]Complete references for the authors cited above are available in the ASCRS Textbook of Colon and Rectal Surgery, 2nd edition, 2011

Table 20.6 Result of two randomized trials examining radiation therapy alone and radiation therapy with chemotherapy for anal canal SCC

			Local control (%)			Overall survival (%)		
	N	Follow-up	XRT	Chemo XRT	*P* value	XRT	Chemo XRT	*P* value
EORTC	110	5 years	50	68	0.02	57	52	0.17
UKCCCR	585	3 years	39	61	<0.001	58	65	0.25

were enrolled in the trial. The primary end point was defined as 4-year disease-free survival. Secondary endpoints were overall survival and time to relapse. Cisplatin-based therapy did not improve disease-free survival compared with mitomycin-based therapy. Additionally, cisplatin-based therapy was associated with a higher rate of colostomy.

- 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 use primary radiation therapy (45–65 Gy), chemoradiation, and selective lymph node dissection followed by radiation which has been reported to maintain disease-free intervals in up to 60 % of

patients. For those with subclinical lymph nodes in the groin, chemoradiation is advocated with doses as low as 30–34 Gy. This minimizes toxicity but is effective in treating small volume disease based on previous studies of small sized tumors. Whether or not inguinal fields should always be included when treating patients for anal canal SCC remains controversial.

Follow-Up

- No consensus has been reached on appropriate follow-up after the 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 exam and anoscopy every 3 months in the first 2 years and every 6 months until 5 years has been recommended.
- Ultrasound examination has also become popular in detecting recurrence although the literature is mixed on its benefit.
- CT scan or MRI performed after the 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 %. Those with positive margins, nodal disease at salvage and persistent disease after chemoradiation have poorer outcomes.
- 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 or alternatively, use of the vacuum assisted-closure (VAC) to promote healing.
- The benefit of adjuvant chemotherapy after APR is currently unknown. Symptomatic inguinal disease after chemoradiation of the primary tumor can be treated with radical groin dissection if radiation has already been administered.
- Additional radiotherapy can be considered if maximal doses of radiation were not delivered. Radical groin dissection in selected patients can result in a 5-year survival of 55 %.
- Distant metastases have been found in 10–17 % of patients treated with chemoradiation and are usually treated with systemic chemotherapy, such as cisplatin or 5-FU for palliation. If the metastases are isolated in the liver or lung and the primary disease is controlled, resection can be considered.

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 SCC. 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.
- Due to the rarity and heterogeneity of this tumor, the role of surgery and chemoradiation has been difficult to assess, thus making definitive recommendations for treatment impossible.
- Many patients present with advanced local or metastatic disease making curative treatment challenging.
- 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 to SCC due to 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. Fewer than 500 cases have been reported in the literature. Patients are frequently female, Caucasian, and in their 60s.
- 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 palpable inguinal lymph nodes common.
- 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.
- Approximately two-thirds of the lesions are grossly pigmented or show histologic evidence of melanin. Amelanotic lesions can be difficult to differentiate from undifferentiated squamous cell carcinoma.
- Surgical management of anorectal melanoma provides the only chance for cure. However, the choice of operation continues to be controversial since the prognosis is so poor. Up to 35 % of patients present with metastatic disease, and those patients with tumors greater than 10 mm in thickness are not cured by any treatment.
- Additionally, long-term survival rates, which range from 0 to 29 %, do not seem to differ when wide local excision or APR is performed. However, some studies have shown fewer locoregional recurrences with a more radical operation, thereby supporting the use of APR for earlier stage tumors. In a study of anorectal melanomas stratified by tumor thickness, tumors greater than 4 mm had inadequate local tumor control with wide local excision alone and APR was advocated. Despite this, 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. If the tumor is bulky and negative margins (1–2 cm) cannot be achieved, it involves the sphincter complex, or local resection will result in incontinence, then an APR is the recommended treatment option. If the patient already has signs of regional or systemic metastasis, radical excision should not be performed.
- The use of endoanal ultrasound and sentinel lymph node biopsies may further guide treatment for this disease.
- Adjuvant therapy for cutaneous melanoma has been studied extensively; however, the applicability of this data to anorectal melanoma remains uncertain.
  - Many immunotherapeutic and chemotherapeutic agents such as dacarbazine, bacillus Calmette-Guérin, levamisole, and interferon-α have demonstrated no benefit. Cytotoxic chemotherapy, including cisplatin, vinblastine, and dacarbazine, combined with interleukin-2 or interferon-α2b, has shown some improvement in survival; however, patients suffered significant treatment-related toxicity.
  - Radiation therapy has also been utilized to improve local and regional control, yet due to the small numbers of patients with anorectal melanoma, its efficacy is unknown.
  - Due to its predilection for developing systemic metastasis, it is unclear whether efforts to achieve better local control are useful.

Gastrointestinal Stromal Tumors

- Gastrointestinal stomal 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.
- Patients present in the fifth to seventh decade of life are more commonly men. Most patients are asymptomatic but bleeding, anal pain, change in bowel habits, or urinary symptoms can occur. Pathologic factors implicated in aggressive tumors with metastatic potential are size greater than 5 cm in diameter and high mitotic counts, pleomorphism, infiltration of muscularis propria, and coagulative necrosis. The presence of symptoms is also associated with a worse prognosis.
- Treatment involves local excision for tumors less than 2 cm and APR for those with larger tumors or worse pathologic features.
  - In a study of anorectal stromal tumors, recurrence rates for local excision and radical resection were 60 and 0 %, respectively.
  - The role of adjuvant therapy in anal GIST is uncertain given the small numbers of patients affected. However, the success of Gleevec® (imatinib mesylate) in treating other GISTs would suggest it as a first line therapy for c-Kit (+) (CD117) GIST of the anus and rectum where compromised bowel control or permanent stoma is an issue.

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.
- Sixty-five to eighty percent of patients with extrapulmonary small cell tumors present with metastatic disease. Therefore, it is important to stage them accurately.
- Those with disseminated disease may benefit from combination chemotherapy regimens used for small cell lung cancer, such as cisplatin and etoposide.

Uncommon Perianal Neoplasms

Basal Cell Carcinoma

- The incidence of basal cell carcinomas (BCC) of the anus, in comparison to sun-exposed areas of the body, is extremely low. It comprises about 0.1 % of all BCC diagnosed and fewer than 200 cases of BCC have been reported on the perianal and genital area.
- The etiology of perianal BCC is likely different from BCC arising in sun-exposed skin. The majority of these carcinomas occur in men (60–80 %)

and the average age at presentation is 65–75 years. Approximately one-third have a previous or concomitant history of BCC at other skin sites.

- The average size at presentation is less than 2 cm, although they can be as large as 10 cm and extend into the anal canal. The clinical appearance can range from erythematous papules to nodules, plaques, and ulcers. They tend to be mobile and superficial with little invasive or metastatic potential.
- Treatment is wide local excision ensuring adequate margins, which is possible in lesions less than 2 cm. Larger lesions may require excision with skin grafting or use of Mohs micrographic surgery to preserve uninvolved tissue. Recurrence rates for local excision range from 0 to 29 %. Cancer-specific survivals in both series were 100 % at 5 years. Recurrences can be treated with re-excision. Large lesions extending into the anal canal may be better treated with radiation or APR.

Paget's Disease

- Paget's disease can be divided into two groups, mammary and extra mammary. Other sites of Paget's disease include the axilla, scrotum, penis, vulva, groin, thigh, and buttock where apocrine glands are found.
- 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 median duration of symptoms is 3 years. The lesions themselves often have an erythematous, eczematous appearance with well-demarcated borders mimicking a rash (Fig. 20.5).
- 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 HSIL, Crohn's disease, condyloma acuminatum, hidradenitis suppurativa, pruritus ani, and squamous cell carcinoma.
- Biopsy is essential to confirm the diagnosis.
- Histologically, Paget's cells have large, round, eccentric, hyperchromic nuclei with pale-staining, vacuolated cytoplasm (Fig. 20.6). The cytoplasm stains positive with periodic acid-Schiff stain due to the abundance of mucin. The incidence of associated visceral malignancies in perianal Paget's disease is elevated with various series reporting rates of 30–50 %.
- 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.

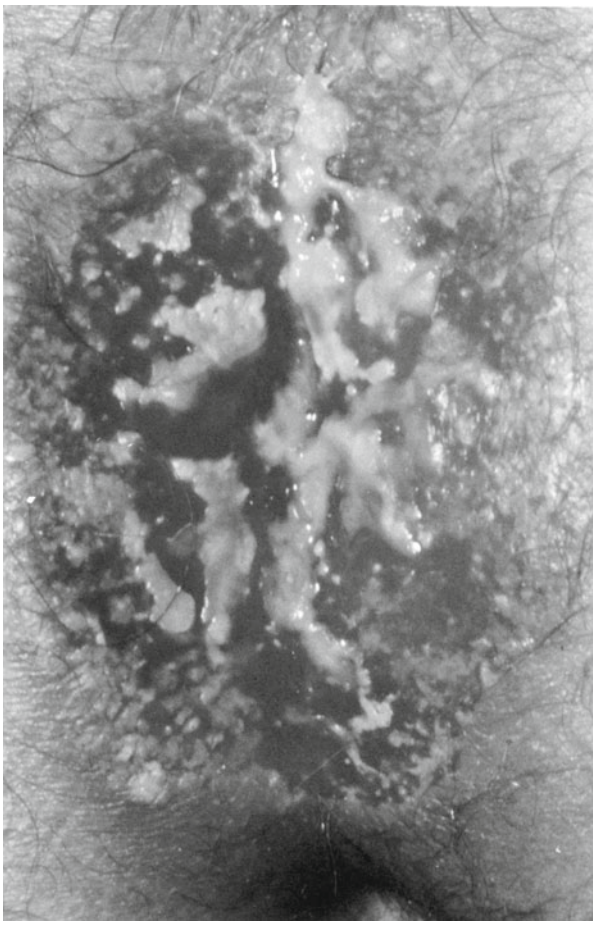

Fig. 20.5 Perianal Paget's disease (With permission from Beck DE, Wexner SD. Anal neoplasms. In: Beck DE, Wexner SD, editors. Fundamentals of anorectal surgery. London: W. B. Saunders; 1998. p. 261–277)

- In addition to resecting the lesion with grossly negative margins, it is important to map the extent of involvement of the lesion microscopically.
  - This can be performed either by taking random biopsies 1 cm from the edge of the lesion in all four quadrants, including the dentate line, anal verge, and perineum, or by using toluidine blue and acetic acid to stain the Paget's cells, thereby directing the site for biopsy. The use of intraoperative frozen sections ensures that any disease that extends beyond the gross lesion is excised to reduce the chance of recurrence. Positive margins requiring re-excision are not uncommon when this technique is not utilized. Preoperative

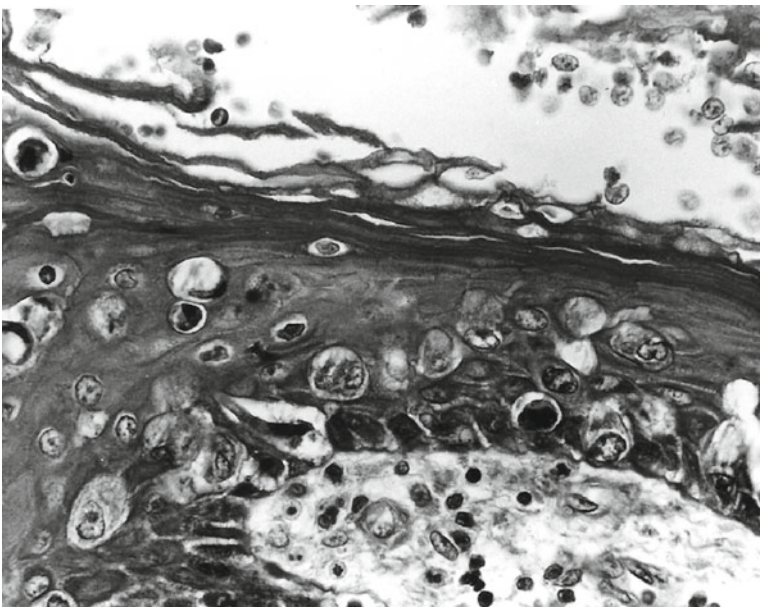

Fig. 20.6 Perianal Paget's disease (Photomicrograph hematoxylin and eosin ×400) (With permission from Beck DE, Wexner SD. Anal neoplasms. In: Beck DE, Wexner SD, editors. Fundamentals of anorectal surgery. London: W. B. Saunders; 1998. p. 261–277)

mapping can also be performed using dermatologic punch biopsies. 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 %. Most recurrences were treated with wide re-excision with excellent results. For those who developed invasion, more radical surgery or adjuvant therapy was utilized.
- Patients who have an invasive component or an associated anorectal malignancy should be considered for radical excision with APR. If positive inguinal lymph nodes are present, then an inguinal lymphadenectomy should be added. Unfortunately, patients with invasive disease present with metastasis 25 % of the time and all patients who die of this disease have an invasive component.
- Too few cases of perianal Paget's disease exist to allow for a comparison of invasive and noninvasive groups. Disease-specific survival for all perianal Paget's disease at 5 years ranges from 54 to 70 % and at 10 years decreases to 39–45 %.
- The role of adjuvant chemoradiation therapy remains uncertain. It is currently used in some cases of invasive or aggressive recurrent disease.

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, fewer than 60 cases have been reported in the literature to date. HPV is frequently detected.
- These tumors are more commonly 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 present most commonly with the complaint of an anal growth. Pain, perianal discharge/abscess, anorectal bleeding, pruritus, and a change in bowel habits may also occur.
- The lesions themselves are generally slow growing with a soft, cauliflower-like appearance that can become nodular as it penetrates the underlying tissues. At presentation, they tend to be quite large measuring anywhere from 1.5 to 30 cm. Regional lymphadenopathy may also occur secondary to infection.
- The tumor, which is clinically difficult to distinguish from a malignancy, is histologically benign. Papillomatosis, acanthosis with hyperplasia of the prickle cell layer, variable hyperkeratosis, parakeratosis, and underlying inflammation are often found. However, of all the cases of giant condyloma acuminatum reported, only 42 % were histologically diagnosed as condyloma without any invasion. A malignant transformation was identified in 58 % of the tumors; 8 % had carcinoma in situ, and 50 % had invasion that was termed verrucous carcinoma, SCC, or basaloid carcinoma.
- 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.

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 to lymphomas found in the general population, these tumors are characterized by B cells of a higher histologic grade that originate from extranodal tissue. They are also more aggressive, prone to dissemination, and resistant to treatment.

- Anorectal lymphomas are extremely rare, comprising less than 1 % of all anorectal neoplasms in the general population.
- Although the anorectal area is devoid of lymphoid tissue, it is postulated that the exposure to chronic infections from anal receptive intercourse or an immunocompromised state may result in an "acquired" mucosa-associated lymphoid tissue (MALT).
- The most common presenting symptoms are pain, pruritus, drainage, or a palpable mass.
- After appropriate staging, patients are treated with a standard regimen for NHL of chemotherapy and radiation therapy of the affected area.
- There is no role for surgical treatment. Usual chemotherapeutic agents include cyclophosphamide, actinomycin, vincristine, and corticosteroids (CHOP). There are too few cases of anorectal lymphoma reported to discuss overall prognosis. However, younger patients without constitutional symptoms may fare better. Additionally, low CD4 counts and performance status may affect a patient's ability to endure aggressive therapy. Isolated reports of immunocompetent patients with anorectal lymphoma have been reported with excellent response to treatment.

21. Presacral Tumors

Eric J. Dozois and Maria Dolores Herreros Marcos

Introduction

- The presacral or retrorectal space is the site of a group of heterogeneous and rare tumors that display indolent growth and produce ill-defined symptoms. As 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 have evolved in recent years due to 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.

Anatomy and Neurophysiology

- The boundaries of the retrorectal region include the posterior wall of the rectum anteriorly and the sacrum posteriorly (Fig. 21.1).
  - This space extends superiorly to the peritoneal reflection and inferiorly to the rectosacral fascia and the supralevator space.
  - Laterally, the area is bordered by the ureters, the iliac vessels, and the sacral nerve roots (Fig. 21.2a).

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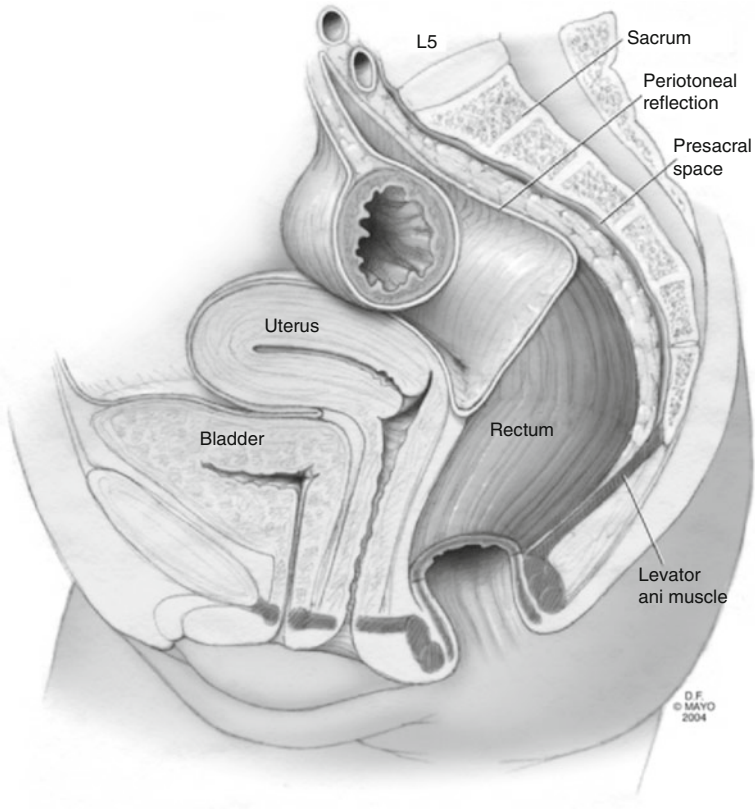

Fig. 21.1 Relationship of pelvic structures to presacral space

- 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 function.
  - Likewise, if the upper three sacral nerve roots are left intact on either side of the sacrum, the patient's ability to spontaneously defecate 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 among the thecal sac, sacral nerve roots, sciatic nerve, piriformis muscle thecal sac, and sacrotuberous and sacrospinous ligaments (Fig. 21.2b).
  - Structurally, 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.

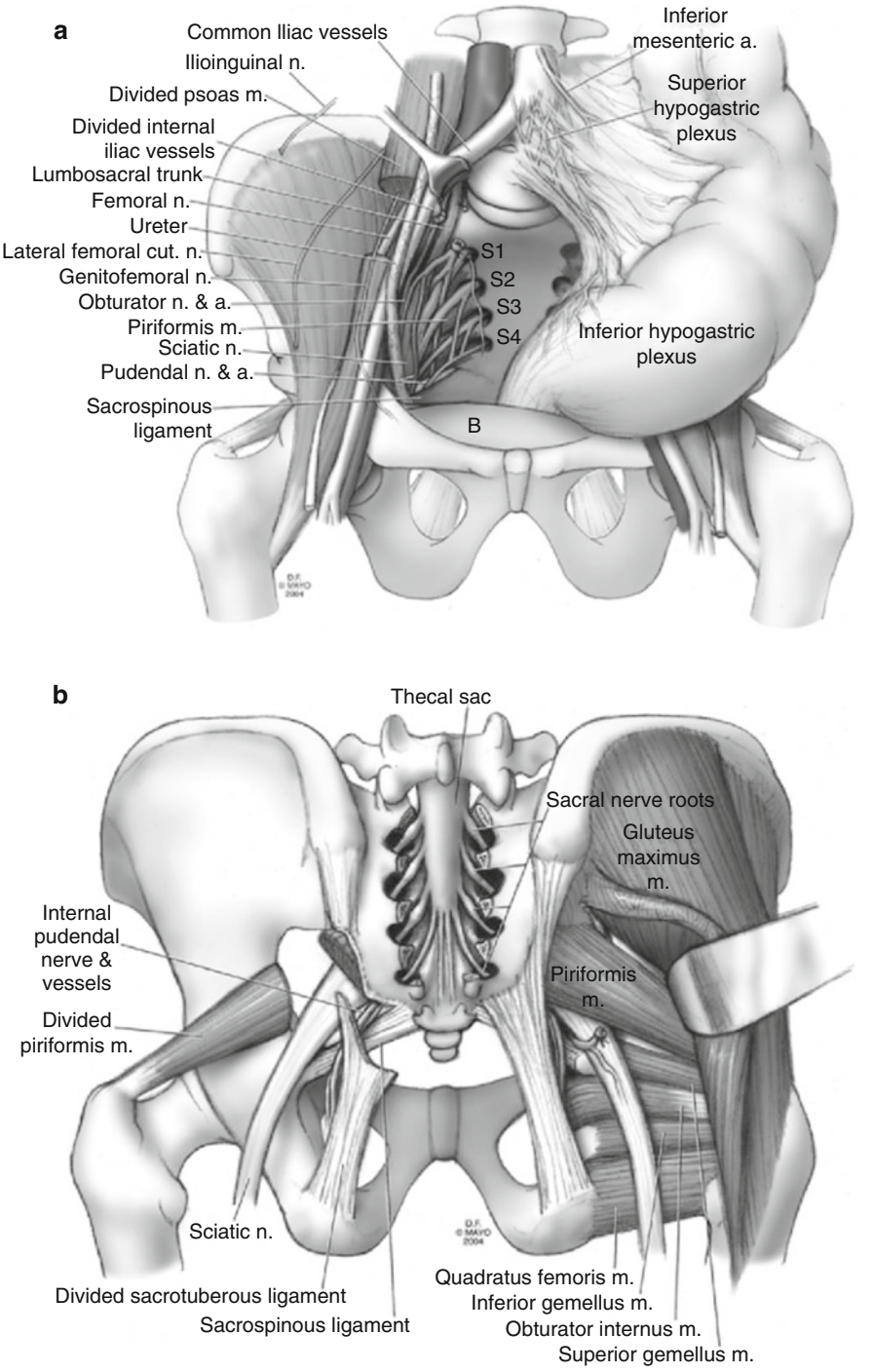

Fig. 21.2 (**a**) Anterior view of pelvic anatomy. (**b**) Posterior view or pelvic anatomy with sacral elements removed

  - 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.
- Knowledge of anatomy of the thigh and lower extremity is also required in complex cases requiring muscle or other 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.

Classification

General Considerations

- Presacral lesions are rare. Reports from various large referral centers have indicated 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 and benign or malignant. Two-thirds of lesions are congenital, two-thirds of which are benign and one-third neoplastic.
- As this area contains totipotential cells that differentiate into three germ cell layers, a multitude of tumor types may be encountered.
- The classification first described by Uhlig and Johnson has been used for many years and divides tumors into broad categories; congenital, neurogenic, osseous, and miscellaneous. We have modified and updated this system to subcategorize tumors into malignant and benign entities, as this greatly impacts therapeutic approaches (Table 21.1).

Gross and Histologic Appearance

- *Epidermoid cysts* result from defects during the closure 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 as they are often misdiagnosed as a perirectal abscess and operatively manipulated.
- *Enterogenous cysts* are lesions thought to originate from sequestration of the developing hindgut; if related with the rectum, they are called rectal duplication cysts. 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. Like dermoid and

Table 21.1 Classification of presacral tumors

Congenital
Benign
Developmental cysts (teratoma, epidermoid, dermoid, mucus secreting)
Duplication of the rectum
Anterior sacral meningocele
Adrenal rest tumor
Malignant
Chordoma
Teratocarcinoma
Neurogenic
Benign
Neurofibroma
Neurilemmoma (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

Modified from Uhlig BE et al. Presacral tumors and cysts in adults. Dis Colon Rectum. 1975;18:581–96

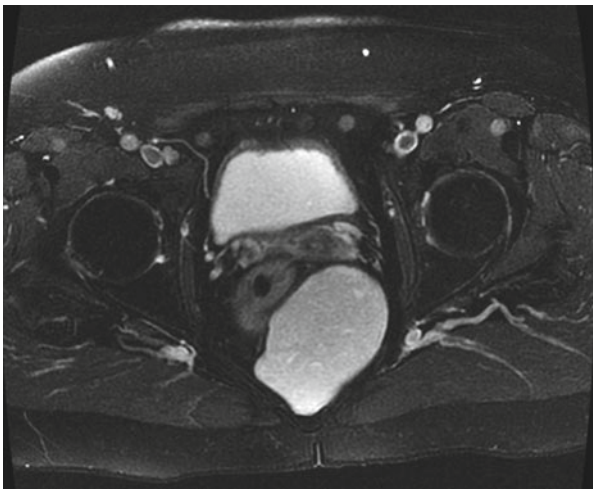

Fig. 21.3 Tailgut cyst

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 congenital lesions arising from remnants of normally regressing postanal primitive gut. They are more common in females and can be seen as multiloculated or biloculated cysts on magnetic resonance imaging (MRI) (Fig. 21.3). 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 differentiates this lesion from an epidermoid or dermoid cyst. Malignant transformation has been reported in up to 13 % in some series.
- *Teratomas* are true neoplasms derived from totipotential cells and include all three germ cell 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 vertebra, urinary tract, or anorectum. In adults, malignant degeneration can occur in 40–50 %. Incomplete or intralesional resection increases the likelihood of malignant degeneration. These lesions can also become infected and be misdiagnosed as a perirectal abscess or fistula. Diagnosis is often delayed and these tumors may reach considerable size.

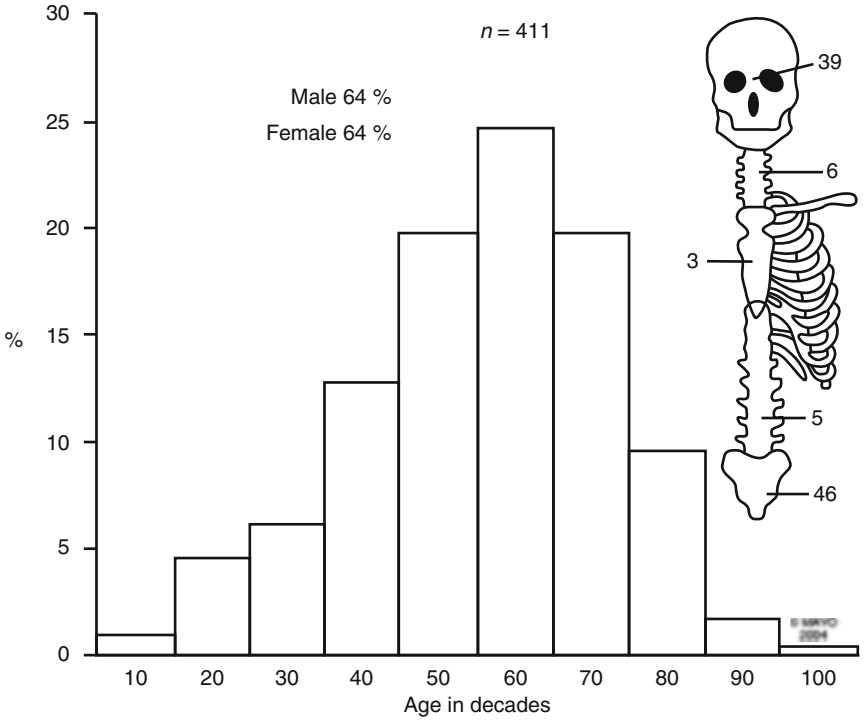

Fig. 21.4 Distribution of chordomas (Mayo Clinic orthopedic database)

- *Sacrococcygeal 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 have a predilection for the pheno-occipital region at the base of the skull and for the sacrococcygeal region in the pelvis (Fig. 21.4). 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. Although chordomas are low- to intermediate-grade malignant lesions, a radical surgical approach that achieves negative margins greatly improves survival.
- *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 exacerbated by straining or coughing. Anterior sacral meningocele 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, and neurogenic sarcomas). In a Mayo Clinic series, schwannomas were the most common benign tumor and malignant peripheral nerve sheath tumors the most common malignant lesions. Although neurogenic tumors tend to slowly grow, they may eventually reach considerable size. Preoperative differentiation between benign and malignant pathology can be difficult without a tissue biopsy but is of paramount importance to guide the operative approach.
- *Osseous tumors* include chondrosarcoma, osteosarcoma, myeloma, and Ewing's sarcoma. These tumors arise from the bone, cartilage, fibrous tissue, and marrow. Due to relatively rapid growth, these lesions often reach considerable size, and pulmonary metastases are common. 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. Carcinoid tumors of the presacral space are unusual but have been reported.
- Overall, most presacral tumors occur in females and are cystic.
  - Most solid tumors are chordomas and more commonly seen in males.
  - Benign lesions are frequently asymptomatic and are incidentally discovered during routine gynecologic examination which may explain the greater incidence in females.
  - By contrast, malignant tumors are more often symptomatic but still commonly found late due to their vague symptomatology.
  - Some presacral tumors present as part of a congenital syndrome, such as Currarino syndrome, which is a combination of presacral mass, anorectal malformations, and sacral anomalies. Diagnosis and Management

History and Physical Examination

- Due to their indolent course, presacral tumors are commonly found incidentally at the time of periodic pelvic or rectal examination.
- Symptomatic patients typically complain of vague, long-standing pain in the perineum or low back.
- Pain may be aggravated by sitting and improved by standing or walking.
- 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 clinicians' inability to ascertain the origin of their chronic, ill-defined pain. Patients with larger tumors may complain of constipation and/or rectal and urinary incontinence and sexual dysfunction due to the sacral nerve root involvement.
- Patients should be carefully examined, focusing on the perineum and rectal examination and assessing for a postanal dimple.
- In a series from our institution, 97 % of presacral tumors could be palpated on rectal exam. Digital rectal exam (DRE) typically reveals 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 exam 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 imaging modalities such as computerized tomography (CT), MRI, and endorectal ultrasound (ERUS). Simple anterior-posterior and lateral radiographs (AP/LAT) of the sacrum can 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, neurilemmoma (schwannoma), and aneurysmal bone cysts, may also cause extensive bony destruction.
- The characteristic "scimitar sign" on plain radiographs denotes the presence of an anterior sacral meningocele, a diagnosis that can be confirmed with conventional myelography or MRI with gadolinium.
- CT, MRI, and positron emission tomography (PET) scan have dramatically changed the way in which these tumors are evaluated. Computerized tomography and MRI complement each other and are the most important radiographic studies in evaluating a patient with a presacral lesion. Computerized tomography can determine whether a lesion is solid or cystic and whether adjacent structures, such as the bladder, ureters, and rectum, are involved (Fig. 21.5a–c). CT is also the best study to evaluate cortical bone destruction. MRI is highly recommended because of its

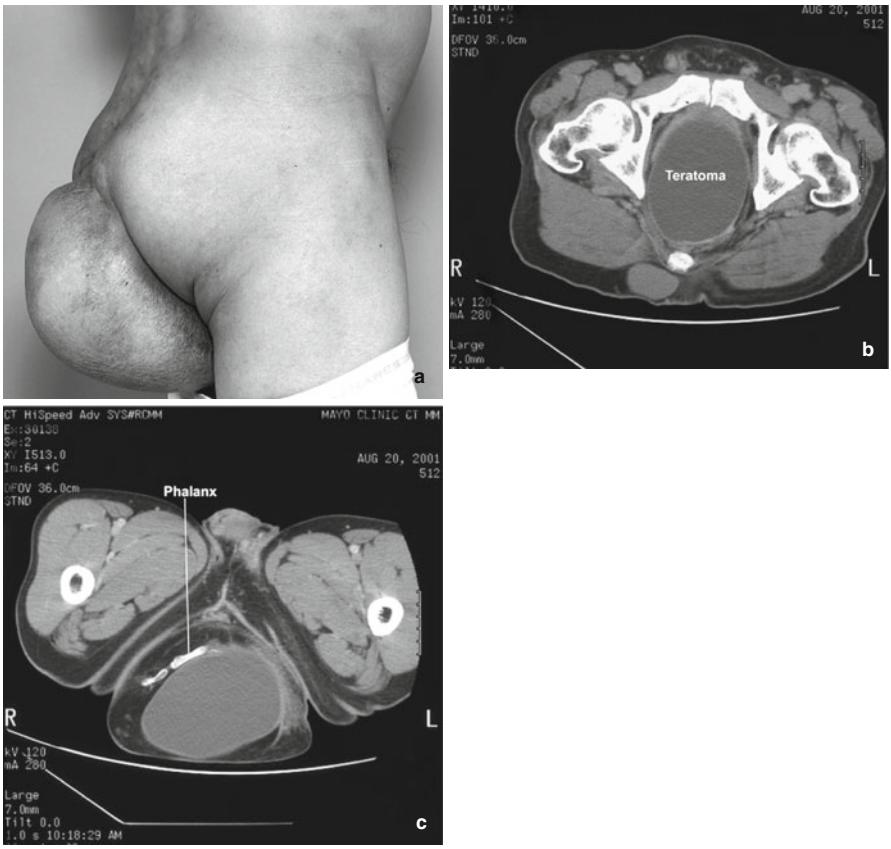

Fig. 21.5 Massive cystic teratoma with sacral appendage. (**a**) CT image of teratoma, intrapelvic portion and (**b**) extrapelvic portion, (**c**) including fully developed phalanx

multiplanar capacity and improved soft tissue resolution that is essential for planning specific lines of resection (Fig. 21.6a, b). Sagittal views assist in decision making in regard to need for and level of sacrectomy (Fig. 21.6c). MRI is also more sensitive than is CT in spinal imaging, showing associated cord anomalies, such as a meningocele, nerve root, and foraminal encroachment by tumor or thecal sac compression.

- In patients with presacral cystic lesions thought to be the source of a chronically draining sinus, fistulogram may occasionally help clarify the diagnosis. ERUS has been used by some to characterize retrorectal tumors and its relationship to the muscularis propria of the rectum.

Preoperative Biopsy

- Historically, the role of preoperative biopsy of presacral tumors has been a controversial topic.

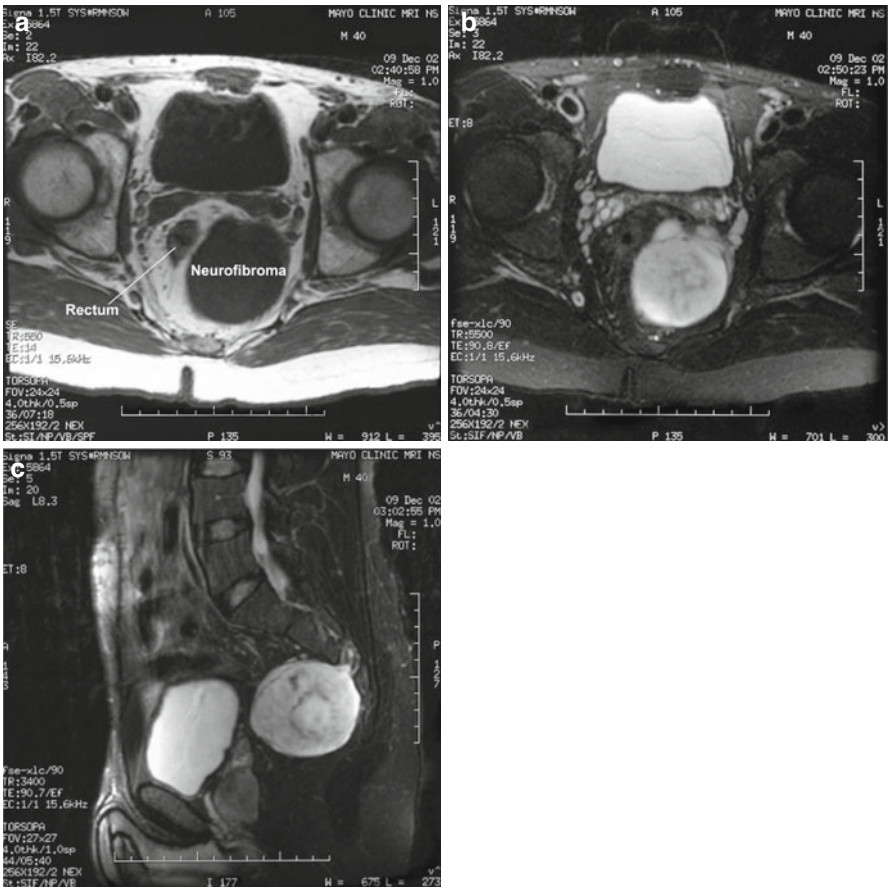

Fig. 21.6 MRI of pelvic neurofibroma displacing the rectum anteriorly and laterally. (**a**) T1-weighted coronal image. (**b**) T2-weighted coronal image. (**c**) Sagittal view with tumor exiting the third sacral foramen

- In the past, some authors have considered any presacral tumor deemed resectable as a contraindication to preoperative biopsy, with only a minority of authors stating that all solid tumors should be preoperatively sampled by biopsy. This recommendation 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 substantially benefit from preoperative chemotherapy and radiation, especially in osseous tumors, such as Ewing's sarcoma, osteogenic sarcoma, and neurofibrosarcoma. Preoperative tissue diagnosis *is* essential to the management of solid and heterogeneously cystic presacral tumors. For example, the surgical approach and necessary margins is dramatically different when faced with a neurofibroma as compared to a neurofibrosarcoma.

- When performed correctly, preoperative biopsy can only improve the overall management, rather than harm it.
- What is clear about preoperative biopsies of presacral tumors is that they should *never* be transrectally or transvaginally performed. 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 postoperative complications and recurrence. More importantly, inadvertent transrectal needling of a meningocele may lead to disastrous sequelae, such as meningitis and even subsequent death. Moreover, as 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. 21.7a, b). Transperitoneal, transretroperitoneal, transvaginal, and transrectal biopsy should be avoided. Biopsy tracts should never traverse neurovascular planes. Normal coagulation studies are required prior to biopsy, as hematoma formation and/or bleeding potentially contaminate(s) 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 have revolutionized the management of patients with complex malignancies. It is in large part due to these new treatment modalities prior to surgery that a preoperative diagnosis is of paramount importance.
- 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. This increased radiation exposure is associated with increased morbidity. Furthermore, 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 the fact that decreased tumor size is often observed. A decrease in tumor size in a pelvic tumor may allow the surgeon to spare vital structures, which

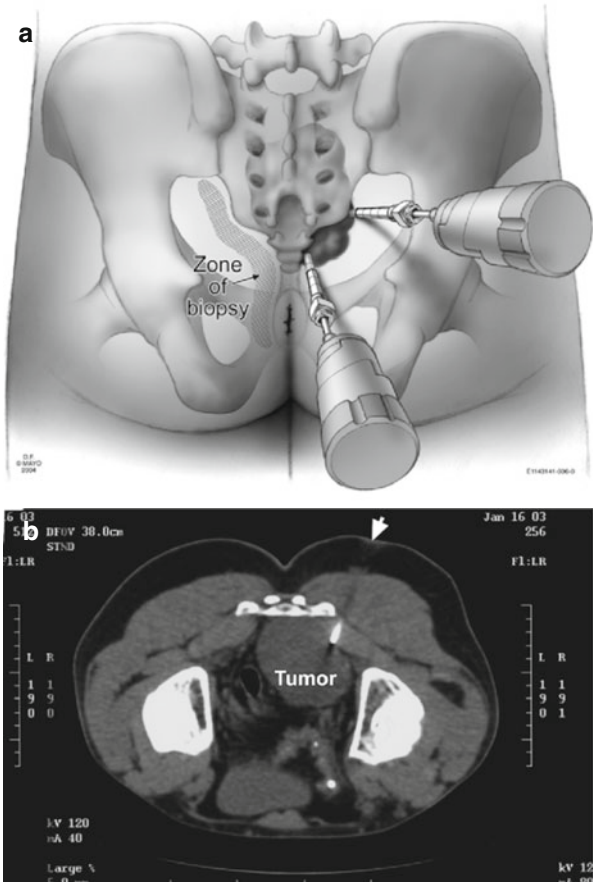

Fig. 21.7 (**a**) Preoperative biopsy technique using CT guidance. (**b**) Parasacral approach to presacral neurogenic tumor

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 intraoperative 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.
- Most non-chordoma malignant presacral tumors are sarcomas. The use of adjuvant therapy for presacral sarcomas in our recent review followed protocols typically for other types of soft tissue sarcomas.
- Regarding malignant neurogenic tumors, the use of adjuvant therapy has been recently reported by our institution.

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 patients in the pediatric age group, the risk of malignant transformation is considerable and continues to dramatically increase 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.
- 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. Presacral tumors may produce 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.
- Finally, and most importantly, tumors in this area have been inadequately treated in the past because of tumor violation, their large size and location, and fear of neurologic complication and/or musculoskeletal instability. Preoperative tumor violation can take place when such tumors are biopsied 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, en bloc removal of adjacent organs, soft tissue, and bone (if locally adherent) is the goal of resection.

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.

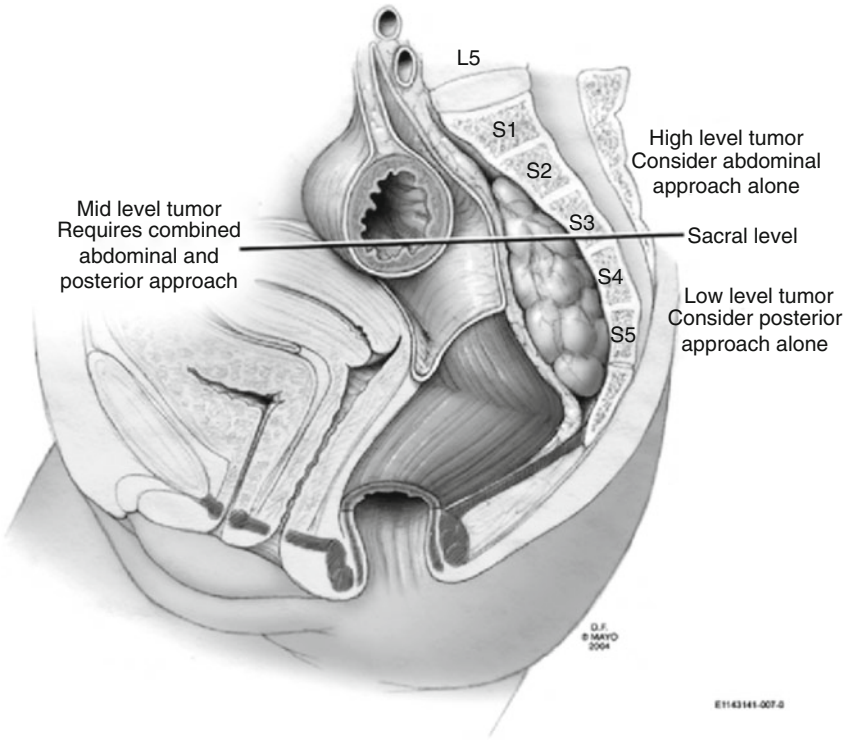

Fig. 21.8 Relationship of tumor to sacral level and proposed approach

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. Computerized tomography and MRI help define the margins of resection and the relationship of the tumor to the sacral level (Fig. 21.8). 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 plays a significant role, as adequate soft tissue coverage can often be difficult. Most often, the authors use the transabdominal rectus abdominis myocutaneous (TRAM) flap, which fills dead space and can cover large cutaneous defects left by the resection.

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 intravena caval filter, since the risk of deep venous thrombosis and pulmonary embolus is high and postoperative anticoagulation may be contraindicated.
  - Preoperative selective coil embolization done by an interventional radiologist may be useful in patients with large, vascular tumors to decrease intraoperative bleeding.
  - A multidisciplinary team should preoperatively review films and plan surgical strategy to avoid 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. 21.9a).
- 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. 21.9b).
- 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. 21.9c) 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.
  - An intersphincteric approach has been described for very low-lying tumors. It is performed in a lithotomy position. Through a V-shaped or radial incision posterior to the anus, the intersphincteric plane is opened and bluntly dissected. The anal canal and internal sphincter are separated from the external sphincter up to the level of the puborectalis sling. The dissection is continued upward in the retrorectal fatty space. The division of Waldeyer's fascia may be necessary to expose the upper surface of the levator ani muscles.

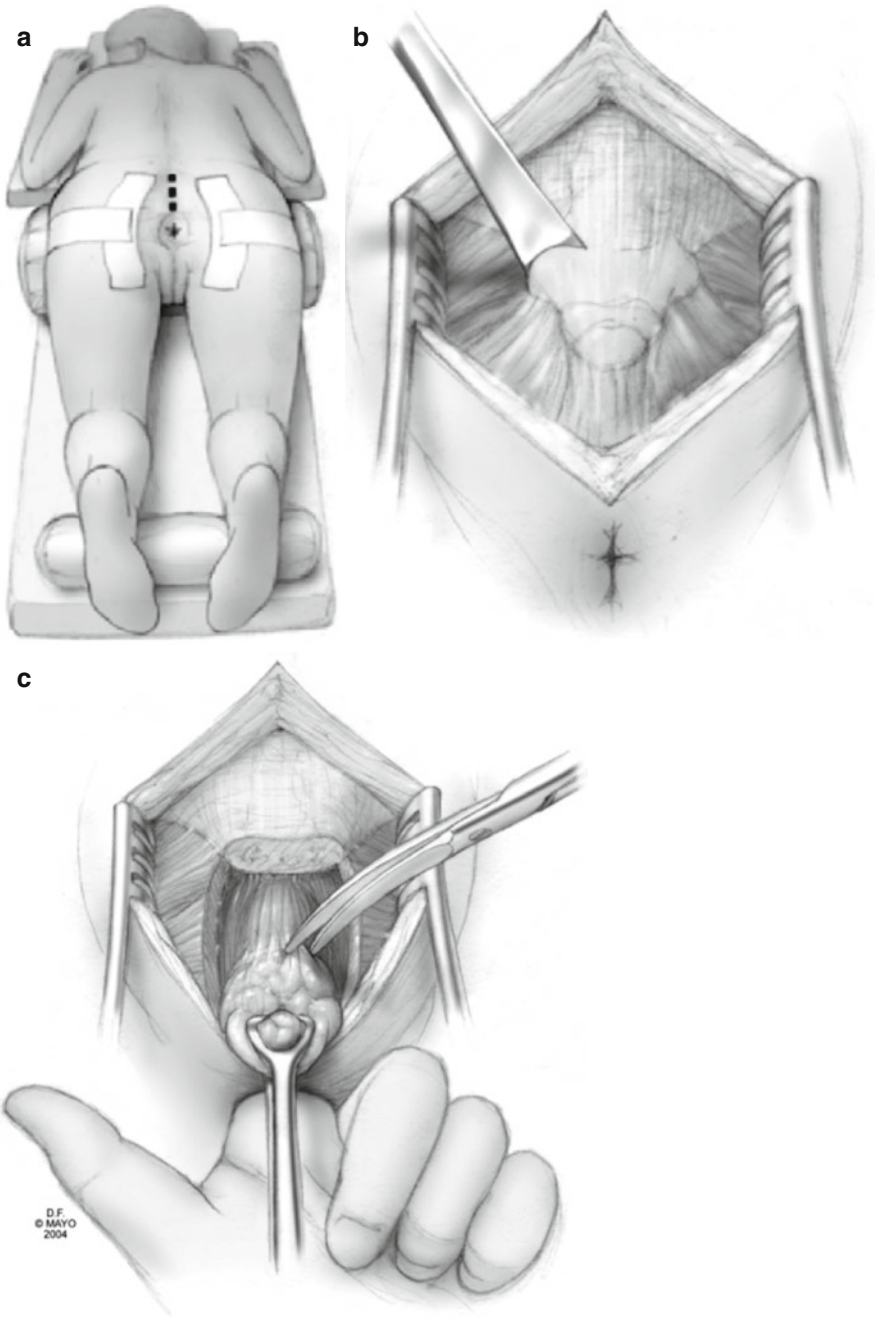

Fig. 21.9 (**a**) Positioning for posterior approach. (**b**) Coccygectomy. (**c**) Index finger in the anal canal to "push" tumor outward facilitating dissection

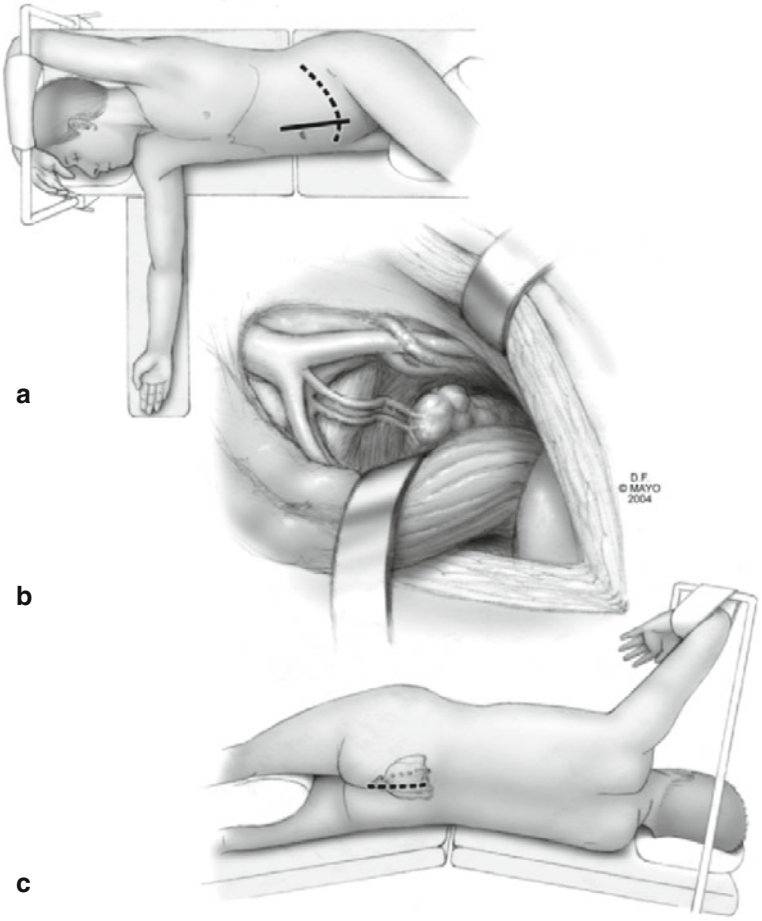

Fig. 21.10 (**a**) Modified lateral position for anterior exposure via a midline (*solid line*) or ilioinguinal (*dashed line*) incision. (**b**) Anterior exposure of the vessels and tumor. (**c**) Posterior approach to the sacrum (*dashed line*)

Combined Abdominal and Sacral-Perineal Approach

- If the upper pole of the tumor extends clearly above the S-3 level, an anterior and posterior approach is usually indicated.
- Patients may be placed in the supine or lateral position, depending on the surgeon's preference and previous experience. 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. 21.10a–c).
- We always recommend cystoscopy and bilateral ureteral stent placement before laparotomy.
- Through a midline incision, the abdomen should be carefully examined to rule out metastasis or other important pathology.

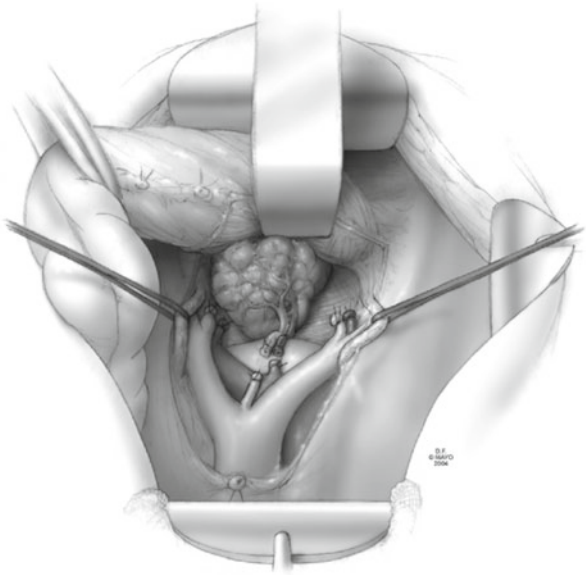

Fig. 21.11 Ligation of the middle sacral and internal iliac vessel

- After the lateral attachments to the sigmoid have been mobilized and the presacral space is entered just below the promontory, the posterior rectum can be dissected from the upper sacrum down to the upper extension of the tumor. The ureters and hypogastric nerves are identified and protected. The rectum can then be mobilized laterally and, if necessary, anteriorly.
- 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. If the tumor is extremely large, markedly compressing and displacing the rectum, making dissection between the rectal vault and the tumor hazardous, one should remove the rectum en bloc with the tumor and the involved segments of the sacrum. It is mandatory in malignant cases that no structures attached to the specimen should be separated with dissection and that they are removed en bloc with the primary tumor mass.
- In the presence of very large tumors, blood loss during the procedure can be substantial. These potentially adverse sequelae may be minimized by ligating the middle and lateral sacral vessels and both the internal iliac arteries and veins (Fig. 21.11). When ligating the internal iliac artery, in order to reduce the risk of perineal necrosis, it is best to preserve the anterior division from which the inferior gluteal artery arises. This maneuver is often performed in conjunction with permissive hypotension. A vascular surgeon can be helpful during this portion of the procedure especially in patients that have had prior irradiation or have distorted vascular anatomy.
- There have been reports using minimally invasive laparoscopic techniques as an approach for presacral tumor resection, both for anterior-only and

for anterior-posterior approaches. If the anterior portion of a combined anterior-posterior approach can be done laparoscopically (rectum divided, colostomy made, tumor partially mobilized, vasculature ligated), it should decrease the morbidity of the overall operation significantly.

Follow-Up Considerations

- The authors recommend an annual visit, including a digital rectal examination, to assess for recurrence of a benign lesion. If digital rectal examination reveals a mass, a CT scan is done. We recommend a baseline CT at 1 year following surgery and then repeated at every 5 years, even if examination is normal.
- In the case of malignant tumors, the patients are closely followed with particular attention to local recurrence and pulmonary metastasis. An annual pelvic MRI and chest CT scan are performed for the first 5 years. If the patient rectum was left in place, annual DRE with possible anoscopy is performed by the colorectal surgeon. Patients are offered repeat resection for locally advanced tumors and for pulmonary metastasis if all disease can be removed operatively.

Results of Treatment

Malignant Lesions

- Results of surgical treatment of presacral lesions depend on both the natural behavior of the tumor and the adequacy of resection. If wide margins were not achieved during resection of a malignant lesion or if the tumor is violated, one can expect a high local recurrence rate and a poor overall outcome. In general, most malignant tumors reported in the literature have had a rather poor prognosis, but many such tumors had been incompletely resected or excised piecemeal, breaking oncologic principles.

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. There continues to be some debate as to whether or not a coccygectomy needs to be done for all resections of congenital cystic lesions.

Algorithm

- Based on the experience at our institution, we have established a decision-making algorithm to guide the management of presacral tumors (Fig. 21.12).

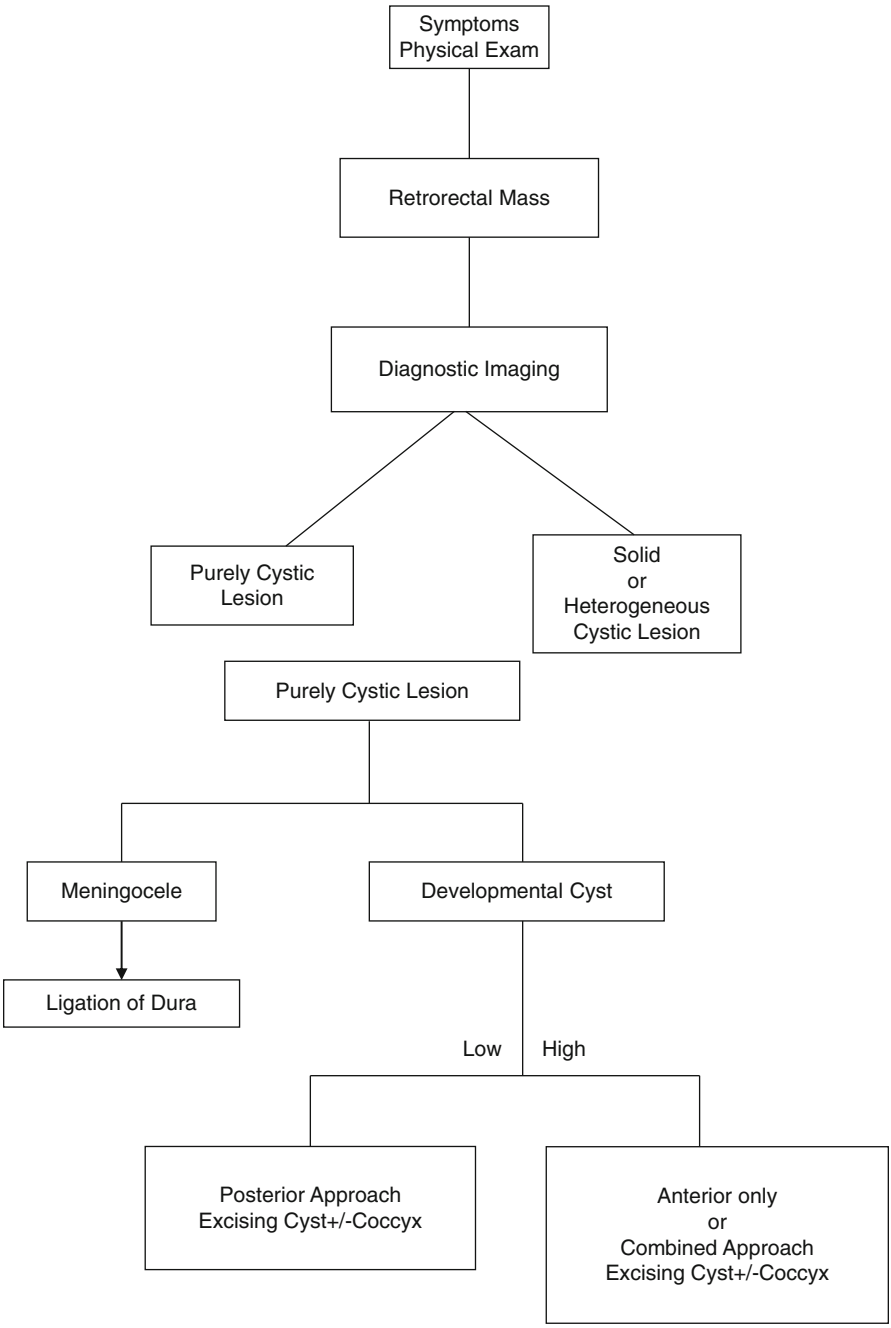

Fig. 21.12 Proposed treatment algorithm

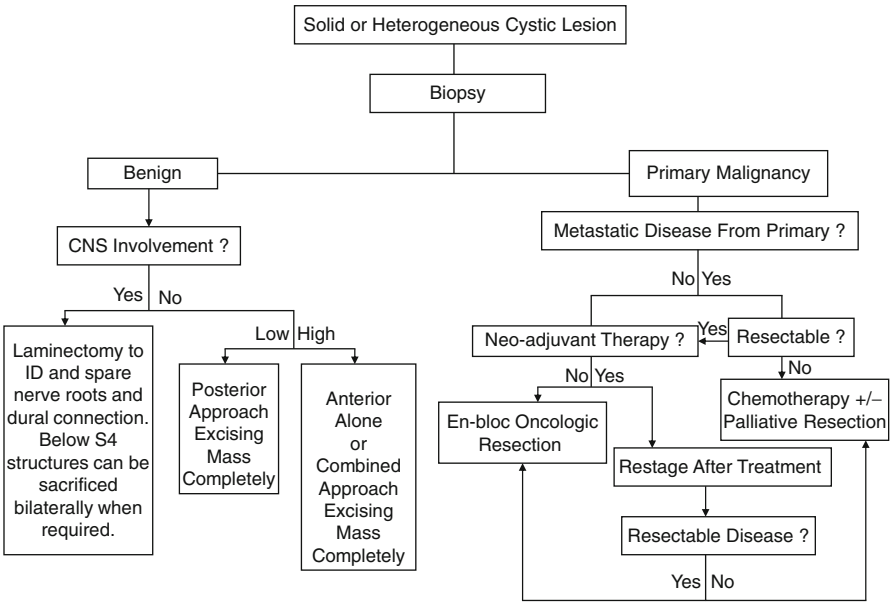

Fig. 21.12 (continued)

Conclusions

- 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 and cystic and solid and accurately define the 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 heterogeneous cysts should be considered for biopsy to rule out malignancy, guide neoadjuvant therapy, and plan the extent of resection.
- 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. Minimally invasive approaches may improve overall recovery and the quality of life in selected patients.

22. Diverticular Disease

Alan G. Thorson and Jennifer S. Beatty

- "Diverticular disease" is a continuum of anatomic and pathophysiologic changes within the colon related to the presence of diverticula.
- These changes most commonly occur in the sigmoid colon but may involve the entire colon.
- The continuum ranges from the presence of a single diverticulum (a sac or pouch in the wall of an organ) to many diverticula (which may be too numerous to count).
- It can refer to an asymptomatic state (diverticulosis) or to any one of a number of combinations of inflammatory symptoms, changes, and complications (diverticulitis).
- Symptoms may 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.
- Bleeding diverticular disease is discussed in Chap. 24.

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Incidence

- Since the early twentieth century, an increasing prevalence of the disease has been recognized in industrialized countries.
- The incidence increases with age and with the adoption of a diet high in red meat, refined sugars, and milled flour but low in whole grains, fruits, and vegetables.
- Although the exact incidence is not well established, numerous autopsy, radiographic, and endoscopic series have shown that the incidence has increased dramatically over the past 75 years, from around 5 % near the turn of the century to 50 % or more by 1975.
- It is now estimated that the risk of developing diverticular disease in the USA approximates 5 % by age 40 and may rise to over 80 % by age 80.
- This increase in observed incidence was originally attributed to new imaging techniques (the introduction of the barium enema in the early twentieth century) and bias inherent to estimates based on a population presenting with symptoms requiring an investigation.
- It is now clear that not only is the incidence of diverticulosis increasing but also the incidence of related complications is increasing. This is exemplified by increasing costs in the treatment of diverticular disease which accounts for nearly 450,000 hospital admissions, two million office visits, 112,000 disability cases, and 3,000 fatalities each year in the USA. It is estimated that costs will continue to increase as the population continues to age over the next several decades.
- Roughly 10–20 % of people with diverticula develop symptoms of diverticulitis.
- 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.
- National Census data estimates that as of July 2006, there would be 89,327,640 adults aged 50 or greater. That would mean that approximately 15 million people would develop diverticulitis and of those, 2.5 million would be admitted. If the 1 % average is correct and taking into account the percentage of patients with diverticulosis based on age, approximately 539,015 people will ultimately require an operation for diverticular disease.
- There is some evidence that males are more frequently affected at a younger age compared to females; however, significant bias may influence this impression. Young females may frequently be under diagnosed due to confusion with gynecologic diseases in women who are of childbearing age. Older females may be overdiagnosed due to confusion with irritable bowel syndrome (IBS).
- The incidence of perforation is higher in males under age 50 and in females over age 50.

Pathophysiology

- Diverticulosis is associated with high intraluminal pressures.
- Pressures in patients with diverticular disease have been found to be as high as 90 mmHg during peak contraction (nine times higher than seen in patients with normal colons). The high pressures lead to segmentation, whereby the colon effectively functions as a series of separate compartments rather than as one continuous tube.
- The high pressures are directed toward the colonic wall rather than as propulsive waves, which predispose to herniation of mucosa through the muscular defects that occur where blood vessels penetrate to reach the submucosa and mucosa (vasa recta brevia).
- Most of these penetrations occur between the mesenteric and antimesenteric tinea where, coincidentally, most diverticula are found. As the mucosa herniates, it does so without dragging the muscular layer along, leaving the diverticula denuded of muscle, which is consistent with the definition of an acquired process.
- Diverticula may be true, containing all layers of the bowel wall (congenital), or false, lacking the muscular layer (acquired or pulsion diverticula). Thus, the most common diverticula are acquired or pulsion diverticula.
- These high pressures are consistent with the sigmoid colon being the most common site of involvement. This can be explained by the law of Laplace which states that the tension in the wall of a hollow cylinder is proportional to its radius multiplied by the pressure within the cylinder. As the narrowest segment of colon, the sigmoid has the highest pressures and, consequently, the highest risk of diverticulum formation.
- It is hypothesized that at least a part of the protective effect of dietary fiber is stool bulking, which maintains a larger lumen within the bowel. The stool bulking and larger lumen prevent segmenting contractions and, therefore, decrease high pressures.
- Complementary to these theories of pathogenesis is the consistent muscle abnormality associated with sigmoid diverticular disease.
  - Both the circular and longitudinal muscle walls are typically thickened resulting in a reduction in the size of the lumen and a shortening of the sigmoid colon.
  - The reduced lumen size may be further enhanced by secondary pericolic fibrosis.
- The source of this muscular thickening is not clear. It has been observed that in the normal process of left colon peristalsis, smooth muscle in the rectosigmoid will relax in response to a stimulus, causing contractions in the colon above and in the rectum below. A combination of poor diet, aging, and constipation could lead to malfunction of this relaxation response leading to a functional obstruction and the hypertrophy seen in the muscle. Cellular hypertrophy, cellular hyperplasia, and elastosis have all been described. Elastosis appears to precede the development of diverticulosis. It is not found in any other inflammatory conditions of the colon.

- Several alternative concepts have been advanced to explain the differences in presentation of diverticular disease. Although the most common finding in diverticular disease is the muscular changes already discussed, some patients fail to demonstrate this characteristic. These patients are more likely to have diffuse diverticula throughout the colon. There is a higher incidence of bleeding with diffuse involvement. There may be an underlying connective tissue abnormality, which could explain the development of diverticula in the absence of high intraluminal pressures. The high incidence of bleeding in these patients could be related to an associated inadequate vascular support in the diverticular wall.
- 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.

Etiology

- The etiology of diverticular disease remains complex and relatively poorly understood.
- Pathophysiologic studies reveal that complications do not occur until there is microperforation through the wall of a diverticulum into the pericolic tissue.
  - A single diverticulum experiences a change in the permeability of its isolated mucosa from physical, biochemical, or physiologic means.
  - It is postulated that perforation then occurs leading to a characteristic response, which results in varying degrees of inflammation.
  - The perforation might cause microabscess, phlegmon, large abscess, fistulas, or even free perforation.
  - Free perforations occur rarely, while fistulas are more likely, with the bladder being the most common site of fistula formation.
- The original communication between the diverticular perforation and the lumen of the bowel is usually rapidly obliterated by the inflammatory process. Occasionally, failure of the diverticular neck to obliterate may lead to a free communication between the bowel and the peritoneal cavity with resultant fecal peritonitis. Rupture of a noncommunicating abscess may lead to purulent peritonitis.
- Low-grade inflammation of colonic mucosa, induced by changes in bacterial microflora, can affect the enteric nervous system and alter gut function, leading to symptom development. This explanation for symptoms in IBS can be easily extrapolated to diverticular disease since some patients with diverticular disease demonstrate bacterial overgrowth.
- Recent clinical investigations have shown that disturbances in cholinergic activity may contribute to diverticular disease.
  - A colon with diverticular disease has more cholinergic innervation than a normal colon. In addition, there is less noncholinergic, nonadrenergic inhibitory nerve activity.

Epidemiology

Diet

- Diets high in red meat and low in fruit and vegetable fiber increase diverticular symptoms by as much as threefold. Vegetables and brown grains have been shown to be protective. Fiber may be protective by increasing stool weight and water content, which decreases colonic segmentation pressures and transit times.
- In a large cohort study, the consumption of nuts, corn, and popcorn did not increase the risk of diverticulosis or diverticular complications, and therefore the recommendation to avoid these foods to prevent diverticular complications should be reconsidered.

Age and Gender

- Female patients present with complications requiring surgery an average of 5 years later than male patients.
- Men have a higher incidence of bleeding than women; however, women have a higher incidence of fistula formation compared to men. Younger men present with fistula more frequently, while older men present more frequently with bleeding.
- Young females are more likely to present with perforation, while older females are more likely to present with chronic disease and stricture.

Nonsteroidal Anti-inflammatory Drugs

- Nonsteroidal anti-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 in providing 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.

Immune Status

- The use of corticosteroids is associated with a higher risk of perforation and more severe inflammatory complications. The postulated mechanism is immunosuppressive and anti-inflammatory effects hinder confinement of perforation in its early stages, resulting in more serious sequelae. The use of other immunosuppressive drugs has also been associated with such increased risks. The main risk appears to be more virulent complications once complications occur.

Smoking

- A recent large case–control study demonstrated that smokers had three times the risk of developing complications from diverticular disease than did nonsmokers. However, a large cohort study involving over 46,000 men in the USA did not find this same association.

Alcohol

- A Danish cohort study showed the risk of diverticulitis was three times higher in female alcoholics compared to the general population and two times higher in male alcoholics. However, the data may be biased due to dietary and smoking habits associated with alcoholics.

Clinical Manifestations

Clinical Patterns

- Diverticular disease may be classified into diverticulosis (asymptomatic) and diverticulitis (symptomatic) (Table 22.1).
- Diverticulosis refers to the presence of diverticula with no related symptoms. This applies to the vast majority (80–90 %) of patients with diverticular disease.
- Diverticulitis can be subclassified into noninflammatory, acute (simple or complicated), chronic (atypical or recurring/persistent), or 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.

Table 22.1 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

Table 22.2 The Hinchey classification (proposed by Hinchey et al. in 1978)

Hinchey Stage I	Localized abscess (para-colonic)
Hinchey Stage II	Pelvic abscess
Hinchey Stage III	Purulent peritonitis (the presence of pus in the abdominal cavity)
Hinchey Stage IV	Feculent peritonitis

- The term "atypical" has been applied to patients with chronic symptoms who never develop the necessary clinical and laboratory criteria to be judged as having acute diverticulitis.

Acute Diverticulitis

- Acute diverticulitis is represented by signs and symptoms of acute inflammation and may be simple (limited to the colonic wall and adjacent tissues) or complicated (with perforation or fistula). Simple acute disease is usually accompanied by systemic signs of fever and leukocytosis, while complicated acute disease may have the added signs of tachycardia and hypotension.
- Complicated acute diverticulitis can be classified according to the extent of spread of the inflammatory process. A common classification for diverticulitis with perforation is the Hinchey classification (Table 22.2).

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. If resection is performed, there will be evidence of inflammatory changes within the specimen.

Complex Diverticular Disease

- Complex diverticulitis refers to disease in those patients who manifest sequelae of chronic inflammation including fistula, stricture, and obstruction.

Presenting Symptoms

- Patients with acute diverticulitis typically complain of left lower quadrant abdominal pain. The pain is generally constant in nature, not colicky. Radiation may occur to the back, ipsilateral flank, groin, and even the leg. The pain may be preceded or accompanied by episodes of constipation or diarrhea. It commonly is progressive in nature if appropriate treatment is not instituted.

- Nausea and vomiting are unusual in the absence of obstruction. Bleeding is not an associated finding. Symptoms of dysuria or urgency suggest possible bladder involvement due to 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.

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. Classically, there is no prodromal epigastric pain with diverticulitis as one might expect to see with appendicitis.
- In the event of a perforation with development of fecal or purulent peritonitis, the area of pain will spread throughout the abdomen. Guarding will become prominent and the abdominal wall will become rigid.

Diagnostic Evaluation

Abdominal X-Rays

- The primary value of abdominal X-rays is to rule out pneumoperitoneum or to assess for a possible obstruction; therefore plain films of the abdomen should include supine and upright or left lateral decubitus views. Computed tomography (CT) scan is often the evaluation of choice in the face of acute abdominal pain, so in many centers, the plain abdominal film is rarely used.

Contrast Studies

- Barium or water-soluble contrast studies have their proponents for utilization; however, CT scans provide a significantly more thorough evaluation, making it the preferred imaging study in many centers (Fig. 22.1). Nonetheless, due to costs, some clinicians will utilize CT scan only if there is clinical suspicion of an abscess or other complicating feature for which an alternative to standard bowel rest and antibiotics might be applied. A water-soluble contrast study can evaluate the lumen of the bowel if there is concern about distal bowel obstruction. It may be an important part of the assessment for the possible use of a colonic stent if malignant disease is suspected.
- In most centers, contrast studies, if used at all, are used in a limited fashion to evaluate the anatomy of the colon prior to an operation.

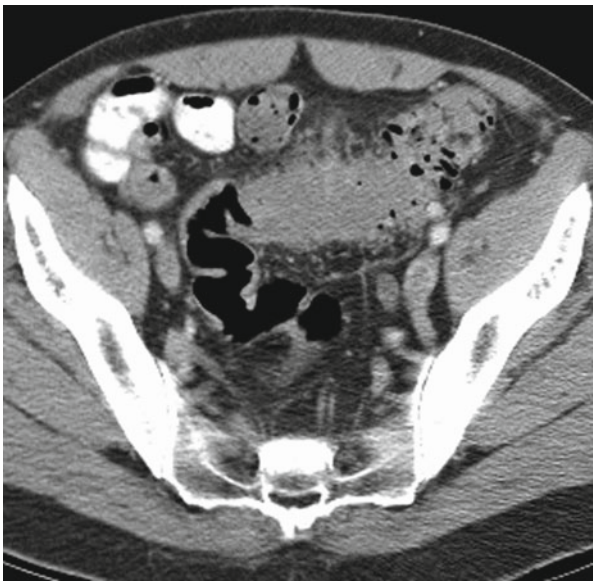

Fig. 22.1 CT scan reveals uncomplicated diverticulitis with bowel wall thickening and streaky fat in the mesentery

CT Scan

- An important advantage of 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 a predictably short length of hospital 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, which is useful for surgical planning.
  - Early CT-guided drainage of abscesses allows down-staging of complicated diverticulitis, converting an otherwise urgent or emergent operation with its attendant increases in morbidity and mortality to the safety of an elective operation. In some selected cases there may be no need for elective resection.

Colonography

- Preliminary studies utilizing magnetic resonance imaging (MRI) colonography have shown a high correlation with CT findings in patients with diverticular disease without exposure to ionizing radiation.

Three-dimensional rendered models and virtual colonoscopy can be performed only in the nonacute setting. These comprehensive 3-D models, rather than barium enema, may have a role in presurgical planning with concurrent assessment of the residual colon.

Ultrasonography

- Transrectal ultrasound (TRUS) has been utilized in the evaluation of diverticular disease in conjunction with transabdominal ultrasound (TAUS). 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.

Endoscopy

- Endoscopy in the face of acute diverticulitis must be undertaken with extreme caution due to risk of perforation and decreased chance of successful cecal intubation. Generally, in the absence of an urgent indication, colonoscopy should be delayed until resolution of the acute episode is complete.
- In the case of elective colonoscopy, the unexpected finding of acute diverticulitis (manifested as erythema, edema, pus, or granulation tissue at a diverticular opening) is distinctly unusual, occurring in just 0.8 % of patients. Treatment with antibiotic therapy for such findings is generally unnecessary as follow-up has shown that symptoms of diverticulitis do not develop following the colonoscopy.

Differential Diagnosis

- The differential diagnosis for diverticular disease includes IBS, carcinoma, inflammatory bowel disease (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

- In many ways, the distinction between chronic diverticulitis and noninflammatory diverticular disease relies upon the pathologist, while the distinction between noninflammatory diverticular disease and IBS relies on the diagnostic acumen of the clinician and the long-term outcomes of resection. Due to the prevalence of diverticular disease, many patients with IBS will have concomitant diverticular disease. However, due to the fact that diverticular disease is most commonly asymptomatic, the

Table 22.3 The Rome II criteria for irritable bowel syndrome

Irritable bowel syndrome 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
2. Onset associated with a change in frequency of stool
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 which are NOT typical of IBS:
Pain that often awakens/interferes with sleep
Diarrhea that often awakens/interferes with sleep
Blood in stool (visible or occult)
Weight loss
Fever
Abnormal physical examination

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 22.3) for the diagnosis of IBS in order to sort through this differential.

Colonic Neoplasia

- Distinguishing diverticular disease from cancer can be difficult and occasionally a resection is necessary. Findings on barium enema (BE) that supports a diagnosis of diverticular disease include preservation of the mucosa, long strictures, and the presence of diverticula. A BE can also assess the extent of the diverticulosis prior to resection. Colonoscopy can frequently resolve this issue, but it is not always possible due to acute angulations or narrowing of the lumen. CT evaluates the entire abdomen, which can identify concurrent disease and may give clues to underlying colonic pathology.
- The increasing incidence of colonic neoplasia with increasing age parallels that of diverticular disease. Polyps and cancer must be considered whenever a diagnostic workup for diverticular disease is begun.

Inflammatory Bowel Disease

- Crohn's disease can be a particularly difficult diagnosis 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 disease. Recurrent "diverticulitis" requiring a repeat resection should always raise the question of possible Crohn's disease.

Other Colitides, Appendicitis, and 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 and gynecologic and urologic disease.

Special Considerations

Diverticulitis in Young Patients

- There continues to be some debate as to the issue of recurrence in patients younger than 50 years old. It does appear that there is an increased incidence in younger patients presenting with diverticulitis.
  - In a recent study by Etzioni et al. evaluating the nationwide inpatient sample data for changing patterns of diverticular disease and treatment, a 73 % increase in the rate of admission for patients aged 18–44 years with diverticulitis was found between 1998 and 2005. While an increase was also found in patients aged 45–74 year, the increase was only 29 %.
- Historically, diverticular disease in patients less than age 50 has been described as more virulent and with more serious complications.
- Despite the increased number of younger patients with the disease, its virulence does not appear to be any different compared to older counterparts. It is now doubtful that age itself should be a primary consideration in the decision to operate.
- Young patients with diverticular disease are more commonly male and obese and have a higher incidence of right-sided diverticulitis.
- Young patients undergoing operation were frequently misdiagnosed preoperatively with appendicitis being the most common misdiagnosis.
- Many recommend that patients less than age 50 have an elective resection after a single episode of acute disease.
- Recent evidence is mixed and supports a more conservative trend to recommending resection for uncomplicated diverticulitis.
- Some 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 %). Some recommendations for elective resection in the young patient are based on cost savings related to definitive surgical management vs. the higher costs of ongoing medical treatment for recurring disease. These types of recommendations assume a high risk of recurrent disease.

- There is evidence that diverticular disease in young patients is changing. It is not as rare as in the past and continues to become more prevalent. And recent evidence suggests there is no increased risk of complications from diverticular disease in the young. Based on these findings, resection following a single episode of diverticulitis is not recommended.
- 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. To improve management, we must become better at predicting who is at risk for recurrent disease. Age alone does not appear to be a reliable factor. The use of CT to identify "severe" or "complex" diverticular disease seems most promising.

Giant Colonic Diverticulum

- Giant diverticula of the colon are rare entities associated with sigmoid diverticular disease. They are generally pseudodiverticula with inflammatory rather than colonic mucosal walls. They usually arise off of the antimesenteric border of the sigmoid colon.
- Diagnosis is by plain film of the abdomen, which demonstrates a large, solitary, gas-filled cavity. Communication with the colon can be demonstrated with contrast enema. The differential diagnosis includes congenital duplication of the colon, cholecystenteric fistula, colonic volvulus, emphysematous cholecystitis, infected pancreatic pseudocyst, pneumatosis cystoides intestinalis, Meckel's diverticulum, intra-abdominal abscess, giant duodenal diverticulum, dilated intestinal loop, gastric dilatation, tubo-ovarian abscess, and mesenteric cyst.
- Most patients will present with vague symptoms of abdominal discomfort or pain and a soft, mobile abdominal mass. A few patients will present with one of the known complications, which include perforation, sepsis, intestinal obstruction, or volvulus. The natural history is slow enlargement over time. The treatment of choice is resection of the diverticulum and adjacent colon at time of diagnosis if the patient is symptomatic.

Rectal Diverticula

- Rectal diverticula are rare. They are typically true diverticula since they include the muscular layer of the rectum in their wall. They are frequently solitary. Inflammation can generally be managed with antibiotics; rarely surgical resection is required.

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. Classically, cecal diverticula are described as true diverticula containing all layers of the bowel wall. However, most cecal diverticula actually are false and frequently not solitary.
- 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.
- Intraoperative diagnosis is relatively easy with Grade I and to a lesser extent with Grade II disease. Most episodes of cecal diverticulitis presenting with Grade III or Grade IV disease are misdiagnosed intraoperatively as perforated carcinoma.
- If a correct diagnosis of uncomplicated cecal diverticulitis can be made preoperatively, then antibiotics and treatment similar to left-sided disease are appropriate. However, this is rare. Intraoperatively, the options for treatment include (1) appendectomy, nonresection of the diverticulum, and postoperative antibiotic therapy; (2) appendectomy with diverticulectomy for Grade I and identifiable Grade II disease; or (3) right hemicolectomy which is the procedure of choice for not readily identifiable Grade II, Grade III, and Grade IV disease, failed treatment, or possible cancer. Appendectomy should always accompany nonresection or diverticulectomy whenever the base of the appendix is not inflamed to avoid confusion at a later date.

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. It is reported to occur in a younger age group than sigmoid disease and is more common in females.
- Treatment parallels that of sigmoid diverticulitis; however, resection is more commonly performed since a preoperative diagnosis is more difficult to make and a carcinoma frequently cannot be ruled out.

Polycystic Kidney Disease

- 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 due to their immunocompromised state.
- Many transplant centers recommend prophylactic sigmoid resection in those polycystic kidney patients scheduled for transplantation with a documented history of diverticulitis.

Treatment of Acute Diverticulitis

Dietary Management

- This is the primary management of uncomplicated diverticular disease.
- 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.

Medical Management

- 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. Recent evidence from Europe suggests that antibiotics may be omitted in selected cases.
- 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 since there is no data to substantiate this practice.
- Appropriate antibiotics should be instituted. 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) and *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 intra-abdominal 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 nil per os (NPO) until there is evidence of clinical improvement making surgical intervention less likely.
- The diet is then gradually advanced from clear liquids to a low-residue diet for a variable period of time before reinstituting a high-fiber diet.
- Symptoms generally improve within 24–48 h. Failure to improve requires further diagnostic workup including repeat CT and reevaluation of the need for surgery.

Surgical Management

- The surgical management of acute diverticular disease is replete with varied options that allow for customizing an operation to meet the needs of the individual patient.
- A thorough knowledge of these options and the indications for each is necessary for the surgeon managing these cases. The goal should always be to manage a complex patient in a way which will maximize the opportunity to avoid an emergency operation 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 procedure) or mucous fistula (Mikulicz operation), simple diversion with drainage of the affected segment, diversion with oversewing of the perforation site, laparoscopic lavage without resection, and, rarely, subtotal colectomy. Adjunctive measures include on-table lavage and the option of a laparoscopic approach.
- The historical discussion of these options would include the use of a three-stage approach with diversion and drainage followed by a second operation for resection and a third operation for reestablishment of intestinal continuity.
- A modification of this approach includes oversewing of a visible site of perforation with an omental patch as a part of the initial operation. Alternatives include a two-stage approach consisting of a Hartmann or Mikulicz procedure followed by a second operation for reestablishment of intestinal continuity and resection with primary anastomosis, with or without proximal diversion, as a single operation. For the most part, current discussions revolve around the relative merits of a single stage vs. 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.

- The following sections will discuss the applications of these approaches to the various presentations of diverticular disease including both chronic and acute forms. Special consideration will be given to the management of intra-abdominal abscesses.

Intra-abdominal Abscess

- For a patient found to have an abscess, there is a large volume of 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 an elective operation.
- An abscess not responding to medical management should be drained percutaneously or transrectally as appropriate to its location (Fig. 22.2).
- 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 Stage 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 resection will be required.
- In a recent study of 511 patients diagnosed with complicated diverticulitis, 99 were diagnosed by CT scan with abscess, and 16 of these underwent percutaneous drainage. Of these patients with continued nonoperative treatment, even after percutaneous drainage, a recurrence rate of 42 % was noted with an associated increased probability of emergent procedure. Based on these findings, it is recommended that all patients with complicated findings undergo at best an elective operation.

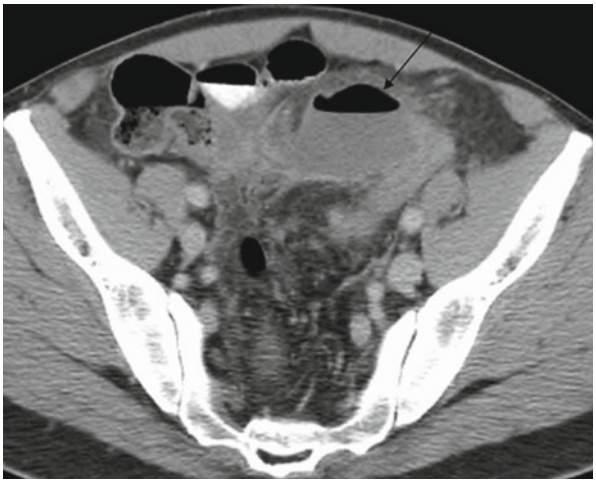

Fig. 22.2 CT reveals pericolic abscess (*arrow*) (Hinchey Stage I)

- This therapy of treating patients with percutaneous drainage and medical management until it was feasible to perform an elective operation has also been evaluated. Salem reviewed all hospitalized patients for the state of Washington and found after evaluating over 25,000 patients that percutaneous drainage was associated with a decrease in emergency operative interventions.
- Ricciardi et al. evaluated the nationwide inpatient sample data from 1991 to 2005 analyzing the incidence of complicated diverticulitis admissions. Despite a significant decline in surgical treatment for diverticulitis during this time period, there was no change in the proportion of patients discharged with complicated diverticulitis.

Indications for Surgery for Acute Disease

- The indications for surgery of acute disease include:
  1. Failure of phlegmon or abscess to respond to nonoperative management with clinical deterioration (increasing fever, leukocytosis, tachycardia, hypotension, signs of sepsis, or a worsening physical examination)
  2. Free perforation with peritonitis
  3. Obstruction

  Perforation without peritonitis may not require operation (Fig. 22.3).

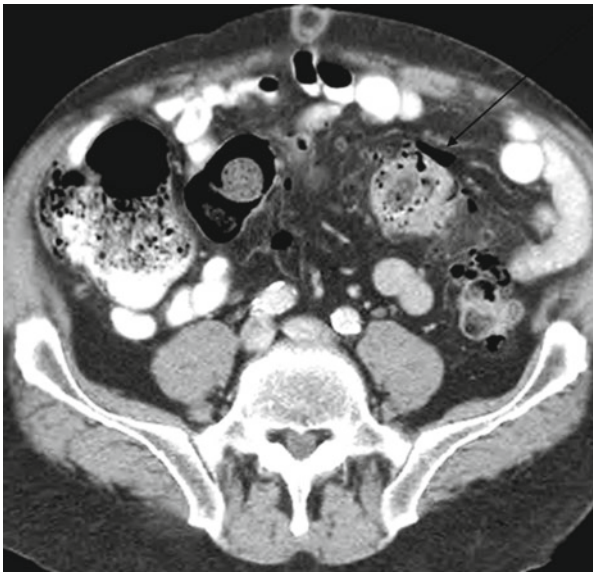

Fig. 22.3 3-Diverticulitis with localized perforation (*arrow*). The patient was treated with antibiotics and improved without the need for emergency surgery

Surgical Procedures

- For acute disease, the choice of operation is highly dependent upon the degree of inflammatory response encountered at the time of operation.
- Since most acute diseases can be managed 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 Stage I and some Stage II disease can be managed with a one-stage procedure (resection and anastomosis) if the patient is stable, the extent of contamination is limited, and adequate bowel preparation is possible recognizing, however, the necessity of mechanical bowel preparation in colon resections has been questioned. Proximal diversion may be necessary.
- Most cases of Hinchey Stage III and IV disease will require a two-stage approach. Some recent evidence suggests a possible role for resection with primary anastomosis and proximal diversion in highly selected cases without gross fecal contamination and also the role of laparoscopic lavage and no resection.
- In a recent review by Salem and Flum, who reviewed 98 articles on the outcome of complicated diverticulitis based on the type of operation performed, 1,051 patients were identified who had a Hartmann procedure from 54 studies, and 569 patients who had a primary anastomosis from 50 studies. Of the 569 cases, 16 % had covering stomas and 10 % underwent on-table lavage. The mortality rates were higher in the Hartmann group, 19.6 % vs. 9.9 % for primary anastomosis. Anastomotic leak rate ranged from 6.3 to 19.3 % in patients undergoing a primary anastomosis. When primary anastomosis was performed with a covering stoma, the lowest rate of leak rate (6.3 %) and the lowest wound infection rate (4 %) were demonstrated. Wound infections were also more frequently seen in the Hartmann group, 24.2 % vs. 9.6 %. Hartmann patients also required a larger second operation than those who had a primary anastomosis with or without a covering stoma. The conclusion was the primary anastomosis is no worse than a Hartmann procedure and has several advantages including higher restoration of continuity rate, less hospitalization, and fewer infectious complications (Table 22.4).

Table 22.4 Outcomes of primary anastomosis and Hartmann procedure

	Patients	Mortality (%)	Wound infection (%)	Leaks (%)
Hartmann procedure	1,051	18.8	24.2	NA
Primary anastomosis	295	8.1	16.4	19.3
Primary anastomosis with stoma	<109	9.2	4	9.6

Modified from Salem L, Flum DR. Primary anastomosis or Hartmann's procedure for patients with diverticular peritonitis. A systemic review. Dis Colon Rectum. 2004;47:1953–64

- A major disadvantage of a two-stage procedure is that 35–45 % of patients never have their colostomy closed. However, in patients with preexisting incontinence, a Hartmann pouch should be the procedure of choice. Women are more likely than men to not have closure. 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 maintains at the same risk for neoplasia as other patients of equal age.

Hartmann Reversal

- Reversal of a Hartmann colostomy carries significant risks that must be entertained when considering this operation for patients who will desire continuity in the future.
  - Failure to reverse the colostomy has been reported in 20–50 % of patients and leak rates on reversal range from 2 to 30 %.
  - Mortality has been reported anywhere from 0 to 10 % and wound infection rates range from 12 to 50 %.
- Maggard et al. reviewed 1,176 patients who had a Hartmann procedure for diverticular disease; only 65 % had a reversal at a mean of 143 days. Younger men were more likely to have their ostomy reversed as opposed to older patients and women. Patients with more comorbidities also had fewer reversals. When evaluating all patients, 35 % never had their ostomy reversed during the 4-year study. The complication rate following Hartmann reversal was 57.4 %, including infection (9.1 %), aspiration pneumonia (8.7 %), pulmonary edema (6 %), and acute renal failure (4.9 %).

Complications from Surgical Resection

- Predictors of complications after resection for diverticular disease include advanced age (greater than 70–75 years), two or more comorbid conditions, obstipation at initial examination, the use of steroids, sepsis, and obesity. 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 %. Anastomotic leaks may lead to localized abscess, stricture, peritonitis, and sepsis. The diagnosis is dependent upon 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, obstruction, and sepsis all should raise the question of a leak. The diagnosis is most commonly confirmed by water-soluble contrast enema or by CT scan with intravenous, oral, and rectal contrast.
- An anastomotic leak without an abscess can usually be managed with intravenous antibiotics and response assessed. 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. An exception

would be a "pinhole" leak with limited inflammatory response, which may be managed with repair, colonic lavage, and proximal diversion.

- An anastomotic leak resulting in an abscess can generally be managed with percutaneous or transrectal drainage. Again, failure to respond will require laparotomy, takedown of the anastomosis, and proximal diversion.
- A colocutaneous fistula related to a diverticular resection will usually respond to nonoperative measures. Provided there is no distal obstruction, no foreign body, and no underlying Crohn's disease, spontaneous closure should be anticipated. Important steps to facilitate closure of colocutaneous fistulas include draining any undrained abscess, maximizing nutrition, and delivering appropriate wound care, which may require the help of enterostomal therapy nurses.
- Strictures are an unusual complication related to diverticular resection, unless the underlying process is Crohn's disease. In the rare instance when stricture does occur, the most likely etiologies include ischemia or localized sepsis due to confined leak. Such strictures can most commonly be managed by dilatation with a balloon or rigid proctoscopy but occasionally will require a formal resection with recreation of anastomosis.
- 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 prior to operation should be a function of clinical suspicion and the extent of inflammation on CT scan.
- General postoperative complications related to colon and rectal surgery and specifics related to the recognition and management of the specific complications mentioned above are discussed more thoroughly in Chap. 10.

Recurrence After Resection

- Recurrence of diverticulitis or its symptoms following resection has been reported in 3–13 % of elective cases. Factors contributing to recurrence of diverticulitis include shorter resection length and anastomosis to the sigmoid colon rather than to the rectum. The level of the anastomosis is the only significant determinant of recurrence after laparoscopic resection for diverticular disease.

Treatment of Chronic and Recurrent Diverticulitis

- Most patients who develop a first episode of symptomatic diverticulitis have been asymptomatic until 1 month prior to presentation. Most will respond to bowel rest and antibiotics as an outpatient. It is difficult to reliably estimate how many outpatients will have recurrence because outpatient data is generally not reflective of a primary care population.

However, 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.

- Data is more readily available on recurrence for patients who were initially treated as inpatients. But our understanding of the natural history continues to evolve as antibiotics become more effective and inpatient status reflects increasingly severe disease. This makes historical data regarding these issues of less value. Presently, inpatients might be expected to be at a greater risk for recurrence. In fact, 20 % or more of these patients will develop a recurrence. Some, but not all, will require a second hospitalization. The interval between acute events may be prolonged (median 5 years). Following a second hospital admission, up to 70 % will continue with symptoms, and over half of those that require another 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 denominator in the number of individuals affected with diverticulosis and better antibiotics for managing infections, this estimate may now be too high.
- The risk of recurrence following an attack of uncomplicated diverticulitis has been shown to be quite low. The range of recurrence following an attack is 1.4–18 %.
- It has been estimated that only 1 in 2,000 patient/years of follow-up will require an urgent Hartmann procedure after resolution of diverticulitis.
- Very few patients presenting and requiring an emergent operation had been previously diagnosed with diverticulitis. An estimated 75–96 % of patients presenting with peritonitis requiring an emergent operation had never been diagnosed with diverticulitis. This supports the notion that operating to prevent complications of diverticulitis is ineffective at achieving the goal.
- Patients with multiple, recurrent episodes of acute diverticulitis documented by CT scan should be considered for resection. Traditional teaching with respect to diverticulitis dictated elective sigmoid resection for patients suffering more than one episode of uncomplicated diverticulitis. In fact, most of the consensus data on elective resection after two documented episodes comes from literature that was published prior to the use of CT scanning and modern day antibiotic therapy. Because of these and other studies, the American Society of Colon and Rectal Surgeons (ASCRS) revised its previous recommendations for resection of diverticular disease. The 2006 revised practice parameters now read as follows: "The decision to recommend surgery should be influenced by the age and medical condition of the patient, the frequency and severity of the attacks, and whether there are persistent symptoms after the acute episode."
- Recent data has suggested that the recommendation for resection following 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 following four documented episodes rather than after two results in fewer deaths, fewer colostomies, and an additional cost savings of over $5,000 per patient in those less than 50 years of age.
- Others question the role of elective resection at all due to 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.
- The ultimate goal is to perform an operation electively rather than as an emergency. This requires correctly predicting those patients who are most likely to have serious complications as a result of their disease. CT evidence of complicated or "severe" disease has shown some promise in predicting risk. The risk of complications within 5 years of a first attack of diverticulitis exceeds 50 % if CT shows severe diverticulitis at the initial episode. Mild findings on CT can be defined as localized thickening of colonic wall and inflammation of pericolic fat. Severe findings are defined as abscess and/or extraluminal air and/or extraluminal Gastrografin. Abscess, extraluminal air, and extraluminal Gastrografin 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 at particular risk for a poor outcome. The risk is due to a higher incidence of perforation and more severe inflammatory complications when perforation does occur.

Surgical Procedures

- Patients undergoing resection for chronic disease will almost always be candidates for single stage resection with primary anastomosis.

Techniques for Appropriate Resection

- The practice parameters of the ASCRS 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. It may be acceptable to retain the proximal diverticular colon as long as the remaining bowel is not hypertrophied.
- All of the sigmoid colon should be removed. When anastomosis is elected, it should be made to a normal rectum and must be free of tension and well vascularized.
- The single most important predictor of recurrence following sigmoid resection for uncomplicated diverticulitis is an anastomosis to the sigmoid

colon rather than to the rectum. In urgent or emergent cases, resection and diversion are generally required. In selected cases where sepsis can be removed, definitive resection with anastomosis (with or without proximal stoma) may be appropriate. On-table colonic lavage may be a useful adjunct to resection and anastomosis.

Laparoscopic Surgery

- The role of laparoscopy in the management of diverticular disease is evolving. Recent data suggest decreased overall costs associated with laparoscopic resections when compared to open resections. Patients who are converted from laparoscopic to open procedures are a concern with regard to added costs, but conversion rates are below 20 %, predictable, and thus probably avoidable in many instances. Higher conversion rates are associated with more complex disease. Recurrence rates match those for open procedures.
- Laparoscopic resection results in a shorter length of stay and fewer complications. Hand-assisted laparoscopic colectomy has also been compared against straight laparoscopic colectomy and has been found to be equivalent in patient outcomes and may result in a lower conversion rate. Marcello et al. in a multicenter prospective randomized trial found the benefit of hand-assisted laparoscopic sigmoid resection compared to laparoscopic resection includes shorter operating time with similar length of hospital stay (Table 22.5).
- Despite the recent eruption of literature and discussion of laparoscopic colectomies, only 5–10 % of all colectomies are currently performed using a laparoscopic technique. As data continues to accumulate, it appears that laparoscopic surgery is set to play a significant role in the management of diverticular disease.
- A therapy unique to laparoscopic surgery is the use of laparoscopic lavage. A new approach has been described by Myers et al., as an alternative to

Table 22.5 Results of a multicenter prospective randomized trial of hand-assisted laparoscopic sigmoid resection compared to laparoscopic resection in diverticular disease

	HA ($n=33$)	LAP ($n=33$)	P value
Operative time (min)	175 ± 58	208 ± 55	0.021
Estimated blood loss (mL)	211 ± 160	198 ± 175	0.074
Ureteral stents	3	4	0.99
Incision size (cm)	8.2 ± 1.5	6.1 ± 2.1	<0.01
Passage flatus (days)	2.7 ± 1.6	2.9 ± 1	0.64
Length of stay (days)	5.7 ± 3.4	5.2 ± 2.6	0.55

Adapted from Marcello PW, Fleshman JW, Milsom JW. Hand-assisted laparoscopic vs. laparoscopic colorectal surgery: a multicenter, prospective, randomized trial. Dis Colon Rectum. 2008;51:818–28

Data are means ± standard deviations

HA hand-assisted colectomy, *LAP* straight laparoscopic colectomy

resection and Hartmann pouch in perforated diverticular disease. They describe using laparoscopic peritoneal lavage for generalized peritonitis for perforated diverticulitis in 100 patients prospectively. They converted 8 patients to a Hartmann procedure who had feculent peritonitis; the remaining 92 were followed with only a 4 % morbidity and 3 % mortality. Only two patients required additional procedures for pelvic abscesses, and two patients had recurrent diverticulitis, one at 12 months and the other at 84 months postprocedure. Additional studies have shown that this approach may be used in selected patients with purulent peritonitis from perforated diverticulitis.

Complications of Diverticular Disease

Bleeding

Bleeding is not recognized as a feature of diverticulitis. Bleeding related to diverticulosis is discussed in Chap. 24.

Perforation

- Perforation occurs in two ways. An abscess forms and then ruptures leading to purulent peritonitis. Large perforations produce fecal peritonitis.
- Mixed fecal and purulent peritonitis results from abscess rupture with ongoing communication with the bowel lumen. Clinically presentation is an 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 seen on abdominal films or CT scan. Rapid progression to diffuse abdominal pain and rigidity can be expected.

Abscess

- Small abscesses frequently resolve with antibiotic therapy. Larger abscesses may require drainage (usually CT-guided percutaneous drainage), which can convert the high risks of an urgent operation to a much safer elective operation.

Fistula

- The incidence of fistulization ranges from 5 to 33 %.
- Colovesical fistula is the most common diverticular fistula, and diverticular disease is the most common cause of colovesical fistula (Fig. 22.4a, b).
- Other diverticular fistulas include colocutaneous, colovaginal, and coloenteric.
- Most colovaginal fistula patients had a previous hysterectomy (Fig. 22.5).

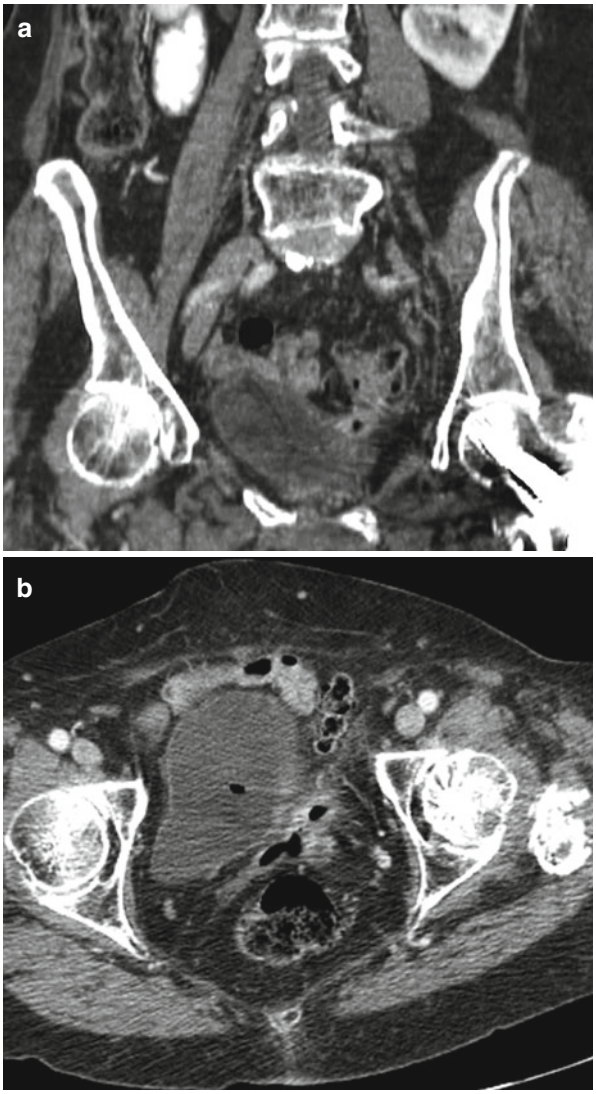

Fig. 22.4 (**a**, **b**) CT scan reveals air in the bladder consistent with a colovesical fistula

- Less common fistulas include colocolic, ureterocolic, colouterine, colosaphingeal, coloperineal, sigmoido-appendiceal, and colovenous and even fistulas to the thigh (a variant of a colocutaneous fistula).
- The diagnosis of diverticular fistula is generally clinical.
- Many fistulas will not be identifiable by imaging studies. Thus, excess efforts should not be undertaken to try to radiographically demonstrate a fistula. The primary aim of a diagnostic workup is not to see the fistula but to determine the etiology (diverticulitis, cancer, IBD, etc.) so that appropriate therapy can be initiated.

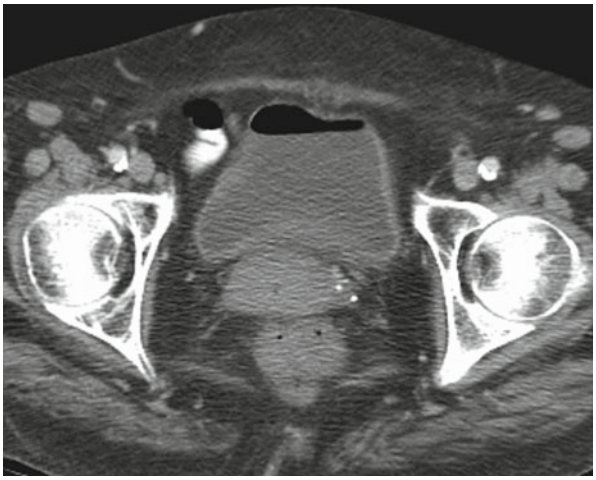

Fig. 22.5 Colovaginal fistula occurs almost exclusively in patient who has undergone prior hysterectomy

- The general principle of management is resection of the colon, usually with primary anastomosis, with varying treatment for the organ involved. For the bladder, simple drainage of the bladder for 7 days is advised.
- No treatment of the vagina is required in most circumstances.
- Cutaneous fistulas will usually require cutaneous closure by delay or secondary intention.
- Enteric fistulas require closure or resection of the involved small bowel or colon.
- Ureteral drainage for fistulas to the ureter, observation or hysterectomy for uterine fistulas, salpingo-oophorectomy for fistulas to the fallopian tubes, and appendectomy for appendiceal fistulas are the most common treatments for uncomplicated fistulas of the other named varieties.
- 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.

Stricture

- The development of a phlegmon with repeated attacks of acute disease or long-term persistent disease may result in a stricture. Although a relatively uncommon complication, patients will present with constipation, abdominal pain, and bloating.

- 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 in the evaluation in such instances, but resection may be necessary to make a diagnosis.

Obstruction

- On rare occasions complete obstruction may occur. If this is due to diverticular disease, most patients will respond to initial medical management allowing for an elective resection at a later date.
- Persistence of an obstruction may require a Hartmann procedure or primary anastomosis with proximal diversion for management.
- The successful use of colonic stents to relieve obstruction secondary to diverticulitis has been described.
- In this setting, the colonic stent is used as a bridge to surgery with later elective resection. However, the use of stents in benign disease is not an indicated use. There is a high incidence of complications leading to emergency surgery for removal of the stent and management of complications.

Ureteral Obstruction

- The ureter is infrequently involved with diverticular disease. When involved, it is most frequently the left ureter.
- Rarely, diverticular disease has been reported as fistulizing to the ureter. A stricture may occur but compression is more common. This can result from retroperitoneal fibrosis secondary to diverticular inflammation. Most commonly this resolves as the underlying diverticular disease process resolves, although occasionally ureterolysis has been advised.

Phlegmon

- A phlegmon represents an inflammatory mass without a surrounding central abscess. A phlegmon can significantly complicate the technical aspects of surgical resection. Many phlegmons will resolve with antibiotic therapy.
- If resection is planned due to recurrent episodes of disease, it is best to treat the acute phlegmon to resolution if possible, prior to resection. Occasionally, operation may become necessary in the face of an acute phlegmon.

23. Colonic Volvulus

Jan Rakinic

Introduction

- Volvulus, from the Latin *volvere*, means "to twist."
- Volvulus may occur in any part of the gastrointestinal tract where there is sufficient length of the gut to twist about a fixed point.
- Colonic volvulus occurs when a mobile portion of the colon has a mesentery with a narrow, fixed base. The colonic segment twists around this fixed point, producing a closed-loop obstruction.
- The most common sites of colonic volvulus are the sigmoid colon and cecum, which are the most mobile parts of the colon.
- Factors that place patients at elevated risk for colonic volvulus include chronic constipation, previous abdominal surgery, and megacolon.
- More than half of the patients with colonic volvulus present acutely with crampy abdominal pain, marked tympanitic abdominal distention, and absence of flatus or stool.
- Colonic volvulus is the cause of 10–15 % of colon obstruction in USA.
- Some institutionalized patients may not complain of pain; rather, a caregiver may notice an unusually long interval between bowel movements associated with significant abdominal distention.
- Pain becomes more constant when ischemia worsens due to compression of the vessels within the twisted mesentery.
- There is a group of patients who have recurring subacute episodes of volvulus, with often painless abdominal distention and tympany. These episodes resolve spontaneously with passage of copious amounts of liquid stool and gas, described as "explosive." These patients should be evaluated for colonic dysmotility and megacolon, as these findings alter the surgical therapy.

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- Total abdominal colectomy is the procedure of choice if megacolon is found, due to the high risk of recurrent volvulus if any abnormal colon is retained.
- In children, colonic volvulus is rare, with a male predominance.
- Volvulus in the pregnant patient merits special consideration.
  - While intestinal obstruction is rare in pregnancy, nearly 45 % is caused by sigmoid volvulus, and it is estimated that 10 % of patients with reports of cecal volvulus are pregnant at presentation.
  - It has been postulated that the enlarging uterus lifts the sigmoid colon and cecum out of the pelvis and that these segments become more prone to torsion about the pelvic sidewall attachments.
  - Volvulus in pregnancy carries a high mortality rate often because diagnosis is delayed.
  - Urgent intervention is often required in the setting of volvulus due to the risk to both mother and fetus.

Sigmoid Volvulus

Epidemiology/Pathogenesis

- The sigmoid colon is the most common site for colonic volvulus in USA.
- American patients with sigmoid volvulus are generally elderly, institutionalized patients on psychoactive medications with chronic constipation, and approximately 80 % are male.
- In regions where a high-fiber diet is the norm, including Africa, India, Pakistan, and the Middle East, the incidence of sigmoid volvulus is much higher than in the West, and patients are several decades younger, with persistence of male preponderance.
- The geographic variation in the incidence of sigmoid volvulus is believed to be linked to the ingestion of a high-fiber diet, which lengthens the sigmoid colon and its mesentery, fostering an anatomic predisposition to volvulize.
- The twist of the sigmoid volvulus is most commonly counterclockwise around the mesocolic axis.
  - Torsion must be at least 180° to produce clinically significant obstruction. The sigmoid colon can tolerate more intraluminal pressure than other parts of the colon, and so the bowel wall can remain viable for a few days; however, strangulation will eventually occur, first with venous occlusion and then followed by arterial occlusion, thrombosis, and necrosis. Gangrene may occur much more quickly due to a sudden, tight compression of the mesenteric vessels caused by rapid distention of the colon lumen.

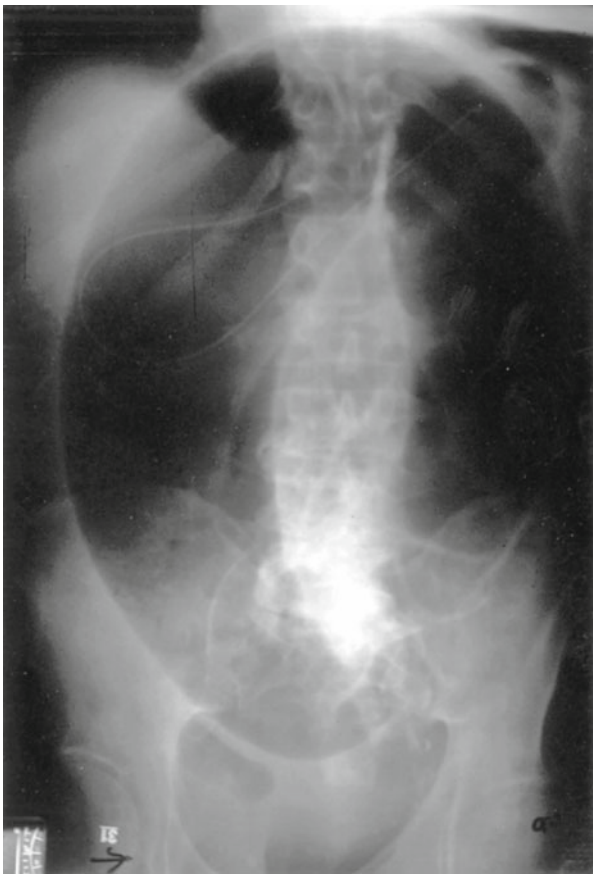

Fig. 23.1 Plain abdominal X-ray of sigmoid volvulus indicating the "bent inner-tube" sign

Diagnosis

- Exploratory laparotomy is mandatory if peritonitis is present.
- A plain abdominal film often confirms the clinical diagnosis, displaying the "bent inner-tube" or "omega loop" appearance of a massively distended bowel loop, with both ends closely adjacent in the pelvis (Fig. 23.1).
- In up to 40 % of cases, the plain film can be equivocal: there may be superimposition of a distended transverse colon or small bowel, the sigmoid loop may be transversely oriented, or a massively dilated small bowel may mimic a sigmoid loop.
- In these situations, a contrast enema or CT scan may clarify the diagnosis.
- If a contrast enema is desired, it should be done with water-soluble contrast material, as the mortality with barium is very high if a perforation is

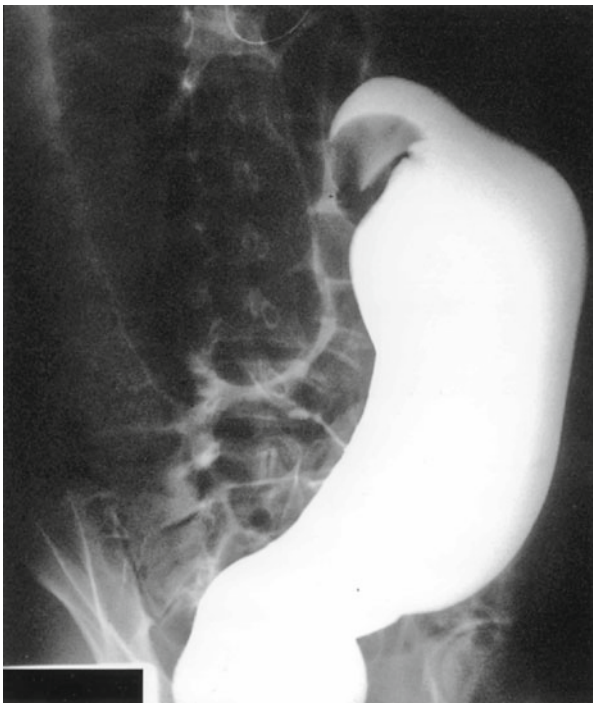

Fig. 23.2 Barium enema study of a sigmoid volvulus indicating the bird's beak deformity and complete obstruction to retrograde flow of contrast

encountered. A water-soluble contrast enema classically shows the contrast column ending sharply in a "bird's beak" shape at the site of torsion (Fig. 23.2).

- The major differential diagnoses that must be considered are obstruction due to colonic neoplasm and colonic ileus or Ogilvie's syndrome, both of which can present in a similar way.
  - In the case of neoplasm, there may be a wisp of contrast through the lesion; if the obstruction is complete, the appearance is distinctly different from the classic "bird's beak" appearance. In Ogilvie's syndrome, the water-soluble contrast enema will show that there is no obstruction and may also be therapeutic.
- Abdominal CT scan can be quite helpful in the identification of colonic volvulus. Much information has been written on the "whirl sign" indicating twisted mesentery and intestinal volvulus, although most reports refer to small bowel volvulus. More recent reports have noted that the "whirl sign" can be observed in settings other than intestinal volvulus and so may not be pathognomonic for intestinal volvulus.
- In the pregnant patient, the diagnosis of sigmoid volvulus is usually made clinically, with subsequent endoscopic confirmation, or intraoperatively due to patient deterioration. The size of the uterus presents a challenge for

operating in the pelvis; this makes simple detorsion or sigmoidopexy appear more attractive when the sigmoid colon is viable but exposes the patient to a high risk of recurrence and need for another, definitive operative procedure.

Treatment and Outcome

- The first volvulus-specific maneuver in the stable patient with a sigmoid volvulus is attempted endoscopic detorsion.
- Successful detorsion converts a surgical emergency into an elective situation.
- If the patient is febrile or has localized tenderness over the distended loop, nonviable colon should be strongly suspected, and attempted detorsion should be abandoned. Attempted detorsion of nonviable bowel risks perforation and peritonitis, with the attendant complications thereof.
- While detorsion was historically done with the rigid proctoscope, the flexible sigmoidoscope or colonoscope has replaced it as the instrument of choice.
- When decompression is successful, as it is in 60–80 % of attempts, there is evacuation of significant flatus and stool with visible lessening of abdominal distention.
- A decompressing tube may be placed into the detorsed loop to allow continued decompression and to prevent retorsion.
- A plain abdominal film should then be obtained to confirm relief of volvulus and absence of intraperitoneal free air.
- The high rate of revolvulus after detorsion alone, coupled with a mortality rate over 20 % for emergent surgery compared to 6 % or less with elective resection, has prompted most surgeons to proceed with elective sigmoid resection during the same hospitalization for most patients.
- Complete colonoscopy should be performed prior to operation to rule out synchronous lesions that would alter management.
- The standard elective surgical procedure is sigmoid resection with primary anastomosis, which may be accomplished with open technique or laparoscopic technique if the colon is sufficiently decompressed.
- Patients successfully endoscopically decompressed prior to definitive resection have an incidence of recurrent volvulus close to zero.
- However, in the setting of megacolon, total abdominal colectomy is the recommended procedure; otherwise, the patient is at very high risk of recurrent volvulus.
- A number of nonresectional techniques have also been described for the treatment of sigmoid volvulus. These include surgical detorsion without resection or fixation or detorsion with methods of either sigmoid or mesenteric fixation.
- The described techniques of sigmoid fixation include extraperitoneal sigmoidopexy, nonsurgical endoscopic sigmoidopexy with or without tube

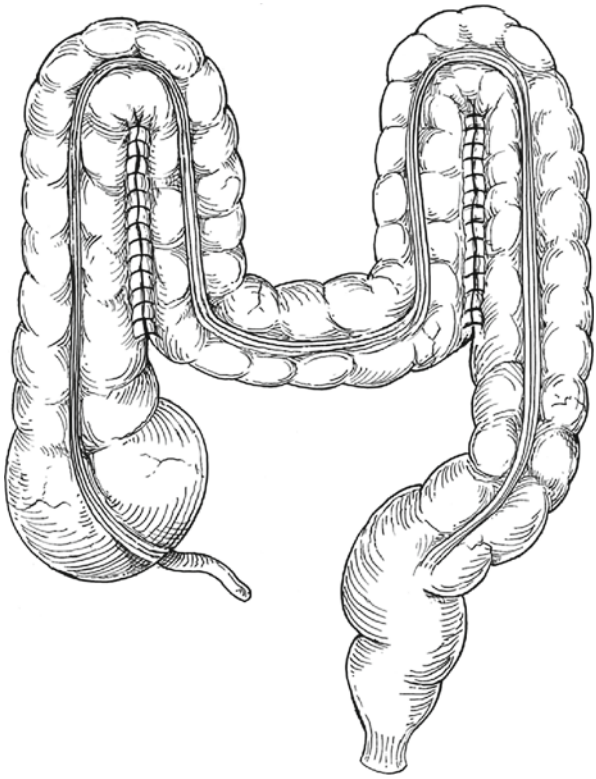

Fig. 23.3 Parallel colopexy as described by Mortensen

fixation, parallel colopexy to the transverse colon (Fig. 23.3), laparoscopic fixation, fixation of the sigmoid colon to the abdominal wall with bands of prosthetic with or without percutaneous colon deflation, and percutaneous endoscopic colostomy.

- Mesenteric fixation techniques include mesosigmoplasty and mesenteric fixation (Fig. 23.4a, b).
- All nonresectional techniques are associated with high morbidity and/or high recurrence rate.
- It is important to understand that the search for alternatives to resection for sigmoid volvulus was based on *historical* rates of morbidity and mortality.
- Considering that modern surgical and anesthetic techniques have significantly reduced surgical complication rates, it seems clear that resection after decompression provides near-zero risk of recurrence with acceptable morbidity and mortality rates.
- If endoscopic decompression is unsuccessful or visualizes gangrenous mucosa, the situation is a surgical emergency, and efforts at detorsion should be halted and preparation of the patient for surgery should be expeditiously done.

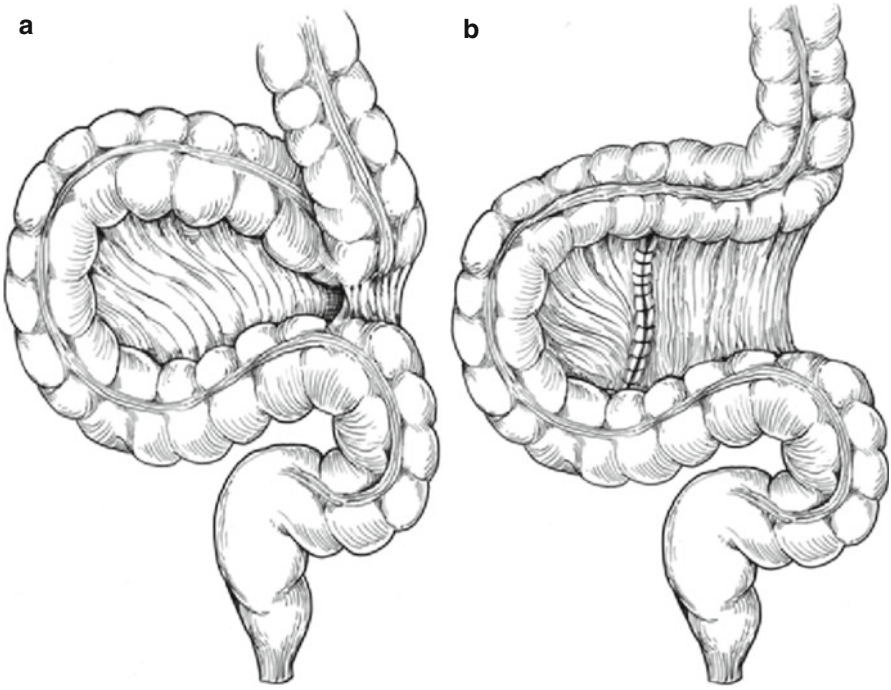

Fig. 23.4 Mesosigmoidoplasty. (**a**) A longitudinal peritoneal incision made in the elongated, narrow mesentery. (**b**) The incision is then closed transversely, broadening the mesenteric base and shortening the height of the sigmoid loop

- Exploration should be done via a midline laparotomy incision or potentially by laparoscopy if the patient is hemodynamically stable. If the bowel appears viable or possibly viable, the twist should be reduced.
- The decision for anastomosis versus Hartmann's procedure should be based on standard surgical criteria: the presence of good blood supply, absence of (or minimal) peritoneal soilage, reasonable nutritional status, and absence of shock would suggest that anastomosis is reasonable.
- When considering stoma formation, it should be remembered that many of the stomas formed in this setting will be permanent, as infirm patients with other medical comorbidities will rarely become candidates for stoma closure. The usual maneuvers used for selecting stoma location are often difficult to employ preoperatively, given the abdominal contour and urgency of the patient's situation. The bowel is often quite dilated, and a large opening in the abdominal wall may be required for a colostomy. This leads to a higher incidence of parastomal hernia.

- Both morbidity and mortality are higher for emergent operations for sigmoid volvulus, compared to those for the elective or semi-elective setting. Deaths and complications increase further if gangrenous colon is encountered. Good outcomes can be achieved with primary anastomosis at the time of emergent sigmoidectomy for sigmoid volvulus with careful patient selection.
- Caring for the pregnant patient with sigmoid volvulus presents the challenge of managing two patients at once:
  - An argument can be made for endoscopic detorsion in the first trimester if mucosa is viable, with an attempt to delay definitive management until the second trimester, when the risk to the fetus is less.
  - In the case of sigmoid volvulus in the third trimester, nonoperative therapy should be pursued when possible until fetal maturity; then delivery and definitive volvulus management can be undertaken.
  - An ischemic sigmoid colon is managed with Hartmann's procedure.

Ileosigmoid Knotting

Epidemiology/Pathogenesis

- Ileosigmoid knotting, also called "compound volvulus" or "double volvulus," although these are now considered misnomers, is unusual in the West.
- It is more common in certain areas of Africa, Asia, and the Middle East, although still quite rare.
- Patients with ileosigmoid knotting are younger than those with sigmoid volvulus, and the condition is more common in males.
- In this condition, loops of the ileum and sigmoid colon wrap about one another, causing a double obstruction of both the ileum and the sigmoid.
- Four patterns of ileosigmoid knot formation have been described, which differentiate between an active or passive segment of the bowel and the direction of rotation (Fig. 23.5a–d). The ileum is most commonly the active component and wraps around the sigmoid. Less commonly, the sigmoid wraps around the ileum. In either instance, the direction of the wrap may be clockwise or counterclockwise.
- Endoscopic reduction attempts are always unsuccessful, and the diagnosis of ileosigmoid knot should be considered when endoscopic reduction has failed.

Diagnosis

- Presentation is acute, with distention, nausea and vomiting, and severe abdominal pain which may be colicky in nature.
- In contrast to other forms of volvulus, there is an absence of previous similar episodes.

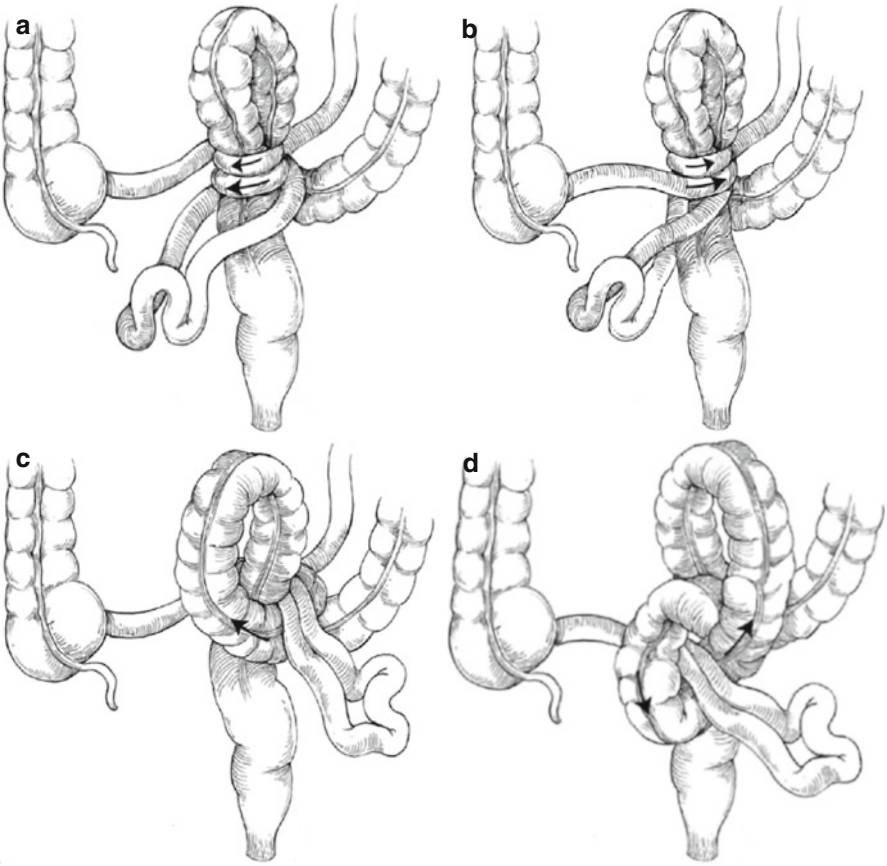

Fig. 23.5 Ileosigmoid knotting: these schematic illustrations indicate the four terms of knotting. The active ileum may rotate around the sigmoid colon in either a clockwise (**a**) or a counterclockwise (**b**) direction. Much more frequently, the sigmoid colon may act as the active loop and rotate in either a clockwise (**c**) or a counterclockwise (**d**) direction around the ileum

- Patients often present in shock with signs of an intra-abdominal catastrophe, including acidosis, hypotension, and tachycardia.
- Preoperative diagnosis is difficult due to the rarity and complexity of the problem. Characteristic radiographic features have been described, consisting of a double obstruction with a distended obstructed sigmoid loop pulled toward the right and a proximal small bowel obstruction on the left. In practice, X-rays are often atypical and difficult to interpret.

Treatment and Outcome

- Patients who present in this manner should be urgently resuscitated and taken for exploration.

- Treatment recommendations range from simple double detorsion to double resection. Advocates of en bloc resection without detorsion reason that attempts to untie the knot are time consuming and difficult, may contribute to systemic release of endotoxin with worsening of shock, and increase the risk of bowel perforation and peritoneal contamination.
- However, others have recommended detorsion if one or both segments are felt to be viable.
- Deflation of the involved segments has been shown to assist in detorsion and diminish the risk of perforation.
- The data on recurrence after detorsion alone are conflicting. Some authors advocate sigmoid resection in all cases, even if the sigmoid is viable, to eliminate the risk of recurrent knot or simple sigmoid volvulus in the future.
- Primary small bowel or ileocolic anastomosis is performed in nearly all patients with a gangrenous ileum.
- Historically, Hartmann's procedure has been the most commonly performed operation when a nonviable sigmoid colon is found, although more surgeons are now performing primary colonic anastomoses in this setting.
- Overall surgical mortality ranges from 30 to 50 %. However, when the colon is not gangrenous, the mortality is lower, approximately10–30 %.

Cecal Volvulus

Epidemiology/Pathogenesis

- Cecal volvulus is the second most common site of colonic volvulus and technically consists of volvulus of the terminal ileum, cecum, and proximal right colon.
- Two variants exist: a true axial rotation of the terminal ileum, cecum, and proximal right colon around its mesentery (Fig. 23.6a) and cecal bascule, which is an anterosuperior folding of a mobile cecum over the proximal right colon without axial rotation (Fig. 23.6b).
- The rotation of a cecal volvulus is most commonly clockwise around the mesenteric axis.
- Cecal bascule accounts for approximately 10 % of cases of cecal volvulus and is less likely to present with vascular compromise.
- Individuals with cecal volvulus are several decades younger than patients with sigmoid volvulus, with a female to male ratio of 1.4:1.
- Mobility of the cecum is required, but that feature alone is not sufficient to cause a clinically apparent volvulus: a cadaver study revealed an 11 % incidence of freely mobile right colons and a 26 % incidence of cecal mobility sufficient to allow anterior folding.
- Previous abdominal surgery is felt to be a major risk factor for cecal volvulus: in published reports of cecal volvulus, 30–70 % of patients had a history of abdominal surgery.

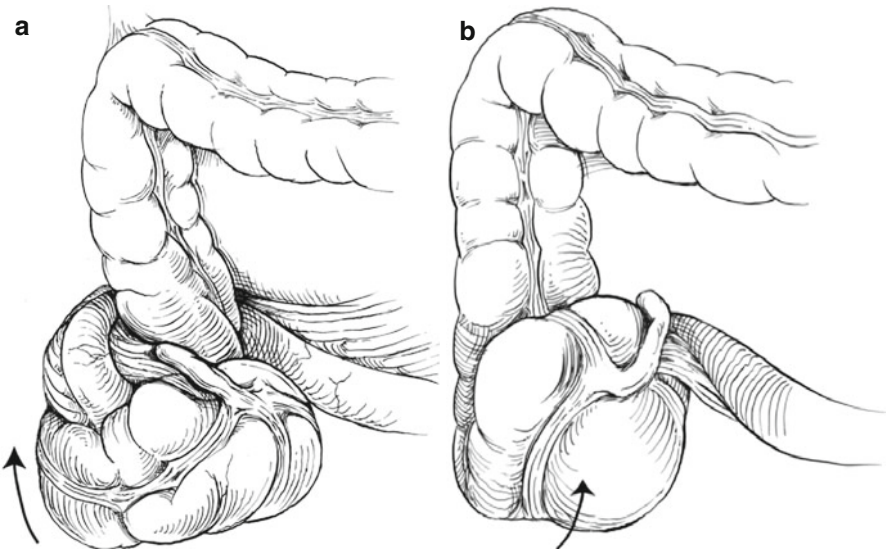

Fig. 23.6 (**a**) Schematic illustration of a cecal volvulus. (**b**) Schematic illustration of a cecal bascule

- Other risk factors include chronic constipation, obstructing colon lesions, and malrotation.
- Upward displacement of the cecum by an enlarged uterus or other pelvic mass may also promote cecal volvulus.
- Several series have reported that 10 % of patients with cecal volvulus are pregnant at presentation.

Diagnosis

- As with sigmoid volvulus, presentation may be that of an acute obstruction or one of an intermittent, recurrent pattern.
- Abdominal distention is generally less marked than that with volvulus of more distal colonic segments.
- The acute presentation is of a closed-loop obstruction with vascular compromise.
- Abdominal pain, distention, obstipation, nausea, and vomiting are common signs. If intervention is not timely, ischemia may progress to gangrene.
- Diagnosis is most often made on the basis of clinical presentation and plain films. Plain abdominal radiographs may identify the classic "coffee bean" deformity directed toward the left upper quadrant (Fig. 23.7).
- While nearly half of the plain films suggest the diagnosis; fewer than 20 % are clearly diagnostic.

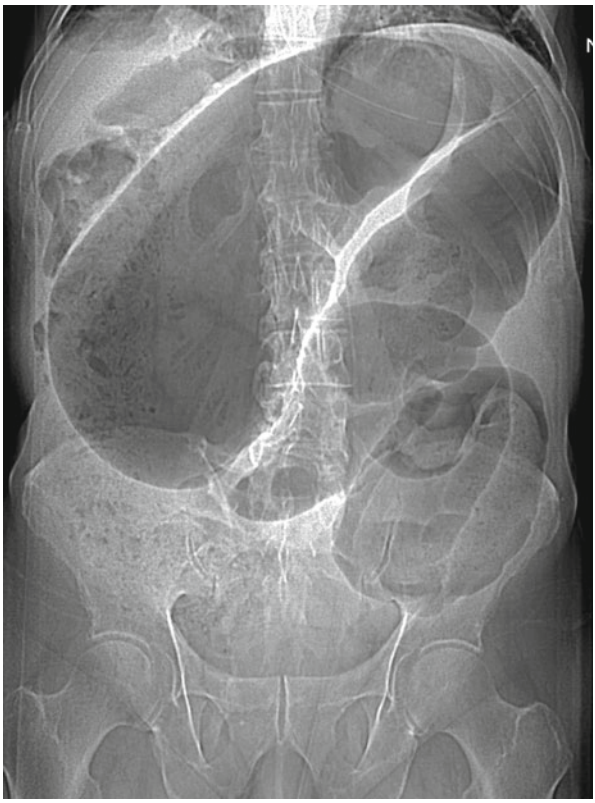

Fig. 23.7 Plain abdominal X-ray of a cecal volvulus with "coffee bean" deformity evident in the *left upper quadrant*

- Contrast enema increases the preoperative diagnostic rate, showing a "bird's beak"-type cutoff in the right colon (Fig. 23.8), and may be employed in stable patients when the diagnosis is in question.
- CT scan has become much more common in the setting of nonspecific abdominal pain and distention (Fig. 23.9).
- CT scan findings in cecal volvulus include the location of the cecum within the abdomen, the "bird's beak" cutoff, and the "whirl sign" of mesenteric torsion. However, about half of the patients with cecal volvulus have the diagnosis made in the operating room.
- Diagnosis of cecal volvulus in the pregnant patient is most often made in the operating room after clinical deterioration. Radiologic studies normally performed in the evaluation of most patients with abdominal pain are often deferred. A case can be made for judicious use of radiologic evaluation of the pregnant abdomen when trying to diagnose the cause of abdominal pain and vomiting in the pregnant patient. Diagnostic laparoscopy is also a viable alternative when the pregnant patient has an acute abdomen.

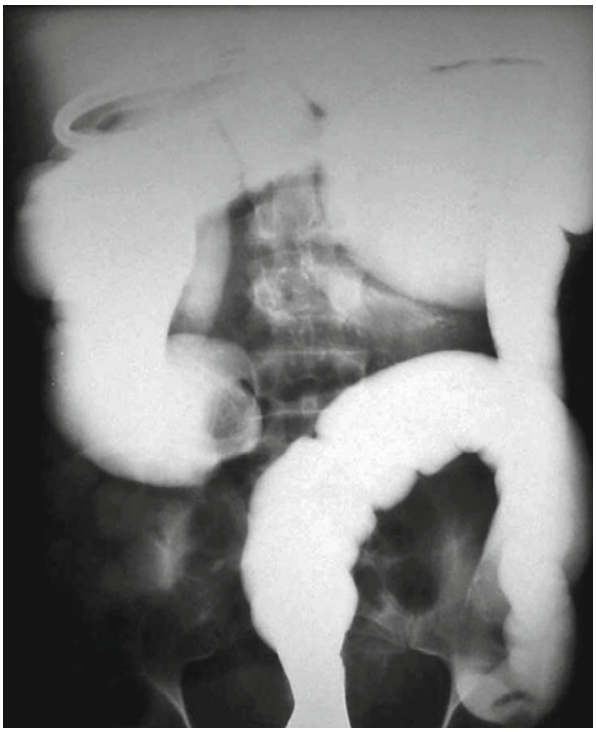

Fig. 23.8 Barium enema study of a cecal volvulus revealing a bird's beak deformity

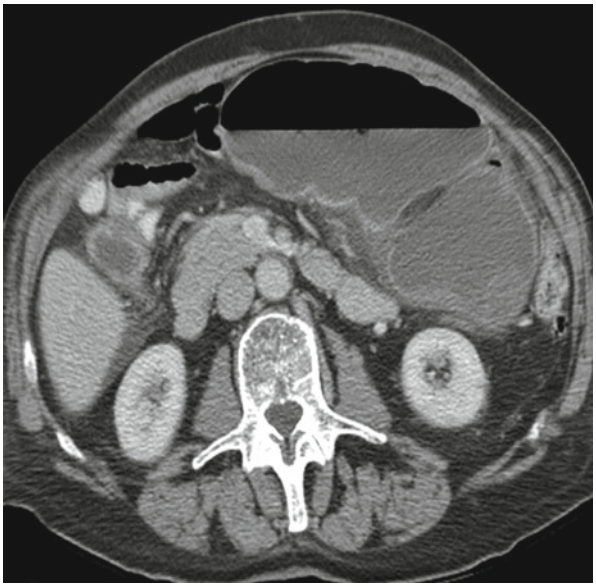

Fig. 23.9 Typical CT findings in cecal volvulus include bird's beak cutoff and location of the cecum on the left side

Treatment and Outcome

- While less efficacious than endoscopic detorsion of more distal colonic volvulus, colonoscopic reduction of cecal volvulus has been reported with some success.
- Reasons cited for limited use of this approach include difficulty in traversing the unprepared bowel to reach the right colon, difficulty in performing the detorsion, lack of clear diagnosis, and a higher rate of ischemia in cecal volvulus.
- Some authors feel that this approach simply delays definitive surgical management and places the patient at higher risk for perforation.
- Proponents feel that when successfully employed, there may be a relatively low rate of recurrence and the subsequent need for surgery may be debatable.
- Cecal gangrene mandates resection, and in most cases primary anastomosis can be safely done. In the circumstance of a malnourished and/or anemic patient or in the presence of other factors that may adversely affect healing, ileostomy with or without mucus fistula may be appropriate.
- If the cecum is viable, detorsion with or without fixation may be considered. Detorsion alone carries a recurrence rate as high as 25 %.
  - Fixation is generally performed by cecopexy and/or cecostomy tube placement (Fig. 23.10). Cecopexy is done by raising a flap of peritoneum along the length of the right colon and suturing it to the serosa of the anterior right colon, effectively placing the right colon in a partially retroperitoneal position, eliminating the abnormal mobility.
  - Tube cecostomy both anchors the cecum and provides a vent for the distended colon. Proponents of cecostomy find it easy to perform and note that spontaneous closure of the cecocutaneous fistula is common after tube removal. However, the rate of recurrent cecal volvulus after cecostomy is significant, and management of the tube and its complications can be troublesome.

Transverse Colon and Splenic Flexure Volvulus

Epidemiology/Pathogenesis

- Volvulus of these colonic segments is exceptionally rare.
- Transverse colon volvulus is estimated to account for 1–4 % of all colonic volvulus, and splenic flexure volvulus for approximately 1–2 %.
- Patients with these disorders are younger than patients with cecal or sigmoid volvulus, with a two- to threefold female predominance.

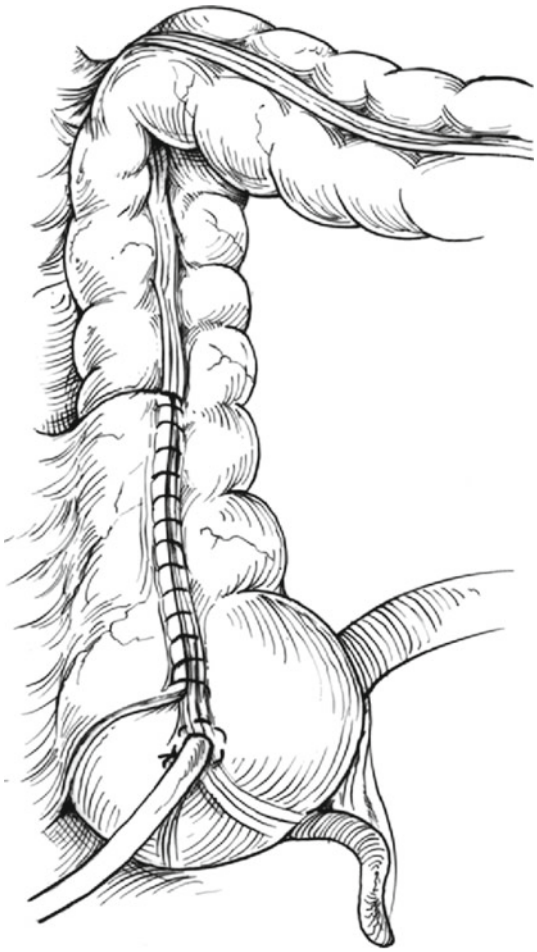

Fig. 23.10 Cecopexy and cecostomy for cecal volvulus

- Common historical points in patients with transverse colon volvulus include chronic constipation, previous abdominal surgery, institutionalization, high-fiber diet, and recurrent distal obstruction.
- In patients with splenic flexure volvulus, previous abdominal surgery is common, and chronic constipation is also felt to increase risk, possibly by leading to redundancy and elongation of the colon.
- Clinical presentation of volvulus of the transverse colon or splenic flexure is that of a large bowel obstruction. As with sigmoid and cecal volvulus, presentation may be acute and fulminating or may be a subacute recurring process, as is seen in up to 50 % of patients.

Diagnosis

- Plain films are rarely diagnostic and may reveal a distended proximal colon with a decompressed distal colon and two air-fluid levels, representing the right colon or right transverse colon and the left transverse colon.
- More often, the films may be misinterpreted as a sigmoid volvulus due to the variable position of the transverse colon.
- Patients may then undergo colonoscopy with no clear transition point seen in the sigmoid colon. In this situation, further attempts to identify a transition point should be terminated, and a contrast study should be obtained.
- Contrast enema will show a bird's beak deformity at the site of the twist. However, definitive management of an acutely ill patient should not be unduly delayed to obtain these studies.

Treatment and Outcome

- Successful endoscopic decompression has been reported with both transverse colon and splenic flexure volvulus. However, as with cecal volvulus, there are the same concerns of difficulty in traversing an unprepared bowel, difficulty in performing detorsion, and the possibility that the diagnosis may not be clarified. There is a risk of excessive insufflation causing cecal distention and vascular compromise. Also, based on the outcomes of endoscopic detorsion elsewhere in the colon, it may be assumed that a high risk of post-decompression recurrence remains.
- Operative procedures include resection, and detorsion with or without colopexy. Resection is mandatory if gangrenous bowel is found.
- Most authors recommend either transverse colectomy or extended right colectomy as definitive treatment for transverse colon volvulus, as this resection eliminates virtually all risk of recurrence.
- The affected colon in splenic flexure volvulus is more likely to be redundant and dilated than in transverse colon volvulus.
  - For this reason, patients with splenic flexure volvulus may be best served with an extended resection and ileosigmoid or ileorectal anastomosis.
- Stomas should be reserved for cases in which perforation and peritoneal contamination are encountered or for other high-risk cases.

24. Lower Gastrointestinal Hemorrhage

Craig A. Reickert and Melissa Times

- Lower gastrointestinal bleeding (LGIB) is defined as measurable bleeding from a source distal to the ligament of Treitz.
- LGIB is a broad term used to encompass the spectrum of symptoms ranging from minimal bleeding noticed on bathroom tissues associated with hemorrhoids to massive bleeding encountered with diverticular hemorrhage.
- Etiologies range from the rare small-bowel tumors to the frequently identified diverticular sources.
- The bleeding may be intermittent, leading to a challenging diagnostic and management dilemma.

Epidemiology

- A population-based study examining the inpatient hospital records of 2,115 patients from 1990–1993 in a California health maintenance organization found the annual incidence rate of LGIB was 22.5 per 100,000 (0.02 % of hospitalizations).
- The three most common etiologies were diverticulosis (41.6 %), colorectal malignancy (9.1 %), and ischemic colitis (8.7 %).

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Etiology

Diverticular Disease

- Diverticular bleeding as a source of LGIB occurs in 20–60 % of cases.
- In 75 % of patients, the bleeding will cease spontaneously.
- Rebleeding rates after the first episode are 25 % and increase to 50 % after two episodes.
- Diverticular bleeding relates to the development of pseudo-diverticula in areas of weakness in the colonic wall where the vasa recta, the intramural branches of the marginal artery, course through the muscular layers to the mucosa and submucosa.
- At the site of the diverticulum, the vasa recta travel in the serosa with no significant tissue between the mucosa, the vasa recta, and the lumen of the bowel.
- Asymmetric and eccentric rupture of the vasa recta leads to intraluminal, and not peritoneal hemorrhage.
- Anecdotally, bleeding diverticula are attributed to mostly right-sided disease despite the greater propensity to have left-sided diverticula.

Anorectal

- Anorectal sources commonly include hemorrhoids, anal fissures, and rectal ulcers. They are the etiology of LGIB in 11–17 % of patients.
- Bleeding from hemorrhoids or fissures is uncommonly associated with hemodynamic instability or large volumes of blood loss.
- Rectal ulcers can cause severe hemorrhage associated with hemodynamic instability, with almost half of them being identified by stigmata of recent hemorrhage, although the etiology of the ulcers is multiple and not frequently defined in the literature in bleeding patients.
- Careful historical elucidation of radiation treatment, sexually transmitted diseases (STDs), anorectal trauma, nonsteroidal anti-inflammatory drug (NSAID) exposure, liver disease associated with rectal varices, and other uncommon etiologies must be included in evaluations.
- Hemorrhoidal bleeding is generally limited to bleeding with bowel movements, although patients may describe spraying or splattering of blood in the bowel (see Chap. 11).

Angiodysplasia

- Angiodysplasias are vascular ectasias that can occur in the small- and large-bowel mucosa and submucosa.
- Small-bowel angiodysplasia is a common source of obscure gastrointestinal bleeding with up to a third of patients having this diagnosis.
- Colonic angiodysplasia has a prevalence of 1 % in the general population with a tendency for right-sided lesions.

- Angiodysplasia had been thought to be associated with aortic valvular disease and renal failure, but these associations have not been found in more statistically rigorous studies.

Malignancy

- Colorectal cancers are a source of LGIB in 9.1–13.6 % of patients and are associated with ulcerated tumors.
- As a symptom, rectal bleeding is seen in 6.5–17 % of patients diagnosed with rectal cancer.

Ischemic Colitis

- Ischemic colitis as an etiology of LGIB occurs in 9–18 % of patients.
- Patient present with abdominal pain (87 %) and bloody bowel movements (84 %) without diffuse peritonitis.
- There are multiple etiologies of ischemic colitis that affect both young and old patients: shock, autoimmune diseases, coagulopathies, long-distance running (with associated dehydration), mesenteric venous thrombosis, acute arterial thrombosis, emboli, small-vessel disease, and cocaine use.
- Despite the multitude of etiologies, the typical patient with colonic ischemia is either an elderly patient or a patient with multiple comorbidities such as cardiovascular disease, hypertension, and renal failure.
- Hospitalized patients with increased risk for ischemic colitis are patients undergoing open and endovascular abdominal aortic aneurysm repair for nonruptured aneurysms. These patients have an incidence of ischemic colitis of 2–3 % in open procedures and 1.3–2.9 % in endovascular interventions.
- The location of ischemic colitis is variable: right-sided, 8–14 %, splenic flexure 23–28 %, and left-sided, 50–87 %.
- Knowledge of the arterial blood supply and areas of collateral circulation is necessary to understand the potential areas for insult and the high likelihood of anatomic variations. Colonic blood supply is dependent on interconnection of the perfusing vessels by the marginal artery of Drummond, which connects the superior and inferior mesenteric arteries through a series of arcades.
- At the splenic flexure, there is an area without vasa recta in 11 % of individuals, which makes the area more susceptible to ischemic insult.
- The arc of Riolan is an artery connecting the left branch of the middle colic artery to the inferior mesenteric artery. It is present in only 7 % of individuals but can allow acceptable perfusion in the absence of other collaterals. The highly variable arterial anatomy of the colon makes it susceptible to ischemia as a complication of surgical and angiographic procedures used to treat LGIB, which can compound the management considerations.
- Acute mesenteric ischemia (small-bowel ischemia) can be either occlusive or nonocclusive.

Other Colonic Etiologies

- Postpolypectomy bleeding after colonoscopy ranges from 0.08 to 0.87 % with mortality in a large Canadian study of over 97,000 colonoscopies estimated at 1/14,000.
- Bleeding from a colorectal anastomosis requiring endoscopic therapy or surgery is rare with a rate of 0.5–1.8 %.
- If bleeding persists after resuscitation, transfusion, and correction of any coagulopathy, endoscopy should be used to identify and stop the bleeding. Therapeutic interventions include cautery, endoclips, and epinephrine injection. If these measures fail, surgical management should be undertaken.
- Gastrointestinal bleeding is a common presenting symptom in ulcerative colitis and Crohn's disease. However, acute hemorrhage with hemodynamic compromise is atypical.
- Patients with human immunodeficiency virus (HIV)/acquired immune deficiency syndrome (AIDS) have additional etiologies for LGIB.
- The most common etiologies are cytomegalovirus (CMV) colitis, idiopathic colonic ulcers, lymphoma, and idiopathic colitis.
- Recurrent bleeding occurred in 17.6–22 % of patients with mortality rates as high as 54.5 %.
- Overall, the 30-day mortality rate was three times higher (14.4 % versus 5 %) for patients with HIV and LGIB than for the routine population.
- Documented adverse effects of NSAIDs on the lower gastrointestinal tract include increased gut permeability (44–70 %), gut inflammation (60–70 %), malabsorption (40–70 %), and blood loss and anemia (30 %). A systematic review of 47 studies examining the use of NSAIDs and lower gastrointestinal (LGI) events found an increase in LGI events with NSAID use. However, the studies included in the review were varied; some were not originally designed to address the proposed hypothesis of the systematic review, and the studies of LGIB and NSAID use were either case controlled or unable to demonstrate a relationship due to the small sample size. NSAID use is common, and physicians should be cognizant of the potential harmful effects of their use on the lower gastrointestinal tract.
- Rectal injury due to pelvic radiation usually presents as bleeding and occurs in 95 % of patients within 1 year from treatment:
  - In most patients, bleeding will resolve, but in the minority of patients who go on to develop chronic radiation proctitis (5 %), management is problematic and repetitive.
  - Thermal coagulation with argon or Nd:Yag laser has been used with positive results.
  - Topical formalin in 3, 4, and 10 % solutions has also been successful for cessation of bleeding. Three or 4 % formalin is instilled in 50-ml aliquots for a total of 500 ml. Due to the associated rectal discomfort, this method is usually employed with some type of

analgesia. After each application, the rectum is irrigated with normal saline. Another option ("Dab" method) is to use 16-Fr cotton-tipped applicator that is soaked in 10 % formalin. This is applied to the rectal mucosa through an anoscope or a proctoscope. The Dab method can be performed in the office without analgesia.
  - Success rates in both procedures range between 75 and 90 %.
- Surgical management is used as a last resort with high morbidity (65–80 %) and mortality rates (6.7–13 %). Surgical options include diverting stoma and limited resections.

Obscure Gastrointestinal Bleeding

- Obscure gastrointestinal bleeding (OGIB) is the bleeding not identified during colonoscopy or esophagogastroduodenoscopy (EGD).
- OGIB accounts for 1.19–9 % of LGIB with lower rates noted in larger studies.
- Angiodysplasia, small-bowel tumors, and ulcers/erosions are the three most common etiologies of OGIB.
- When diagnosing the source, patients with OGIB undergo more procedures than patients with upper gastrointestinal and colonic bleeding, 5.3 versus 1.5 and 2.1, respectively (Table 24.1).
- The diagnosis of OGIB was limited to upper and lower endoscopy and conventional radiography until 2001, when capsule endoscopy and double balloon enteroscopy (DBE) were introduced.
- Prior to these two technical advances, intraoperative enteroscopy was used to identify bleeding in the small bowel.
- Indications for capsule endoscopy include OGIB, unexplained iron-deficiency anemia, and suspected Crohn's disease, small-bowel tumors, or refractory malabsorptive syndromes. Contraindications are related to the structure and transmission signal of the capsule as well as the need for normal peristalsis for capsule efficacy.

Table 24.1 Diagnosis by etiology for patients admitted to an urban emergency medical center, 1998–2006

Etiology	*N* (%)
Diverticulosis	227 (37.34)
Hemorrhoids	128 (21.05)
Neoplasia	72 (11.84)
Colitis	65 (10.69)
Inflammatory bowel disease	33 (5.43)
Vascular ectasias	14 (2.30)
Other colonic disease	40 (6.58)
Small-intestine disease	8 (1.32)
Unknown	21 (3.45)
Total	608 (100)

- Therefore, patients with swallowing disorders, pacemakers or implanted devices, obstruction, fistula, or stricture are not candidates for capsule endoscopy. Entrapment of the capsule occurs in 3.3 % of procedures and is associated with Crohn's disease, radiation, and NSAID-induced strictures. Indications for DBE include a positive capsule endoscopy and a high suspicion of a small-bowel source in the setting of a normal capsule study.
- DBE has the ability to perform therapies such as sclerotherapy, polypectomy, dilations, and clippings. DBE can be performed from anterograde (oral) or retrograde (rectal) approach. Patients undergoing the anterograde approach require a 6–8-h fast prior to the procedure, while those having a retrograde exam need a bowel preparation.
- The diagnostic yield of capsule endoscopy and DBE is 38–83 % and 58 %, respectively. Two meta-analyses comparing capsule endoscopy and DBE found similar diagnostic yields.

Clinical Presentation, Physical Exam, and Management

- LGIB has many presentations reflecting the diverse pathology found in the upper and lower gastrointestinal tract.
- Evaluation of a patient's hemodynamic stability upon presentation is imperative.
  - Tachycardia and hypotension represent acute hemorrhagic shock associated with a blood loss of more than 500 ml or 15 % of the total blood volume. These patients require two large-bore IVs or central venous access for resuscitation if peripheral access cannot be obtained. Continuous monitoring of vitals and urine output with a urinary bladder catheter is standard. Nasogastric tube (NG) placement has been recommended routinely to rule out an upper gastrointestinal source of bleeding. NG placement is a fast and inexpensive diagnostic test that, if positive (clots, coffee-ground emesis, blood), can quickly direct the workup toward identification of an upper gastrointestinal source. Upper gastrointestinal sources are seen in 11 % of patients who present with an LGIB. The NG tube can be left in and used for the bowel preparation if an urgent colonoscopy is needed.
    - After intravenous access has been obtained, resuscitation should start immediately. However, there are no systematic reviews, and only one randomized controlled trial evaluating the role of transfusions in gastrointestinal bleeding is available.
    - A Cochrane systematic review evaluating the resuscitation of trauma, burn, and surgical patients with either crystalloid or colloids found no survival benefit using colloids instead of crystalloids.
    - Despite the lack of large, randomized trials evaluating transfusion requirements in patients with LGIB, there is mounting evidence that limiting or eliminating transfusions leads to

improved outcomes such as decreased mortality and morbidity.

- The patient's history should be taken simultaneously with the placement of intravenous access and monitors if the patient is hemodynamically unstable. Important aspects of the history that should be elucidated are given as follows: frequency, volume, color, and duration of bloody stools; comorbid conditions such as liver and cardiovascular disease; medication use such as clopidogrel, warfarin, and NSAIDs; and date of last colonoscopy/EGD.
- Visual inspection of the perineum for prolapsed or thrombosed hemorrhoids, anal fissures, or masses are the first part of the anorectal exam.
- After visual inspection, digital rectal exam and anoscopy are performed. It is imperative to assess the anus, anal canal, and distal rectum prior to further diagnostic tests. Anoscopy can be performed efficiently at the bedside, and if a source is found, such as internal hemorrhoids, therapy can be provided.
- Laboratory studies should include a chemistry panel, complete blood count, coagulation profile, and a type and cross. Any identified coagulopathies must be corrected with appropriate factors or products. Patients with cardiovascular disease should undergo an electrocardiogram, and if it turns out to be abnormal, cardiac enzymes are obtained.
- After the initial clinical evaluation and review of laboratory values, the volume of hemorrhage can be classified into one of the following three groups: (1) minor and self-limited, (2) major and self-limited, and (3) major and ongoing.
- Patients with minor and self-limited lower gastrointestinal bleeding with no or minimal change in hematocrit are unlikely to be hemodynamically unstable. These patients can undergo a colonoscopy during their admission or as an outpatient.
- Patients with massive, ongoing bleeding who remain hemodynamically unstable after initial resuscitation need urgent diagnosis and treatment either with angiography or with surgery.
- Patients in the middle of the spectrum with major bleeding who are stable or their bleeding has ceased are the patients at the core of the diagnostic dilemma surrounding LGIB.
- The most common diagnostic tests that can be employed for identifying the etiology of an LGIB are colonoscopy, angiography, CT angiography, and nuclear scintigraphy.

Colonoscopy

- Colonoscopy can be both diagnostic and therapeutic.
- The likelihood of identifying the source of bleeding with colonoscopy ranges from 45 to 95 % with the majority of studies with greater than 100 patients showing diagnostic yield rates of 89–97 %.
- The timing of colonoscopy is debatable. Urgent colonoscopy has been performed within 24 h, within 12 h, and after a fast oral purge, making comparison between studies challenging.
- In some studies, early colonoscopy has been associated with decreased length of stay.
- All studies evaluating urgent colonoscopy except one had patients undergo a bowel preparation, which would improve visualization and decrease the difficulty of the procedure and any endoscopic therapy. Endoscopic interventions were performed in 10–15 % of patients who underwent an urgent colonoscopy. Interventions include heater probes, argon plasma coagulation, bipolar coagulation, topical and intramucosal epinephrine, and endoclips (Fig. 24.1).
- Overall complication rate of colonoscopy in LGIB is 1.3 %.
- Patients with major, self-limited hemorrhage who have been resuscitated should undergo a bowel preparation with a polyethylene glycol solution and colonoscopy within 24 h.
- The goal of colonoscopy is to identify a source of bleeding and, if possible, treat it endoscopically. If a bleeding source is noted, the area should be marked, and the patients who rebleed require emergent surgery. Anatomic localization during endoscopy has known limitations and errors, and without a definitive mark (clip or tattoo) resection can be prone to error.

Angiography

- Angiography can be both diagnostic and therapeutic (Fig. 24.2).
- Angiography has both broad positivity (27–77 %) and sensitivity (40–86 %), with specificity being 100 %.
- For angiography to be positive, bleeding must occur at 0.5 ml/min or faster. Small, single-institution retrospective studies have shown blood pressure less than 90, transfusion requirement greater than 5 units, and a blush within 2 min on nuclear scintigraphy to be associated with positive angiograms.
- Superselective embolization is the preferred treatment for positive angiograms. Recent studies have demonstrated success rates from 60 to 90 %, rebleeding rates of 0–33 %, and significant ischemia of less than 7 %.
- In addition, a meta-analysis found embolization of diverticular disease was three to four times more effective than embolization of nondiverticular sources.
- Superselective embolization occurs at the level of the vasa recta or marginal artery.

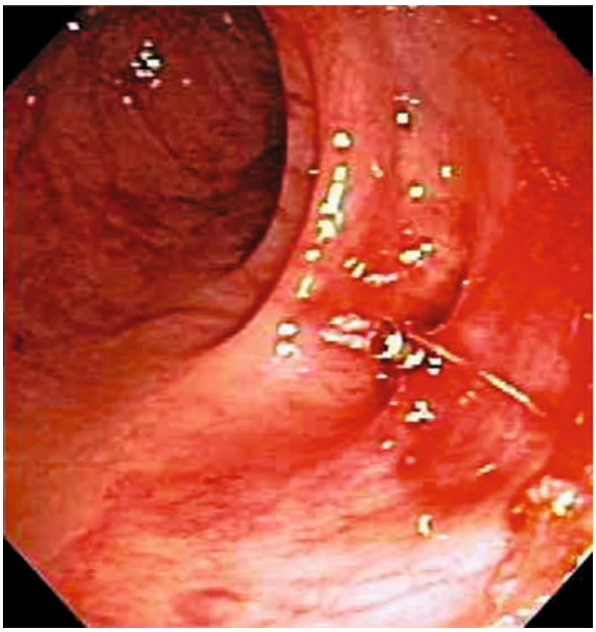

Fig. 24.1 Clip applied to bleeding diverticular vessel

- Materials used for embolization include microcoils, polyvinyl alcohol particles, and gelfoam. They may be used individually or in combination. Microcoils are permanent materials with multiple sizes that are easily visible during fluoroscopy.
- Polyvinyl alcohol particles are also permanent and will be carried by the circulation to the bleeding site which has the least resistance to flow. These particles have decreased selectivity and are poorly visualized. Gelfoam is not a permanent agent with vessel recannulization in days to weeks but it is not routinely used. Material choice is decided by location, angiographer expertise, and microcatheter position in relation to the bleeding vessel. Technical aspects that can lead to failure or inability to embolize are atherosclerosis, vascular tortuosity, and vasospasm.
- Patients with major, ongoing hemorrhage or patients who rebleed need angiography.
- Similar to colonoscopy, the goal of angiography is to localize the source of bleeding and provide directed therapy.
- If superselective embolization is unable to be performed, but a bleeding site is localized, angiographers can inject methylene blue into the artery providing a temporary marker for the surgeon.
- Another option is highly selective, intra-arterial vasopressin infusion. The potent arterial contraction may reduce or halt the hemorrhage. Infusion rates of vasopressin being at concentrations of 0.2 U/min may

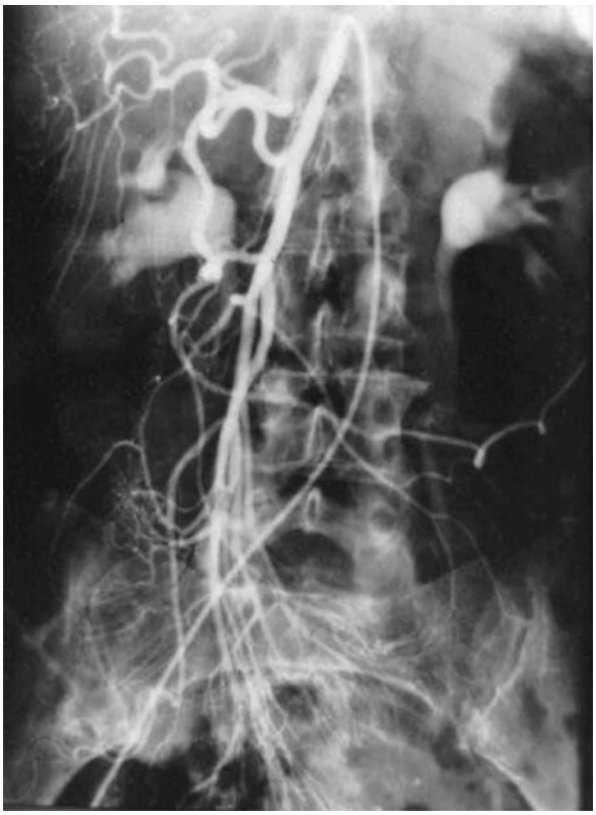

Fig. 24.2 Angiogram demonstrating extravasation (hemorrhage) in cecum

progress to 0.4 U/min. The systemic effects and cardiac impact of vasopressin may limit maximizing the dosage. 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.

- In patients who have negative upper and lower endoscopy with continued evidence of bleeding, angiography can be used to localize the source. However, superselective embolization for sources other than diverticula has higher failure rates.
- Since most LGIB is sporadic, it is not uncommon to be unable to localize the source, even after an EDG, a colonoscopy, and an angiography. Provocative angiography, which uses anticoagulants, vasodilators, or fibrinolytics to induce bleeding, can be used in these cases. Agents used in these procedures include urokinase, streptokinase, and tissue plasminogen activator. Studies evaluating provocative angiography are small and from single institutions with identification of the bleeding source varying from 20 to 80 %. If a bleeding site is identified, superselective embolization can be used for treatment.

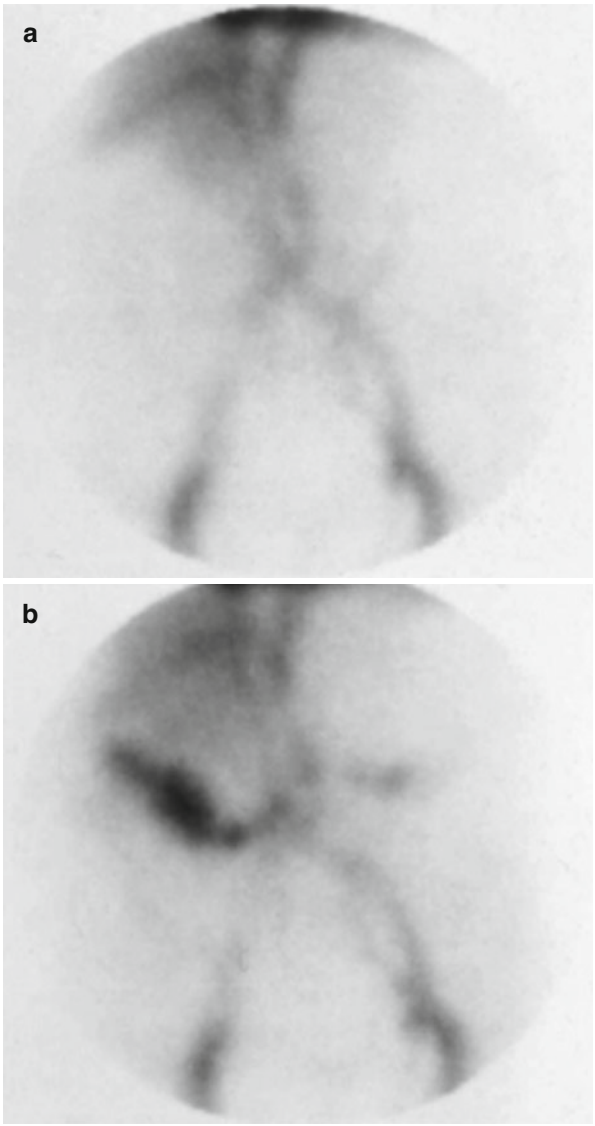

Fig. 24.3 Selected images from a 99mTc-labeled RBC gastrointestinal bleeding study in a patient with known diverticulosis. Images acquired at 1 min (**a**) and 14 min (**b**)

Radionuclide Scintigraphy

- Nuclear scintigraphy or the radioactive labeling of red blood cells is used to evaluate patients with LGIB (Fig. 24.3a, b).
- In comparison to colonoscopy or angiography, it does not have any therapeutic capabilities. However, it is not invasive, does not require a bowel preparation, or requires specialists to be called in to perform the study.

- Bleeding at rates as low as 0.1 ml/min can be detected. Red blood cells are labeled with technetium or sulfur colloid.
- Technetium-labeled red blood cell (TRBC) scanning is positive in 16–91 % of patients.
- A number of studies have attempted to define characteristics of positive TRBC scans. Scans that are positive early have shown increased positivity on angiography and accuracy rates in some studies, but not in others.
- The largest study examining the predictive value of scintigraphy retrospectively reviewed 249 scans and 271 arteriograms. Using a positive scintigraphy as a requirement for angiography led to an increase in positive angiograms from 22 to 53 %. Common clinical parameters such as hemodynamic instability and the number of blood transfusions are not associated with a positive TRBC scan. A more reliable indicator than the overall number of blood transfusions may be the number of units transfused within the 24 h preceding scintigraphy. Multivariate analysis confirmed that patients who received more than 2 units of packed red blood cells within 24 h prior to the scan were twice as likely to have a positive study.

Abnormal increased isotopic activity developed in the proximal transverse colon, which progressed antegrade to the descending colon.

- The role of radionuclide scintigraphy in the management of LGIB continues to be poorly defined.
- In patients who have major, self-limited hemorrhage and are stable to go to radiology, this test, if positive early, can direct further workup and management.
- However, if radionuclide scintigraphy is negative, rebleeding rates are not negligible.
- One advantage of TRBC is that rebleeding within 24 h can be restudied promptly without a second labeling procedure.
- Surgical resection based on radionuclide scintigraphy is not recommended.

Multidetector Row CT

- Multidetector row computed tomography (MDCT) or CT angiography (CTA) may have an increasing role in the diagnostic workup of LGIB.
- MDCT is considered positive when vascular contrast material is extravasated into the bowel lumen.
- MDCT offers the following advantages over radionuclide scintigraphy: (1) it is easy to perform and readily available in emergency rooms with CT scanners, (2) accurate localization of the bleeding site, which allows for a directed angiogram and less contrast use, and (3) identification of other pathologies.

Surgery

- Emergent surgery is necessary in hemodynamically unstable patients who have massive ongoing bleeding and are unresponsive to the initial resuscitation, patients who have had the source of bleeding localized but no therapeutic measures were performed or they failed, and patients who have required at least 6 units of packed red cells within 24 h.
- The need for emergent, exploratory surgery without a localized source of bleeding is uncommon. Prior to surgery, ileostomy, and colostomy, sites should be marked when possible.
- An open laparotomy through a midline incision that allows access to both the upper and lower gastrointestinal tract should be performed. Examination of the entire intra-abdominal gastrointestinal tract is required with focus on identifying blood within the bowel lumen. The stomach, duodenum, small bowel, and colon are visually examined and palpated.
- If there is no identifiable bleeding source and localization was not successful, push intraoperative enteroscopy (IOE) can be considered. Transillumination of the bowel may identify a source such as angiodysplasia or small tumors. IOE is technically challenging and time-consuming. The identification of bleeding pathology occurs in 70–87 % of patients. However, rebleeding rates are 19–30 %. If a source of bleeding is identified, then resection is warranted.
- If no bleeding site is identified in the upper gastrointestinal tract or small bowel and the source is presumed to be colonic, then a total abdominal colectomy should be performed.
- If the patient was on vasoactive medication or is hemodynamically unstable, then an end ileostomy should be created. Postoperatively, these patients will require further resuscitation and possibly continued or intermittent pressor use, which can jeopardize a bowel anastomosis. In addition, the majority of patients with LGIB are elderly with multiple comorbidities augmenting the complexity of their management.
- The aim of the preoperative diagnostic workup is to localize the source of bleeding. If a colonic source is localized, then a segmental rather than subtotal colectomy can be performed. Nonlocalized segmental colectomy based on a clinical "best guess" is not a safe or reliable option.
- Mortality can be as high as 50 % and rebleeding rates as high as 75 %. Mortality rates associated with segmental and subtotal colectomy for LGIB are 4–14 % and 0–40 %, respectively.

Outcomes in Lower Gastrointestinal Bleeding

- The heterogeneity of patients with LGIB and the lack of randomized data concerning the diagnostic workup have led to studies attempting to characterize prognostic indicators (Table 24.2).

Table 24.2 Mortality of lower gastrointestinal bleeding by etiology

Investigator [ref]	Diverticulosis (%)	Angiodysplasia (%)	Cancer/polyp (%)	Colitis/ulcer (%)	Anorectal (%)	Other (%)	Mortality (%)
Jensen and Machicado (1997)	23	40	15	12	5	4	NA
Longstreth (1997)	41	3	9	16	5	14	3.6
Bramley et al. (1996)	24	7	10	21	9	4	5.1
Richter et al. (1995)	48	12	11	6	3	6	2
Rossini et al. (1989)	15	4	30	22	0	11	NA
Jensen and Machicado (1988)	20	37	14	11	5	5	NA

- The following clinical data are independent predictors of severity in LGIB: initial heart rate greater than or equal to 100, initial systolic blood pressure less than or equal to 115 mmHg, initial hematocrit less than or equal to 35 %, gross blood on rectal exam or rectal bleeding within the first 4 h of evaluation, aspirin use, and more than two active comorbid conditions.
- Severe LGIB was defined by one or more of the following clinical characteristics: transfusion of greater than or equal to 2 units of blood, decrease of hematocrit by greater than or equal to 20 % in the first 24 h, and recurrent rectal bleeding after 24 h of stability coinciding with a further decrease in hematocrit of greater than or equal to 20 %, more transfusions, and readmission within 1 week of discharge.
- Patients were considered high risk if they had greater than three risk factors and low risk if they had no risk factors. High-risk patients had increased rates of surgery and death, increased number of transfusions, and longer hospital stays.
- Prognostic factors for urgent surgery are hypotension on arrival (systolic blood pressure 70–80 mmHg) and the etiology of the bleeding. Urgent surgery and associated comorbidities (neuropathies, diabetes, hepatic, cardiovascular and pulmonary disease) were risk factors for morbidity and mortality. Postoperatively, only transfusion needs greater than 10 units predicted mortality and morbidity after multivariate analysis. The average number of units transfused prior to surgery in this study was 9.3. These findings support an earlier study from 1991 where patients who received less than 10 units had a 7 % mortality rate and patients who received greater than 10 units had a mortality rate of 27 %.
- The literature has shown that there are multiple options in the workup of LGIB that can be used interchangeably with adequate results. Urgent endoscopy can be performed as the first diagnostic step, followed by other localizing studies if not successful, but evaluation with TRBC followed by selective angiography if TRBC is positive can also be successful for localization. Studies have shown clearly that segmental colon resection after radionuclide scintigraphy alone is ill advised and that blind resections have high rebleeding rates and lead to worse patient outcomes. The steps in the workup remain variable but should be tailored to a physician's expertise and hospital resources.
- Billingham's description, in 1997, of LGIB as a conundrum with five main problems continues to reflect the current management issues.
  - First, bleeding can be from any location in the gastrointestinal tract.
  - The second problem faced by surgeons is the sporadic nature of lower gastrointestinal bleeding.
  - The third problem is the necessity of surgical intervention prior to localization.

  - Fourth, rebleeding after extensive resections remains a concern.
  - Finally, there are few consensus statements regarding diagnosis and management.
- Certainly, the conundrum has not been solved. However, a variety of new technologies and evolving methods of treatment are allowing clinicians to make progress with less dramatic interventions for patients.
- New imaging techniques such as MDCT may be able to efficiently identify sources of bleeding and guide management with less delay and better anatomic definition.
- Superselective angiography can provide safe and accurate diagnostic and therapeutic options.
- Capsule endoscopy can assist in locating obscure bleeding sources and has become the standard of care for workup in a nonacute setting.
- DBE will become more available and may provide multiple therapeutic options for lesions not reached by traditional endoscopic techniques, but is not advocated in the urgent or emergent setting at this time.
- Acceptance and practice of urgent colonoscopy and superselective angiography provide opportunities to identify the source prior to surgery and even avoid surgery entirely.
- In addition, the diagnostic and therapeutic options available with colonoscopy, capsule endoscopy, DBE, and superselective angiography offer a variety of options to localize and treat the source with minimal risk compared to emergent surgery.
- Nevertheless, LGIB can be a challenging event for the patient and physician.
- Successful treatment of LGIB requires the ability to perform massive resuscitation, expeditious workup, and skilled surgical assessment with prompt operative intervention when required.
- An algorithm summarizing the management is provided in Fig. 24.4.

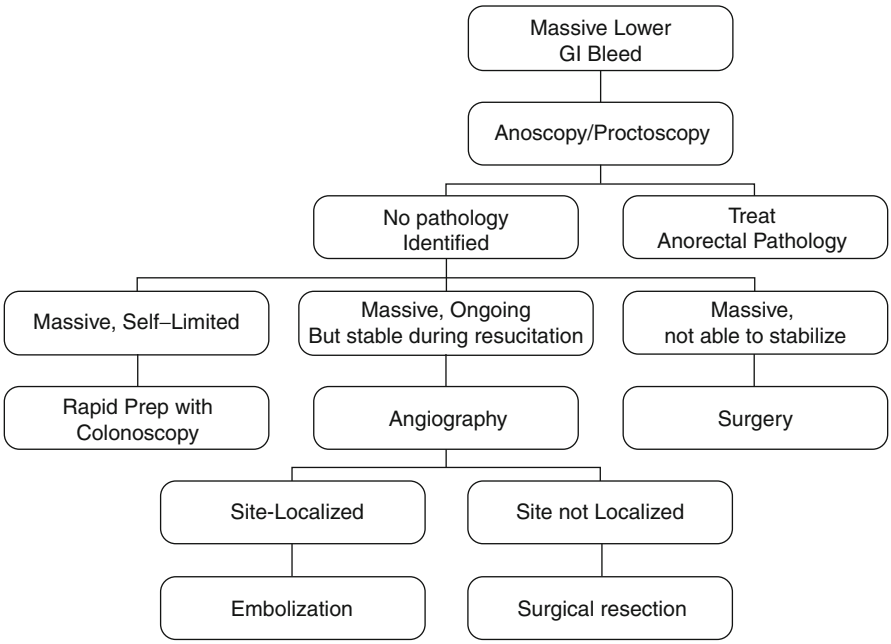

Fig. 24.4 An algorithm summarizing the management

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25. Endometriosis

Michael J. Snyder

Introduction

- Endometriosis is a disease characterized by the presence of endometrial glands and stroma outside the uterine cavity.
- Endometriosis may be associated with disabling pain and intractable infertility.
- Treatment for endometriosis is usually multimodal and may require surgery in those patients with infertility, pelvic pain, obstruction, or a poor response to hormonal suppression.

Epidemiology

- The true prevalence of endometriosis is unknown.
- Up to 15 % of all women of reproductive age and one-third of infertile women have endometriosis.
- 6.2 % of premenopausal women have endometriosis.
- The widespread use of exogenous estrogens and increasing obesity in our society have made it more prevalent in postmenopausal women.
- There is a decrease in the incidence of the disease when women use oral contraceptives or experience multiple pregnancies.
- Uninterrupted menstrual cycles predispose susceptible individuals to the development of endometrial implants.
- There is no racial predilection for endometriosis other than in Japanese women who have double the incidence of the disease than do Caucasian women.

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Etiology

- The two most popular theories as to its etiology are coelomic metaplasia and the implantation of viable endometrial cells from retrograde menstruation through the fallopian tubes.
- Coelomic metaplasia suggests that under the correct hormonal milieu, the coelomic epithelium will undergo metaplastic changes and transform into endometrial tissue.
- Retrograde menstruation remains the most plausible explanation.
- 7 % relative risk for blood relatives of affected individuals as opposed to a 1 % relative risk for non-blood controls.
- Investigators have confirmed alterations in both cellular and humoral immunity in humans.
- High concentration of activated macrophages and decreased functional capacity of natural killer cells.
- The most significant abnormality in humoral immunity is the presence of autoantibodies against different cellular components.

Clinical Manifestations

- The most common sites where endometriosis occurs are summarized in Table 25.1.
- The most common presenting complaints relate to menstrual irregularities, pelvic pain, and infertility.
- Mild endometriosis can spontaneously resolve and that medical therapy may only suppress the disease until hormonal stimulation resumes.

Table 25.1 Sites and incidence of endometriosis

Common	
Ovaries	60–75 %
Uterosacral ligaments	30–65 %
Cul-de-sac	20–30 %
Uterus	4–20 %
Rectosigmoid colon	3–10 %
Less common	
Appendix	2 %
Ureter	1–2 %
Terminal ileum	1 %
Bladder	<1 %
Abdominal scars	<1 %
Rare	
Diaphragm	
Inguinal canal	
Liver	
Spleen	
Kidney	

Pelvic Pain and Dysmenorrhea

- Pain is the most common symptom of endometriosis, affecting up to 80 %.
- Pelvic pain associated with endometriosis presents as dysmenorrhea, dyspareunia, or chronic noncyclic pelvic pain.
- Total lesion volume does appear to correlate directly to the degree of pain.
- Pain is typically most intense just prior to 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. Dyspareunia is most pronounced just prior to menstruation.
- Adhesions, very common in endometriosis, may also be associated with pain. Adherence of the colon and small bowel along with retroflexion of the uterus from extensive posterior adhesions may occur. Such retroflexion and fixation of the rectosigmoid can result in pressure on the sacrum with consequent back and rectal pain.
- Macrophages are responsible for the removal of foreign material such as the endometrial implants. They are present around the endometrial implants and are potent producers of inflammatory mediators such as the prostaglandins.

Infertility

- In women with known endometriosis, the infertility rate is 30–50 %.
- Pelvic endometriosis and the resulting inflammatory response can produce dense, fibrotic adhesions that may significantly interfere with both the oocyte release from the ovary and the ability of the fallopian tube to pick up and transmit the oocyte to the uterus.
- Endometriosis was the etiology in 14 % of patients undergoing tubal reconstruction for occlusion.
- In moderate or severe endometriosis, the pregnancy rates following surgery are 50 and 40 %, respectively, compared with only 7 % when expectant management is practiced.

Intestinal Symptoms

- Intestinal complaints are found in most women with moderate-to-severe disease.
- Bowel involvement occurs in 12–37 % of cases of endometriosis.
- Rectosigmoid is involved in over 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.
- Intestinal resection in asymptomatic patients is probably unwarranted.
- Acute or chronic small bowel obstruction develops from extensive fibrotic adhesions.
- The next most frequent site of intestinal endometriosis is the appendix.
- Endometriosis of the appendix may produce a chronic obstruction of the intestinal lumen with formation of a mucocele or periappendiceal inflammatory mass that is difficult to distinguish from a neoplasm.
- Finally, endometrial implants of the appendix and cecum may serve as lead points for an intussusception.

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.
- Symptoms of pelvic pain and an enlarging pelvic mass are the most common symptoms.
- In women with known endometriosis, a cyst larger than 10 cm, cyst rupture, or a change in the nature of the chronic pelvic pain is a potential sign of malignancy.
- The rectosigmoid colon is the most common site for extragonadal tumors arising from endometriosis.
- Recurrent symptoms of pelvic endometriosis following hysterectomy and bilateral salpingo-oophorectomy can be possible signs of malignant degeneration. Endometrial carcinoma is the most common tumor type.

Diagnosis

Physical Examination

- Careful bimanual and rectal examination may reveal nodularity or induration especially in the uterosacral ligaments or cul-de-sac of Douglas.
- Fixed tender retroversion of the uterus in a patient without previous pelvic surgery may raise suspicion for endometriosis.

Laboratory Evaluation

- CA-125, an antigen expressed on tissues derived from human coelomic epithelium, is elevated in women with moderate-to-severe endometriosis.
- The concentration of CA-125 does correlate with the severity of the disease.

- It may also be of value in following women post-resection who had elevated levels preoperatively and are again exhibiting symptoms of endometriosis.

Endoscopy

- Endoscopically, the mucosa is generally intact, occasionally associated with significant luminal narrowing. Infiltration of the submucosa, while uncommon, may produce nodularity and distortion of the overlying mucosa (Fig. 25.1).
- 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 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.
- Endorectal ultrasound is a potentially valuable tool to determine rectal wall invasion by endometrial implants in the cul-de-sac.
- Barium enema examination is another imaging technique often obtained by gynecologists for the intestinal complaints associated with deep pelvic endometriosis.

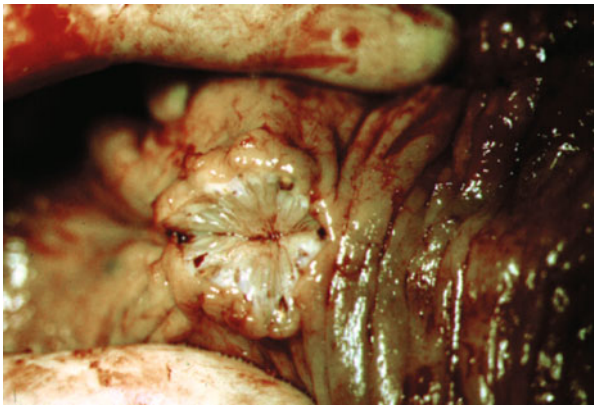

Fig. 25.1 Polypoid endometrial implant of the colon

- Computerized tomography is the imaging technique probably used most frequently for the evaluation of abdominal and pelvic pain. Unfortunately, there is no standard CT appearance for a mass caused by endometriosis to clearly differentiate it from pelvic masses due 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.
- Colorectal involvement on MRI is strongly suspected when there is disappearance of the fat plane between the rectum and the vagina, loss of the hypointense signal of the anterior bowel wall on T2-weighted images, and a contrast-enhanced mass on T1-weighted images involving the bowel wall.
- Sagittal images are particularly valuable in imaging the cul-de-sac of Douglas.
- MRI is superior to CT scanning for extraperitoneal lesion and the evaluation of pelvic masses.

Laparoscopy

- Both ovaries should be mobilized to evaluate the pelvic peritoneum, and the uterus should be manipulated to allow complete visualization of the cul-de-sac of Douglas, uterosacral ligaments, sigmoid colon, and ureters.
- The extent of endometriosis should be carefully documented and staged (Fig. 25.2).
- 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, popular, or hemorrhagic.

Treatment

- Treatment is primarily begun to ameliorate symptoms.
- Not all women with endometriosis require treatment.
- Medical therapy is designed to treat the symptoms of endometriosis, notably pelvic pain.
- In limited disease, medical therapy is comparable with surgery in terms of relief of symptoms, recurrence of disease, and subsequent pregnancy rates. Finally, medical therapy does not require specialized training or equipment and is much less costly than surgery.
- Estrogen/progestogens result in the induction of pseudopregnancy with hyperhormonal amenorrhea. Pituitary and ovarian function is thereby suppressed, and in the later stages of the treatment regimen, endometrial implants resorb and resolve.
- Synthetic progestogens alone may induce a pseudopregnancy by acting in concert with endogenous estrogens. Ovarian suppression is often inconsistent.

Patient's name _____ Date _____

Stage I (Minimal) - 1–5
Stage II (Mild) - 6–15
Stage III (Moderate) - 16–40
Stage IV (Severe) - > 40
Total _____

Laparoscopy _____ Laparotomy _____ Photography _____
Recommended treatment _____
_____
Prognosis _____

Peritoneum	Endometriosis	< 1 cm	1–3 cm	> 3 cm
	Superficial	1	2	4
	Deep	2	4	6
Ovary	R Superficial	1	2	4
	Deep	6	16	20
	L Superficial	1	2	4
	Deep	4	16	20

	Posterior cul-de-sac obliteration	Partial	Complete
		4	40

Ovary	ADHESIONS	< 1/3 Enclosure	1/3–2/3 Enclosure	<2/3 Enclosure
	R Filmy	1	2	4
	Dense	4	8	16
	L Filmy	1	2	4
	Dense	4	8	16
Tube	R Filmy	1	2	4
	Dense	4•	8•	16
	L Filmy	1	2	4
	Dense	4•	8•	16

•If the fimbriated end of the fallopian tube is completely enclosed, change the point assignment to 16.
Denote appearance of superficial implant types as red [(R), red, red-pink, flamelike, vesicular blobs, clear vesicles], white [(W), opacifications, peritoneal defects, yellow-brown], or black [(B) black, hemosiderin deposits, blue]. Denote percent of total described as R___ %,W___ % and B___%. Total should equal 100%.

Additional endometriosis: _____

Associated pathology: _____

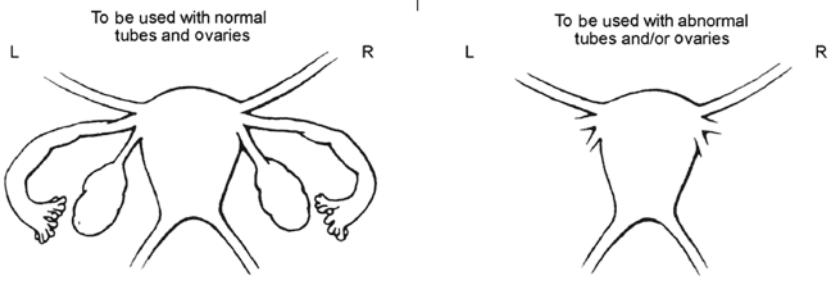

Fig. 25.2 Revised American Society for Reproductive Medicine 1996 classification of endometriosis

- Depot progestogens have been effective in ameliorating pelvic pain with equivalent efficacy to danazol. Side effects include breakthrough vaginal bleeding, weight gain, and fluid retention.
- Danazol lowers peripheral estrogen and progesterone levels by a direct effect on ovarian steroidogenesis and pituitary production of FSH and LH.

- Danazol also binds directly to endometrial cellular receptors leading to atrophy and suppression of proliferation.
- Danazol also raises free testosterone levels and produces a hyperandrogenic state, especially at lower doses. Hirsutism, acne, weight gain, and deepening voice changes may occur.
- The introduction of GnRH-a as a new treatment modality for endometriosis has improved results primarily by a reduction in side effects.
- Pain relief is complete in over 50 % of women and significantly decreased in over 90 %.
- GnRH-a is not recommended for women with osteoporosis.
- The major goal of surgical therapy for endometriosis is to completely excise or ablate the endometrial implants. Secondary goals include the preservation of ovarian function and minimizing postoperative adhesion formation.
- Utilizing surgical techniques that minimize injury to the surrounding tissue, such as a cutting current to outline lesions to be removed by electrocautery and high-power density settings with the CO_2 laser, is desirable.
- Laparoscopic hydrodissection is also very useful in identifying normal surrounding tissue.
- Ureteral stents are liberally used and are especially useful in women with severe obliterative disease in the cul-de-sac and in reoperative pelvic surgical procedures.
- Small superficial lesions involving the intraperitoneal rectum may be vaporized with the CO_2 laser or electrocautery.
- Cutting current as opposed to coagulating current is preferred.
- After the lesion is removed, the bowel wall is carefully assessed.
- Excision of the implant either with a disk of rectal wall or with a formal anterior resection is recommended.
- For severe disease laparoscopic ablation, when possible, had similar crude pregnancy rates in comparison to laparotomy, and both techniques were clearly superior to medical management alone.
- Disk excision of the anterior rectal wall, by either laparoscopic or open technique, is performed for single lesions usually less than 3 cm in diameter.
- Segmental resection of the rectosigmoid is performed for larger lesions or when neoplasia is a concern.
- Place omentum between the rectum and the vagina, if the suture lines are in contact.
- Superficial small bowel implants may be treated with sharp excision, electrocautery, or 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.
- For those patients with asymptomatic endometriosis, observation is probably sufficient, but hormone replacement therapy should be avoided.

- Combination medical and surgical 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.
- Improvement in pregnancy rates with 6 months of danazol given preoperatively with all stages of endometriosis has been noted. The optimal length of therapy and long-term (and not just delayed) recurrence rates must still be elucidated.
- Postoperative treatment with danazol and oral contraceptive pills has not been shown to have durability, and the initial excitement over improved recurrence rates at 12 months has not been duplicated.

Conclusion

- The diagnosis and management of intestinal endometriosis has evolved tremendously over the last 20 years with the widespread availability of laparoscopy and a clear understanding of the necessity to remove all endometrial implants in symptomatic patients.
- With the advent of stapling devices that facilitate low pelvic anastomoses, the intestinal surgeon should be able to resect the endometrial implants and restore bowel continuity in virtually all patients with minimal morbidity and preserved fertility, when desired.
- Further improvements in outcomes will probably not occur until a better understanding of the precise etiology and growth of the endometrial implant is discovered.

26. Trauma of the Colon and Rectum

David B. Hoyt and Michael E. Lekawa

Colon Injuries

- Reduction of colon-related mortality from about 60 % during World War I.
- 40 % during World War II.
- 10 % during the Vietnam War.
- Lower than 3 % in the last few decades.
- The abdominal sepsis rate has remained significant at about 20 %.
- No other organ injury is associated with a higher septic complication rate than colon injury.
- In patients with colon injuries with a Penetrating Abdominal Trauma Index (PATI) >25 or with multiple blood transfusions, the incidence of intra-abdominal sepsis is as high as 27 %.
- In patients with destructive colon injuries requiring resection, the reported incidence of abdominal complications is about 24 % (Table 26.1).

Epidemiology

- In American urban centers, firearms are by far the most common cause of injury.
- The colon is the second most commonly injured organ after the small bowel, and it is involved in about 27 % of cases undergoing laparotomy.
- In stab wounds, the left colon is the most commonly injured segment.

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Table 26.1 Incidence of abdominal septic complications in colon injuries (prospective studies)

Author, year	Number of patients	Abdominal sepsis (%)
George, 1989	102	33
Chappuis, 1991	56	20
Demetriades, 1992	100	16
Ivatury, 1993	252	17
Gonzalez, 1996	114	24
Demetriades, 2001	297	24
Overall	921	22

- In anterior abdominal stab wounds, the colon is the third most commonly injured organ after the liver and small bowel and is found in about 18 % of patients.
- In posterior stab wounds, the colon is the most commonly injured organ and is injured in about 25 % of patients undergoing laparotomy.
- In abdominal gunshot wounds, the transverse colon is the most commonly affected segment.
- 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.
- Only 3 % of blunt trauma patients undergoing laparotomy have full-thickness colon perforations.
- Seat belts increase the risk of hollow viscous perforations, and the presence of a seat-belt mark sign is a predictor of hollow viscous injury.

Diagnosis

- A rectal examination may show blood in the stool, especially in cases with distal colon or rectal injuries.
- A preoperative upright chest film may show free air under the diaphragm.
- The colon can reliably be evaluated by water-soluble contrast enema studies or abdominal CT scan with soluble rectal contrast. Retroperitoneal gas or contrast extravasation is diagnostic, and an exploratory laparotomy should be performed.
- Ultrasound or diagnostic peritoneal lavage is unreliable in the evaluation of suspected colon injuries due to its retroperitoneal location.
- The preoperative diagnosis of colon injury following blunt trauma can be a major challenge, especially if the patient is unevaluable due to associated head injuries.
- Intraoperatively, every paracolic hematoma due to penetrating trauma should be explored.
- Paracolic hematomas due to blunt trauma should not undergo routine exploration unless there is evidence of colon perforation (Table 26.2).

Table 26.2 American Association for the Surgery of Trauma (AAST) colon injury scale

Grade	Injury description
I	(a) Contusion of hematoma without devascularization
	(b) Partial-thickness laceration
II	Laceration ≤50 % of circumference
III	Laceration >50 % of circumference
IV	Transection of the colon
V	(a) Transection of the colon with segmental tissue loss
	(b) Devascularized segment

Operative Management

Historical Perspective

- The first guidelines were published by the United States Surgeon General in 1943 and mandated proximal diversion or exteriorization of all colon wounds.
- The policy of mandatory colostomy for all colon injuries remained the unchallenged standard of care until the late 1970s.
- Stone reported the first major scientific challenge of this policy in 1979. It was concluded that primary repair was associated with fewer complications than colostomy.
- In the 1990s and 2000s, primary repair became the standard of care except in the presence of certain risk factors such as destructive colon injuries, severe contamination, multiple injuries, and delays in treatment.

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, i.e., AAST Grade I or II, irrespective of risk factors).
- Primary repair is the method of choice of treatment of all penetrating colon injuries in the civilian population despite any associated risk factors for adverse outcome.
- Numerous prospective observational studies (class II evidence) demonstrated the superiority of primary repair over diversion in nondestructive injuries.
- In conclusion, there is sufficient class I and II data to support routine primary repair of all nondestructive colon injuries, irrespective of risk factors for abdominal complications.
- No study has ever shown that colostomy is associated with better results than primary repair.

Destructive Colon Injuries

- Until 2000, the available prospective randomized studies, which include only a small number of cases, recommend resection with anastomosis irrespective of risk factors.

- Two large retrospective studies advocate diversion in the subgroups of patients with certain risk factors such as PATI ≥25, multiple blood transfusions, or associated medical illness.
- Subsequently, the guidelines of the Eastern Association for the Surgery of Trauma (EAST) published in 1998 supported resection and primary anastomosis in the subgroups of patients with destructive colon injuries if they (a) are hemodynamically stable intraoperatively, (b) have minimal associated injuries (PATI <25, ISS <25), (c) have no peritonitis, and (d) have no underlying medical illness.
- The guidelines suggest that patients with shock, significant associated injuries, peritonitis, or underlying disease should be managed with resection and colostomy.
- In view of the lack of large prospective studies in the literature, the AAST sponsored a prospective multicenter study This study, published in 2001, included 297 patients with penetrating injuries requiring colon resection (rectal injuries were excluded) that survived at least 72 h.
- The overall colon-related mortality was 1.3 % (four deaths) and all deaths occurred in the diversion groups ($P = 0.01$).
- The overall incidence of abdominal complications was 24 %, and the most common complication was an intra-abdominal abscess.
- The incidence of anastomotic leaks was 6.6 %. 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 the 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 %.
- The method of colon management, delay of operation >6 h, shock at admission, site of colon injury, PATI >25, ISS >20, or associated intra-abdominal injuries were not found to be independent risk factors.
- Colon-related mortality was significantly higher in high-risk patients undergoing diversion rather than primary anastomosis.
- 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.
- The study concluded 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.

Risk Factors for Abdominal Complications

- The abdominal complication rate in colon injuries is very high, with a sepsis rate of about 20 % (Table 26.1).

- In destructive colon injuries the AAST colon resection study of 298 patients recorded an overall incidence of 24 % of abdominal complications.

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 anatomical sides should be treated differently.

Associated Abdominal Injuries

- Class I and II studies have shown that although multiple associated intra-abdominal injuries are significant risk factors for intra-abdominal sepsis, the method of colon management does not affect the incidence of abdominal sepsis.
- 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 intra-operative shock is neither an independent risk factor for abdominal sepsis nor a contradiction for primary colon repair or anastomosis.

Blood Transfusions

- Multiple blood transfusion ($\geq$4 units of blood within the first 24 h) has been shown to be a major independent risk factor for abdominal septic complications.

Injury Severity Score

- The injury severity score (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

- Severe fecal contamination of the peritoneal cavity is a major independent risk factor for abdominal sepsis.
- 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 have 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

- Multivariate analysis failed to identify time delay as an independent risk factor.

Retained Missiles

- Missiles that passed through the colon and remained lodged in the tissues are not associated with increased risk of local sepsis.

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.
- However, multivariate analysis failed to identify this method as an independent risk factor.

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, there were 66 (2.2 %) leaks.
- In prospective studies including 534 patients with colon repair or resection and anastomosis, there were 17 (3.2 %) leaks.
- The leak rate after resection and anastomosis is significantly higher than in simple repairs.
- It seems that colocolostomies are associated with a higher incidence of anastomotic leaks than ileocolostomies.
- Univariate analysis identified PATI $\geq$25, $\geq$6 units of blood transfusion, and hypotension in the emergency room as risk factors for anastomotic leak.
- A multicenter prospective AAST study reported a leak rate of 4.2 % for ileocolostomies and 8.9 % for colocolostomies. No significant independent risk factors could be identified.

- Many cases of anastomotic leak that do not result in diffuse peritonitis can be managed safely nonoperatively with a low-residue diet.
- Leaks result in fecal fistulas, which heal spontaneously within a few days. In other cases, the leak results in a local abscess which can be drained percutaneously. However, in some patients, the colonic leak causes severe intra-abdominal sepsis, and a proximal diversion procedure may be required.
- The overall mortality due to colon leak-related complications in a collective review of 3,161 trauma patients treated with primary repair or resection and anastomosis was only 0.1 %.

Technique of Colon Repair

- In nondestructive injuries, repair of the injured colon should be performed after debridement of the perforation.
- In destructive injuries, resection to normal and well-perfused edges should be performed, and the anastomosis should be tension-free.
- The method of anastomosis, hand sewn or stapled, does not influence the incidence of abdominal complications or leak rate.
- Further protection of the anastomosis with adjacent omentum is recommended whenever possible.

Rectal Injuries

- The mortality related to rectal trauma has decreased dramatically from 67 % during World War I down to today's civilian reports of 0–10 %.
- Likewise, the morbidity, which was as high as 72 % during the Vietnam War, is now as low as 10 %.
- 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.

Epidemiology

- Injuries to the rectum occur infrequently and are usually the result of penetrating trauma.
- In a series of 59 patients with gunshot wounds to the buttocks, only 3.4 % had rectal injuries.
- Of 192 patients with gunshot wounds to the back, 2.6 % had a rectal injury.
- In a series of 309 anterior abdominal gunshot wounds and a series of 37 transpelvic gunshot wounds, no rectal injuries were identified.
- Rectal injuries have been reported in nearly 2 % of all pelvic fractures.

Diagnosis

- Extraperitoneal rectal injuries may not always be obvious.
- The cornerstone for diagnosing an extraperitoneal injury is the combination of a digital rectal exam and rigid proctoscopy.
- However, the false-negative rate of the two has been reported to be as high as 31 %.
- Further evaluation by means of a water-soluble contrast study should be considered.
- In mechanisms of injury other than foreign body insertion, intraluminal blood on proctoscopy should generally be considered positive for rectal injury

Rectal Organ Injury Scale

- The grading system developed by the AAST for rectal injuries is similar to that for colonic injuries (Table 26.2).

Operative Management

- Presently, there is no acceptable gold standard for the treatment of rectal injuries, as most studies have been unable to demonstrate any advantage of the various treatment options.
- Several studies do indicate that injuries to the intraperitoneal rectum can be managed like left-colon injuries with primary repair and without the need for colostomy.
- No increase in abdominal complications was found in these series when primary repair without colostomy was performed, making primary repair in this group of patients a reasonable option.

Fecal Diversion with Colostomy

- Ever since World War II, the mainstay of management of extraperitoneal injuries has been proximal colostomy.
- Extensive destruction of the rectum that requires a resection may best be served with a Hartmann's procedure.
- Recently, there have been reports of primary repair without fecal diversion in selected extraperitoneal rectal injuries.
- Similarly, injuries right at the peritoneal reflection, or injuries encountered with minimal dissection, may also be primarily repaired without the need for colostomy.

Presacral Drainage

- Over the last 15 years, the use of presacral drainage has diminished considerably.
- It involves an additional procedure and dissection into an uninvolved space.

- The drains that are placed may malfunction or become malpositioned, and most importantly, there is no evidence that their use improves outcome.
- The addition of presacral drainage is unnecessary.

Distal Rectal Washout

- The overall value of distal washout is questionable.
- There is no proven benefit, and it may be associated with a high risk of infection due to spillage of intraluminal contents out of unrepaired rectal injuries.

Rectal Repair

- Rectal repair with or without a diverting colostomy is infrequently performed for extraperitoneal injuries.
- In the majority of cases, repair is not technically feasible, with some series reporting successful repair in only 20–37 % of cases.
- Even when repair is performed, no outcome advantage has been proven.
- Attempts at repair are associated with extensive dissection and unnecessary contamination of the peritoneal cavity.
- Attempts at repair should only be made when the rectal injury is encountered during the exposure of an associated injury such as bladder or iliac vessel or if the injury is easily accessible at the peritoneal reflection.

Associated Injuries

- Associated injuries are commonly seen with rectal injuries and have been reported to occur in as many as 77 % of cases.
- Genitourinary, and in particular bladder, injuries are usually the most commonly seen associated injuries, occurring in 30–64 % of cases.
- Every effort should be made to close both injuries and separate both sites with well-vascularized tissues such as omentum.

Wound Management

- The incidence of wound sepsis in patients with colon or rectal injury is high.
- Primary wound closure in the presence of severe fecal spillage is a significant risk factor for wound sepsis and fascia dehiscence.

Antibiotic Prophylaxis

- Appropriate antibiotic prophylaxis is critical. It is a standard practice to cover against both aerobes and anaerobes.
- The reported overall incidence of intra-abdominal abscess in abdominal trauma series is about 3 %, while in severe colon injuries it is about 19 %.

- It is possible that although single agents may be effective in minor or moderate trauma, they might be suboptimal in severe colon injuries.
- It is also possible that it might be necessary to cover against *Enterococcus*.
- 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.

Stoma-Related Complications

- The incidence of complications directly related to the ostomy construction is a significant one. The most common serious complications include necrosis, retraction, prolapse, parastomal abscess, and parastomal hernia.
- Less serious complications include troublesome skin irritation and poor location with difficulties in the application of the collection bag.
- The morbidity of colostomy closure is significant.
- The incidence of complications following colostomy closure is approximately 13–15 %.
- The timing of colostomy closure does not seem to play 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.

Rectal Foreign Bodies

- Most objects can be safely removed in the emergency department.
- A small percentage of patients will require general anesthesia and operative management with or without laparotomy.
- Patients with a history of retained foreign body who present with peritonitis should be taken directly to the operating room.
- 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 colotomy may be necessary for foreign body retrieval.

27. IBD: Diagnosis and Evaluation

Walter A. Koltun

History

- In 1932, Crohn, Ginzburg, and Oppenheimer described 13 patients with "regional ileitis."
- It was their published description that established the formal classification of the disease syndrome and association with noncaseating granulomas.
- The surgeon involved in the care of the majority of the patients, Dr. AA Berg, did not want his name included in the article.
- Brooke and Lockhart-Mummery pointed out both the segmental and granulomatous nature of the colitis in CD.
- Brooke contributed significantly by introducing pioneering surgical techniques in the 1950s that created a more functional ileostomy.
- Truelove and Witts in 1959 reported on a double-blind, controlled study demonstrating the value of high-dose cortisone as treatment for severe colitis.
- The ileal pouch anal anastomosis (IPAA) was first described by Parks and Nicholls in 1978 and subsequently refined by Utsunomiya.
- The IPAA is now the standard of care for the surgical correction of UC.

Epidemiology

- The causes of UC and CD remain unknown.
- Prevalence and associated risk factors are shown in (Table 27.1).
- The prevalence of IBD (incidence x disease duration) greatly varies throughout the world.

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Table 27.1 Epidemiologic and associated risk factors for inflammatory bowel disease

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
Gender:
CD: Female > Male
UC: Male > Female
Age:
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 socioeconomical status ↑ IBD
Oral contraceptive use ↑ IBD
Cigarettes – ↑ CD
↓ UC
Appendectomy ↓ ulcerative colitis
NSAIDS – ↑ symptoms of IBD

ETOH alcohol, *UC* ulcerative colitis, *CD* Crohn's disease, *NSAIDS* nonsteroidal anti-inflammatory drugs

- IBD is found in the more temperate climates of North America and Europe. Studies from these 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 suggesting an environmental effect, since a genetic factor would probably not influence disease rates so rapidly.
- CD most commonly occurs in the third decade of life, while UC is more common in the fourth decade.
- There may be a bimodal distribution of disease incidence with a second peak in the sixth or seventh decade
- Recent case–control studies in USA suggest a similar incidence in blacks and whites.
- The incidence is consistently higher in Jews than in the non-Jewish population in most countries studied.

- IBD is more common in urban, "indoor" populations of individuals of middle to upper socioeconomic status, suggesting the "hygiene" hypothesis that relates the lack of early exposure to environmental antigens to the later development of disease.
- There is very little evidence that a specific dietary factor causes disease.
- Childhood diarrheal illness and oral contraceptive and nonsteroidal anti-inflammatory drugs (NSAIDs) use are measurable risk factors for IBD.
- Smoking increases risk of developing Crohn's de novo and increases risk of recurrence after surgical resection.
- Conversely, smoking is protective for UC, as is prior appendectomy.

Genetic Disease Determinants in IBD

- Approximately 20 % of patients with IBD will have a family member also afflicted.
- Genome-wide association studies (GWAS) have identified areas (loci) in the human genome that are associated with the various forms of IBD.
- As of mid-2009, an excess of 32 loci (most containing several potential disease-causing genes) was found for CD alone.
- UC appears to have less of a genetic component to its pathobiology but similarly has at least 15 loci associated with it (Fig. 27.1).
- IBD may be the consequence of an altered host immune response to various environmental factors, most probably enteric or commensal bacteria within the gut.
- Other factors may also play a role, such as smoking or NSAID use that further alters the host immune system or affects its function (Fig. 27.2).
- The first CD-associated genetic mutation was found in the NOD2/CARD 15 gene on chromosome 16.
- This gene's protein product recognizes muramyl dipeptide, a component of bacterial cell walls, and activates NF-kappa B, a potent second messenger involved in immune regulatory mechanisms.
- Though a homozygous (double) mutation in this gene increases the risk of CD approximately 30-fold, any one patient with a mutation will still only have an approximately 2.5 % risk of developing CD.
- Autophagy, i.e., the cell's ability to destroy and recycle defective cytoplasmic molecules including invading bacteria, is compromised by mutations in the ATG16L1 and IRGM genes, which have been associated with CD.
- Mutations in the acquired immune system, especially those involving the IL-23 and IL-12 signaling pathways, have been found.
- Various alleles in other molecules found in the IL-23 pathway including JAK2, STAT3, and IL12B have also been linked with CD and UC.
- Experimentally, blockade of the IL-23 pathway may compromise bacterial clearance in some models, reinforcing the concept that IBD is the consequence of an abnormal immune response to commensal gut bacteria.

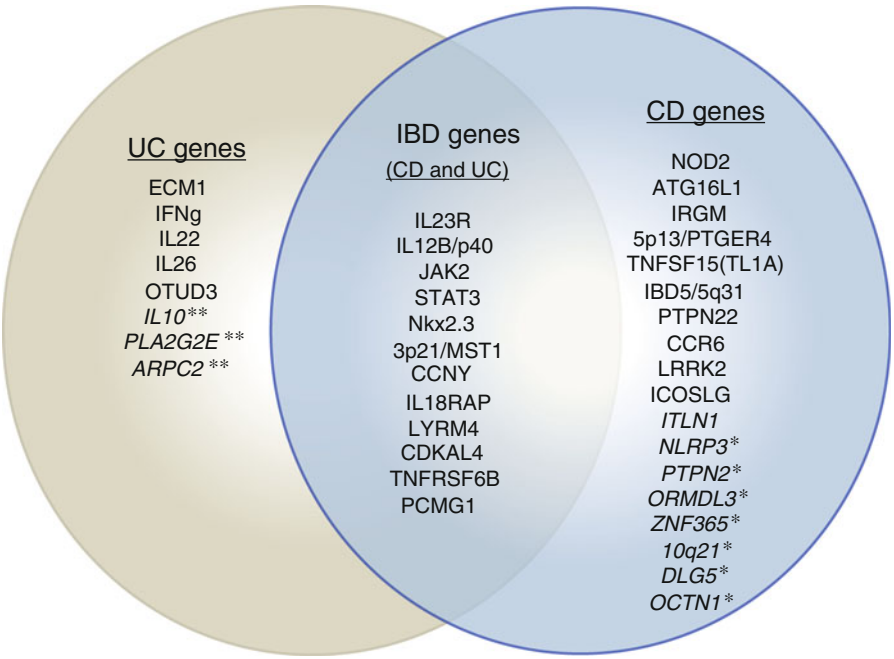

Fig. 27.1 Genes implicated in the pathogenesis of Crohn's disease and ulcerative colitis (as of late 2009). Some genes seem to play a role in both diseases. Not all genes have been confirmed by second investigators. * CD genes not fully tested in UC. ** UC genes not fully tested in CD

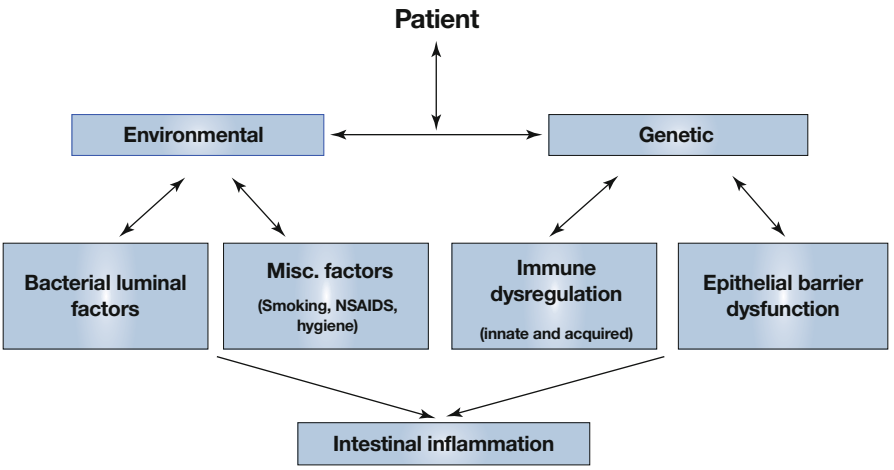

Fig. 27.2 Pathogenesis of inflammatory bowel disease incorporating a genetic (predisposition) component and an environmental aspect, each of which may play a varying role in the individual patient

- IBD-associated mutations have been found in many other genes, including DLG5 (coding for an epithelial cytoplasmic scaffolding protein), NKX2-3 (a developmental protein found in the lymphoid tissue of gut and involved in the expression of lymphocyte trafficking molecules), PTPN2 (involved in T-cell-dependant B-cell function), and IL-10R (receptor).

Signs and Symptoms

Crohn's Disease

- CD can affect any portion of the gastrointestinal (GI) tract from the mouth to the anus and it is usually discontinuous.
- The inflammation of CD involves the entire bowel wall.
- The most common complaints of any patient with CD are abdominal pain and diarrhea, being found in over 75 % of patients.
- Weight loss, fever, and bleeding are present in approximately 40–60 % of patients.
- Anal symptoms of abscess and/or fistula occur in 10–20 % of patients.
- CD is most frequently found in the ileocecal region (approximately 40 %).
- Colonic disease is found in approximately 30 % and correlates with diarrhea and bleeding.
- 30 % have disease confined to the small bowel proximal to the terminal ileum and correlates with abdominal pain and bloating.
- Anal disease is associated with terminal ileal and colonic distributions of disease.
- Vienna classification of CD segregates patients into three categories based on behavior: inflammatory (B1), stricturing (B2), and fistulizing (B3).
- Patients will frequently change categories as disease progresses.
- Approximately 50 % of CD patients will be in clinical remission.
- The majority of patients (60–75 %) will have alternating years of quiescence and disease activity.
- 10–20 % will have either a chronic, unremitting course or repetitive annual flaring of disease.
- The inflammation of UC characteristically starts in the rectum and extends proximally.
- If small bowel is involved, CD should be suspected.
- Thus rectal disease results in increased stool frequency, hematochezia, and tenesmus. Diarrhea is a frequent symptom.
- Constipation with a sense of incomplete evacuation can be a complaint in 20–25 % of patients.
- With increasing severity and extent of disease, nausea, vomiting, and weight loss ensue.
- Toxic megacolon is a moniker that should be discarded, since severe life-threatening colitis may occur without colonic dilatation.

Extraintestinal Manifestations

- The most common non-GI complaints in IBD patients relate to the musculoskeletal system.
- Osteopenia and osteoporosis are very common, in part due to therapeutic steroid use, occurring in as many as 50 and 15 %.
- There is a 40 % increased risk of bone fractures in IBD patients.
- Peripheral arthritis usually affects multiple small joints and has little relation to gastrointestinal disease activity.
- Axial arthritis (ankylosing spondylitis) is associated with certain HLA subtypes (B27) and is found in approximately 5 % of both CD and UC patients. Its severity commonly parallels disease activity.
- Recently, anti-tumor necrosis factor (TNF) therapies have been shown to be effective in both CD and the arthropathy of IBD.
- Pyoderma gangrenosum and erythema nodosum occur in approximately 0.5–5 %.
- These and oral lesions such as aphthous stomatitis and pyostomatitis vegetans are more commonly associated with CD than UC and commonly parallel underlying gastrointestinal disease activity.
- There is a reported increased rate of psoriasis and eczema in IBD patients that does not parallel disease activity.
- Primary sclerosing cholangitis (PSC) has a reported incidence of approximately 3 % in both CD and UC patients.
- It may present independent of intestinal disease activity.
- Colectomy in UC patients does not affect the progression of liver disease.
- PSC in the UC patient increases the risk for malignant disease in both the colon and the hepatobiliary system.
- Iritis, uveitis, and episcleritis can affect 2–8 % of patients with UC and CD, respectively, and are generally unrelated to disease activity.
- Iritis and uveitis present as blurred vision, eye pain, and photophobia. These require prompt treatment to avoid scarring and even blindness.
- There is an identified increased risk of deep venous thrombosis (DVT), mesenteric thrombosis, and pulmonary embolism (PE).
- Decreased protein S and antithrombin III levels due to mucosal loss and increased levels of acute-phase reactants including factors V and VIII have been implicated.

Disease Severity Assessment

- The CD activity index (CDAI) is the most commonly used method for quantification of disease severity in CD (Table 27.2).
- It is generally accepted that a total score less than 150 points indicates quiescent disease, whereas over 450 indicates severe, active disease.

Table 27.2 The Crohn's disease activity index (CDAI)

Item calculation	Data-collected weighing factor	
No. of liquid stools	7-day diary 2	Sum of 7 days
Abdominal pain	0–3 scale, 7-day diary 5	Sum of score for each day
General well-being	0–4 scale, 7-day diary 7	Sum of score for each day
Symptoms[a]	At clinic visit 20	Sum (6 total) possible
Lomotil use	7-day diary 30	Yes = 1, No = 2
Abdominal mass	At clinic visit 10	None = 0, questionable = 2, definite = 5
HCT	At clinic visit	M: (47 subtract patient's HCT) F: (42 subtract patient's HCT)
Weight	At clinic visit	% below ideal weight

HCT hematocrit
[a]See table in chapter of text for explanation

Table 27.3 Truelove and Witts ulcerative colitis activity index

	Mild	Severe
Bowel frequency	<4	>6
Blood in stool	+	+++
Fever	Absent	>37.5
Pulse	<90	>90
Hgb	>75 % nl	<75 % nl
ESR	<30	>30

- Relapses are defined as a score rising to over 150 or an increase of 100 points over baseline.
- Symptoms 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.
- Clinical assessment tool for severity assessment in UC (Table 27.3).

Evaluation

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, tubelike colon that can be seen with air contrast (Fig. 27.3).

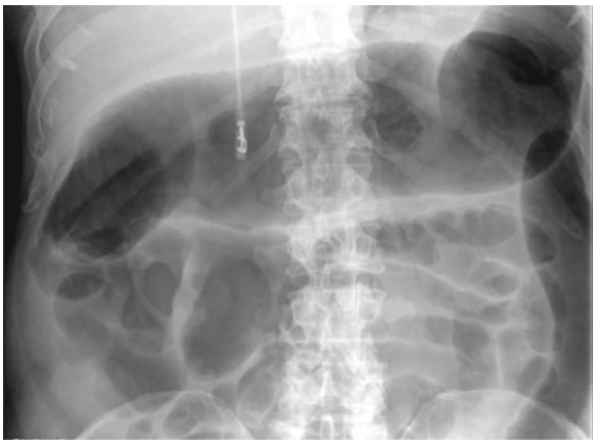

Fig. 27.3 Plain radiographs of a patient with worsening symptoms of ulcerative colitis. Note the ahaustral left and transverse colon, signs of small-bowel ileus, and enlarged ("mega") transverse colon

- Fulminant colitis may result in toxic dilatation (toxic megacolon) that mandates surgical intervention.

Contrast Radiologic Studies

- Colonic contrast studies in the patient with CD can reveal segmental disease, strictures, and fistulas (Fig. 27.4).
- Reflux into the terminal ileum occurs in approximately 85 % and can more effectively reveal ileal disease than small-bowel follow-through.
- When fistulas or near-obstructing strictures are suspected, a water-soluble dye such as Gastrografin is preferred.
- A small-bowel series can effectively show areas of stricturing and upstream dilatation (Fig. 27.5).
- Enteroclysis is preferred over simple small-bowel follow-through.
- Gastrointestinal contrast studies surpass computed tomography (CT) for detecting enteroenteric and enterocolic fistulas (Fig. 27.4).
- Sinography or fistulography can be used to delineate the path or origin of fistulous disease in patients with CD.
- Such contrast studies can also be done via the drainage catheter after percutaneous drainage of an abscess to document intestinal communication.

Computed Tomography

- Abdominal and pelvic CT is probably the most commonly obtained study in the acute evaluation of patients with IBD, especially CD.
- Such studies should be undertaken with orally ingested low-density barium or iodinated contrast material.
- Rectal administration of contrast material will sometimes be necessary.

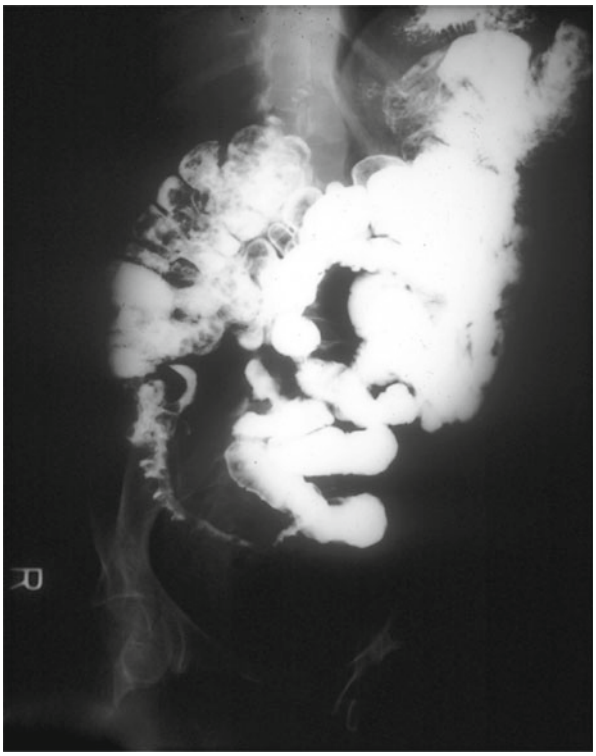

Fig. 27.4 Small-bowel follow-through contrast study showing terminal ileal stricturing disease, with displacement of adjacent bowel loops due to ileal thickening

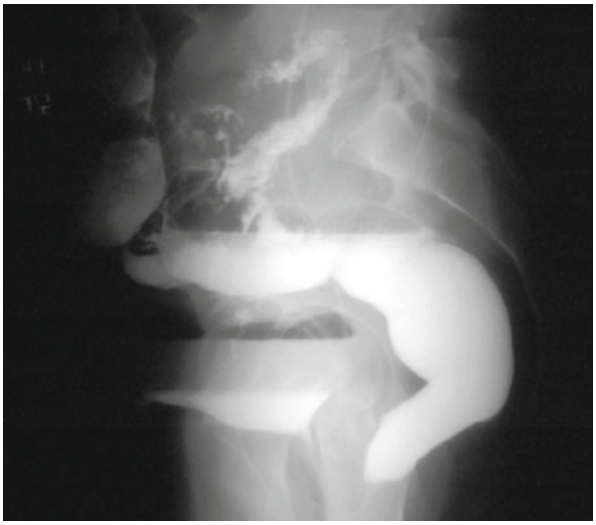

Fig. 27.5 Colonic contrast study in Crohn's disease patient showing complex fistulizing disease. Contrast is present in the proximal, diseased ileum and air and contrast in the bladder due to fistulizing disease

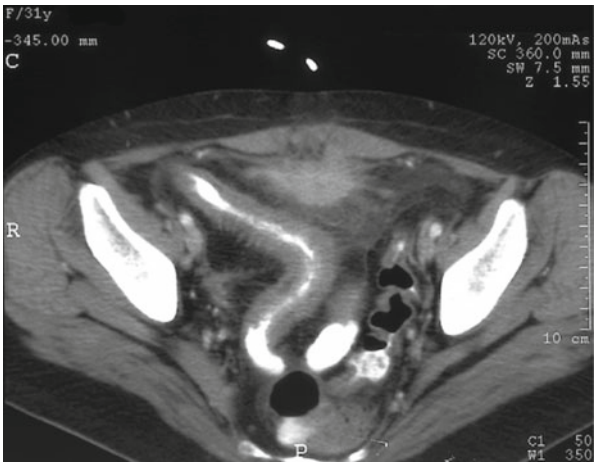

Fig. 27.6 Computed tomography scan of Crohn's disease patient with severe terminal ileal thickening and early abscess formation under anterior abdominal wall

- CT scanning is useful for 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.
- Fistula formation is a sign of CD that can be found on CT scan (Fig. 27.6).
- Percutaneous drainage of abscess collections done under CT guidance can also be performed.

Magnetic Resonance Imaging

- Intestinal CD can be identified simply by thickened bowel loops on conventional MRI.
- The intensity of T2-weighted signals from areas of disease correlates with the severity of inflammation, especially after gadolinium administration.
- The value of MRI in defining perineal disease in the CD patient approaches – and may exceed – that achieved with examination under anesthesia.
- Endorectal coil placement may improve sensitivity.
- Intravenous injection of gadolinium highlights the fistula tract, and combined with MRI's ability to define soft tissue anatomy accurately, it can result in remarkable delineation of disease.

Ultrasound

- The role of ultrasound in IBD is presently very limited.
- Transabdominal bowel sonography (TABS) can look for bowel wall thickening and fistula formation and can even assess functional effects of strictures by observing bowel peristalsis and distention in the vicinity of such.

Table 27.4 Indications for colonoscopy in inflammatory bowel disease

Diagnosis	Gross appearance
	Tissue biopsy
Disease extent	
Disease complications	Fistulas
	Stricture
	Bleeding
Preoperative "staging"	
Monitor response to therapy	
Stricture management	Biopsy
	Dilatation
Cancer surveillance	

- Intrarectal ultrasound can be used to document and map perianal fistula formation by injecting a solution of hydrogen peroxide into the external opening.

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.
- Indium^{111} has the advantage of a long half-life that allows scanning at 6, 12, and 24 h.
- Newer techniques using technetium-99m hexamethylpropylene amine oxime (HMPAO) provide for better image quality, with lower radiation exposure.

Endoscopy

- Colonoscopy is the study of choice for the patient with suspected UC since it can directly visualize the entire extent of the disease process. It is similarly relevant for CD.
- There are numerous indications for colonoscopy in the patient with IBD (Table 27.4).
- The gross appearance of the colon as seen on colonoscopy can frequently differentiate between CD and UC (Table 27.5).
- Colonoscopy is generally avoided in the acute setting.
- Rigid or flexible proctoscopic evaluation with biopsies done in the lower rectum may be performed in the acute setting below the peritoneal reflection in order to minimize risk of free preforation.
- There is an increasing experience with through-the-scope (TTS) pneumatic dilatation of colonic or ileocolonic strictures in CD.
- The technique incorporates repetitive insufflation of the TTS balloon for 15–60-s periods, with the larger balloons (25 mm) being associated with more patient pain and complications than the smaller ones (12 mm).
- Esophagogastroduodenoscopy (EGD) will infrequently be used in the management of CD since gastroduodenal CD occurs in less than 5 % of patients.

Table 27.5 Gross (colonoscopic) features of colitis

	Ulcerative colitis	Crohn's disease
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	Mucosal bridging of colon
	Mucosal bridging	

- EGD is useful in the evaluation of the differential diagnosis of upper abdominal pain or dysphagia in the IBD patient.
- Push enteroscopy using specially designed flexible scopes has been developed to improve access of the endoscopist to the jejunum, but its use is very limited.

Wireless Capsule Endoscopy

- An 11×26 mm capsule is swallowed that transmits two video images per second to a receiver worn on the belt.
- 50,000 images are transmitted and stored that are subsequently evaluated at 25 frames per second by dedicated software and the human eye.
- Its role in CD is still being clarified.
- The size of the capsule may cause it to impact at a stricture, precipitating acute bowel obstruction requiring surgery.

Pathology

Ulcerative Colitis

- UC begins in the rectum and extends proximally to a variable distance, with the worst disease being distal and the least disease being proximal.
- The disease is in continuity, and segmental or "skip" disease does not occur.
- Gross appearance of the inflammatory process depends on the severity and duration of the disease (Table 27.5).
- The histopathologic features of UC are listed in Table 27.6.
- There are no pathognomonic features of UC, and in its extreme form, it can resemble CD.

Table 27.6 Histology of inflammatory bowel disease

	Ulcerative colitis	Crohn's disease
Early	Crypt distortion, branching	Patchy crypt distortion
	Goblet cell mucin depletion	Minimal goblet cell mucin depletion
	Vascular congestion (without inflammation)	Aphthoid ulcers
	Mucosal inflammation	
Intermediate	Uniform crypt abscesses	Focal crypt abscesses
	Loss of mucosa with retention of crypts	Vasculitis (20 %)
	Noncaseating granulomas	
	Lamina propria neutrophils	(20–60 %) Mononuclear cell infiltrate
Advanced/late	Crypt destruction	Transmural inflammation
	Neuronal hyperplasia uncommon	Neuronal hyperplasia common
	Deeper submucosa inflammation	Mucosal and submucosal
	Pseudopolyp, mucosal thickening bridging	Fibrosis and strictures

- 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 UC from CD where mucin depletion is uncommon and the inflammation is usually mononuclear.
- More severe UC leads to the entire loss of the crypt, with deeper submucosal and transmural inflammation and ulceration.
- In the chronic, more quiescent phase, UC will have mucosal reconstitution but will still have crypt distortion, foreshortening, and branching. Dysplasia in long-standing UC is common but can be interpreted only in the setting of non-inflamed bowel, since many of its features are common with inflammation, namely, crypt distortion, increased mitotic index, and nuclear atypia.

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.
- On the mucosal surface, the earliest changes are aphthous ulcers.
- These lesions are thought to then enlarge and coalesce into the larger, deeper longitudinal serpiginous ulcers.
- Microscopically, the inflammatory infiltrate is commonly mononuclear and there is minimal goblet cell dropout in the mucosa.

- When crypt abscesses occur, they are nonuniform, affecting some crypts and not others.
- Vasculitis is sometimes seen (20 %) and neuronal hyperplasia is common, both features that are rarely seen 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 patients with colitis will have either clinical or pathologic features that do not allow a clear diagnosis of either CD or UC.
- The diagnosis of more than half of indeterminate cases can usually be resolved with consideration of the entire clinical picture in conjunction with discussion with the pathologist.

Serum Tests for IBD

- The prototypic acute-phase reactant is the erythrocyte sedimentation rate (ESR), which is commonly used, especially in CD in spite of its imperfect correlation with disease activity.
- Some have suggested that ESR correlates better with colitis, either CD or UC, than with small-bowel CD.
- The fecal excretion of alpha-1-antitrypsin when measured as a clearance ratio has some correlation to active intestinal disease, but difficulty with collection methodology makes this test rarely used.
- Presently, ESR and possibly CRP are the only two tests commonly used in the clinical arena.
- Albumin, prealbumin, and iron (transferrin and serum iron) studies 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 commonly decreased in CD patients with ileal disease or after surgical resection.
- IL-1, IL-2, IL-6, IL-8, TNF, CD45, soluble IL-2, and interferon gamma have not been used beyond investigative protocols.
- Perinuclear antineutrophil cytoplasmic antibody (pANCA) is an autoantibody found in the serum of approximately 50–70 % of UC patients but only in 20–30 % of CD patients.
- It does not correlate with disease activity but is thought to indicate a more aggressive disease type. A serum antibody, to a common yeast, *Saccharomyces cerevisiae* (ASCA), has been shown to be present in 50–70 % of CD patients but only in 10–15 % of UC patients.

- The measurement of both ANCA and ASCA is increasingly being used to try to differentiate between CD and UC when the disease is limited to the colon and confusing features, such as rectal sparing, exist.
- Three mutations affecting the CARD15/NOD 2 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 play a role in innate immunoresponsiveness to enteric bacteria.
- Mutations in this gene are found in approximately 10–30 % of CD patients versus 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 in the general population.
- The presence of this mutation in a patient with CD is associated with ileal disease, earlier age of onset, and possibly fibrostenosing characteristics.

Evaluation of the Acute Patient with Acute Exacerbation of IBD

- There is no one good test for IBD, so the clinical judgment, experience and acumen of the caregiver is key.
- A basic outline of evaluation of the acutely presenting IBD patient is found in Table 27.7.

Table 27.7 Evaluation of the patient with inflammatory bowel disease

	Test	Purpose
Serum labs	CBC	r/o anemia, leukocytosis
	Electrolytes, renal function	r/o electrolyte disturbance 2° diarrhea, dehydration
	ESR, +/− CRP	↑ in systemic disease
	LFTs, albumin	r/o PSC, nutritional compromise
Stool studies	C. difficile	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, and distribution of disease
	CT scan	For abscess, obstruction, fistulas, and adjacent organ involvement
Endoscopy	Flexible/rigid scope colonoscopy	For biopsy to r/o CMV, granulomas, pseudomembranes
		For biopsy, visualize extent and severity of disease

SBFT small-bowel follow-through, *r/o* rule out, *CMV* cytomegalovirus, *LFTs* liver function tests, *CT* computed tomography, *O&P* ova and parasites, *ESR* erythrocyte sedimentation rate, *CRP* C-reactive protein, *CBC* complete blood cell count, *PSC* primary sclerosing cholangitis

28. IBD: Medical Management

Bruce E. Sands

Introduction

- The cause of inflammatory bowel disease (IBD) is unknown, but it is believed to be an uncontrolled immune response within the intestinal mucosa leading to inflammation in genetically predisposed individuals.
- Multifactorial evidence suggests a defect of innate immune response to microbial agents and abnormalities in adaptive immunity and epithelial barrier function.
- The goals of therapy include controlling symptoms, improving quality of life, and minimizing short-term and long-term complications of disease and treatment.
- There are two phases of treatment: (1) inducing remission in active disease and (2) maintaining remission.
- Surgery is usually reserved for treating medically refractory disease or for specific complications.

Crohn's Disease: Medical Management

- CD is a chronic inflammatory condition that can affect any area of the gastrointestinal tract from the mouth to the anus.
- The disease most commonly affects the ileum and colon.

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Mild-to-Moderate Crohn's Disease

- Individuals with mild-to-moderate disease have fewer than four stools daily and are ambulatory and able to tolerate solid foods and liquids.
- Aminosalicylates and antibiotics are often used to treat mild-to-moderate Crohn's disease.
- The topically acting steroid, budesonide, is increasingly used as a drug of choice for mild-to-moderate disease of the terminal ileum or proximal colon.

Sulfasalazine and 5-Aminosalicylates

- Sulfasalazine (SSZ) and 5-aminosalicylates (5-ASA) are often used as first-line therapy.
- The National Cooperative Crohn's Disease Study demonstrated the benefits of SSZ 6 g/day over placebo for up to 16 weeks in patients with active ileocolonic and colonic CD.
- In contrast, SSZ did not induce remission at 3 g/day as monotherapy but was shown to be beneficial in combination with methylprednisolone.
- SSZ is not consistently effective for patients with active disease limited to the small intestine.
- Delayed-release formulations of mesalamine include Eudragit-S-coated mesalamine (Asacol®) that releases 5-ASA in the terminal ileum and cecum at pH 7 and Eudragit-L-coated mesalamine formulations (Salofalk®, Mesasal®, and Claversal®) that release in the mid-ileum at pH 6.
- 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 dimers, olsalazine (Dipentum®) and balsalazide (Colazal®), which are composed of 5-ASA molecules azo-bonded to the inert carrier molecule 4-aminobenzoyl-β alanine.
- Lialda® is a delayed-release tablet containing mesalamine that allows for once-daily dosing and releases at pH 7 or above, normally in the terminal ileum.
- Apriso®, also a mesalamine compound, is an extended-release capsule that is taken once daily and dissolves at pH 6 starting in the small intestine and continuing throughout the colon.
- 5-ASA has not consistently demonstrated efficacy in controlled clinical trials.
- Table 28.1 describes dosing guidelines for SSZ and 5-ASA. Response to therapy should be evaluated after 6–12 weeks.
- Topically delivered preparations of 5-ASA (suppositories, enemas) have not been evaluated in controlled trials in patients with distal colonic CD.
- SSZ and 5-ASA are not recommended for maintenance of remission.

Table 28.1 Sulfasalazine and 5-aminosalicylates

Generic	Brand	Daily dose	Site of action
Sulfasalazine	Azulfidine	4–6 g daily in divided doses	Colon
	Azulfidine EN-Tabs	4–6 g daily in divided doses	Colon
Mesalamine	Canasa (suppositories)	500–1,000 mg daily QHS	Rectum
	Rowasa (enemas)	1–4 g daily QHS	Rectum/distal colon
	Asacol	2.4–4.8 g daily in divided doses	Terminal ileum/colon
	Pentasa	2–4 g daily in divided doses	Distal small bowel/colon
	Lialda	2.4–4.8 g daily in a single dose	Colon
	Apriso	1.5 g daily in a single dose QAM	Colon
Olsalazine	Dipentum	1.5–3 g daily	Colon
Balsalazide	Colazal	6.75 g daily	Colon

- Headache and gastrointestinal upset are common dose-dependent side effects of SSZ.
- SSZ depletes folate and should therefore be given with a folate supplement.
- SSZ may cause reversible sperm abnormalities, leading to relative infertility that reverses within 3 months of stopping the drug.

Antibiotics

- Antibiotics are valuable in treating perianal or perforating complications of CD.
- Side effects occur in up to 50 % of patients who take metronidazole short term and include gastrointestinal intolerance, metallic taste, and reaction to alcohol.
- Peripheral neuropathy, possibly irreversible, may occur with long-term use.
- Ciprofloxacin was shown in one study to be as effective as 5-ASA for achieving remission in mild-to-moderate active disease.
- Combination treatment with metronidazole and ciprofloxacin may be an alternative to steroid treatment in mild-to-moderate active CD.
- Side effects include gastrointestinal upset, skin reactions, and an increase in transaminase levels.
- Ciprofloxacin has been associated with rare cases of tendonitis and Achilles tendon rupture.

Budesonide

- Multiple randomized controlled trials have demonstrated the efficacy of budesonide over placebo for the induction of remission in patients with mild-to-moderately active ileal or ileo-right colonic disease.

- Budesonide has also been shown to be a more effective treatment than 5-ASA.
- Several studies have compared budesonide with prednisone and found that rates of clinical remission were similar in each group and the occurrence of corticosteroid-related side effects was considerably less.

Moderate-to-Severe Crohn's Disease

- The treatment options for these patients include corticosteroids, biologic agents, and the early addition of immunomodulator therapy with azathioprine (AZA), 6-mercaptopurine (6-MP), or methotrexate (MTX) as an adjunct or a bridge to maintenance therapy.

Oral Corticosteroids

- Oral corticosteroids are effective for the induction of remission in patients with moderate-to-severe CD.
- Prednisone doses of 40–60 mg daily are often prescribed for 2–6 weeks to induce remission.
- 50–70 % of patients will achieve remission at these doses. Higher doses of prednisone (1 mg/kg) or methylprednisolone (1 mg/kg) have had somewhat higher response rates of 80–90 %; however, there is an increased incidence of side effects.
- Prednisone doses are tapered by 5–10 mg/week until 20 mg and then by 2.5–5 mg weekly from 15 or 20 mg until discontinuation of therapy.
- Corticosteroids are not recommended as maintenance agents.
- 50 % of patients treated for active symptoms with a corticosteroid will become "steroid dependent" or "steroid resistant."
- Studies suggest that younger patients, smokers, and/or those with colonic disease have the highest risk of becoming corticosteroid dependent.
- Common findings include insomnia, fluid retention, acne, moon face, abdominal striae, weight gain, hypertension, hyperglycemia, glaucoma, cataracts, and mood disturbances. Musculoskeletal complications, such as osteoporosis, osteonecrosis, and myopathy, are important side effects.

Immunomodulators

- AZA and 6-MP are effective for maintaining a corticosteroid-induced remission and are beneficial as steroid-sparing agents.
- In clinical practice, AZA 2.0–2.5 mg/kg and 6-MP 1.01.5 mg/kg are used for maintenance therapy.
- Clinical benefit may not be evident for 3–4 months after initiation but may be durable.
- Adverse events include leukopenia, liver function abnormalities, pancreatitis (3–7 %), and lymphoma.

- Monitoring of complete blood counts, initially every 1–2 weeks, then, at least every 3 months, is recommended.
- Nonmelanoma skin cancers and cervical cancer may also occur more frequently. There is a slightly increased risk of lymphoma.
- Genetic polymorphisms of thiopurine methyltransferase (TPMT), the primary enzyme metabolizing 6-MP, have been identified, and drug metabolite levels may be measured.
- Prior to starting AZA or 6-MP, TPMT enzyme activity or genotype should be determined.
- AZA and 6-MP should be avoided in patients deficient in TPMT.
- Patients with heterozygous genotype of intermediate activity should initiate therapy at reduced doses, generally, AZA 1.0–1.25 mg/kg or 6-MP 0.5–0.75 mg/kg daily.

Methotrexate (MTX)

- MTX may be used to induce remission and as a steroid-sparing agent in patients with corticosteroid-refractory or corticosteroid-dependent CD.
- Folic acid 1 mg daily is routinely given.
- MTX is an alternative agent to AZA and 6-MP for maintenance of remission.
- MTX is contraindicated in pregnancy as it is teratogenic and abortifacient.

Biologic Therapy

- Biologic therapies (primarily anti-tumor necrosis factor antibodies) have been considered when CD is moderately to severely active despite therapy with aminosalicylates, corticosteroids, and/or immunomodulators or if corticosteroids or immunomodulators are contraindicated, not tolerated, or ineffective.
- Biologic therapy may also be indicated if patients are corticosteroid dependent or refractory.
- Patients with complications such as draining fistulas or extraintestinal manifestations may derive particular benefit from biologic therapy.
- Infliximab (chimeric monoclonal antibody) has been shown to effectively induce remission in patients with moderate-to-severe CD and to maintain remission in those patients.
- Infliximab is also useful for treating patients with corticosteroid-dependent and fistulizing disease.
- Patients treated with infliximab experience fewer hospitalizations and surgeries related to CD.
- The occurrence of extraintestinal manifestations, such as spondyloarthropathy, arthralgias, and pyoderma gangrenosum, may be reduced with infliximab.
- Approximately 30 % of patients have no response to infliximab, and not all responders have a complete response.

- Elevated C-reactive protein (CRP), nonstricturing and pure colonic disease subtypes, and concomitant use of immunomodulators have been described as positive predictors for response to infliximab. AZA and 6-MP are most commonly used as concomitant suppression. Methotrexate (MTX) may also be used.
- Initial response rates to adalimumab and certolizumab pegol were 58 % (the Netherlands randomized patients).
- Initiation of more intensive treatment early in the course of disease may result in better outcomes.
- Significantly more patients treated with infliximab alone or the combination of infliximab and azathioprine had relief of symptoms than patients treated with azathioprine alone.
- Patients with CD who are naive to immunomodulators and biologic agents are more likely to have enhanced mucosal healing when they are treated with infliximab and AZA and attain a corticosteroid-free clinical remission.
- Response to anti-TNF agents decreases with longer duration of disease.
- Natalizumab is a humanized monoclonal antibody that targets human α_4 integrin, thereby interfering with trafficking of leukocytes into the mucosa.
- Natalizumab is indicated for the induction and maintenance of response or remission in patients with moderate to severely active CD.
- Natalizumab should only be used in patients who are refractory or intolerant to immunomodulators and anti-TNF therapy and for whom surgery is not an acceptable option. See Table 28.2 for specific indications and Table 28.3 for dosing guidelines for biologic therapies.
- Anti-TNF agents and natalizumab have been shown in randomized placebo-controlled trials to be effective for maintenance of remission in patients with moderate-to-severe CD

Loss of Response to Anti-TNF Agents

- One-third of patients who initially respond to an anti-TNF agent will subsequently lose response over the course of 6–12 months.
- Therefore, a reasonable approach to loss of response to infliximab is to test for HACA and levels of infliximab. Patients with detectable HACA (normal <1.69 mcg/ml, levels ≥8 mcg/ml associated with loss of response) should be changed to an alternative anti-TNF agent, or less desirably, the dose could be increased.
- Concomitant immune suppression with AZA, 6-MP, or MTX reduces the development of antibodies.

Adverse Events Associated with Biologics

- Infusion or injection site reactions, autoimmunity (positive ANA, anti-double-stranded DNA antibodies; rare lupus-like reactions), activation of latent tuberculosis, and development of opportunistic infections.
- Fungal infections caused by *Histoplasma capsulatum*.

Table 28.2 Indications for biologic therapies

	Crohn's disease				Ulcerative colitis
Indication	Infliximab	Adalimumab	Certolizumab	Natalizumab	Infliximab
Induction of response and remission	X	X	X	X[1]	X
Maintenance of response and remission	X	X	X	X	X
Mucosal healing	X	X	X		X
Induction of response in adults with draining perianal fistulas	X	X			
Induction of response in adults with draining abdominal or rectovaginal fistulas	X				
Steroid-sparing agent	X	X		X	X
Treatment of spondyloarthropathy, arthritis/arthralgia, pyoderma gangrenosum and erythema nodosum, uveitis, and other ocular manifestations of Crohn's disease	X	X			X
Loss of response or intolerance to infliximab		X	X	X	

X[1] Must have also failed anti-TNF therapy and have evidence of inflammation

- All patients should be screened for tuberculosis with tuberculin skin testing (and chest X-ray if skin testing is positive) prior to initiating therapy with infliximab.
- Leukopenia, neutropenia, thrombocytopenia, or pancytopenia.
- Rarely, liver toxicity may occur and present as acute liver failure, jaundice, hepatitis, and cholestasis.
- Neurologic disorders including optic neuritis, seizures, and new onset or exacerbation of central nervous system demyelinating disorders, including multiple sclerosis.
- Hepatosplenic T-cell lymphoma, a lethal form of non-Hodgkin's lymphoma. Natalizumab may cause headache or rare infusion reactions.

Contraindications to Biologic Therapies

- Contraindications to anti-TNF agents are consistent across the class and include the following:
  1. Known hypersensitivity to agent, if severe.
  2. Active infection.

Table 28.3 Dosing guidelines for biologic therapy

Biologic agent	Induction regimen	Maintenance dose	Attenuated response	Discontinue therapy
Infliximab	5 mg/kg IV at weeks 0, 2, and 6	5 mg/kg IV every 8 weeks beginning at week 14	10 mg/kg at 8-week intervals, or 5 mg/kg every 4 weeks	No response after two doses or infusions are required more frequently than every 4 weeks
Adalimumab	160 mg SC on day 1 of week 0, then 80 mg SC on day 1 of week 2	40 mg SC every other week	40 mg SC weekly or 80 mg every other week	No response to induction therapy or duration of response decreases to less than 1 week
Certolizumab	400 mg SC at weeks 0, 2, and 4	400 mg SC every 4 weeks	Extra dose of 400 mg SC 2 weeks after last dose	No response to induction therapy or when the duration of response decreases to 2 weeks
Natalizumab	300 mg IV at weeks 0, 4, and 8	300 mg IV every 4 weeks	Other dosing regimens have not been adequately evaluated	Lack of response or inability to discontinue steroids by week 12

3. Untreated latent tuberculosis.
4. Preexisting demyelinating disorder.
5. Moderate-to-severe congestive heart failure.
6. Current or recent malignancy, without advice from an oncologist.
7. Further treatment with infliximab is contraindicated when the patient presents with uncontrolled infusion reactions.

Contraindications to Natalizumab

1. Known hypersensitivity to agent, if severe
2. Active infection
3. Current or past PML
4. Liver disease
5. Continued treatment with an immune modulator or anti-TNF antibody

Tacrolimus

- Various small studies have shown a trend toward clinical benefit especially in fistulizing disease.
- Oral therapy is usually started with 0.1–0.2 mg/kg/day as a twice-daily divided dose.
- Adverse effects: renal insufficiency, liver function abnormalities, infection, hyperglycemia, hypertension, and myelosuppression.

- Drug levels, blood counts, liver enzymes, renal function, glucose level, and blood pressure need to be monitored.

Severe Crohn's Disease

- Symptoms include high fever, frequent vomiting, evidence of intestinal obstruction, rebound tenderness, cachexia, or evidence of an abscess.
- Severe disease may be treated with high-dose intravenous corticosteroids.
- AZA or 6-MP should be initiated in patients who respond to IV corticosteroids.
- A patient who does not respond after 5–7 days of therapy may benefit from infliximab or intravenous (IV) cyclosporine (CSA).
- Failure to respond to medical therapy or worsening symptoms are indications for surgery.

Indications for Surgery in Crohn's Disease

- Approximately two-thirds of patients with CD will require surgery.
- The disease predictably recurs at the anastomotic site, and stricturoplasty is a reasonable surgical alternative if previous small-bowel resections place the patient at risk of short bowel syndrome.
- Any patient who fails to respond to 7–10 days of intensive inpatient management should be strongly considered for surgery.
- The indications for emergency surgery include primary free perforation or secondary rupture of an abscess into the peritoneal cavity and massive, uncontrollable hemorrhage.
- Urgent surgical procedures are required for fulminant Crohn's colitis with or without toxic megacolon and severe perianal sepsis.
- Elective procedures are an option for definitive treatment of intra-abdominal abscesses, complete or incomplete obstruction of the bowel, or an intractable course of disease (including steroid dependence or steroid resistance) and neoplastic or preneoplastic lesions.

Crohn's Disease: Maintenance Therapy After Medical Induction of Remission

- Randomized controlled trials investigating the use of SSZ or 5-ASA have not demonstrated significant maintenance benefits in CD.
- 5-ASA (at a dose of 4 g daily) has not been efficacious in preventing relapse after corticosteroid-induced remissions.
- Immunomodulators, including AZA, 6-MP, and MTX, as well as anti-TNF agents and natalizumab may be effective maintenance agents.

Postoperative Reoccurrence of Crohn's Disease and Prophylaxis

- Factors associated with an increased risk of early postoperative recurrence include smoking, absence of prophylactic postoperative therapy, and extent of disease greater than 100 cm.
- SSZ has not been statistically superior to placebo in preventing postoperative relapse. 5-ASA is associated with a modest pooled risk reduction of 13 % for those patients with surgically induced remissions with isolated small-bowel disease.
- Data supporting the use of AZA and 6-MP for prevention of postoperative recurrence are limited; however, the data suggest possible efficacy.
- Infliximab may be used as a postoperative prophylactic agent. It has been shown to prevent postoperative clinical and endoscopic recurrence after ileocecal resection.
- Imidazole antibiotics, including metronidazole, decrease short-term, but not long-term, endoscopic recurrence and are limited by side effects. Corticosteroids do not prevent postoperative relapse.
- There is insufficient evidence to support the use of probiotics in preventing postoperative recurrence of CD.
- Overall, there are no consistent recommendations regarding medical therapy after surgical resection for Crohn's disease.

Perianal Crohn's Disease

- Medications commonly used for the treatment of perianal fistulas include antibiotics, immunomodulators, and anti-TNF agents.
- There is no role for the use of 5-ASA or corticosteroids in the treatment of perianal fistulas.
- Perianal fistulas typically respond to metronidazole alone or in combination with ciprofloxacin; however, continuous therapy may be necessary.
- Simple, superficial fistulas may respond completely to fistulotomy and antibiotics. Complex fistulas may respond best to combined medical/surgical approaches.
- Infliximab is effective at acutely closing fistula and maintaining closure with maintenance dosing.

Ulcerative Colitis: Medical Management

Proctitis

- Treated with topical therapies such as enemas or suppositories or oral agents.
- Topical formulations of 5-ASA are considered first-line therapy for the treatment of proctitis. These agents are considered more effective than

rectal steroids and have been shown to be more effective than oral 5-ASA.
- Suppositories are preferred over enemas.
- Response is usually seen within 2–3 weeks with increased response rates (63–79 %) at 4–6 weeks.
- For patients not responding to rectal 5-ASA alone, combination treatment with topical corticosteroids (foam or enema) is better than either therapy alone.

Distal Ulcerative Colitis

- Patients with distal colitis can be treated with topical 5-ASA (suppositories, enemas), topical corticosteroids (suppositories, enemas), oral 5-ASA, or a combination of these agents.
- Rectal therapies may have a more rapid effect than oral therapies. Rectal 5-ASA is considered superior to rectal corticosteroids for inducing remission; however, combination therapy with a topical corticosteroid may be more effective than monotherapy.
- Therapy with a combination of oral and rectal 5-ASA achieves higher remission rates than either therapy alone.

Mild-to-Moderate Extensive Ulcerative Colitis

Sulfasalazine and 5-Aminosalicylates

- SSZ and oral 5-ASA are considered first-line agents for induction of remission in mild-to-moderate UC. SSZ achieves remission in 64–80 % of patients at doses of 2–6 g daily.
- Clinical response can be achieved in up to 84 % of patients taking a 5-ASA.
- Combining oral 5-ASA with topical 5-ASA preparations has been shown to be well tolerated and more efficacious in patients with extensive UC.

Corticosteroids

- Oral corticosteroids successfully induce remission in the majority of patients.
- Doses of prednisone 20–60 mg/day are often used, but doses greater than 60 mg/day have no additional benefit.
- Prednisone is tapered by 5–10 mg weekly until 15–20 mg, then tapered by 2.5–5 mg weekly.

Severe and Fulminant Extensive Ulcerative Colitis

Intravenous Corticosteroids

- Approximately 60 % of patients with severe/fulminant colitis treated with IV corticosteroids respond fully.
- Doses of hydrocortisone 100 mg IV three times daily or methylprednisolone 60 mg IV daily are used to induce remission.
- Continuous infusion of corticosteroids is not more efficacious than bolus dosing. Patients who fail to improve within 3–7 days (depending on severity of illness) should be considered for colectomy or rescue therapy with CSA or infliximab.

Azathioprine/6-Mercaptopurine

- In patients with persistently active, steroid-dependent, or steroid-refractory UC, immunomodulators (AZA or 6-MP) should be considered.
- AZA or 6-MP can induce a clinical remission or response in 30–50 % of patients, improve overall symptoms, and allow the dose of steroids to be reduced or discontinued.
- Infliximab is an alternative agent for refractory disease.

Cyclosporine

- Intravenous CSA is used as rescue therapy for severe corticosteroid-refractory UC.
- Studies report response rates between 70 and 80 % in patients with this type of UC.
- CSA is initiated as a continuous infusion while continuing IV corticosteroids.
- General improvement is seen within 4–5 days of initiating treatment.
- If no improvement is noted within 7 days or the condition deteriorates during treatment with CSA, surgery should be considered.
- Symptoms of CSA toxicity include infection, paresthesia, nausea, tremors, headache hypertension, and permanent or temporary renal toxicity.
- Patients who are noncompliant, have a history of uncontrolled seizures, or active infection should not receive CSA.

Tacrolimus

- Tacrolimus is a steroid-sparing agent.
- The most common affect is mild finger tremor.

Infliximab

- Infliximab is the only anti-TNF agent approved for use in UC.
- It has been shown to successfully induce and maintain remission in patients with moderate-to-severe and corticosteroid-dependent UC.

- Infliximab is used as a steroid-sparing agent in patients with corticosteroid-dependent or corticosteroid-refractory UC.
- Infliximab appears to decrease the rate of colectomy at 3 months and 1 year.

Ulcerative Colitis: Maintenance Therapy After Medical Induction of Remission

- Rectal and oral 5-ASA are effective for maintaining remission of distal UC and proctitis even when used on an intermittent basis. Up to 90 % of patients with extensive colitis can be maintained in remission using oral once-daily 5-ASA therapy.
- AZA and 6-MP are useful as corticosteroid-sparing agents, for maintaining remission in patients not adequately controlled by 5-ASA alone and for maintaining CSA-induced remission.
- Infliximab is able to maintain remission in patients with UC for up to 54 weeks.

Indications for Surgery in Ulcerative Colitis

- Between 20 and 30 % of UC patients will eventually require surgery.
- Indications for emergency surgery include massive hemorrhage, toxic megacolon, perforation, and severe colitis unresponsive to medical therapy.
- Elective surgery may be performed for cancer/dysplasia, failure of therapy, adverse events resulting from medial therapy, malnutrition, growth retardation in children, and control of certain extraintestinal manifestations.

Preoperative Treatment Effect on Postsurgical Complications

- Studies have shown that corticosteroid use prior to surgery increases the risk of postoperative infectious complications.
- Patients taking corticosteroids preoperatively may have doubled the risk of infectious complications.
- Patients taking >40 mg had a considerably higher risk of developing postoperative complications.
- Treatment with AZA or 6-MP prior to surgery is not a risk factor for postoperative complications.
- Effect of preoperative infliximab on postsurgical complications is controversial.
- Two retrospective studies in patients with CD suggest that infliximab infused within 8–12 weeks before abdominal surgery is not associated with an increased rate of postoperative complications.

- Analysis of a third retrospective series found that infliximab use within 3 months prior to surgery is associated with increased rates of postoperative sepsis, abscess, and hospital readmission in patients with CD. The data regarding postsurgical complications in UC patients receiving infliximab prior to surgery are limited. Infliximab use prior to surgery may be associated with an increased risk of pouch failure and infectious complications related to the pouch.

Pouchitis

- Pouchitis is the most common long-term complication of ileal pouch anal anastomosis (IPAA).
- Patients respond to 2 weeks of ciprofloxacin at 500 mg twice daily or metronidazole 750–1,200 mg/day.
- 60 % will go on to develop a second episode, and approximately 20 % of patients will have refractory or relapsing symptoms.
- If patients relapse at least three times within 1 year, chronic maintenance therapy with lower doses of antibiotics is recommended.
- Approximately 20 % of patients develop chronic refractory pouchitis.
- Combination antibiotic therapy may be the most effective.
- Rifaximin alone or in combination with ciprofloxacin is an effective treatment. Budesonide and infliximab may be used as alternative treatments.
- Maintenance with VSL #3, a probiotic, is an option.

Crohn's Disease of the Pouch

- CD of the pouch may be treated with topical and oral 5-ASA, oral or topical corticosteroids, antibiotics, and immunomodulators.

Conclusion

- Aminosalicylates are first-line agents for the treatment of mild-to-moderate disease and for maintaining remission; however, in the case of CD, evidence of efficacy is sparse.
- Antibiotics are somewhat effective in colonic CD but are not considered useful as treatment for UC, although efficacious for the treatment of pouchitis.
- Corticosteroids are effective for inducing remission in more severe disease but are associated with multiple side effects.
- Corticosteroids are not recommended as maintenance therapy.
- Immunomodulators, AZA, 6-MP, and MTX, are best employed as maintenance agents and, in the case of AZA and 6-MP, require approximately 3–4 months to be effective.
- Infliximab is the only anti-TNF agent currently approved for use in UC.

29. Ulcerative Colitis: Surgical Management

Zuri Murrell and Phillip R. Fleshner

Introduction

- Ulcerative colitis (UC) is a diffuse inflammatory disease of the mucosal lining of the colon and rectum.
- UC manifests clinically as diarrhea, abdominal pain, fever, weight loss, and rectal bleeding.

Indications for Surgery

- Approximately 10 % of UC patients will undergo surgery for very specific reasons, including an acute flare unresponsive to medical measures; development of a life-threatening complication such as 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 either cyclosporine or infliximab in the acute setting, yet long-term effectiveness of these treatment modalities remains undefined.
- There is no reported increase in the incidence of perioperative complications after subtotal colectomy in patients treated before surgery with cyclosporine.
- There is some controversy as to whether infliximab increases the perioperative complication rate.

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- The *combined* use of cyclosporine and infliximab is not advised as there may be a higher incidence of infectious complications.Medical intractability is the most common indication for operation.
- The question of timing of surgery for cancer prophylaxis remains undefined.
- Identification of dysplasia of any grade by an experienced pathologist, especially in the absence of severe inflammation, is an indication for colectomy.
- Dysplastic mass lesions detected within colitic mucosa should be viewed with a high degree of suspicion for malignant potential.
- Elective colectomy may be indicated for severe extraintestinal manifestations such as recurrent monoarticular arthritis, uveitis, or iritis.
- Primary sclerosing cholangitis, ankylosing spondylitis, and sacroilitis are not improved by colectomy.
- The response of pyoderma gangrenosum to colectomy is unpredictable.

Emergency Versus Elective Procedures

- The four elective surgical options are:
  1. Total proctocolectomy and Brooke ileostomy
  2. Total proctocolectomy and continent ileostomy
  3. Abdominal colectomy with ileorectal anastomosis (IRA)
  4. Ileal pouch–anal anastomosis (IPAA)
- Total proctocolectomy and Brooke ileostomy remains the operation with which alternative procedures should be compared. With this procedure, patients avoid any risk for cancer, and steroid medications are eliminated. The loss of fecal continence is a significant drawback, and nonhealing of the perineal wound and the high incidence of small bowel obstruction (SBO) and ileostomy revision are not to be minimized.
- Total proctocolectomy and continent ileostomy is an attractive option since no external appliance is needed and the stoma can be placed in a less conspicuous position on the abdominal wall. Troublesome complications leading to incontinence continue to plague the postoperative course of a substantial number of patients.
- Total colectomy and IRA avoids perineal complications, has minimal risk of sexual dysfunction, is technically easy to perform, and provides near-perfect control of feces and flatus. Ileorectostomy does not achieve total excision of colorectal mucosa, 25 % patients will require subsequent rectal excision for persistent proctitis, a small percentage of patients will develop cancer in the rectal remnant, and only one-half of the patients have satisfactory long-term functional results.
- Ileal pouch–anal anastomosis 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.

- Problems such as small bowel obstruction and pouchitis continue to be a cause for concern.
- With toxic colitis, it is seldom necessary to perform a proctectomy at the time of colectomy.
- When performing an emergent operation for acute disease:
    1. Mesenteric dissection in the vicinity of the ileocecal valve should be flush with the colon in order to preserve ileal branches of the ileocolic artery and vein.
    2. It is unnecessary to mobilize the rectum within the pelvis.
    3. A Hartmann procedure is recommended.
    4. A transanal rectal drain may prevent leakage from the diseased Hartmann pouch closure site.
    5. Laparoscopic-assisted or hand-assisted subtotal colectomy is both feasible and safe.
    6. Although an IPAA can be successfully performed in patients undergoing surgery for emergent complications, this approach is generally not safe.
    7. Patients with UC receiving high-dose steroids (more than 40 mg/day) have a significantly greater risk of developing pouch-related complications.

Brooke Ileostomy

- The preoperative period should include effective patient education.
- 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.

Operative Technique

- A modified lithotomy–Trendelenburg position is chosen. The proctectomy phase is performed with the dissection close to the rectal wall, especially anteriorly in the area of Denonvilliers' fascia.
- Meticulous dissection to minimize the risk of injury to pelvic autonomic nerves is essential.
- Perineal dissection should be performed in the intersphincteric plane.
- The ileum may be anchored to the abdominal wall fascia with nonabsorbable sutures to prevent retraction of the stoma. These sutures may also help prevent parastomal herniation, but there is no controlled study demonstrating that they are effective in preventing this complication.
- A defect remains lateral to the small bowel mesentery. It is unclear whether this defect needs to be routinely closed.
- The stoma is routinely matured by removing 3–5 cm of mesentery from the end of the ileum and folding the edge of the bowel upon itself.

- To anchor the edge of the bowel, use the "three-bite" suture that includes the full thickness of the bowel, the seromuscular layer of the bowel, and the dermis of the skin.

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).
- Permanent impotence or retrograde ejaculation can occur.
- Almost 30 % of women complain of dyspareunia.
- Intestinal obstruction is a troublesome complication that can be managed conservatively in most patients.
- 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.
- 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.

Continent Ileostomy

- The continent ileostomy should be reserved for patients who have failed Brooke ileostomy or those individuals 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.
- Suspicion of CD contraindicates construction of a continent ileostomy.
- Obesity and age over 40 years are associated with an increased risk of pouch loss.
- The patient must comprehend that by learning to care for and intubate the reservoir, he or she plays an important role in its functional outcome.
- Only highly motivated, emotionally stable individuals should consider this procedure.

Operative Technique

- Using the terminal 45 cm of the ileum, an aperistaltic reservoir is created by making a 3-limb S pouch or a folded 2-limb pouch originally described by Kock (Fig. 29.1).

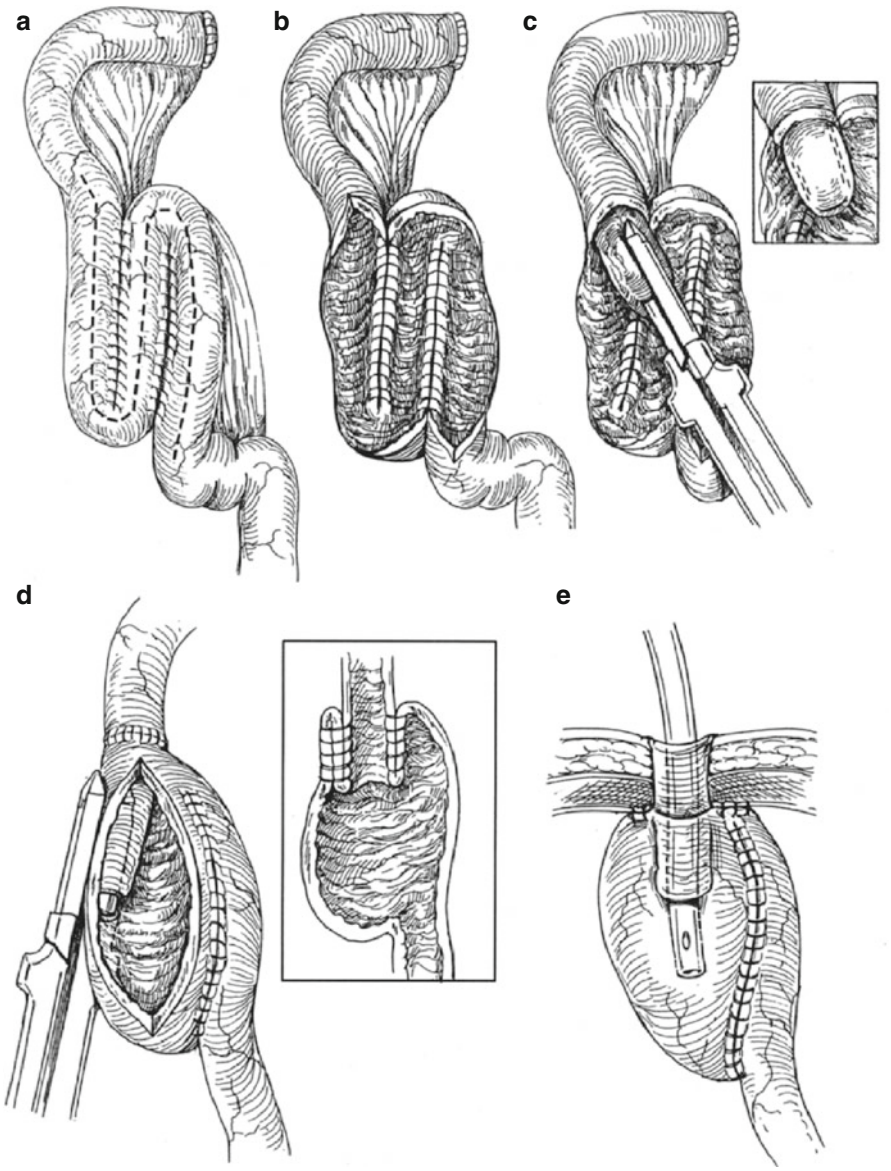

Fig. 29.1 Continent ileostomy. (**a**) Three limbs of small bowel are measured, and the bowel wall is sutured together. (**b**) After opening the bowel (see the *dotted lines* in **a**), the edges are sewn together to form a two-layered closure. (**c**) A valve is created by intussuscepting the efferent limb into the pouch and fixing it in place with a linear noncutting stapler (*inset*: staples in place on valve). (**d**) The valve is attached to the pouch sidewall with the linear noncutting stapler (a cross section of the finished pouch is shown). (**e**) After closure of the last suture line, the pouch is attached to the abdominal wall, and a catheter is inserted to keep the pouch decompressed during healing

- Intussusception of the terminal 15 cm of ileum into the pouch is performed to construct a valve.
- The intussusception is secured with multiple nonabsorbable sutures and staples.
- The stoma is sutured flush with the skin and the pouch firmly anchored to the posterior rectus sheath.
- A wide plastic tube with large openings is placed into the pouch to allow gravity drainage of the pouch in the early postoperative period.
- This tube is occluded for progressively longer periods beginning 10 days after surgery until it can be removed for 8 h without distress.

Postoperative Complications

- Nipple valve slippage occurs because of the tendency of the intussuscepted segment to slide and extrude on its mesenteric aspect.
- Nipple valve slippage results in difficult pouch catheterization, chronic outflow tract obstruction, and incontinence. It remains the most common complication (30 %).
- Pouchitis refers to nonspecific inflammation that develops in the reservoir and is thought to result from stasis and overgrowth of anaerobic bacteria. It occurs in 25 % of patients:
  - Pouchitis patients present with a combination of increased ileostomy output, fever, weight loss, and stomal bleeding.
  - The diagnosis is made by history and confirmed by pouch endoscopy.
  - Pouchitis usually responds to a course of antibiotics and continuous pouch drainage.
- Other complications include intestinal obstruction (5 %) and fistulas (10 %).
- Fistulas most commonly originate in the pouch itself or at the base of the nipple valve.
- 90 % of patients eventually have total continence after one or more procedures.
- Barnett modification of the Kock pouch (Fig. 29.2) uses the afferent limb of small bowel to construct the nipple valve and wraps a portion of the residual efferent limb around the nipple valve.
- There are no controlled data to suggest that this modification is any better than the standard procedure.

Ileorectal Anastomosis (IRA)

- 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 where rectal compliance remains adequate.

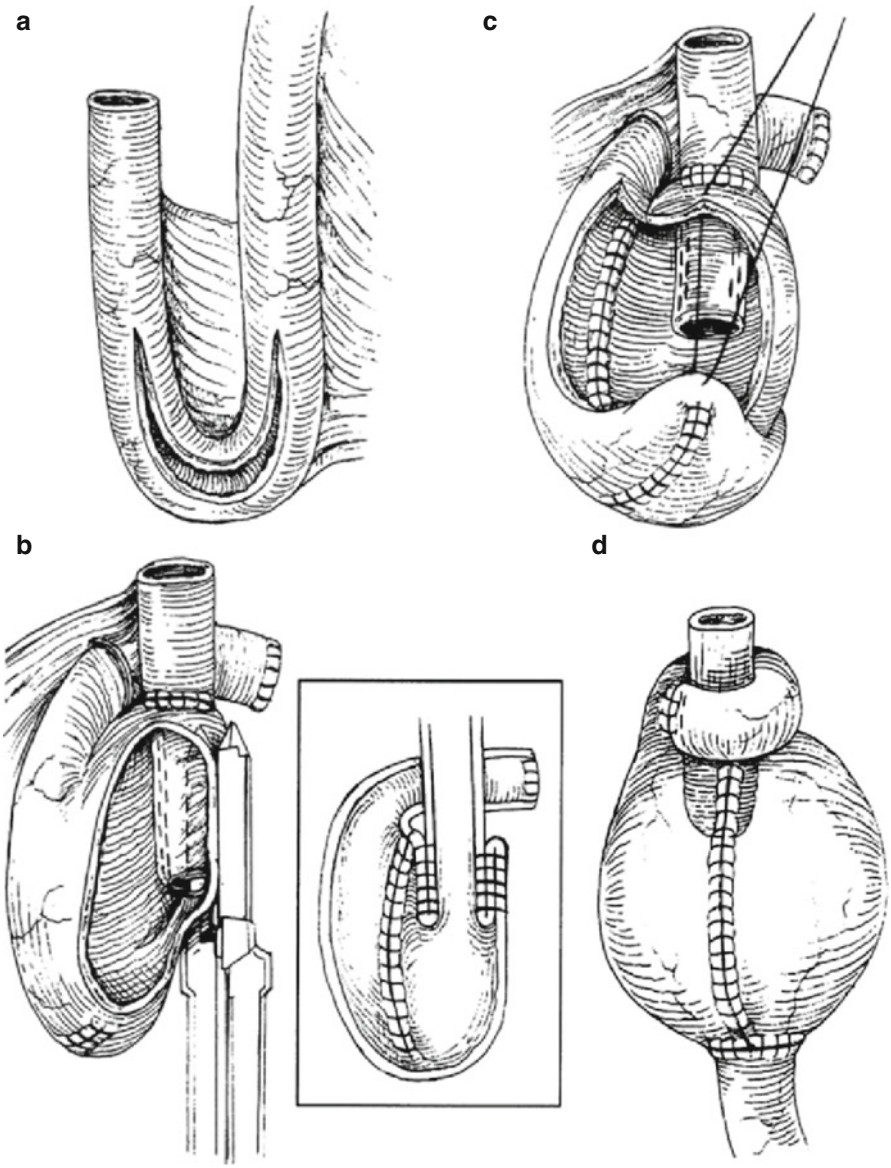

Fig. 29.2 Barnet continent ileostomy reservoir (BCIR). (**a**) Two limbs of small intestine are sewn together and opened. (**b**) The afferent limb is intussuscepted to form a valve, and the valve is stapled to the side of the reservoir. (**c**) The pouch is folded back and sutured closed. *Inset* shows cross section of pouch. (**d**) Completed BCIR. The afferent limb of bowel has been divided and reattached to the apex of the pouch, and the efferent limb is wrapped around the valve to form a collar

- The operation may also be indicated in the teenager or young adult in order to rapidly regain good health, avoid a stoma, and return to school or work quickly.
- In addition, it can also be considered in young females in an attempt to preserve fertility.
- Contraindications to IRA include a very diseased and noncompliant rectum, dysplasia or nonmetastatic cancer, perianal disease, and a severely compromised anal sphincter.

Postoperative Complications

- Mortality is low, particularly when it is performed as an elective procedure.
- Anastomotic leak occurs in less than 10 %, and major sepsis is very uncommon.
- Sexual function is well preserved.
- Most patients pass between two and four semiliquid stools a day. Nocturnal defecation is common, but true incontinence is rare.
- The overall risk of cancer developing in the rectum after IRA approximates 6 %.
- Most cancers appear 15–20 years after operation.
- Patients being offered IRA must realize the need for semiannual 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.

Ileal Pouch–Anal Anastomosis

- The anorectal sphincter mechanism must be intact to prevent leakage of watery ileal contents.
- Laparoscopic ileal pouch surgery is associated with longer operating time and less blood loss but may have short-term benefits such as diminished postoperative pain, reduced narcotic requirements, and shorter hospital stay compared to open surgery (Figs. 29.3, 29.4 and 29.5).

Operative Technique

- The abdomen is explored to rule out evidence of Crohn's disease.
- Omentectomy is avoided as there is a lower incidence of postoperative sepsis when the omentum is preserved.

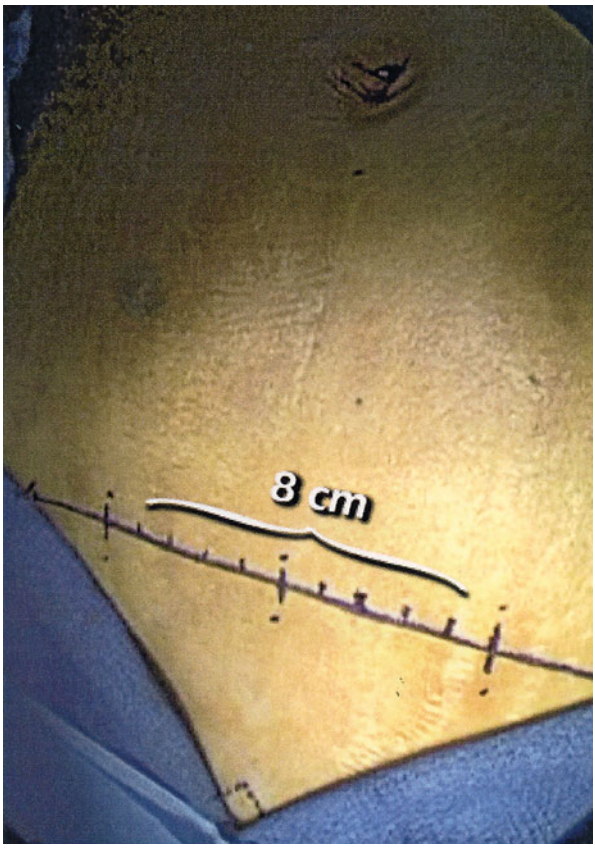

Fig. 29.3 Hand-assisted colectomy begins with 8 cm Pfannenstiel or lower midline incision. Note how positioning of towels from the root of penis or top of the introitus to the anterior superior iliac spine creates a right angled triangle, assuring a straight transverse incision

- Stapling of the distal ileum flush with the cecum is very important, as is preservation of the ileal branches of the ileocolic artery and vein. These vessels provide perfusion of the pouch after mesenteric division.
- Mobilization of the rectum should be flush with the fascia propria to minimize damage to nearby autonomic nerve.
- If desired, mucosal stripping is performed from a perineal approach (Figs. 29.6 and 29.7).
- The terminal ileum is aligned in a J configuration and the pouch constructed with either a continuous absorbable suture or stapling device (Figs. 29.8, 29.9, 29.10 and 29.11).
- Both limbs of the J are approximately 15–25 cm in length, the exact length guided by where the pouch reaches deepest into the pelvis.
- The prospective apex of the pouch must reach beyond the symphysis pubis in order to accomplish a tension-free ileoanal anastomosis (Fig. 29.12).

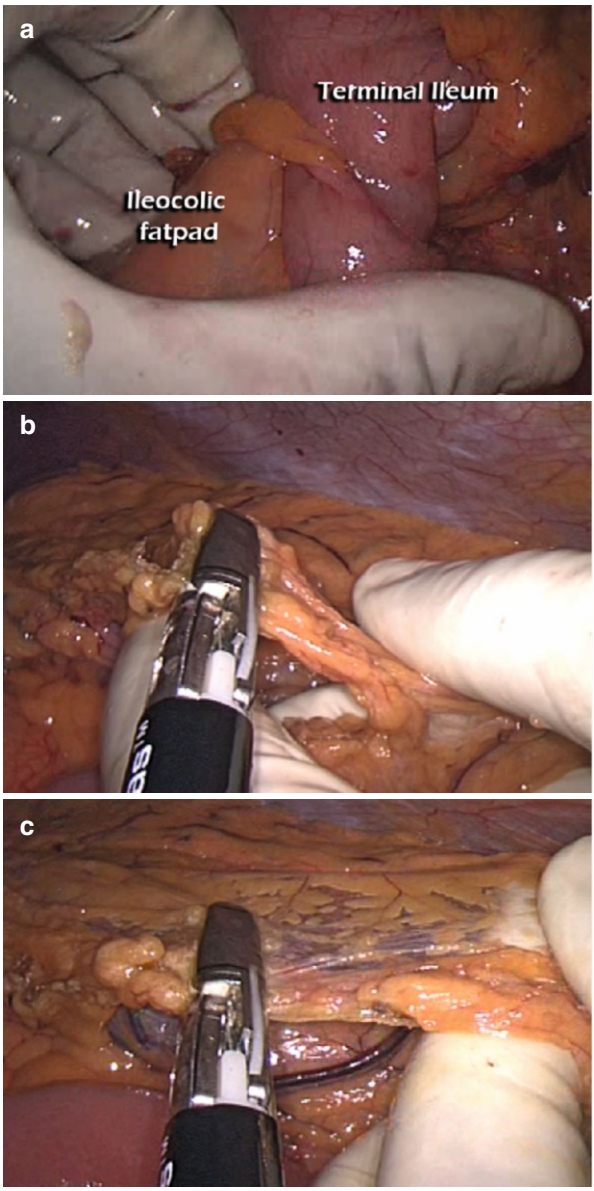

Fig. 29.4 Technical maneuvers during hand-assisted laparoscopic total colectomy. (**a**) Traction of the ileocolic fat pad with traction towards the right lower quadrant will facilitate identification and preservation of the ileocolic artery. The omentum and transverse colon mesentery are divided either together (**b**) or separately after entry into the lesser sac (**c**)

Fig. 29.5 Typical wound appearance at completion of surgery

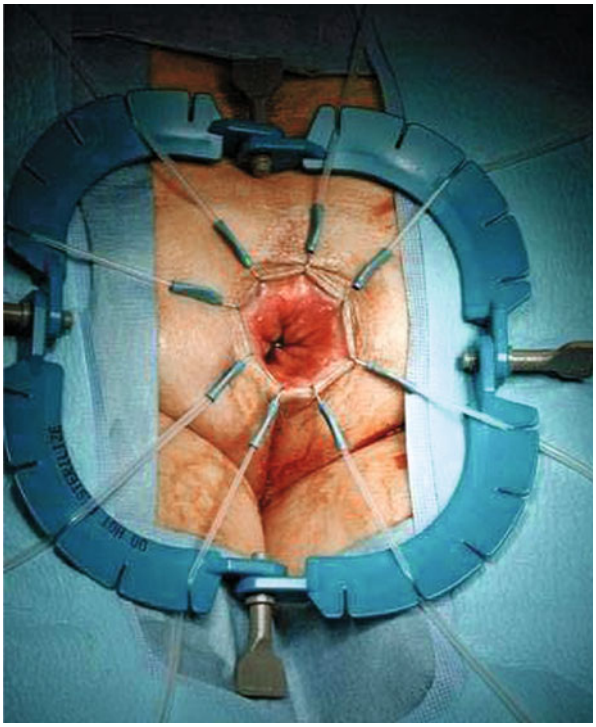

Fig. 29.6 Lone Star™ retractor

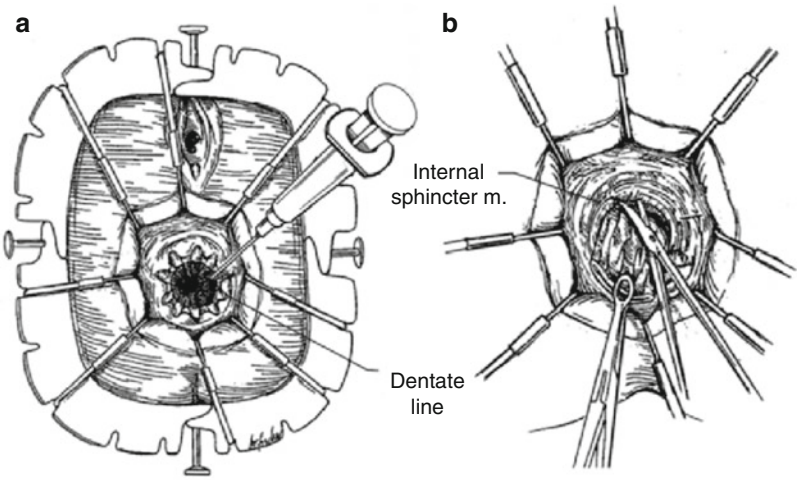

Fig. 29.7 Mucosectomy. In (**a**), a spinal needle is used to inject saline solution with epinephrine (1:200,000) into the submucosa from the dentate line to the levators. A circumferential incision through the mucosa is made at the dentate line. A sleeve of mucosa is dissected free from the internal sphincter using sharp dissection (**b**)

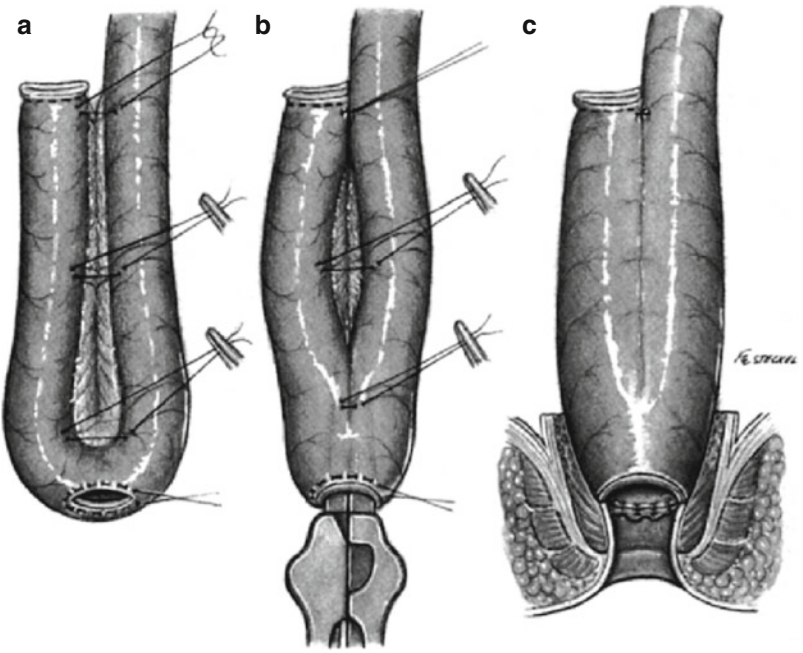

Fig. 29.8 Ileal J-pouch creation. (**a**) The limbs of the ileum are oriented using stay sutures. (**b**) The common wall of the two limbs is then divided using a linear cutting stapler placed through an apical antimesenteric enterotomy. (**c**) The J-reservoir is then placed within the rectal muscular sleeve and sutured to the dentate line (From Veidenheimer MC. Mucosal proctectomy, ileal J-reservoir, and ileoanal anastomosis. In: Braasch JW, Sedgwick CE, Veidenheimer MC, Ellis FH Jr., editors. Atlas of abdominal surgery. Philadelphia: WB Saunders; 1991)

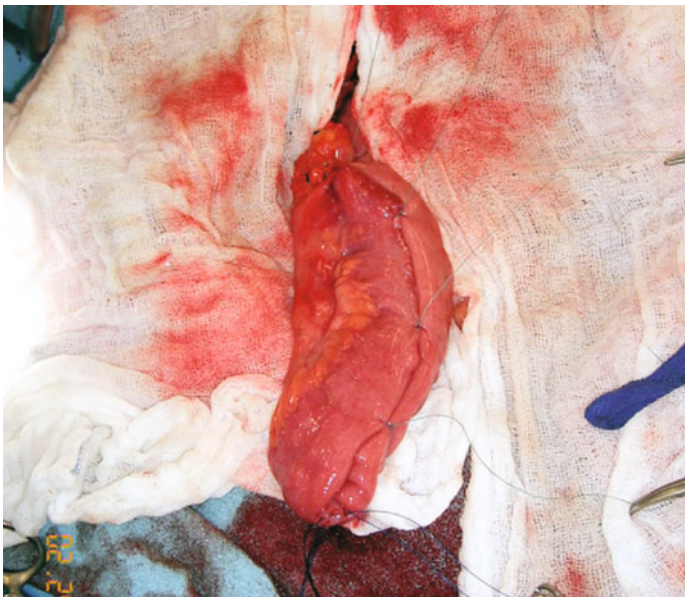

Fig. 29.9 Ileal J-pouch. Intraoperative photograph showing the two limbs of the ileum properly oriented using stay sutures

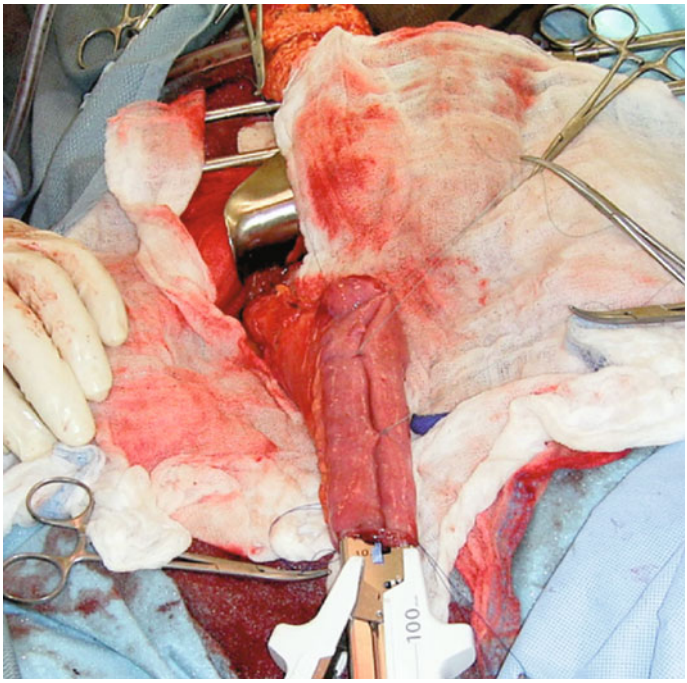

Fig. 29.10 Ileal J-pouch. Intraoperative photograph showing application of the linear stapler through the apical enterotomy. Note how the stay sutures are helpful in advancing the bowel over the stapler

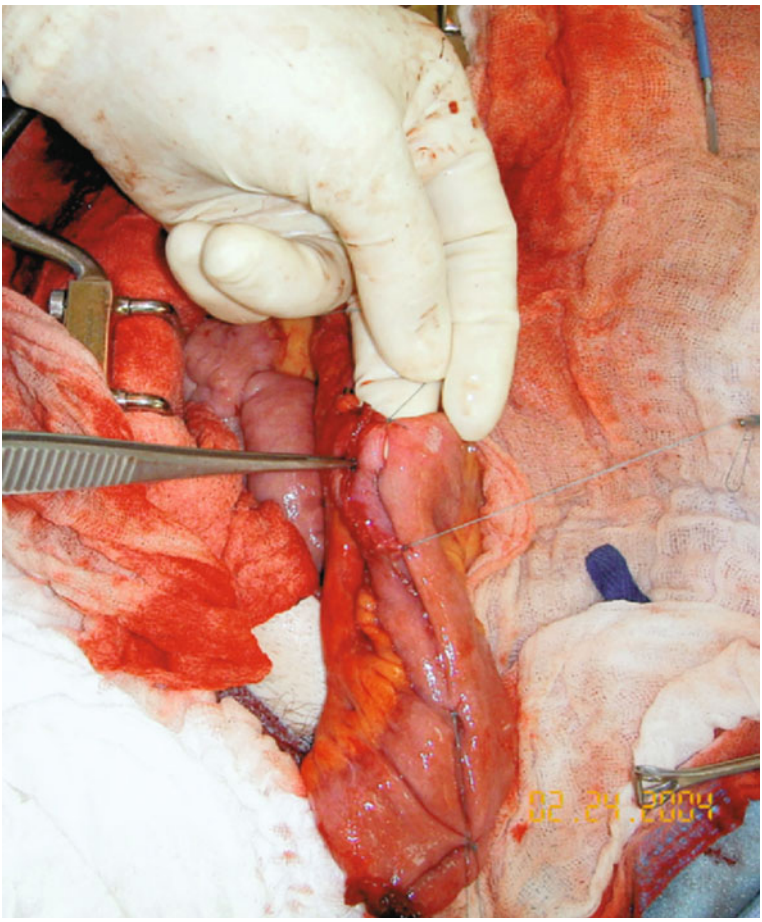

Fig. 29.11 Ileal J-pouch. Intraoperative photograph showing the completed J-pouch

- The pouch is then pulled into the pelvis and the anastomosis carried out between the apex of the pouch and the dentate line (Fig. 29.13).
- A proximal defunctioning loop ileostomy is created in the RLQ.
- More commonly, a double staple technique is used to perform the ileoanal anastomosis (Figs. 29.14).
- Patients are usually discharged after 3–7 days in the hospital and return 6–8 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.
- A contrast study is performed to detect pouch leaks, fistulas, and sinus tracts.

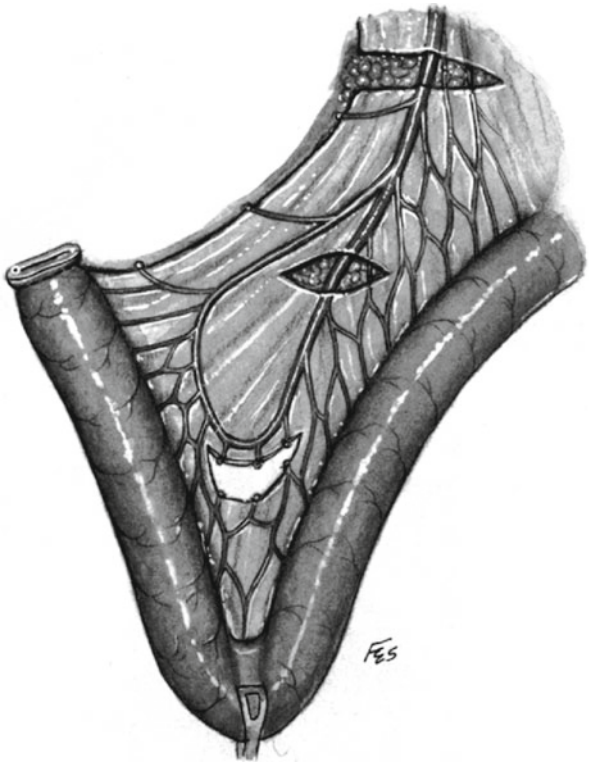

Fig. 29.12 Ileal J-pouch. The peritoneum is scored to lengthen the mesentery. Selective division of mesenteric arcades is used to produce additional length (From Veidenheimer MC. Mucosal proctectomy, ileal J-reservoir, and ileoanal anastomosis. In: Braasch JW, Sedgwick CE, Veidenheimer MC, Ellis FH Jr., editors. Atlas of abdominal surgery. Philadelphia: WB Saunders; 1991)

- In over 90 % of patients, the ileostomy can be closed through a peristomal incision. However, in the remainder, the midline abdominal incision must be reopened.

Postoperative Complications

- Reported mortality ranges from 0 to 1 %.
- Morbidity after IPAA remains considerable.
- Small bowel obstruction occurs in 20 % of patients.
- Pelvic sepsis still occurs in 5 % of patients after IPAA. Septic complications result from anastomotic dehiscence or an infected pelvic hematoma.
- Symptoms suggestive of early pelvic sepsis are fever, anal pain, tenesmus, and discharge of pus or secondary hemorrhage through the anus.

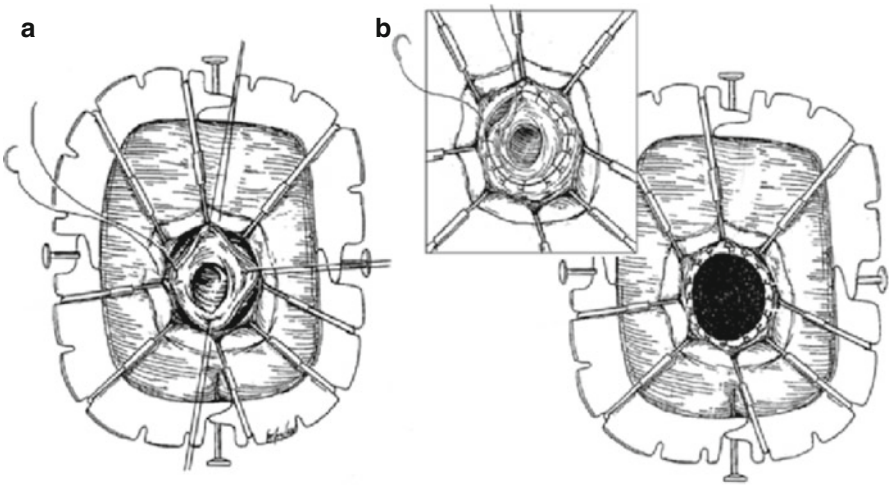

Fig. 29.13 Handsewn ileoanal anastomosis. After the pouch is gently pulled through the anal canal by the perineal surgeon, four sutures incorporating full thickness of the pouch and a generous bite of the internal sphincter are placed at right angles to anchor the efferent limb within the anal canal (**a**). The anastomosis is completed by placing sutures between each anchoring suture (**b**). Completed anastomosis (**c**)

- Diagnosis is confirmed using computed tomography (CT) or magnetic resonance imaging (MRI).
- As 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.
- Patients with ongoing sepsis and an organized abscess should undergo early operative endoanal or imaging-guided percutaneous drainage.
- If drainage of the cavity is unsatisfactory, an attempt should be made to deroof the abscess and curette the cavity through the anus, creating a large communication between the abscess and the reservoir.
- A catheter should be placed into the cavity to promote drainage and irrigation. Sometimes several local procedures are needed to eradicate sepsis.
- Laparotomy may be indicated when these measures are ineffective.
- The reported incidence of ileoanal anastomotic stricture has varied between 5 and 38 %.
- An apparent stricture may be noted when digital examination is carried out for the first time after the operation.
- Occasionally the insertion of graded dilators under anesthesia is necessary.
- Rarely, a transanal approach involving excision of the stricture and pouch advancement distally is necessary.
- Anastomotic separation is seen in approximately 10 % of patients.
- The reported incidence of pouch–vaginal fistula ranges from 3 to 16 %.

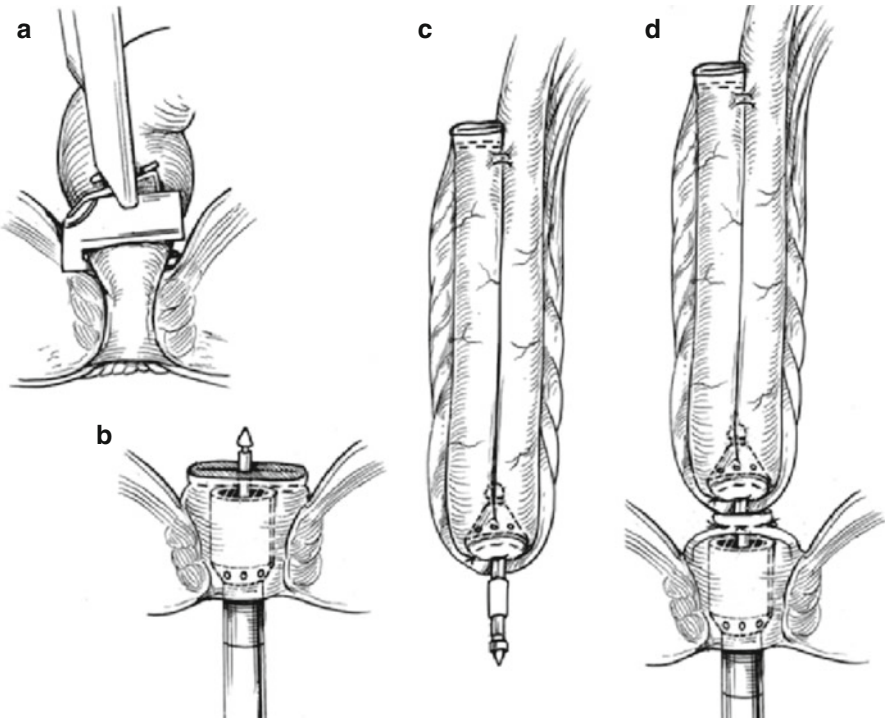

Fig. 29.14 Double-stapled J-pouch anastomosis. The anvil of a midsized circular stapler is tied into the apex of the J-pouch (**a**). The anorectum is divided with a stapler within the levator muscles about 1–2 cm above the dentate line. Adjacent tissue such as the bladder or vagina must be excluded from incorporation in the staple line. The integrity of the staple line should be tested with air insufflation through an anoscope (**b**). The perineal operator advances the midsized circular stapler against the anorectal transaction site and advances the trocar through the transverse staple line (**c**). The anvil mechanism is positioned onto the rod of the circular stapler. Before completing the anastomosis, the abdominal operator must prevent extraneous tissue from being trapped into the stapling device (**d**)

- 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.
- Simple defunctioning alone does not often lead to fistula closure.
- 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.
- Pouch–vaginal fistula from an anastomosis at or above the anorectal junction should be approached abdominally with pouch dissection, repair of the vaginal defect, and creation of a new ileoanal anastomosis.
- A fistula arising from an anastomosis within the anal canal should not be treated with an abdominal procedure as there is not sufficient distal anal

canal length to be clear of the fistula. A local procedure is necessary in such circumstances, and most surgeons have used either an endoanal ileal advancement flap.

- Although both approaches result in fistula closure in 50–60 % of cases, the transvaginal repair may have an advantage over the endoanal technique as it allows a direct approach to the fistula without the possibility of sphincter damage.
- Another alternative is the use of a gracilis muscle interposition.
- The most frequent long-term complication after IPAA for UC is a nonspecific inflammation of the ileal pouch commonly known as pouchitis.
- Acute pouchitis responds rapidly to oral antibiotic treatment.
- Clinical factors associated with acute pouchitis include the use of steroids before colectomy and smoking.
- Factors directly related to chronic pouchitis are the presence of extraintestinal disease such as primary sclerosing cholangitis, elevated platelet count, and length of follow-up after IPAA. Smoking appears to protect against the development of chronic pouchitis.
- The etiology of this nonspecific inflammation is unclear.
- 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.
- A mixture of probiotics is useful in most IPAA patients after resolution of the acute symptoms to prevent recurrence of pouchitis.
- The number of bowel movements after successful ileoanal pouch procedures averages six per 24 h.
- Major incontinence is very unusual.
- 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.
- 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.
- Two large studies showed a significant decrease in postoperative fertility.
- Results of a recent systematic review were more promising, revealing an infertility rate of 12 % before restorative proctocolectomy and only 26 % after surgery based on seven studies and 945 evaluable patients.
- Application of an anti-adhesion membrane around the fallopian tubes and ovaries during surgery is recommended.
- Surgeons may also consider delaying proctectomy until a family has been established.
- Minimally invasive surgery should be strongly considered in all young females.

Controversies

- A large, prospective study recently reported the incidence of acute pouchitis, chronic pouchitis, and de novo CD after ileal pouch–anal anastomosis does not differ significantly between patients with UC, inflammatory bowel disease unclassified (IBDU), or indeterminate colitis (IC).
- Patients with IBDU and IC can undergo ileal pouch–anal anastomosis and expect a long-term outcome equivalent to patients with UC.
- It appears that chronologic age should not itself be used as an exclusion criterion. Pouch procedures are feasible in suitably motivated elderly individuals who understand the risks and problems of this procedure.
- The presence of distant metastatic disease is generally a contraindication to IPAA.
- Patients with middle and low rectal tumors, in accordance with basic principles of cancer surgery, may not be eligible for this procedure.
- A pelvic pouch should not be subjected to radiation because of a high incidence of pouch loss.
- Studies examining the use of the ileoanal pouch in patients with locally invasive cancers of the colon and upper rectum have been conflicting.
- 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.
- Although inflammation in the rectal cuff after double-stapled IPAA is commonly seen, only about 10 % of these patients are symptomatic.
- Mesalamine suppositories might be an effective treatment for symptomatic cuffitis.
- Shape and size of the pelvic reservoir do not make significant differences.
- A diverting loop ileostomy does not prevent leaks but reduces the clinical significance of leaks that do occur.

30. Crohn's Disease: Surgical Management

Scott A. Strong

- Crohn's disease is a chronic, unremitting inflammatory bowel disease.

Prevalence

- The worldwide prevalence of Crohn's disease is increasing.
- High-incidence areas include Canada, France, New Zealand, the Netherlands, Scandinavia, and Scotland.
- Affluence and living in industrialized areas do not currently appear to have an etiological role.
- There is a bimodal age distribution with the first peak occurring between the ages of 15 and 30 years and the second between 60 and 80 years.
- The prevalence of Crohn's disease in patients aged younger and older than 20 years is 43 and 201 per 100,000, respectively.
- Crohn's is more common in whites than in blacks, Hispanics, and Asians, and there is a two- to fourfold increase in the prevalence among the Jewish population in the USA, Europe, and South Africa.

Etiopathology

- Two biologic pathways have generated significant interest.
- The first involves autophagy, which is responsible for the recycling of cellular organelles and long-lived proteins, and plays an important role in tissue homeostasis as well as intracellular bacteria processing.

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- The second is the IL-23/Th17 pathway. IL-23 stimulates the Th17 cell population to produce IL-17 and other pro-inflammatory cytokines involved in intestinal inflammation.
- In normal intestine, the immunologic character is typified by suppression or tolerance of immune responses against nonpathogens present within the gut lumen. These nonpathogens include both commensal flora and dietary antigens. This tolerant state, at least to specific components of the flora, is lost in patients with Crohn's disease.
- Crohn's disease likely arises in a genetically susceptible individual exposed to an ordinarily harmless trigger that initiates a dysregulated inflammatory response causing an aggressive and persistent inflammatory response that becomes progressively resistant to medical therapy during the patient's lifetime.

Classification

- Table 30.1 shows the Montreal classification system of Crohn's disease.
- While only 15 % of patients experience an alteration in anatomic location, nearly 80 % of individuals with inflammatory disease ultimately demonstrate stricturing or penetrating behavior.

Symptoms and Signs

- Chronic diarrhea is the most common presenting symptom and is defined as a decrease in fecal consistency for more than 6 weeks to adequately differentiate this from self-limited infectious diarrhea.
- Abdominal pain and weight loss are seen in about 70 and 60 % of patients before diagnosis, respectively.
- Blood or mucus in the stool can be seen in 40–50 % of patients with Crohn's disease of the colon but is unusual in patients with ileal or isolated upper gastrointestinal disease.

Table 30.1 The Montreal classification system of Crohn's disease

Age of diagnosis	A1 <16 years
	A2 17–40 years
	A3 >40 years
Location	L1 ileal
	L2 colonic
	L3 ileocolic
	L4 isolated upper
Behavior	B1 nonstricturing nonpenetrating
	B2 stricturing
	B3 penetrating
	P perianal disease

- The most common of the recognized extraintestinal manifestations are abnormalities involving the axial and peripheral joints of the musculoskeletal system, which are most frequently seen when Crohn's disease affects the colon.
- Table 30.2 shows the Perianal Crohn's Activity Index.

Table 30.2 Perianal Crohn's disease activity index

Feature	Score
Abscess	
None *or* 0	
First occurrence, single abscess *or*	1
First occurrence, multiple abscesses *or*	3
First recurrence, single or multiple abscesses *or*	4
Multiple recurrence, single or multiple abscesses	5
Maximum abscess score 8	
Fistula	
None	0
Short-term (<30 days) fistula *or*	1
Long-term (>30 days) fistula *or*	2
Persistent postsurgery fistula *or*	3
Recurrent fistula	3
Multiple fistulas	3
Rectovaginal/rectourethral fistula *or*	4
Recurrent rectovaginal/rectourethral fistula	6
Maximum fistula score	14
Ulcer and fissure	
None	0
Short-term (<30 days) ulcer/fissure *or*	1
Long-term (>30 days) ulcer/fissure *or*	2
Single ulcer/fissure *or*	1
Multiple ulcers/fissures	2
Maximum ulcer/fissure score	4
Stenosis	
None	0
Short-term (<30 days) stenosis *or*	1
Long-term (>30 days) stenosis	2
Recurrent stenosis	4
Maximum stenosis score	6
Incontinence score	
No incontinence *or*	0
Incontinence score of 1–6 *or*	1
Incontinence score of 7–14 *or*	3
Incontinence score >14	5
Maximum incontinence score	5
Concomitant disease[a]	
None *or*	0, 0, 0
Moderate *or*	3, 2, 1
Severe	4, 3, 2
Active fistula	4, 3, 2
Maximum concomitant disease score	18

[a]Scores are for rectal, colonic, and small bowel disease, respectively

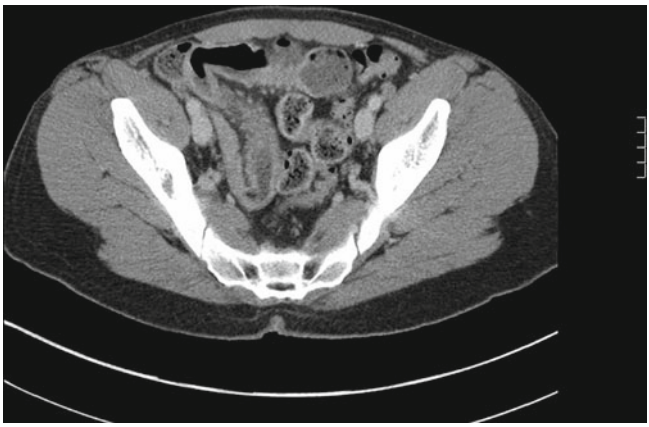

Fig. 30.1 CT enterography

Diagnosis

- The initial diagnosis of Crohn's disease is based on an amalgamation of clinical, laboratory, imaging, endoscopic, and histologic findings.
- No single diagnostic test provides an unequivocal verdict.
- Anemia and thrombocytosis represent the most common changes in the complete blood count.
- The C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR) are standard laboratory surrogates of the acute-phase response to inflammation.
- CRP broadly correlates with disease severity.
- The ESR less accurately measures intestinal inflammation because it reflects changes in both plasma protein concentration and packed cell volume.
- Computed tomographic (CT) enterography and enteroclysis differ from standard CT imaging by using intraluminal bowel distention with neutral enteric contrast, multidetector CT with narrow slice thickness and reconstruction interval, and intravenous contrast administration followed by delayed scans that optimize bowel wall enhancement.
- CT enterography has largely supplanted barium examinations because the CT study is more sensitive and allows improved visualization of small bowel loops within the pelvis.
- Contrast-enhanced magnetic resonance imaging (MRI) enterography (Fig. 30.1) and enteroclysis appear to provide results comparable to those seen with CT studies without the risk of exposure to ionizing radiation.

Natural History

- Patients' initial presentations are equally distributed among ileitis, colitis, and ileocolitis.
- Disease location remains relatively stable over time.
- The majority of patients have nonstricturing, nonpenetrating disease at the time of diagnosis but tend to evolve into a stricturing or penetrating phenotype over their lifetime.
- It is too early to accurately understand how immunomodulators and biologic agents will impact long-term disease activity and relapse rates.
- The cumulative risk for surgery within 10 years of diagnosis is 40–55 %, and the risk of a second operation has been estimated to be 16, 28, and 35 % at 5, 10, and 15 years following the initial procedure, respectively.
- Overall mortality was slightly but significantly higher than that seen in the general population.
- Regarding the cause-specific mortality, there is a significantly increased risk of cancer death.
- Chronic obstructive pulmonary disease, gastrointestinal diseases, and genitourinary diseases are more commonly implicated as a cause of death.

Operative Indications

- The indications for operative management of Crohn's disease include acute disease complications, chronic disease complications, and failed medical therapy. The acute complications are hemorrhage, perforation, and severe colitis with or without associated megacolon.
- Chronic disease complications include extraintestinal manifestations, growth retardation, and neoplasia.

Hemorrhage

- Crohn's disease may infrequently cause life-threatening lower gastrointestinal hemorrhage and even exsanguination.
- Localization of the bleeding site is essential.
- In a stable patient with colonic disease, endoscopic evaluation is preferred.
- A patient who requires ongoing resuscitation to maintain hemodynamic stability or in whom a small bowel source of active bleeding is suspected should undergo emergent mesenteric angiography to localize the source of hemorrhage and arrest ongoing bleeding through superselective angiographic embolization.

- If the hemorrhage is localized but cannot be controlled, the catheter is left in position and intraoperative angiography is performed to accurately identify the bleeding site and guide a limited bowel resection.
- An operation is warranted if the patient's hemodynamic state cannot be sustained, bleeding persists despite 6 units of transfused blood, hemorrhage recurs, or another indication for surgery exists.
- Resection with or without anastomosis is usually required for ongoing hemorrhage, whereas intraoperative enteroscopy with endoscopic therapy might be employed in less emergent settings.

Perforation

- Free perforation of the small bowel is unusual and typically occurs at or immediately proximal to a stricture site.
- The most appropriate treatment is resection of the involved bowel with or without anastomosis.
- A primary anastomosis without proximal diversion is avoided in the setting of delayed treatment, malnutrition, significant comorbidity, or severe sepsis.
- Resection and proximal ileostomy with or without anastomosis has a mortality rate of 4 % compared to 41 % with simple suture closure alone.
- Perforation of the colon is rare, occurs in the setting of severe colitis or steroid use, and typically requires a subtotal colectomy.

Severe Colitis

- A disease flare is defined as at least six or more bloody stools per day with evidence of systemic toxicity as demonstrated by anemia (<10.5 g/dL), elevated ESR (>30 mm/h), fever (>37.8 °C), or tachycardia (>90 beats/min).
- Initial management is 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.
- If a patient has acute colitis and does not require emergent surgery, infection with Clostridium difficile and cytomegalovirus should be excluded.
- Anticholinergics, antidiarrheals, and narcotics are avoided as they may worsen already impaired colonic motility or conceal ominous symptoms.
- Any worsening of the clinical course over the ensuing 24–72 h mandates urgent operation.
- This approach reduces operative mortality rates to 2–8 % vs. 40 % if perforation has occurred.
- If the patient does not improve after 5 days of conventional therapy, the plan should be altered to include hyperalimentation, biologic therapy, or surgery.

- No controlled data exists regarding treatment with cyclosporine, tacrolimus, infliximab, or adalimumab in this setting.

If medical biologic therapy is pursued, patients who do not improve within 5–7 days should be referred for surgery.

- The principal options for patients with severe or fulminant Crohn's colitis include subtotal colectomy with end ileostomy, total proctocolectomy with end ileostomy, and loop ileostomy with decompressive blowhole colostomy. Subtotal colectomy with end ileostomy is the most common option.
- The most difficult aspect of the surgery is managing the distal bowel stump which may be closed and left in the pelvis, or it can be delivered to the anterior abdominal wall where it can lie in the subcutaneous fat of the lower midline wound.
- If the bowel wall is too friable to hold sutures or staples, a mucous fistula is primarily created.
- An ileoproctostomy can be recommended 6 months later in selected persons who demonstrate minimal mucosal inflammation, adequate rectal compliance, absence of significant perianal disease, and sufficient sphincter strength.
- The diseased rectum is left in place and the patient is counseled about the risk of neoplasia and the need for appropriate surveillance endoscopy.
- Proctocolectomy with end ileostomy is rarely performed in the severely ill patient with severe colitis because of the excessive rates of morbidity and mortality.
- Proctectomy increases the difficulty of the procedure and risks pelvic bleeding as well as autonomic nerve damage.
- Loop ileostomy combined with decompression blowhole colostomy is of historical interest because of improved and more sophisticated management of severe colitis. Contraindications to the procedure include colorectal hemorrhage, intra-abdominal abscess, and free perforation.

Extraintestinal Manifestations

- Some forms of peripheral arthritis, episcleritis erythema nodosum, and oral aphthous ulcers are temporally related to intestinal Crohn's disease activity.
- Primary sclerosing cholangitis, pyoderma gangrenosum, spondyloarthropathy, and uveitis typically follow a course independent of disease activity.

Neoplasia

- Patients with Crohn's disease are at increased risk for developing colon cancer, but not of rectal cancer.

- A recent meta-analysis of 60,122 patients with Crohn's disease showed the relative risk of small bowel, colorectal, and extraintestinal cancer and lymphoma compared with the baseline population was 28.4 (95 % CI, 14.46–55.66), 2.4 (95 % CI, 1.56–4.36), 1.27 (95 % CI, 1.1–1.47), and 1.42 (95 % CI, 1.16–1.73), respectively.
- A significant association exists between the anatomic location of the diseased bowel and the risk of cancer in that segment.
- It is recommended that patients with Crohn's disease with one-third or more of the colon involved and 8 years or more of chronic colitis should be enrolled in an endoscopic surveillance program.
- The finding of multifocal low-grade dysplasia, high-grade dysplasia, or invasive cancer warrants review by a second experienced pathologist; confirmation would prompt a colectomy.
- Patients with primary sclerosing cholangitis have a heightened risk of colorectal cancer. Accordingly, yearly surveillance is recommended after a diagnosis of primary sclerosing cholangitis is made in the background of colonic Crohn's 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.
- Alternatively, some patients request an operation before exhausting all available medical therapies. Seventy-six percent of gastroenterologists are willing to gamble to avoid an ileocolic resection compared with only 37 % of colorectal surgeons and 39 % of patients.

Operative Considerations

- Fundamental observations must be considered:
  - Crohn's disease is incurable.
  - Surgery is most often indicated for intestinal complications.
  - Operative options are influenced by myriad factors.
  - Asymptomatic disease should be ignored.
  - Nondiseased bowel can be affected.
  - Resection margins should be conservative (2 cm) as only a grossly normal and not microscopically normal margin is necessary.
  - Mesenteric division can be difficult.
- Nondiseased bowel can be affected by the disease process through inflammatory adhesions or internal fistulas.
- Every attempt should be made to conserve the nondiseased bowel.
- Most internal fistulas are best managed by wedge excision and primary closure of the fistula site in the secondarily affected small bowel.

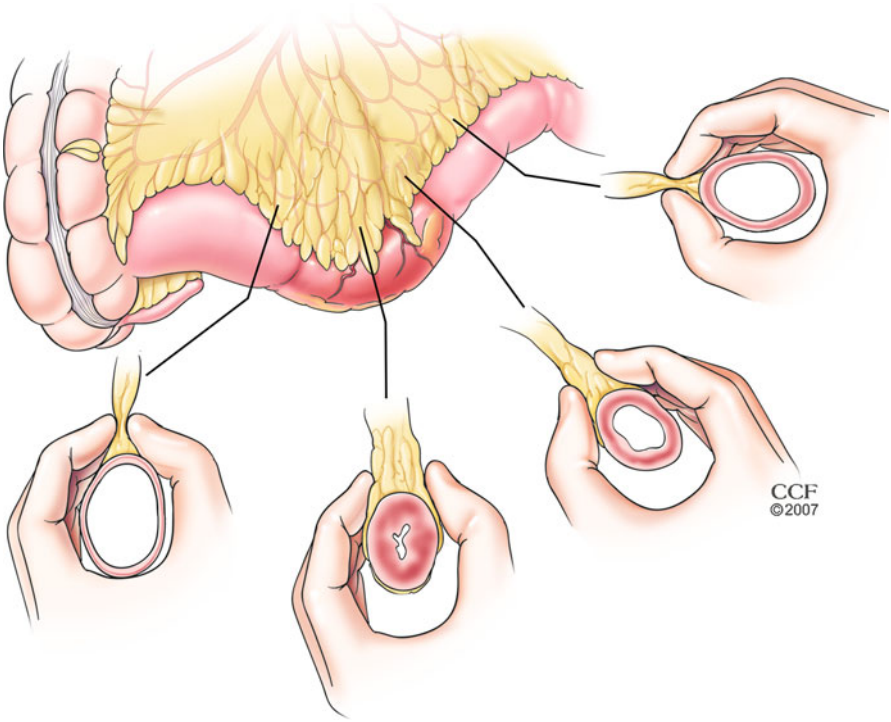

Fig. 30.2 Mesenteric thickness associated with intestinal disease

- A short segmental resection with primary anastomosis may be required for fistulas targeting the rectosigmoid region as these often enter the bowel at the mesenteric margin and simple wedge excision may be predispose to dehiscence of the suture line.
- The small bowel lumen will be macroscopically free of disease if the mesenteric margin can be palpated (Fig. 30.2).
- Conversely, the extent of large bowel involvement is best determined by endoscopic inspection of the mucosa. Frozen section analysis of the margins has no role, and microscopic finding of disease at the margin need not necessitate any additional surgical intervention.

Operative Options

Internal Bypass

- With the advent of supportive modalities and recognition of complications, such as recrudescent disease, mucoceles, and malignancy arising in diverted segments, this procedure has been largely abandoned.
- Bypass operations may be reasonable or desirable in circumstances such as a complicated ileocecal phlegmon with dense attachment to the iliac vessels or retroperitoneum or refractory gastroduodenal Crohn's disease.

External Bypass

- Many of the stomas created to permanently bypass unresected disease fail to control symptoms, and resection is ultimately warranted.
- High complex fistulas and deep ulcerations are among the disease characteristics likely to mandate proctectomy.
- Temporary diversion intended to heal distal disease or its sequelae is usually unsuccessful unless combined with a secondary procedure, such as a rectal mucosal advancement flap that directly addresses the problem.

Strictureplasty

- This technique was initially described for the successful treatment of tubercular small bowel strictures and later utilized in strictures secondary to Crohn's disease.
- Patients undergoing strictureplasty alone experience significantly shorter recurrence-free survival than those undergoing resection and tend to be more likely to develop surgical recurrence.
- The situations for which strictureplasty may be considered are:
  - 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 presenting as an obstruction
  - Stricture in a patient with short bowel syndrome
  - Nonphlegmonous fibrotic stricture
- The contraindications to strictureplasty are:
  - 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)
- Factors that do not appear to be associated with increased operative risk include perforative or phlegmonous disease remote from the strictureplasty site, steroid dosage, synchronous resection, number of strictureplasties, and length of stricture.
- The length of the strictured segment dictates the type of strictureplasty technique utilized (Fig. 30.3).
- Short (<10 cm) strictures are best managed by a Heineke-Mikulicz type of strictureplasty, while medium length (10–20 cm) strictures can be corrected by a Finney-type strictureplasty.
- Long (>20 cm) strictures are best managed by a side-to-side isoperistaltic strictureplasty.

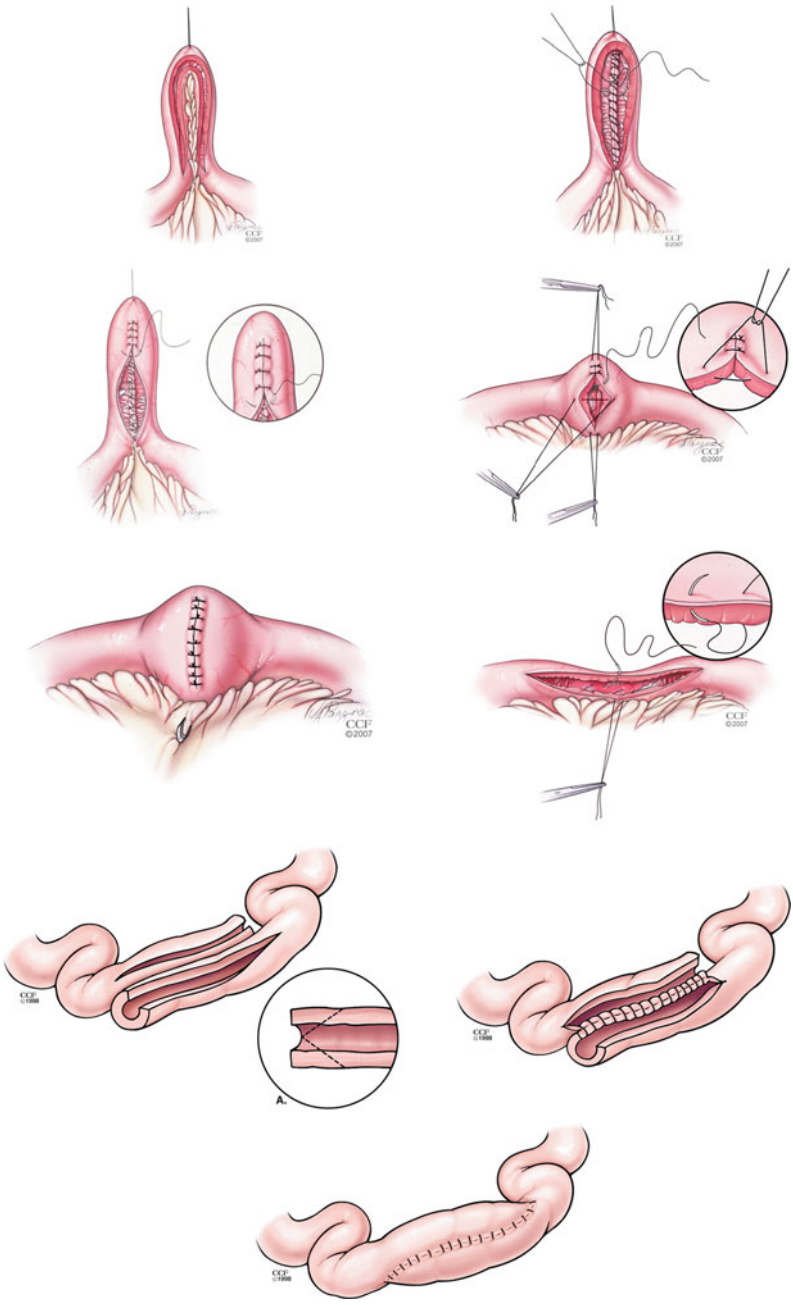

Fig. 30.3 Strictureplasty techniques

- Biopsy of any suspicious mucosa is performed to exclude carcinoma, and closure is achieved using an absorbable suture in a one- or two-layer fashion.
- The mesentery at each of the strictureplasty sites is then labeled with metallic clips to allow discrimination among the multiple sites in the unlikely event that postoperative hemorrhage occurs.
- Selective mesenteric angiography with intra-arterial vasopressin infusion controls most bleeding episodes.

Resection

- Basic principles of resection include mobilization of both diseased intestine as well as sufficient nondiseased bowel to facilitate creation of a tension-free anastomosis or construction of an ostomy.
- Enteric fistulas commonly originate from diseased bowel that communicates with nondiseased intestine. While the primary site usually requires resection, the secondarily affected bowel segments are typically treated by conservative wedge excision and simple closure of the resultant defect or sometimes closure without wedge resection.
- The specimen should be opened to assure macroscopic disease-free resection margins.
- An anastomosis can be safely created assuming a few general principles are respected specifically:
  - Adequate blood supply must be assured.
  - Tension or torsion is unacceptable.
  - Luminal size needs to be equivalent.
- A temporary diverting stoma should be considered to protect the anastomosis in instances of incompletely drained sepsis, excessive blood loss following a long operation, severe hypoalbuminemia (<2.5 g/dL), or significant immunosuppression.

Disease Locations

Ileal Disease

- In the majority of cases, resection with construction of an ileal-ascending colon anastomosis is feasible and desirable.
- All nondiseased ascending colon should be preserved to provide the largest possible surface area for water absorption.
- With mesenteric division, managing the small bowel vessels with simple ties can be catastrophic because the transected vessels might retract.
- Instead, clamps and suture ligatures should be applied in an overlapping fashion to best assure adequate hemostasis (Fig. 30.4).

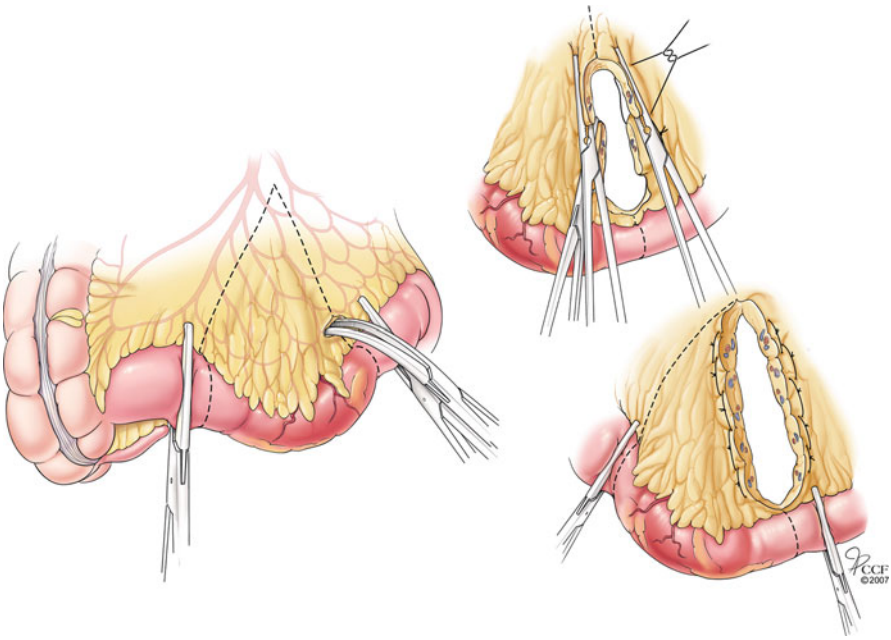

Fig. 30.4 Ligation of thickened mesentery

- The anastomotic leak rate is significantly reduced with a side-to-side anastomosis compared to an end-to-end anastomosis.
- Postoperative complications, other than anastomotic leak, and postoperative hospital stay are significantly reduced in the side-to-side anastomosis.
- No significant difference is noted between the groups in perianastomotic recurrence.
- The stapled anastomosis may be associated with fewer leaks than the hand-sewn anastomosis.
- It is important to utilize a hand-sewn technique when the bowel wall is abnormally thickened because the stapling instruments are not designed to safely construct an anastomosis under these conditions.
- A bowel resection may be avoided by creating a large Finney-type ileocolostomy encompassing the entirety of the diseased bowel.
- Terminal ileal disease with sparing of the ileocecal valve and cecum may be treated with resection and enteroenterostomy provided there is sufficient length (5–7 cm) of normal-appearing distal ileum after definitive ileal resection.
- Preservation of the ileocecal valve helps to minimize the risk of postoperative diarrhea.

- Laparoscopic resection can be employed with an overall conversion rate of 6.8 %. Operative time is significantly longer, but total costs of hospitalization are comparable. Times to the first liquid and solid diets, times to the first flatus and bowel movement, and hospital stay are all significantly shorter.
- Long-term monitoring suggests that patients undergoing laparoscopic resection are not at any greater risk for disease recurrence than those undergoing an open resection.

Colonic Disease

- Nearly one-third of patients suffer from this disease distribution.
- Persons presenting with segmental disease are best treated with segmental resection to protect against dehydration and electrolyte imbalances.
- A meta-analysis comparing segmental colectomy to subtotal/total colectomy revealed no significant difference regarding the incidence of postoperative complications, disease recurrence, or need for a permanent stoma.
- The time to recurrence was shorter in the segmental resection group by 4.4 years.
- Patients with two or more affected colonic segments are best treated by subtotal or total colectomy.
- Disease limited to the ascending colon: the transverse colon is divided at the level of the middle colic vessels so that the mesenteric root naturally separates the anastomosis from the retroperitoneum, minimizing the risk for recurrent disease and complex fistulas.
- Alternatively, a more proximal anastomosis may be wrapped with a pedicle of omentum.
- Disease involving the ascending and transverse colon: an extended right colectomy is advised.
- Disease of the transverse, descending, or sigmoid colon is treated with segmental resection, and colocolonic or colorectal anastomosis is most commonly employed.
- Laparoscopic colectomy can also be safely employed in patients with colonic Crohn's disease.
- The laparoscopic clip appliers and bipolar thermal energy devices can safely manage arteries and veins <7 mm in diameter, but the thickness of the surrounding tissue that must be additionally incorporated may limit the utility of these devices.
- Laparoscopic staplers, on the other hand, can manage arteries <17 mm and veins <22 mm in diameter.
- A conversion rate of 26 % has been noted with laparoscopy.
- Laparoscopic colectomy patients may experience a shorter time to first bowel movement and shorter hospital stay.
- Colonic strictureplasty has been described; however, given the 7 % incidence of malignancy arising in a colonic stricture, some surgeons argue that resection should be employed.

- Patients with extensive colonic involvement, relative rectal sparing, and adequate fecal control are candidates for colectomy with ileoproctostomy.
- Rectal compliance can be subjectively judged by distending the rectum during proctoscopy or objectively quantified with anorectal physiology testing; patients whose maximum tolerated rectal volume measures <150 mL do poorly with an ileoproctostomy.
- Patients with proctocolitis who warrant operative treatment usually require a total proctocolectomy.
- If proctectomy is required, the entirety of the rectum should be resected because of the significant risk of cancer developing in the defunct rectal stump.
- Total proctocolectomy with ileal pouch-anal anastomosis for colonic Crohn's disease is associated with a pouch excision rate of 10–15 % after 10 years of follow-up. The need for pouch excision is higher in some series.

Ileocolonic Disease

- The surgeon must conserve as much of the nondiseased colon as possible and avoid large mesenteric defects.

Upper Gastrointestinal Disease

- The prognosis for Crohn's disease diffusely involving the small bowel is significantly worse than that of localized disease.
- Intestinal bypass is rejected by most clinicians because of concerns about bacterial overgrowth and malignant degeneration.
- Resection risks immediate or future short bowel syndrome and is not generally recommended.
- Multiple strictureplasties are the procedures of choice.
- Gastroduodenal Crohn's disease is relatively rare, and its most common presenting complaints are upper abdominal pain and symptoms of duodenal obstruction.
- Endoscopy demonstrates macroscopic abnormalities in the majority of patients with the antrum most frequently involved.
- Isolated gastric disease is exceedingly rare, and any reports of successful treatment are purely anecdotal.
- For duodenal disease, medical therapy is the mainstay of treatment for inflammatory and penetrating disease, while strictures present a different challenge.
- Ulcer-like lesions are nonspecific, rarely cause stenosis, spontaneously regress, and are usually associated with other diseased sites.
- Stenotic duodenal segments are typically unifocal and often respond poorly to medical management.
- Endoscopic balloon dilatation has been safely used to treat short duodenal strictures, and the procedure appears to be well tolerated while providing marked symptom relief.

- Success with duodenal strictureplasty has been reported by several centers, and the technique appears to be the procedure of choice if the affected bowel is sufficiently supple and devoid of associated sepsis.
- Occult malignancies can complicate stricture sites involving the stomach and duodenum.

Perianal Disease

- Crohn's disease is a likely diagnosis if multiple abnormalities, such as laterally located fissures, cavitating anal canal ulcers, and anorectal ring stenosis, are noted.
- Endoanal ultrasound can be a useful tool for the diagnosis of anorectal sepsis.
- Pelvic MRI is a similarly valuable means of identifying abscesses and classifying fistulas.
- Uncontrolled studies have shown a reduction in fistula-associated pain and drainage in adults treated with metronidazole or ciprofloxacin after 6–8 weeks of therapy, but symptoms typically recur immediately after antibiotic discontinuation.
- Immunomodulation with optimized azathioprine or 6-mercaptopurine is as effective as de novo therapy in nearly one-half of patients.
- Immunomodulators have also been found to successfully delay fistula recurrence following antibiotic discontinuation in patients initially responding to treatment.
- Continuous therapy with biologic agents, such as infliximab, is associated with complete arrest of fistula drainage in nearly one-half of adults.
- Surgical treatment of skin tags, whether conservative or aggressive, is often associated with morbidity due to chronic, nonhealing anal or perianal ulcers.
- Fissures should be relatively asymptomatic, and nearly one-half heal with medical treatment, especially those that are painless or acute in nature.
- Refractory symptoms from an uncomplicated fissure may respond to lateral internal sphincterotomy, especially if anal hypertonicity is present and rectal inflammation is absent.
- Symptoms secondary to large, cavity-forming ulcers can often be controlled with debridement of overhanging edges and intra-lesion corticosteroid injection.
- An anorectal abscess, regardless of its etiology, is best treated with simple incision and drainage.
- Medical therapy to optimize control of disease-related inflammation is typically recommended to increase the likelihood of healing without adversely impacting surgical outcomes.
- Most low-lying, simple fistulas without concomitant proctitis can be appropriately managed by fistulotomy.

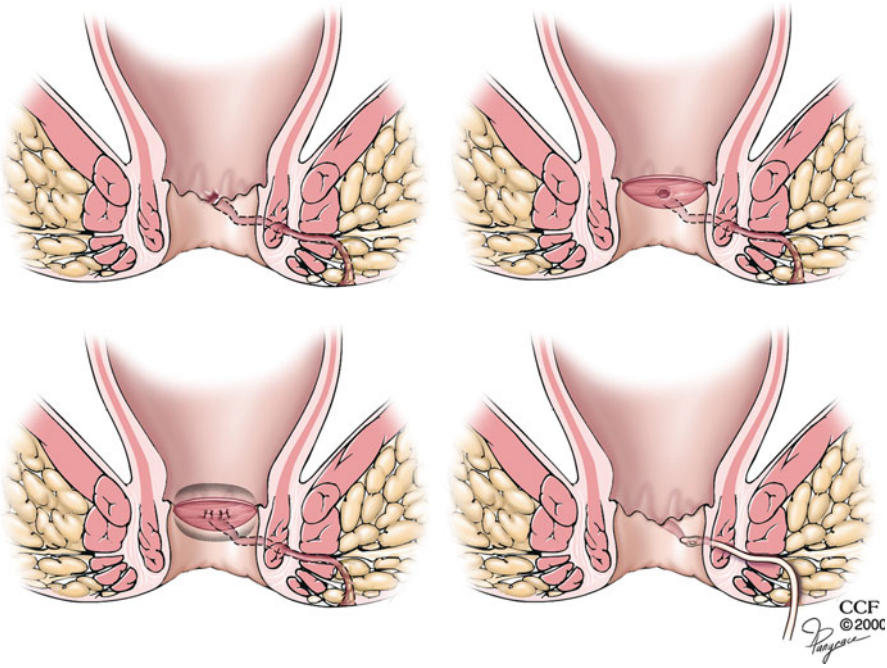

Fig. 30.5 Rectal mucosal advancement flap

- If partial sphincter division would compromise fecal continence, a noncutting seton or rectal mucosal advancement flap is indicated for low-lying, simple fistulas without significant proctitis.
- Noncutting setons establish drainage of the fistula, minimize the risk for future abscesses arising from the fistula tract, rarely cause discomfort, and do not interfere with personal hygiene.
- The rectal mucosal advancement flap is a versatile procedure that can be used when rectal inflammation is limited and no cavitating ulceration or anal stenosis is present (Fig. 30.5).
- In the event that the above is complicated by anal canal ulceration or stricturing, a rectal sleeve advancement with temporary fecal diversion can be performed in selected patients.
- If moderate or severe proctitis complicates a low-lying, simple fistula, medical therapy is then employed with or without a noncutting seton.
- In a patient with a high, complex fistula and no evidence of Crohn's proctitis, a rectal advancement flap can be performed with the expectation that one-third of complex fistulas treated in this fashion completely heal.
- The presence of proctitis with a high, complex fistula relegates the patient to medical therapy in combination with seton drainage, temporary fecal diversion, or proctectomy.

- Results with fibrin sealant for fistulas related to Crohn's disease have been inconsistent.
- Some centers have reported high success rates (>80 %) in patients treated by collagen plug occlusion, while others have encountered somewhat discouraging outcomes.
- In selected patients with severe perianal disease, fecal diversion is required.
- A temporary ileostomy does not generally influence the long-term outcome of perianal Crohn's disease because less than one-quarter of individuals have intestinal continuity restored.
- The majority of patients who undergo successful closure of their stoma require a secondary procedure (e.g., rectal mucosal advancement flap) to achieve stoma closure.
- An endoanal proctectomy is necessary in approximately 5 % of Crohn's disease patients solely to control perianal disease, especially if high, complex fistulas, deep ulcerations, colonic disease, or anal canal stenosis are present.

Prophylaxis Against Recurrent Disease

- Probiotics are not superior to placebo for any outcome measured.
- The use of nitroimidazole antibiotics appeared to reduce the risk of clinical and endoscopic recurrence when compared to placebo.
- Mesalamine therapy is associated with a significantly reduced risk of clinical and severe endoscopic recurrence relative to placebo.
- Azathioprine and 6-mercaptopurine are also associated with a significantly reduced risk of clinical and severe endoscopic recurrence when compared to placebo.
- Mesalamine relative to azathioprine and 6-mercaptopurine is associated with a higher risk of endoscopic recurrence but a lower risk of serious adverse events.
- Infliximab therapy after intestinal resection is significantly effective at preventing endoscopic and histologic recurrence without increasing the occurrence of adverse events.

31. Intestinal Stomas

Laurence R. Sands and Floriano Marchetti

The History of the Stoma

- The colostomy was initially described by Littre in 1710.
- Dr. John Young Brown of St. Louis introduced the ileostomy as part of the therapy for ulcerative colitis in 1913.
- In 1952, when Brooke designed the everted stoma.

Stoma Incidence

- In the late 1970s, there were 10,000 patients in the United Kingdom with an ileostomy, and 400–500 ileostomies were being created per year.
- It has been estimated that about 4,000 ileostomies were created in 1968 in the Unites States.

What Is an Ostomy?

- An ostomy is a surgically created opening between a hollow organ and the body surface or between any two organs.
- Ostomy comes from the Latin word ostium, meaning mouth or opening.

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Table 31.1 Indications for a stoma

Protection of distal anastomosis
Treatment of anastomotic leak
Large bowel obstruction
Bowel perforation
Abdominal or perineal trauma
Rectal injury
Diverticular disease
Complex anorectal disease
Complications from radiation
Fecal incontinence
Inflammatory bowel disease
Motility and functional disorders including idiopathic megarectum and megacolon
Infections – necrotizing fasciitis, Fournier's gangrene
Congenital disorders – imperforate anus, Hirschsprung's disease, necrotizing enterocolitis, intestinal atresias

Indications and Types of Stomas

- Indications for a stoma are listed in Table 31.1.
- Permanent stomas are indicated for:
  - Removal of the anus along with its associated musculature.
  - Distal rectal cancers which require an abdominoperineal resection.
  - Severe inflammatory bowel disease with involvement of the sphincter mechanism.
  - Patients of any age with weak sphincter muscles and/or fecal incontinence may be better served with permanent fecal diversion in order to prevent perineal skin breakdown, improve perineal hygiene, and prevent decubitus ulcer formation.
- Temporary stomas are indicated for:
  - Diffuse peritonitis from a perforated colon due to inflammatory conditions
  - Patients who undergo a high-risk distal bowel anastomosis (e.g., following neoadjuvant radiation)
  - Patients who may be symptomatic enough that fecal diversion should be considered as the initial management for their rectal cancer

Ileostomy vs. Colostomy

- Ileostomy may be preferable because of ease of reversal, easier stoma management, and lower incidence of parastomal hernia and sepsis and more effective in diverting the fecal stream.
- Loop colostomies have more complications such as parastomal and incisional hernias, stomal prolapse, and fecal fistulas.

Stoma Creation

- Stomas may be created as either a loop stoma or an end stoma.
- Loop stomas are often used when they are temporary and in the presence of a distal intestinal obstruction, whereby the primary cause of the obstruction is left undisturbed.
- Loop stomas are often larger than end stomas since both limbs of bowel must be exteriorized through the same fascial defect.
- Loop stomas may be more prone to develop parastomal hernias.
- End stomas are often smaller and easier to manage. They are rarely associated with stomal prolapse and may have a lower incidence of parastomal hernia formation.
- End stomas often require more extensive surgery for reversal.
- Another alternative in stoma creation is the loop end stoma. This may be performed in the obese patient.

Stoma Physiology

- The physiological changes that occur are primarily related to the loss of continence and reduced colonic absorptive surface area. These affect fluid and electrolyte balance.
- However, once more than 50 cm of terminal ileum has been removed or taken out of continuity, nutritional consequences are likely.
- Distal left or sigmoid colostomies normally produce formed 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.
- 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.
- Most patients with an ileostomy 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 quantity is reduced by 80–90 % to 100–200 ml of fluid volume in normal stool as it passes through the colon.
- The average colostomy produces 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 one-half and may be as low as 50–100 ml per day.

- 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. Output above this level is usually associated with dehydration.
- Ileostomy effluent is generally weakly acidic at a pH of about 6.3.

Transit

- It appears that small bowel transit times decrease after ileostomy, possibly related to mucosal hypertrophy and adaptation. The specific mechanisms are not known.
- Gastric emptying is not altered in ileostomy patients. Yet, small bowel transit is longer than in control subjects (348 vs. 243 min).

Fluid and Electrolyte Balance

- The average ileostomy puts out about 500 ml of water and 60 mmol of sodium per day and amounts approximately two to three times higher volumes than found in normal fecal output.
- Urinary volume is relatively decreased in patients with ileostomies by as much as 40 %, while renal sodium losses may be decreased by 55 %.
- Total body water and sodium reductions may be a chronic condition in ileostomy patients.

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.
- Staphylococci, streptococci, and fungi are increased, while Bacteroides fragilis is rarely found in ileostomy effluent.

Nutrition

- The colon plays little role in the maintenance of normal 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.
- Vitamin B12, necessary for normal hemoglobin synthesis, may not be adequately absorbed in patients with terminal ileal loss or significant Crohn's disease. This loss results in pernicious or macrocytic anemia.
- Kidney stones may be a consequence of chronic dehydration and acidic urine.
- Adding sodium bicarbonate to the diet as well as increasing fluid intake may help to prevent uric acidic stone formation.

Fig. 31.1 Stomal placement. The site is selected to bring the stoma through the rectus abdominis muscle (With permission from Beck DE. Intestinal stomas. In: Beck DE, ed. Handbook of Colorectal Surgery, 2nd ed. Taylor and Francis, 2003)

Preoperative Considerations

- Preoperative planning needs to be initiated. This planning includes both preoperative counseling and stoma marking.
- Often times it is beneficial for the patient to speak to other willing patients.
- Support group participation may be very valuable.
- Lastly, the patients should be properly marked by the enterostomal therapist for the ideal site(s) of the stoma (Fig. 31.1).
- Stoma sites should be modified to avoid scars, skin creases, and other skin disorders. Stoma markings should be done with the patient in both the sitting and standing positions, and attention must be given to the beltline and pant height. The site must be 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.
- Stomas should be placed through the rectus sheath and reduce the incidence of parastomal hernias.
- Siting a stoma through the umbilicus is a reasonable alternative when there is no other good location.
- There is no data to suggest that tacking the mesentery or bowel to the fascia may in fact be effective in reducing prolapsed or hernia formation.

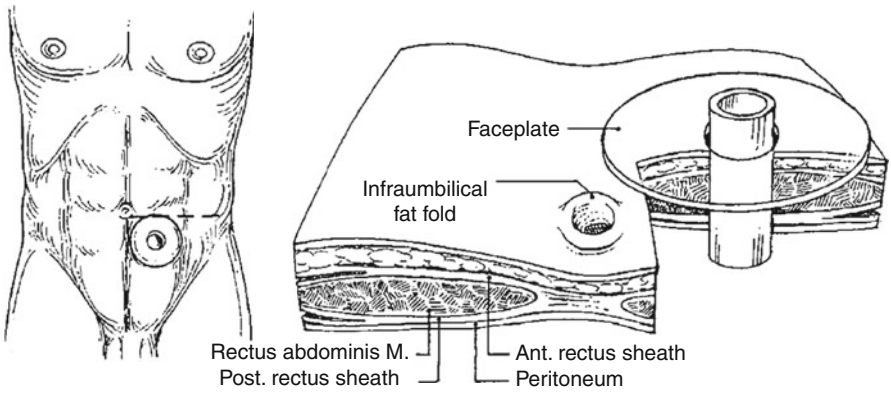

Fig. 31.2 Colostomy creation. (**a**) Circular skin disk is removed. (**b**) Fascia is divided. (**c**) End of colon is brought through the fascia and skin opening (With permission from Beck DE. End sigmoid colostomy. In: MacKeigan JM, Cataldo PA, eds. Intestinal Stomas. Principles, Techniques, and Management. Taylor and Francis, 1993)

Techniques of Stoma Creation

- The basic surgical principles that apply to stoma creation include the following:
  1. The bowel to be exteriorized must be well vascularized, and the mesentery must not be stretched to the point of inducing stomal ischemia or necrosis.
  2. The bowel must reach the skin without tension in order to prevent stomal retraction.
  3. The intestine must be brought through the rectus sheath, and the facial opening should be just two fingerbreadths in width in order to reduce the incidence of parastomal hernia and prevent obstruction of the bowel as it exits through the opening.
  4. A disk of skin should be excised where the stoma is to be placed rather than simply creating a slit in the skin. This will prevent stomal stenosis and obstruction (Figs. 31.2 and 31.3).

Laparoscopic Stoma Creation

- Surgeons will often place a port at the site of the stoma marking and exteriorize the bowel through this area at the completion of the surgery (Fig. 31.4).
- However, some care must be taken upon using this laparoscopic technique with regard to bowel orientation.
- Twisting of the bowel at this level may result in a mechanical obstruction at the level of the stoma site.
- More importantly, one must assure that the proximal portion of the bowel is exteriorized in those patients undergoing an end stoma.
- Many surgeons now believe that laparoscopy should be the primary means of stoma creation.

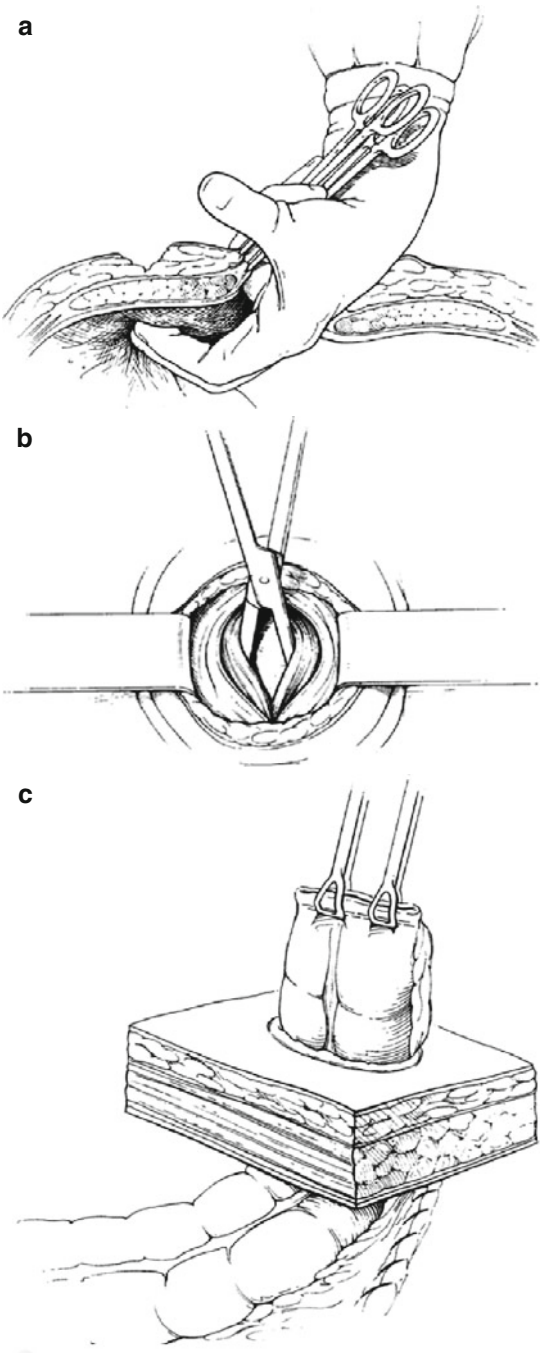

Fig. 31.3 Method of creating an end colostomy

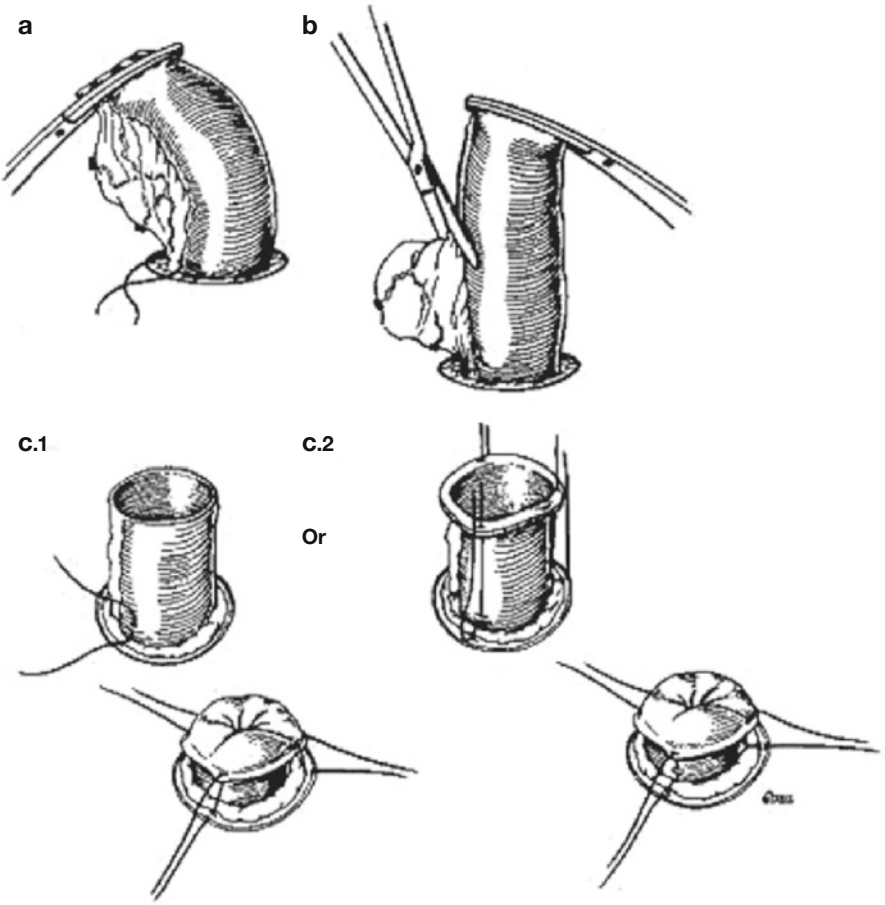

Fig. 31.4 Ileostomy maturation. (**a**) Ligation. (**b**) Trimming of the ileal mesentery. (**c**.1) Serosa is attached to Scarpa's fascia and the mucosal edge sutured to the dermis. (**c**.2) Triangular stitch from ileal end to serosa to dermis; tying sutures inverts the ileum to the skin (With permission from Beck DE. Intestinal stomas. In: Beck DE, ed. Handbook of Colorectal Surgery, 2nd ed. Taylor and Francis, 2003)

Controversies of Intestinal Stomas

When Should Stomas Be Used to Provide Distal Anastomotic Protection

- While the retrospective studies did not show any difference in the anastomotic failure rate with a defunctioning stoma in place, they did prove that there were far fewer major problems once these leaks occurred.
- Many studies suggest that proximal diversion at the time of low anterior resection may not alter the leak rate, but it does lower the rate of septic complications and should therefore be considered in most if not all cases.

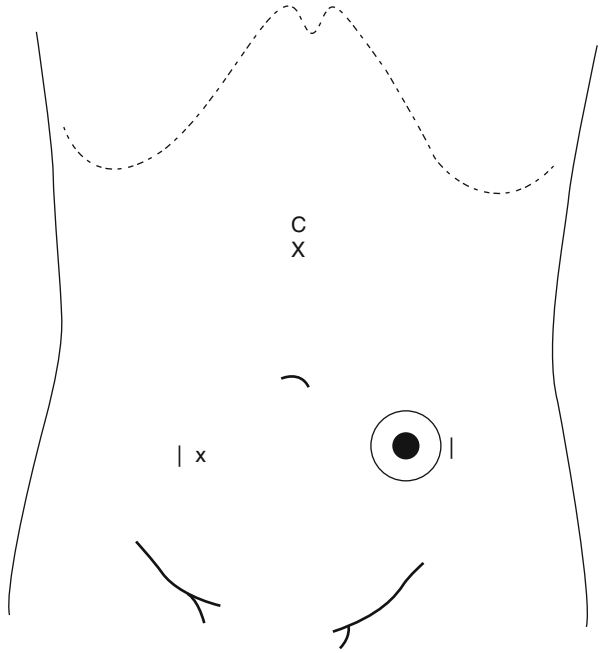

Fig. 31.5 Stoma with severe skin problems

Stomal Complications

- The difficulties of a stoma should not be underestimated.
- Most of the skin issues related to the stoma do not require surgery. Many surgeons will refer their patients to an enterostomal therapist in order to help with this problem.
- It is imperative that surgeons have a good understanding of stomal care.
- Many of the skin problems from a stoma may be traced back to poor site selection in the first place whereby the stoma was placed under a skin crease.
- Surgical correction for severe skin problems from the stoma may need to be done if enterostomal care has failed (Fig. 31.5).
- Parastomal hernia remains a major problem following stoma creation.
- A recent prospective audit of parastomal hernias found that the overall rate of parastomal hernia was 33 % and that aperture size and patient age were independent predictors of this problem.
- They found that for every additional millimeter increase in aperture size, there was a 10 % increase in risk of developing an hernia and for every additional year of patient age, the risk increased by 4 %. In addition, colostomies were at higher risk for hernia formation than ileostomies.
- Incisional hernia rate of 31 % at the previous stoma site.

- It has been found that waist circumference over 100 cm was associated with a 75 % probability of developing a parastomal hernia.
- Parastomal hernia prevention is perhaps the best method of treatment.
- As a general rule, stomas should be placed through the rectus sheath for additional muscular support, fascial openings should be of the appropriate size for the portion of exteriorized bowel, prophylactic use of mesh may be considered for those patients requiring a permanent stoma, and extraperitoneal tunneling of the bowel may also be considered.
- Once parastomal hernias are present and repair is necessary, there are several surgical options available.
- The stoma may be resited to an area on the opposite side of the abdomen that has never been used.
- Other options for parastomal hernia repair include a laparoscopic approach with mesh implantation around the stoma and covering the fascial defect or an open technique around the stoma itself either with suture closure of the fascial defect or with the placement of mesh. Biologic meshes may be more suitable for this approach since the operation is considered a clean contaminated field.

High-Output Stomas

- But the more voluminous and more liquid effluent typical of the ileostomy may make these patients more prone to electrolyte disturbances and dehydration with marked diarrhea and dehydration occurring in 5–20 % of ileostomy patients particularly in the early postoperative period.
- Patients should be told to drink plenty of fluids should they have a stoma with many of the popular sport drinks being suitable for fluid and electrolyte replenishment.
- The stoma output will need to be controlled with antidiarrheal agents or bile salt binders. Opiates may also be used to slow down small bowel transit. In extreme cases, injections of somatostatin may be used to reduce salt and water excretion and slow gastrointestinal tract motility.

Stone Formation

- It has been estimated that up to 12 % of patients with an ileostomy may develop urinary stones and the numbers seem to be higher in those patients who have had small bowel resected in addition to having an ileostomy.
- It appears that a high level of uric acid is the main cause of the stone formation.
- The hyperuricemia may allow the calcium oxalate crystals to form more readily by lowering the saturation index. This may also be facilitated by the excess loss of fecal water, sodium, and bicarbonate, all of which reduces urinary pH and volume.

- Patients should be advised to increase their fluid intake and possibly eliminate foods rich in oxalate such as spinach and some leafy vegetables.
- Whether there is a higher incidence of gallstone formation in patients with an ileostomy remains controversial.

Intestinal Obstruction

- However, there have been papers reporting bowel obstruction occurring in up to 20 % of patients with an ileostomy. As in most cases, adhesions are probably the most common cause, but small bowel volvulus, internal hernia, or even incarcerated parastomal hernias may also be contributing factors.
- Some surgeons have suggested closing off the lateral peritoneal reflection around the stoma site or even bringing the bowel up to the skin in an extraperitoneal fashion in order to prevent internal hernia formation and torsion. However, there has never been proven true benefit to any of these methods.

Ischemic Stomas

- Many stomas may initially appear edematous and congested after stomal creation due to mechanical trauma and the compression of the small mesenteric vessels as they traverse the abdominal wall.
- This often resolves within a few days to weeks after surgery.
- If there is concern about bowel viability after surgery, one can simply insert a glass test tube or sigmoidoscope into the stoma in order to determine if the bowel is viable beneath the tip of the stoma. If the stoma is viable at the fascial level, then the patient may be carefully observed.
- However, if there is question about the viability of the stoma at the fascial level, the patient should be returned to the operating room in order to undergo stoma revision.

Stoma Prolapse

- Stomal prolapse is a more common complication of loop than end stomas.
- The best way to treat a stomal prolapse is to reverse the stoma.

Stomal Irrigation and Continence

- For those patients not desiring to wear an appliance, colostomy irrigation may provide an alternative.
- However, colostomy irrigation requires a level of motivation, intelligence, and dexterity on the part of the patient.
- The Kock pouch or continent is an option for selected patients.

Stoma Reversal

- Prior to stoma reversal, the patients must be appropriately studied to ensure that it is safe to reverse the stoma.
- The patient may require a sigmoidoscopic evaluation of this portion of the bowel or a contrast enema.
- In addition, the proximal colon should always be evaluated prior to end colostomy reversal to ensure that there are no lesions present.
- If the patient has a loop stoma that was performed to protect a distal anastomosis, one must ensure that this anastomosis is healed prior to the stoma reversal.
- The length of time from stoma creation to reversal makes a difference in terms of whether or not another stoma was used in the reversal procedure suggesting that increased time made the reversal a more difficult operation.
- Not all patients are candidates for Hartman's reversal. In fact, many studies have suggested that many patients may never undergo stoma reversal because of their comorbidities.

32. Constipation and Functional Bowel Disorders

Madhulika G. Varma and Brooke H. Gurland

Definition and Prevalence

- Prevalence in North America estimated between 2 and 27 %.
- Complaints of constipation are two to three times more common in women than men.
- Of 2,004 patients evaluated by transit study at three European tertiary referral centers for intractable constipation, 92 % were women.
- The incidence of constipation increases with age, and it is higher in non-whites than whites, in people from a lower socioeconomic and educational status, and in the southern USA.
- The Rome criteria for constipation are as follows:
  - Less than three bowel movements per week
  - Straining more than 25 % of the time
  - Hard stools more than 25 % of the time
  - Incomplete evacuation more than 25 % of the time
- When utilizing the standardized definitions of the Rome criteria, the prevalence of constipation in North America is estimated at 15 %.
- The Bristol Stool Scale is a visual representation of stool form and helps to subtype functional bowel disorders (Fig. 32.1).

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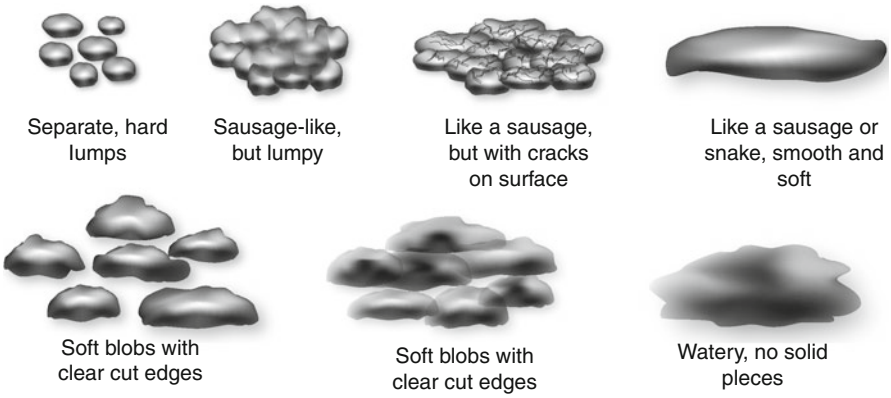

Fig. 32.1 Bristol Stool Scale (Adapted with permission from Lewis and Heaton, © 1997 Informa Healthcare. Reproduced with permission)

Etiologies of Constipation

- Diet affects the size, consistency, and frequency of bowel movements; dietary fiber intake is highly correlated with stool bulk.
- Factors associated with constipation are summarized in Table 32.1.

Subtypes of Constipation

- Patients can be further classified by associated findings such as slow transit (motility disorders), irritable bowel syndrome (IBS), and pelvic floor dysfunction, also described as obstructed defecation syndrome (ODS) or mixed disorders.
- Motility disorders can be isolated to the colon (colonic inertia aka slow-transit constipation) or can affect the stomach and small bowel.
- Colonic inertia (CI) is frequently associated with constipation since childhood, fewer than 3 BMs per week, and laxative dependence.
- IBS-C (constipation subtype) is associated with abdominal pain, irregular bowel habits, and pain relieved by defecation.
- ODS refers to a constellation of symptoms such as prolonged repeated straining at bowel movements, sensation of incomplete evacuation, and the need for digital manipulation.

History and Physical Examination

- The evaluation of constipation begins with a thorough history.
- Query into psychiatric illness and sexual and physical abuse must be performed as they are often associated with defecation difficulties.

Table 32.1 Factors associated with constipation

Lifestyle
Inadequate fluid intake
Inadequate fiber intake
Inactivity
Laxative abuse
Medications
Opiates
Anticholinergics
Iron
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

- Multicompartment pelvic floor symptoms such as urinary dysfunction, pelvic organ prolapse, and sexual dysfunction need to be elicited.
- Evaluation for pelvic floor dysfunction includes vaginal, perineal, and rectal examination.
- Bulging of the posterior vaginal wall beyond the hiatus is consistent with advanced prolapse and may represent a rectocele, enterocele, or sigmoidocele. *Examination in the standing position with a finger in the rectum and vagina may be performed to elicit the maximal prolapse of the pelvic organs as they descend through the pouch of Douglas and genital hiatus.

- A gaping patulous anus may indicate neurological injury, intra-anal intussusception, or full-thickness rectal prolapse.
- Digital examination evaluates resting anal tone and squeeze strength and can identify a large rectocele, sphincter defect, or no movement of the pelvic floor muscles.
- Valsalva maneuver or simulated defecation on a commode is useful to elicit full-thickness rectal prolapse.

Diagnostic Testing

- Laboratory testing with thyroid studies and calcium levels is useful to exclude metabolic etiologies of constipation.
- Obstructing colon lesions and inflammatory conditions such as IBD or diverticulitis must be excluded by colonoscopy or GI contrast studies before considering functional etiologies.

Diagnostic Studies to Evaluate Intestinal Transit

- The most widely available technique for determining colonic transit uses radiopaque markers and radiographs of the abdomen.
- The patient should refrain from all enemas, laxatives, and most medications for 2 days prior to 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, and the distribution and number of markers present in the colon is noted. A variation is to obtain radiographs on days 1, 3, and 5.
- Eighty percent of normal patients will have passed all the markers by 5 days.
- If the markers remain scattered throughout the colon and more than 20 % of the markers remain in the colon, colonic inertia can be diagnosed.
- If the markers are found to have accumulated in the rectum, traditional teaching suggests that this is a diagnostic of outlet obstruction constipation (Fig. 32.2); however, this is controversial and there may be no correlation between the pattern of marker distribution and type of constipation.
- In the general population, 95 % of patients will have a transit time of less than 65 h in men and 75 h in women. Patients with normal transit constipation will have a colon transit time that is in the normal range.
- Transit times obtained through scintigraphy are generated by following the passage of a radiolabeled meal.
- Small-bowel transit time may also be measured with a lactulose hydrogen breath test. The principle of this examination is that hydrogen produced through lactulose fermentation only occurs in the colon. If one records the time from ingestion of lactulose to hydrogen production, small-bowel transit time can be inferred.

Fig. 32.2 Marker study revealing colonic inertia

Diagnostic Studies to Evaluate Pelvic Floor Dysfunction

- Anal manometry evaluates resting and squeeze pressure; often with constipation, patients exhibit internal sphincter hypertonia with poor incremental squeeze pressures.
- The volume noted at first sensation can be blunted, i.e., requiring larger volumes to obtain a sensory response, and the maximum tolerated volume can also be blunted.
- The presence of the rectal anal inhibitory reflex (RAIR) is useful to exclude Hirschsprung's disease.
- Electromyography aids in the diagnosis of puborectalis syndrome by indicating a paradoxical or nonrelaxing muscle.
- Balloon expulsion is an inexpensive method to assess ability to evacuate. Normal studies indicate the ability to evacuate a 50–100 cm^3 balloon in less than 1 min.

- Defecography is the gold standard to confirm evacuatory dysfunction due to intussusception, rectal prolapse, enterocele, sigmoidocele, rectocele, and perineal descent.
- Some centers use a dynamic MRI, but the technique varies. For the best images, complete evacuation of the contrast during the MRI after Valsalva will most likely simulate defecation.
- Defecating MRI has advantages over traditional defecography because it involves less radiation and provides multicompartment images. However, defecating in the supine position is not physiologic.
- For patients with pelvic floor dysfunction who demonstrate dysnergic defecation, randomized controlled trials show that biofeedback is superior to laxatives, sham treatments, and alternative therapies.
- In the setting of rectal intussusception, rectocele, and mucosal prolapse, stapled transanal rectal resection (STARR) can be offered.
- STARR employs a double stapled technique
- Prospective multicenter trials reveal initial and long-term symptom improvement of obstructed defecation after STARR.
- A randomized controlled trial of STARR versus biofeedback revealed that STARR is more effective for treatment of evacuatory dysfunction.
- For patients with a clinical or radiologic rectocele and retained rectal contrast, rectocele repair can be suggested.
- Rectocele repair can be performed via transvaginal transanal or transperineal approach with 75–80 % reported bowel symptoms improvements.
- Enterocele involves descent of small bowel into the lower pelvic cavity, leading to mechanical obstruction of the rectum.
- A sigmoidocele refers to descent of the sigmoid colon into the lower pelvic cavity leading to compression and mechanical obstruction of the rectum.
- Sigmoid resection or sigmoidopexy in conjunction with posterior compartment repair has been shown to be effective in relieving symptoms of obstructed defecation in a limited number of patients.

Medical Treatment of Constipation

- Simple measures that can influence the passage of colonic content are increasing physical activity and fluid intake.
- Osmotic laxatives, stimulants, and enemas should be reserved for treatment of acute bouts of discomfort.
- Bulking agents promote these changes by delivering a mass of nondigestible substrate to the colon and, due to their hydrophilic nature, facilitate the absorption and retention of fluid in the stool.
- These substrates are derived from the nondigestible components of plants or are synthetic methylcellulose derivatives.
- Osmotic laxatives are a class of medications that promote the accumulation of large volumes of fluid in the colon.

- The osmotically active particles can be derived from sugars or salts such as sucrose-based sorbitol and lactulose.
- Lactulose is degraded in the colon yielding the production of fatty acids, hydrogen, and carbon dioxide.
- MiraLAX® (polyethylene glycol 3350) is an over-the-counter osmotic laxative that increases the frequency of bowel moments and softens the stool, so it is easy to pass.
- Osmotic laxatives can also be based on nonabsorbable ions, commonly derived from magnesium or phosphate.
- Caution must be exercised in patients with renal insufficiency as hypermagnesemia and renal failure can result.
- Colonic irritants are a class of agents that diminish constipation through stimulation of colonic motility. Examples are anthracene derivatives, which include senna and cascara and are found in Senokot® and Peri-Colace®.
- Long-term anthracene intake can generate a characteristic brown discoloration of the mucosa called pseudomelanosis coli.
- Bisacodyl is another irritant and can be found in the agent Dulcolax®.
- Long-term utilization of anthracene irritants may lead to poor colon function; therefore, such use is discouraged.
- Mineral oil coats the stool bolus, preventing fluid loss.
- Docusate sodium lowers the surface tension at the stool–water interface, allowing greater penetration of the stool with fluid.
- Lubiprostone (Amitiza®) is still commercially available for use in patients with functional constipation and IBS-C. It is a chloride channel activator that induces intestinal secretion without elevating serum electrolyte levels. It activates C1C-2 chloride channels in the apical membrane of the intestinal epithelium. It is Food and Drug Administration (FDA) approved for the treatment of chronic idiopathic constipation in the adult population (including patients > 65 years old) at the dose of 25 μg bid and for IBS constipation subtype patients at 8 mg bid.

Colonic Inertia

- In the majority of patients, symptoms have been present since childhood, while others present with symptoms later in life without a sentinel event.
- Slow-transit constipation may be part of a more widespread disease affecting the whole gut, and patients with gastric and small-bowel dysmotility have less favorable results after surgical intervention than patients with colonic inertia alone.
- Patients with slow-transit constipation and concomitant pelvic floor dysfunction represent a challenging subgroup to treat. Postoperative symptoms of difficult evacuation may persist but the literature is not conclusive in this regard.
- Psychological evaluation and management is important, especially in patients in whom surgery is being contemplated.

Colectomy

- Preoperative functional evaluation is very important but does not guarantee successful outcome following colectomy for constipation.
- Routine evaluation of the entire GI tract is recommended by some author.
- Furthermore, patients with prior sexual trauma have been shown to have more functional diagnosis and more precolectomy operations and require more postcolectomy medical care for abdominal complaints.
- Patients should be extensively counseled prior to surgery about the postoperative persistence of preoperative symptoms and the occurrence of new symptoms (Table 32.2).

Segmental Colon Resection

- Since the ability to define segmental colonic transit is inexact and not universally available, total abdominal colectomy remains the most widely accepted surgical treatment option in the treatment of CI.

Proctocolectomy and Ileal Pouch Anal Anastomosis

- Proctocolectomy with ileoanal pouch reconstruction has been described as a salvage operation for patients with recurrent constipation after abdominal colectomy with ileorectal anastomosis for slow-transit constipation. Results are mixed, patients may still have constipation.
- Proctocolectomy has also been used as initial treatment for slow-transit constipation and rectal inertia. Overall, significant improvements in lifestyle scores were recorded.

Stoma

- Fecal diversion with a permanent stoma is a last resort for the patients who fail other modalities.

Sacral Nerve Stimulation

- In general, the number of weekly BMs increases with SNS, and difficulty with evacuation (here defined as unsuccessful visits to the toilet) and time necessary to evacuate are decreased.
- The exact mode of action is not known.

Antegrade Colonic Enema

- Patients with severe bowel dysfunction who are contemplating a permanent colostomy may find the antegrade colonic enema (ACE) procedure as an affirmative viable option. This procedure allows easy access to the colon through the abdominal wall with intermittent catheterization, irrigation of the colon, and rapid, controlled bowel purging (Fig. 32.3).

Table 32.2 Surgical therapy for constipation

Authors	*N*	Surgery/anastomosis type	Study design	Study subjects		Study subjects age	Follow-up time	#BM	Patient reported outcomes	30-day complications
				F	M	Mean/median	Mean/median	Mean/median		
Nyam et al.	74	TAC with ileorectostomy CI group: 52 patients CI+PFD group: 22 patients	R	68	6	M: 43 (23–71)	M: 56 (2–101) months	Md: CI: 4 (0–20)/day CI+PFD: 2 (1–6)/day	72 (97 %) patients satisfied	*23 (31 %) patients* 9 (12 %): ileus 7 (9.45 %): SBO 4 (5 %): wound infection 3 (4 %): UTI
Pikarsky et al.	30	TAC with IRA	R	21	9	M: 60 (28–85)	M: 106 months	M: 2.5 (1–6)/day	Good/excellent: 100 %	6 (20 %): SBO
Webster et al.	55	50 (91 %) patients: TAC with ileoproctostomy 5 (9 %) patients: TAC w/Brooke ileostomy	R	47	8	M: 40 (13–78)	FU: 12 months	M: 3/day	Good/excellent: 89 % Poor: 11 %	*23 (42 %) patients* 24 %: ileus 8 %: SBO 4 %: anastomotic leak
Mollen et al.	21	TAC with IRA	R*	19	2	M: 42.8 (16–75)	FU: 12 months	2.8/day	52 %	*7 (33 %) patients* 3 (14 %) patients: SBO
Verne et al.	13	ST: 7 patients: ISA 6 patients: IRA	R	13	0	M: 46.2 (26–67)	Not reported	M: 15 (±4.5)/week	85 % patients satisfied	Not reported
Fitz Harris et al.	75	ST with primary anastomosis	R	75	0	Not reported	M: 3.9 (0.5–9.6) years	69 (92 %) patients: 2–3/week	70 (93 %) patients: willing to have SC again	*40 (53 %) patients:* 29 (37 %): SBO 11 (15 %): wound infection

(continued)

Table 32.2 (continued)

Authors	*N*	Surgery/anastomosis type	Study design	Study subjects		Study subjects age	Follow-up time	#BM	Patient reported outcomes	30-day complications
				F	M	Mean/median	Mean/median	Mean/median		
Thaler et al.	17	TAC with IRA	R*	17	0	M: 47.8 (±14.3)	M: 58.3 (±27.3) months	M: 3.7 (±2.8)/day	Good/excellent: 100 %	*6 (35.2 %) patients* 2 (12 %): hernias 4 (23.5 %): SBO
Hassan et al.	110	TAC with IRA	P	104	6	Md: 40 years	Md: 11 (1.5–16.5) years	Md: 4/day	Good/improved: 90 %	Not reported
Zutshi et al.	69	TAC with IRA	R	67	2	M: 38.6 (20–79)	Md: 10.8 years	M: 21/week	77 % patients: surgery was beneficial	*20 (29 %): patients* 11 (16 %): ileus 4 (6 %): prolonged fever 3 (4 %): diarrhea 1 (1.5 %): bleeding 1 (1.5 %): anastomotic leak

TAC total abdominal colectomy, *ST* subtotal colectomy, *ISA* ileosigmoid anastomosis, *IRA* ileorectal anastomosis, *CI* colonic inertia, *PFD* pelvic floor dysfunction, *R* retrospective study, *P* prospective study, *R** data prospectively collected, *M* mean, *Md* median, *SBO* small-bowel obstruction.

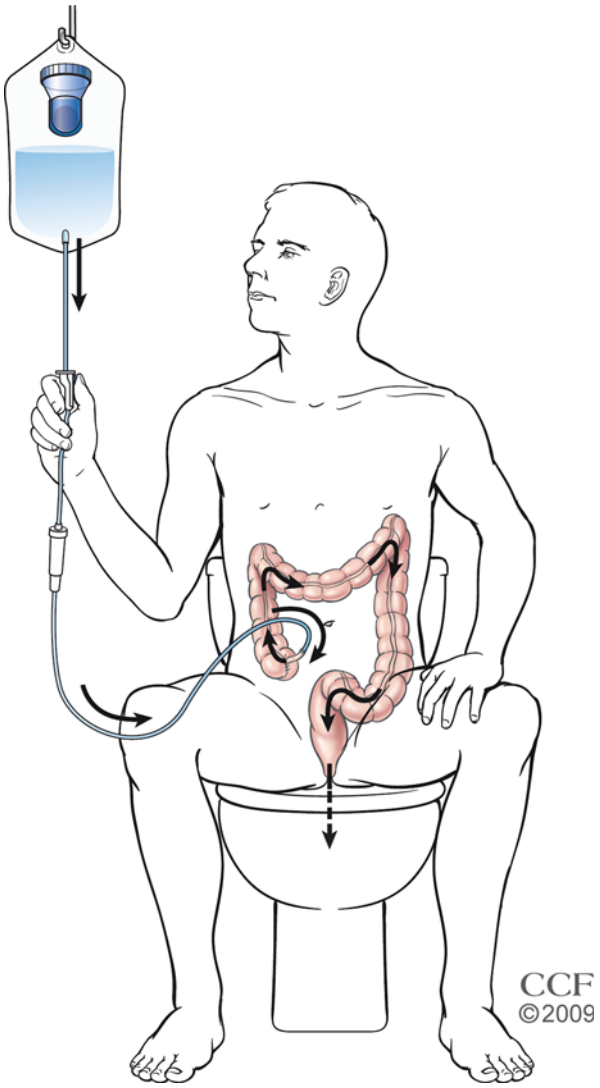

Fig. 32.3 Antegrade colonic enema (ACE) procedure for colonic inertia. This procedure allows easy access to the colon through the abdominal wall with intermittent catheterization, irrigation of the colon, and rapid, controlled bowel purging (Reprinted with permission, Cleveland Clinic Center for Medical Art and Photography © 2009. All Rights Reserved)

Irritable Bowel Syndrome

- Irritable bowel syndrome (IBS) is a functional bowel disorder in which abdominal pain or discomfort is associated with defecation or a change in bowel habits.

- Organic pathology is absent, and diagnosis is made on clinical symptoms and exclusion of other disease states.
- These symptoms are variably associated with mucorrhea and/or abdominal bloating.
- IBS can be categorized into the following: constipation predominant (IBS-C), diarrhea (IBS-D), or mixed (IBS-M). The Rome criteria for a clinical diagnosis of IBS are listed in Table 32.3.

Epidemiology

- Population-based studies in Western countries report an overall prevalence of IBS of 10–20 %.
- In non-Western countries in Asia and Africa, some studies suggest that IBS incidence may be lower.
- In Western countries, women are two to three times more likely to develop IBS than men; in India, this phenomenon is reversed.
- Patients with IBS who present for evaluation are at least twice as likely to meet criteria for psychiatric disorders as patients with organic disease.
- However, no specific pattern of personality traits in patients has been identified.

Pathophysiology

- The pathophysiology of IBS remains uncertain. Despite extensive investigations, no specific physiologic abnormality has been identified, and IBS remains a diagnosis of exclusion.

Gastrointestinal Motility

- The current theories regarding the pathophysiology of IBS are of a complex interaction between altered gut motility and/or visceral hyperalgesia and neuropsychopathology.

Table 32.3 Rome criteria for irritable bowel syndrome

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

- Patients with IBS have variations in the colonic slow wave frequency and a blunted late peaking postprandial response of spike potentials in the colon.
- Studies suggest an underlying generalized hyperresponsiveness of smooth muscle in patients with IBS.

Visceral Hypersensitivity

- Visceral hyperalgesia appears to be another component of this disorder.
- It appears 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.
- It is thought that patients with IBS may have sensitization of the intestinal afferent nocioreceptive pathways in the spinal cord.
- Patients with IBS may process visceral afferent input in the central nervous system in an abnormal way, and this response may be modified by attentional factors acknowledging that stress, anxiety, and prior unpleasant life events increase the perception of painful events.
- On a biochemical level, patients with IBS have been demonstrated to have increased hypothalamic corticotropin-releasing factor in response to stress, as well as an exaggerated colonic motility response.

Small Intestinal Overgrowth Syndrome

- Small intestinal bacterial overgrowth (SIBO) syndrome ($>10^5$ bacteria/ml) has been implicated as possible etiology for IBS.
- 78 % of patients with IBS have an abnormal hydrogen breath test.
- Studies have found higher bacterial counts in IBS patients compared to placebo (43 % vs. 12 %). Treatment with oral antibiotics has become an accepted course of therapy for some patients with suspected SIBO and IBS.

Mucosal Inflammation

- The presence of low-grade inflammation and immune activation suggests that alterations in the indigenous intestinal flora may play a role.
- A correlation between abdominal pain in IBS and the presence of activated mast cells in proximity to colonic nerves has been reported. Probiotics may be helpful to restore the depleted bifidobacteria species found in the human intestine.

Psychological Abnormalities

- The relationship between psychopathology and IBS is unclear.
- Patients with IBS have a higher incidence of panic disorder, major depression, anxiety disorder, and hypochondriasis than do normal populations.
- In addition, they report a higher prevalence of physical or sexual abuse.

Symptoms

- The altered stool habits reported by patients with IBS can be constipation, diarrhea, or alternating constipation and diarrhea.
- What differentiates these patients from those with functional constipation is the presence of significant abdominal pain and bloating.
- Abdominal pain is usually perceived as diffuse and is most common in the lower abdomen.
- 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 such as mucorrhea, either white or clear.
- Overall symptoms may be worse in times of stress.
- Symptoms not typical of IBS that should alert the clinician to organic disease include the following: onset in middle age or older, progressive or nocturnal symptoms, anorexia, weight loss, fever, hematochezia, and painless diarrhea or steatorrhea.

Treatment of IBS-C

- Much of the current medical therapy depends on diet modification and reassurance.

Medical Therapy

- Fiber supplementation may improve symptoms of either constipation or diarrhea, although studies are inconclusive due to a strong placebo effect.
- Similarly, ingesting more water and avoiding caffeine and legumes are all reasonable patient advice.
- 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 MiraLAX®, Milk of Magnesia®, or sorbitol may be tried.
- Lubiprostone (Amitiza®) chloride channel activator has been approved for patients with IBS-C at a lower dose 8 mcg bid to decrease constipation, abdominal discomfort, and bloating.
- Antibiotics have been recommended to treat patients with SIBO and IBS. The following oral antibiotics have been suggested: neomycin orally for 10 days, levofloxacin or ciprofloxacin for 7 days, metronidazole for 7 days, and rifaximin (Xifaxan®) for 10 days at higher than normal doses of (1,200 mg/day) compared to standard lower doses (800 or 400 mg/day).
- Retrospective studies suggest that rifaximin is superior to other oral antibiotics.

Probiotics

- Probiotic bacteria may inhibit other symptom-causing bacteria in the intestine, or the probiotic bacteria may act on the host's intestinal immune system to suppress inflammation.
- The most common probiotic bacteria are lactobacilli (also used in the production of yogurt) and bifidobacteria.
- Both of these bacteria are found in the intestine of normal individuals.
- Fedotozine is clinically available for this indication and has shown to be helpful in reducing symptoms of pain in patients with IBS.
- An adjunctive therapy to medication is psychological treatment. Psychological treatment is appropriate when there is evidence that stress or psychological factors are contributing to an exacerbation of symptoms.

Conclusion

- The Standards Practice Task Force of the American Society of Colon and Rectal Surgeons has published practice parameters for the evaluation and management of constipation.

33. Rectal Prolapse

Steven D. Mills

Rectal prolapse is a telescoping of the rectum out of the anus.

Rectal intussusception is when the telescoping does not protrude through the anal canal.

Many patients have other associated pathologies of the pelvic floor.

Fecal incontinence is a common associated symptom.

There is also a frequent association with anterior compartment pathologies such as urinary incontinence, voiding disorders, cystocele, or rectocele.

Nearly 100 years ago, Moschcowitz suggested that rectal prolapse occurs as a sliding hernia through a defect within the pelvic fascia. Later, Broden and Snellman demonstrated, with the aid of cinedefecography, that rectal prolapse is an intussusception of the rectum.

Rectal prolapse is more common in women than in men and is associated with childbirth, prolonged straining at stool, and/or anatomical considerations such as a wider pelvis. In women, the disorder increases in frequency with age and associated with damage to the pudendal nerves during childbirth and/or chronic straining at stool.

Many different procedures have been described to treat rectal prolapse (Table 33.1).

Choice of procedure is based upon patient and procedural factors. The key issues are gender, the patient's overall medical condition, bowel function, and whether fecal incontinence is present.

There is a dearth of high-quality data regarding the optimum treatment method.

A comprehensive review, in 2008, of randomized trials found a few patterns:

The method of fixation during rectopexy did not change outcome.

Division of the lateral stalks was associated with a higher incidence of constipation.

Resection and rectopexy was associated with less constipation.

Laparoscopy was associated with a shorter hospitalization and less morbidity.

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Table 33.1 Operations described for rectal prolapse

Transabdominal procedures
1. Repair of the pelvic floor
Abdominal repair of levator diastasis
Abdominoperineal levator repair
2. Suspension–fixation
Sigmoidopexy (Pemberton–Stalker)
Presacral rectopexy
Lateral strip rectopexy (Orr–Loygue)
Anterior sling rectopexy (Ripstein)
Posterior sling rectopexy (Wells)
Puborectal sling (Nigro)
3. 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)

Patient Evaluation

Most patients present with complaints associated with the prolapse itself.

Constipation and/or fecal incontinence symptoms should be elucidated.

Physical examination may demonstrate a spontaneous prolapse (Fig. 33.1), while straining may be needed to demonstrate the prolapse in the squatting or sitting position.

A differentiation should be made between full-thickness and mucosal prolapse.

Digital rectal examination detects concomitant anal pathology and evaluates adequacy of sphincter resting tone and squeeze pressure and function of the puborectalis muscle.

Colonoscopy or flexible sigmoidoscopy with air-contrast barium enema excludes and associated mucosal abnormalities.

Defecography adds little in full-thickness prolapse; however, it can be essential in the evaluation of internal or occult procidentia (rectorectal intussusception) or as part of pelvic floor musculature evaluation.

Anal manometry assesses sphincter function, as chronic prolapse typically damages the internal anal sphincter, resulting in poor resting pressures. A manometric study by Spencer reported that the anorectal inhibitory reflex was frequently absent or abnormal, that resting anal pressures were abnormally low, and that squeeze pressures were normal.

Surgical Procedures

There are two general approaches: abdominal and perineal operations.

The most common abdominal operations are rectopexy with or without concomitant sigmoid resection.

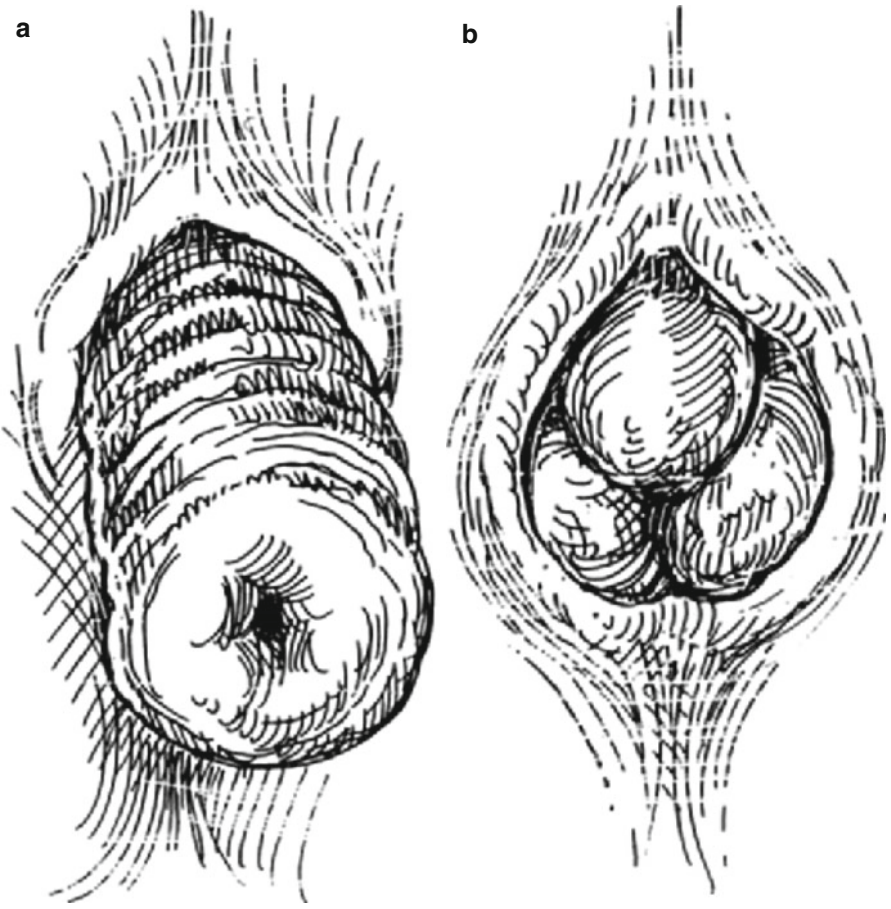

Fig. 33.1 Mucosal versus full-thickness prolapse. (**a**) Circumferential full-thickness prolapse with concentric mucosal folds. (**b**) Radial folds seen with hemorrhoidal prolapse (From Beck and Whitlow. Copyright 2003 by Taylor & Francis Group LLC. Reproduced with permission)

The typical perineal procedures are perineal rectosigmoidectomy (Altemeier) or a mucosal sleeve resection (Delorme).

The specific operation must be tailored to the condition and pathology of each patient, but some generalizations can be made.

Elderly, high-risk patients are best treated with perineal procedures (possibly with regional anesthesia).

An abdominal resection/rectopexy should be considered for a healthy patient with constipation and no incontinence.

The risk of impotence for abdominal rectopexy should approach 1–2 % in skilled hands.

A rectopexy with or without levatorplasty can be performed in patients without constipation symptoms

Perineal Procedures

Rectosigmoidectomy

Rectosigmoidectomy (Altemeier procedure) can be performed under a general or spinal anesthetic in either the prone, left lateral, or lithotomy position. A circumferential incision is made in the rectal wall approximately 1–2 cm above the dentate line (Fig. 33.2). The incision is deepened until the full thickness of the rectal wall has been divided. The rectum is withdrawn out of the body while progressively dividing and ligating the mesorectum, advancing more cephalad.

Anteriorly, the peritoneal reflection (hernia sac) is opened. The dissection continues until there is no further redundancy remaining in the rectum/sigmoid colon. A hand-sutured or circular-stapled coloanal anastomosis is performed. A levator plication can be performed prior to the coloanal anastomosis, which has been reported to improve continence in two-thirds of patients.

Several studies have been reported on perineal rectosigmoidectomy, and clinical outcomes are summarized. An improvement in incontinence is reported in the majority of patients in whom levatorplasty was performed.

Mucosal Sleeve Resection (Delorme Procedure)

The Delorme procedure is ideally suited to those patients with a less extensive prolapse (e.g., about 5 cm in length) or with full-thickness prolapse limited to partial circumference (e.g., anterior wall).

In Delorme procedure, only the mucosa and submucosa are excised from the prolapsed segment (Fig. 33.3).

It can be performed under general, spinal, or local anesthesia. Prone position is preferred, but left lateral or lithotomy position can be used.

Results of Delorme procedure are summarized in Table 33.2. Recurrence rates (6–26 % at 1–13 years postoperatively) are generally higher than with a perineal rectosigmoidectomy. Incontinence is improved in 40–50 % of patients.

An alternative to the mucosal resection with muscular plication is the mucosal plication procedure (Gant–Miwa procedure). The best results seem to be when the mucosal plication is combined with an anal encircling procedure (see section "Thiersch Procedure" below).

Thiersch Procedure

Anal encirclement (Thiersch procedure) was originally performed with a silver wire placed subcutaneously around the anus under local anesthesia. The goal of this procedure was to mechanically supplement or replace the anal sphincter and stimulate a foreign body reaction in the perianal area, thereby increasing resistance at the anus.

William Gabriel in the 1950s reported 25 cases of incontinence or minor rectal prolapse. He did not recommend this operation for major degrees of prolapse.

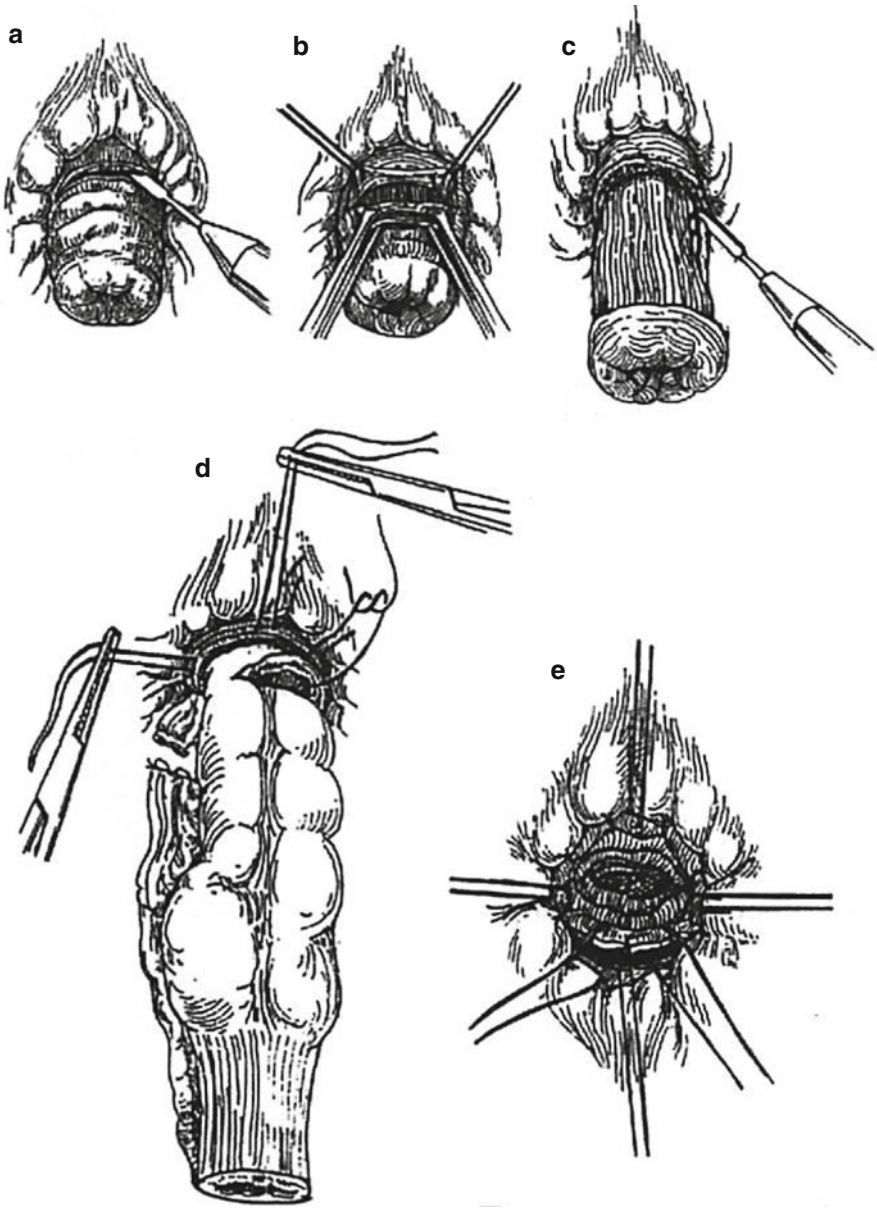

Fig. 33.2 Perineal rectosigmoidectomy. (**a**, **b**) Incision of rectal wall. (**c**) Division of vessel adjacent to bowel wall. (**d**) The prolapsed segment is amputated. Stay sutures previously placed in distal edge of outer cylinder are placed in cut edge of inner cylinder. (**e**) Anastomosis of distal aspect of remaining colon to the short rectal stump (From Beck and Whitlow. Copyright 2003 by Taylor & Francis Group LLC. Reproduced with permission)

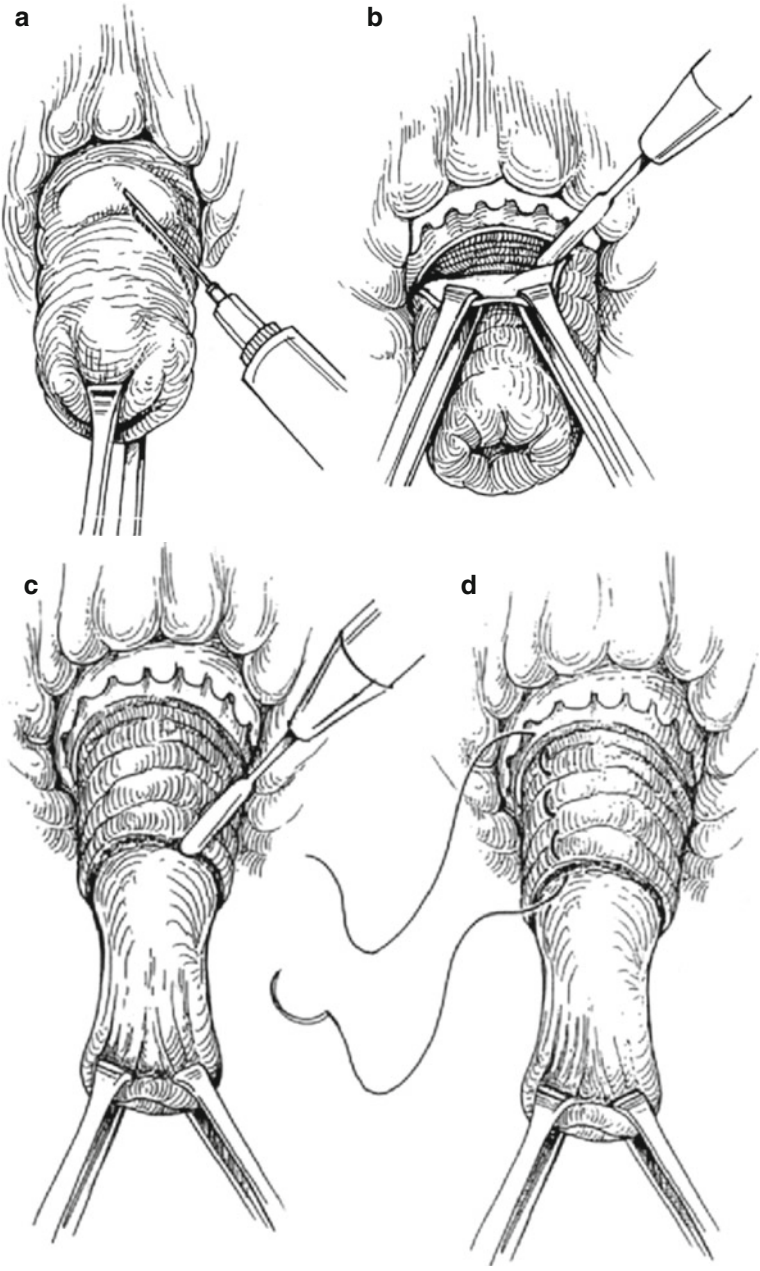

Fig. 33.3 Delorme procedure. (**a**) Subcutaneous infiltration of dilute epinephrine solution. (**b**) Circumferential mucosal incision. (**c**) Dissection of mucosa off muscular layer. (**d**) Plicating stitch approximating cut edge of mucosa, muscular wall, and mucosa just proximal to dentate line. (**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 (B) in the format Textbook via Copyright Clearance Center)

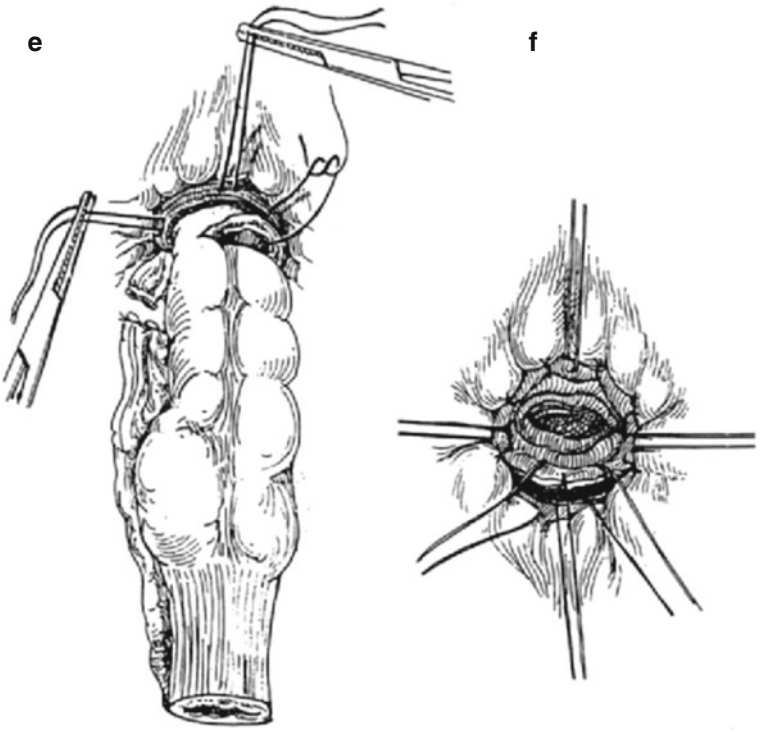

Fig. 33.3 (continued)

Table 33.2 Results of Delorme procedure

Authors	Number of patients	Recurrence	Mortality	Morbidity
	n	(%)	(%)	(%)
Uhlig and Sullivan	44	7	0	34
Monson et al.	27	7	0	0
Senapati et al.	32	13	0	6
Oliver et al.	41	22	2	62
Tobin and Scott	43	26	0	12
Graf et al.	14	21	0	–
Watkins et al.	52	6	0	77
Lieberth et al.	76	14	0	25

Anal encirclement is performed with the patient placed in the prone jackknife, lithotomy, or left lateral position (Fig. 33.4). A variety of materials used for encirclement include nylon, silk, Silastic rods, silicone, Marlex mesh, Mersilene mesh, fascia, tendon, and Dacron.

Complications of this procedure include breakage of the suture or wire, fecal impaction, sepsis, and erosion of the encircling material into the skin or anal canal.

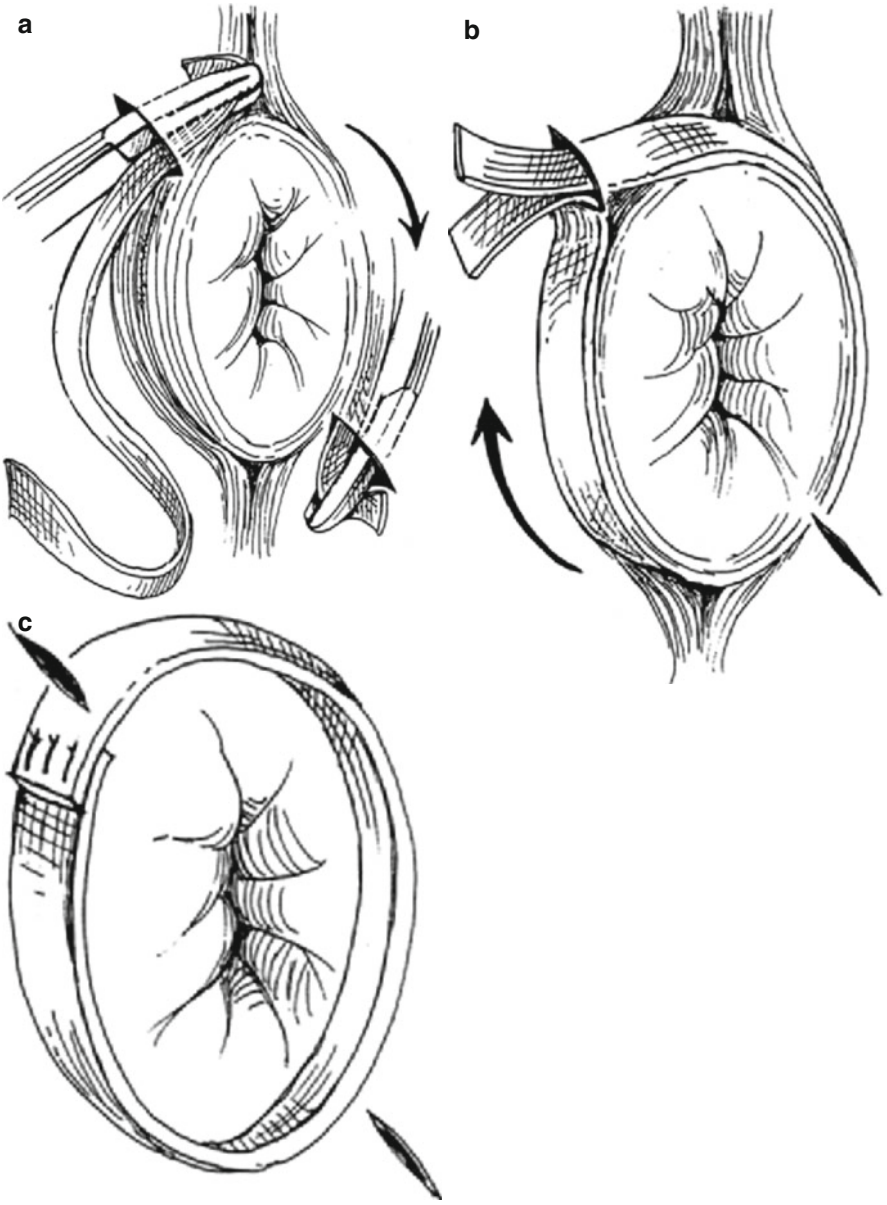

Fig. 33.4 Anal encirclement (Thiersch). (**a**) Lateral incisions with prosthetic mesh tunneled around the anus. (**b**) Mesh completely encircling the anal opening. (**c**) Completed anal encirclement procedure (From Beck and Whitlow. Copyright 2003 by Taylor & Francis Group LLC. Reproduced with permission)

Table 33.3 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
Sainio et al.	14	15	–	–

Results of the Thiersch procedure are summarized in Table 33.3.

Abdominal Procedures

Abdominal Rectopexy and Sigmoid Colectomy

Initially described by Frykman in 1955.

The four essential components are shown in Fig. 33.5 and results in Table 33.4.

Abdominal Rectopexy

Simple suture rectopexy without sigmoid colectomy has been reported.

Rectopexy without resection can lead to worsening of constipation.

Results are summarized in Table 33.5.

Ripstein Procedure

The Ripstein operation was popular in the past, but is infrequent today, due to the success of alternate therapies, the incidence of postoperative constipation, and use of prosthetic material.

The rectum is mobilized posteriorly with preservation of the lateral stalks. A 5-cm piece of prosthetic mesh (Marlex or Prolene) is sutured to the presacral fascia within the sacral hollow, about 5 cm below the sacral promontory in the midline (Fig. 33.6).

Care must be taken to avoid making the wrap too tight thus causing an obstruction.

The results are summarized in Table 33.6.

Posterior Mesh Rectopexy

- Posterior mesh rectopexy is a modification of the Wells Ivalon sponge wrap operation.
- The sponge is no longer available and has been replaced by using a posterior mesh attached to the sacrum and the mesorectum.

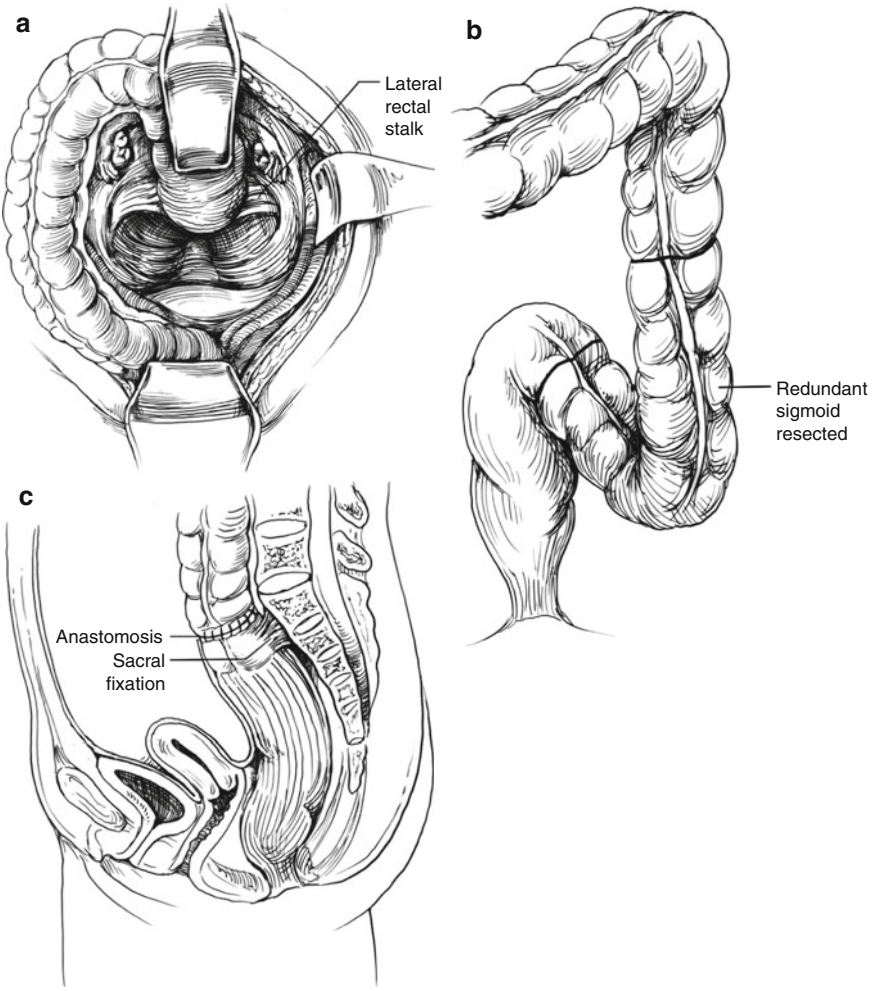

Fig. 33.5 Abdominal rectopexy and sigmoidectomy. (**a**) Rectum is fully mobilized in the posterior avascular plane. (**b**) Redundant sigmoid colon is resected. (**c**) Anastomosis is completed and rectopexy sutures are placed (From Beck and Whitlow. Copyright 2003 by Taylor & Francis Group LLC. Reproduced with permission)

Table 33.4 Results of abdominal rectopexy and sigmoid colectomy

Authors	Number of patients	Recurrence (%)	Mortality (%)	Morbidity (%)
Watts et al.	102	2	0	4
Husa et al.	48	9	2	0
Sayfan et al.	13	0	0	23
McKee et al.	9	0	0	0
Luukkonen et al.	15	0	7	20
Canfrere et al.	17	0	0	–
Huber et al.	39	0	0	7
Ashari et al.[a]	117	2.5	0.8	9

[a]Laparoscopic approach

Table 33.5 Results of abdominal rectopexy

Authors	Number of patients	Recurrence	Mortality	Morbidity
	n	(%)	(%)	(%)
Loygue et al.	140	4	1	
Blatchford et al.	42	2	0	20
Novell et al.	32	3	0	9

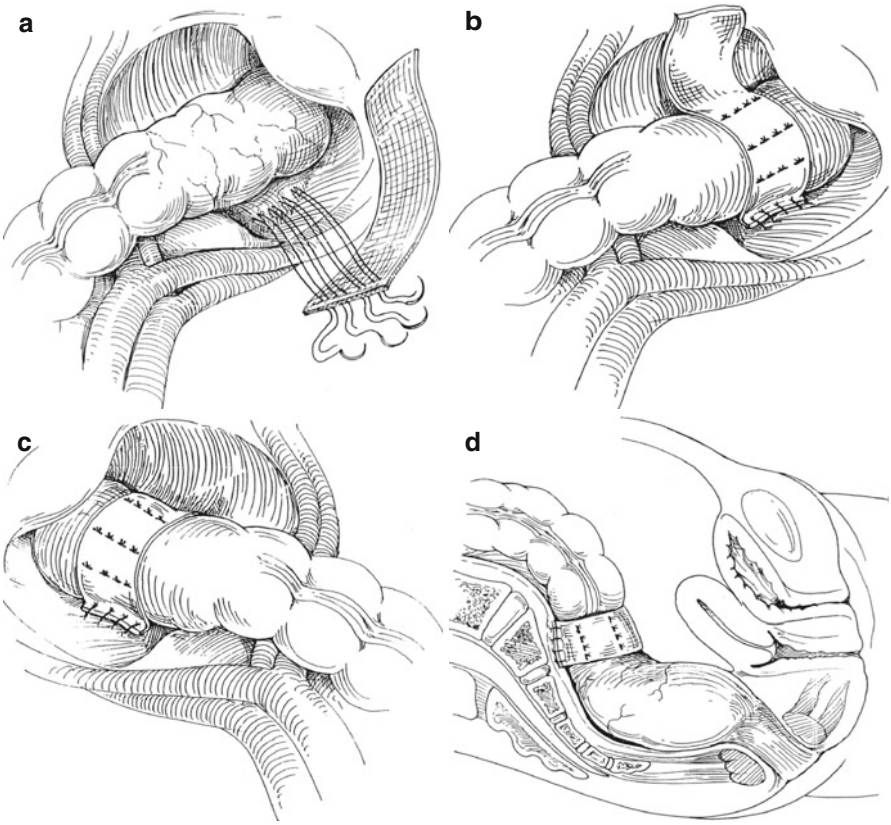

Fig. 33.6 Mesh rectopexy (Ripstein). (**a**) Posterior fixation of sling on one side. (**b**) Sling brought anteriorly around mobilized rectum. (**c**) Sling fixed posteriorly on the opposite side. (**d**) Sagittal view of the completed rectopexy (From Beck and Whitlow. Copyright 2003 by Taylor & Francis Group LLC. Reproduced with permission)

- Mobilization of the rectum is analogous to all other procedures.
- Results of posterior wraps are summarized in Table 33.7.

Anterior Mesh Procedures

- Multiple other mesh procedures have been described, some of which employ an anterior suspension technique. Among the most popular of these has been the Orr–Loygue procedure with placement of two ribbons of synthetic mesh

Table 33.6 Results of Ripstein procedure

Authors	Number of patients	Recurrence (%)	Mortality (%)	Morbidity (%)
Ripstein and Lanter	289	0	0.3	–
Gordon and Hoexter	1111	2	–	17
Eisenstadt et al.	30	0	0	13
Tjandra et al.	134	8	0.6	21
Winde et al.	35	0	0	28
Schultz et al.	69	1.6	1.6	33

Table 33.7 Results of Ivalon sponge/posterior mesh rectopexy operation

Authors	Number of patients	Recurrence	Mortality	Morbidity
	n	(%)	(%)	(%)
Sayfan et al.	16	0	0	13
Luukkonen et al.	15	0	0	13
Novell et al.	31	3	0	19
Dulucq et al.[a]	77	1	0	4

[a]Laparoscopic posterior mesh rectopexy

is sutured to the anterior–lateral rectum (one on each side) after mobilization of the rectum as described earlier. A modification is the more recent ventral mesh rectopexy with placement of the mesh to the anterior rectum and closure of the peritoneum over the mesh. These procedures offer similar outcomes.

Laparoscopic Approaches

- Laparoscopic approaches are analogous to all of the previously described abdominal procedures.
- Success and morbidity are comparable to traditional approaches, with the benefit of shorter hospitalizations and a rapid recovery.
- A meta-analysis by Purkayastha et al. of six studies comparing laparoscopic versus open suture rectopexy found no significant difference in terms of morbidity or recurrence of prolapse between the two approaches but a decrease in the length of hospitalization by 3.5 days as compared to the open group.
- Robotic-assisted laparoscopic surgery is associated with increased cost but no clinical advantages.

Recurrent Prolapse

- Though rectal prolapse has historically had a high recurrence rate (up to 50 % or more), recent reports note recurrent prolapse following resection with rectopexy to be less than 10 %.
- Perineal operations for prolapse have a higher risk of recurrence compared to abdominal approaches.

Table 33.8 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
	(+/– sigmoidectomy)
	Perineal rectosigmoidectomy
Abdominal rectopexy + resection	Redo abdominal rectopexy (+/– re-resection)
	Avoid perineal rectosigmoidectomy

- With recurrent rectal prolapse, it is important to reevaluate the patient for both constipation and other pelvic floor abnormalities.
- An important consideration is the residual blood supply of the remaining large bowel due to the initial operative procedure (Table 33.8).
- For example, if the patient has undergone an initial perineal rectosigmoidectomy, then a repeat perineal rectosigmoidectomy or abdominal rectopexy (without resection) can be safely performed.
- 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.
- Successful treatment of recurrence has been reported between 85 and 100 %.
- Pikarsky et al. reported on 27 patients with recurrent full-thickness rectal prolapse in a case-match study. Re-recurrence of prolapse occurred in 4/27 (15 %) after a median follow-up period of 24 months, with similar results for abdominal and perineal approaches.
- Steele et al. reported on 78 patients with recurrent rectal prolapse and found that abdominal operations to treat a recurrent rectal prolapse were associated with a lower re-recurrence rate.

Solitary Rectal Ulcer Syndrome and Colitis Cystica Profunda

- Solitary rectal ulcer syndrome (SRUS) and colitis cystica profunda (CCP) are uncommon and controversial conditions associated with rectal prolapse.
- CCP and SRUS are closely related diagnoses and some authors consider them interchangeable.
- Symptoms include rectal bleeding, copious mucous discharge, anorectal pain, and difficult evacuation.
- There may be single, multiple, or no rectal ulcers, usually located on the anterior rectal wall just above the anorectal ring.

- CCP is a benign condition characterized by mucin-filled cysts located within the submucosa. These lesions generally appear as nodules or masses, most commonly on the anterior rectal wall.
- CCP is a pathologic diagnosis whose most important aspect is to differentiate it from adenocarcinoma, especially a well-differentiated mucinous adenocarcinoma. Obtaining the correct diagnosis can prevent unnecessary radical operations to treat a benign process.
- The differential diagnosis of both CCP and SRUS includes polyps, endometriosis, inflammatory granulomas, infectious disorders, drug-induced colitides, and mucus-producing adenocarcinoma.
- SRUS is associated with characteristic obliteration of the lamina propria by fibrosis and a thickened muscularis mucosa with muscle fibers extending to the lumen.
- Mucous cysts lined by normal columnar epithelium located deep to the muscularis mucosa characterize CCP pathologically.
- The etiology of these conditions remains unclear, but a common feature is chronic inflammation and/or trauma.
- An endoscopic evaluation of the distal colon and rectum in symptomatic patients will reveal the above-described lesions.
- Defecography is generally abnormal in most patients.
- 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.
- If symptoms persist, a localized resection may be considered in selected patients. Those few patients potentially suitable for localized resection should be highly symptomatic, be good surgical risks, have failed all conservative nonoperative management, and have localized, accessible areas of disease.
- Patients with prolapse are considered for surgical treatment via an appropriate procedure as outlined previously. Those without prolapse may be offered excision, which varies from a transanal excision to a major resection with coloanal pull through.

Conclusion

- Management of patients with rectal prolapse requires careful patient evaluation for synchronous functional bowel disorders and associated anterior compartment problems such as urinary incontinence, voiding disorders, cystocele, and rectocele.
- Management of any associated constipation is important.
- Fecal incontinence is frequent and successful treatment results in only a 50 % improvement.

- Operations are divided into abdominal and perineal approaches. Generally, abdominal procedures have a higher morbidity but a lower rate of recurrence compared to the perineal approaches. Selection is at the surgeon's discretion and remains dependent upon such variables as the patient's general medical condition, comorbid disorders, the presence of incontinence or constipation, and any prior history of colon resection.
- Laparoscopic approaches are safe and effective.
- SRUS and CCP are uncommon colorectal conditions often associated with prolapse. They are benign and efforts are directed to establishing the diagnosis, excluding malignancy, and treating symptoms. Initial conservative therapy is to modify bowel movements and habits and is associated the most success. Surgical therapy is used if these measures fail and should be directed at correcting any coexisting rectal prolapse or to excise locally the lesions.

34. Other Benign Colorectal Disorders

Justin A. Maykel and Scott R. Steele

Introduction

- A wide range of benign pathology ranging from infectious, radiation-induced, and vascular etiologies to more obscure and difficult to diagnose conditions such as collagen vascular and microscopic colitides.
- Patients may present with a variety of clinical symptoms spanning from chronic, nonspecific diarrhea; vague abdominal pain; low-grade fevers; to florid sepsis.

Infectious Disorders

Bacterial Enteritis/Colitis

Escherichia coli

- *Escherichia coli* normally resides in the human gastrointestinal (GI) tract; however, there are five pathologic variants: enterotoxigenic *E. coli* (ETEC), enteropathogenic *E. coli* (EPEC), enterohemorrhagic *E. coli* (EHEC, also called Shiga toxin-producing *E. coli* or STEC), enteroinvasive *E. coli* (EIEC), and enteroaggregative *E. coli* (EAEC or EAggEc).
- EHEC H7-O157 is the only strain readily identified in the clinical laboratory.

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- Typically, infection from all strains leads to variable degrees of diarrhea, from mild to severe, resulting in large-volume GI tract losses and electrolyte abnormalities.
- Enteropathogenic *E. coli* (EPEC) primarily causes outbreaks of severe diarrhea in nurseries due to a toxin that results in watery diarrhea, vomiting, and fever.
- ETEC is a major cause of traveler's diarrhea, with 30–50 % of travelers from industrialized nations spending 3 weeks or more in developing nations experiencing this infection.
- EHEC has occurred in the United States (USA) during outbreaks associated with undercooked hamburger meat. Cases caused by EHEC can result in severe dysentery more commonly with bloody diarrhea than the other strains.
- Treatment in all cases is typically supportive, although antibiotics (fluoroquinolone or trimethoprim-sulfamethoxazole) are added for complicated and persisting cases, and in those with underlying immunosuppression.
- Duration of diarrhea from EAEC is decreased with antibiotics (i.e., ciprofloxacin) administration.

Shigella

- Shigella is the classic cause of dysentery in developing and industrialized countries.
- Shigella bacteria, *Shigella flexneri* (~1/3) and *Shigella sonnei* (~2/3), are far and away the most common causes of Shigellosis.
- Transmission is via person-to-person or through contaminated food, milk, or water.
- These bacteria are resistant to the low gastric pH, multiply in the small bowel, and eventually infiltrate colonocytes, resulting in clinical infection.
- Shigella is capable of colonizing the intestinal epithelium by exploiting epithelial-cell functions and circumventing the host innate immune response.
- Patients commonly present with high fevers, abdominal cramps, tenesmus, and initially watery (though later bloody/mucoid) diarrhea.
- Diagnosis is confirmed by elevated fecal leukocytes and stool cultures.
- Endoscopic exam reveals a nonspecific friable, edematous, erythematous mucosa with focal ulcerations and bleeding especially the rectum and sigmoid.
- Symptoms typically last 4–7 days.
- Toxic megacolon (3 %), intestinal obstruction (2.5 %), and perforation may also develop.
- Treatment is generally supportive, while in the immunocompromised host or when dysentery develops, trimethoprim-sulfamethoxazole, ciprofloxacin, and ampicillin are appropriate.

- Paradoxically, antidiarrheal agents such as loperamide (Imodium™) or diphenoxylate with atropine (Lomotil™) can make the illness worse.

Salmonella

- Salmonella are gram-negative bacilli that grow under both aerobic and anaerobic conditions.
- They are the most commonly isolated pathogens from the stool of patients with gastroenteritis.
- *Salmonella enteritidis* most frequently causes gastroenteritis.
- *Salmonella typhi* more often causes enteric fever in underdeveloped countries.
- In the United States, the incidence rate of nontyphoidal Salmonella infection has doubled in the last two decades, with an estimated 1.4 million cases occurring annually.
- Salmonella is usually transmitted to humans by eating foods contaminated with animal feces, including beef, poultry, milk, or eggs.
- Gastroenteritis due to Salmonella is clinically indistinguishable from gastroenteritis caused by many other pathogens, commonly presenting with nausea, vomiting, fever, diarrhea, and cramping but is usually self-limited.
- Up to 8 % of patients with nontyphoidal Salmonella gastroenteritis develop bacteremia and 5–10 % also develop severe localized infections, including endocarditis, mycotic aneurysm, and osteomyelitis.
- Clinical diagnosis is confirmed via stool culture.
- Treatment remains controversial and depends in part on the host immune status. In general, fluid and electrolyte replacement are administered. Based on available data, antibiotic therapy is not recommended in healthy immunocompetent individuals. Fluoroquinolones are the most frequent first-line therapy, followed by trimethoprim-sulfamethoxazole, and are given for a 3-to-7-day course, with a longer minimum 14-day period in the immunosuppressed.

Campylobacter

- This gram-negative rod is the most frequently identified cause of acute diarrheal illness in the United States and industrialized nations. Of the various species, Campylobacter jejuni is the most common.
- Outbreaks generally occur during warm weather and are most frequently traced back to poor handling or preparation of beef or chicken products at barbecues.
- The organism can produce a spectrum of disease from watery diarrhea to dysentery, depending upon the strains' ability to produce enterotoxin, cytotoxin, or directly invade the mucosa. Most cases present with fever, abdominal pain, diarrhea, nausea, and malaise within 2–5 days after exposure.

- Symptoms are generally self-limited, resolving within 1 week, though may linger up to 3 weeks or longer.
- The terminal ileum and cecum are most commonly involved sites.
- Long-term consequences of infection include arthritis, Reiter's syndrome, and Guillain-Barre syndrome.
- Disease limited to the ileocecal region may also mimic Crohn's disease.
- Organisms that are identifiable only by dark-field or phase-contrast microscopy. Definitive diagnosis requires stool cultures as the disease clinically resembles both Salmonella and Shigella.
- As in other bacterial colitis, treatment with ciprofloxacin or erythromycin should be reserved for severely ill or immunocompromised patients.

Yersinia

- Three species of *Yersinia* produce human illness: *Yersinia pestis* (the causative agent of human plague), *Yersinia pseudotuberculosis* (rare in the United States), and *Yersinia enterocolitica* (i.e., yersiniosis).
- Contaminated food (typically pork) and water serve as the major routes of transmission of infection and typically affect children and young adults.
- These bacteria invade the intestinal epithelium, localize to lymphoid tissues of the intestinal mucosa (i.e., Peyer's patches) and regional mesenteric lymph nodes.
- Symptoms associated with yersiniosis include diarrhea, abdominal pain (especially right lower quadrant), fever, and less frequently nausea and vomiting.
- Symptoms typically develop 4–7 days after exposure and may last 1–3 weeks or longer and mimic other conditions such as appendicitis and Crohn's disease, often called pseudoappendicitis or mesenteric adenitis.
- As the bacteria tend to infect lymphoid tissue throughout the body, concomitant tonsillar symptoms of pharyngitis symptoms can help distinguish *Yersinia* from other causes of colitis.
- Gastrointestinal complications of acute yersiniosis include suppurative appendicitis, diffuse ulcerative ileitis and colitis, intestinal perforation, peritonitis, intussusception, toxic megacolon, small bowel necrosis, cholangitis, and mesenteric vein thrombosis.
- Stool cultures remain the gold standard for diagnosis, although specific culture for Campylobacter is normally not standard, and typically requires a special request.
- Serologic tests are commercially available to help in diagnosis.
- While antimicrobial treatment has been shown to decrease fecal shedding, there are no studies that have demonstrated a benefit in uncomplicated enterocolitis.
- If clinically indicated for the treatment of complicated illness (i.e., septicemia), a fluoroquinolone (adult) and trimethoprim-sulfamethoxazole (children) are first-line therapy choices, with a third-generation

cephalosporin combined with gentamicin intravenously used in more severe disease.

- Following treatment, chronic sequelae are frequent, including erythema nodosum and reactive arthritis. These usually develop approximately 1 month following the initial episode of diarrhea and generally resolve spontaneously after 1–6 months.

Tuberculosis

- Tuberculosis affecting the gastrointestinal tract in the United States is almost always due to either Mycobacterium tuberculosis or Mycobacterium bovis.
- Tuberculous enterocolitis is generally contracted via consumption of unpasteurized milk or from swallowing sputum infected from pulmonary tuberculosis.
- Gastrointestinal tuberculosis manifestations can be divided into three categories: the ulcerative form (60 %), hypertrophic form (10 %), and mass-like lesions (30 %) that mimic malignancies. Which type the patient exhibits depends in part on the host's immune system.
- Distal small bowel and cecal infections are most common and present with abdominal pain, weight loss, and fever, often mimicking Crohn's disease or malignancy.
- Ulcers of varying depth, fistulas, and stenosis may also result from the infectious process, thus causing further difficultly in distinguishing this entity from inflammatory bowel disease.
- Significant lymph node reaction may be seen, so-called tuberculous peri-colonic adenitis, producing extrinsic compression leading to symptoms of partial or complete intestinal obstruction.
- Tuberculous peritonitis can present as a surgical emergency mimicking acute appendicitis or a perforated hollow viscous.
- Colonoscopic biopsy or fine needle aspiration have permitted detection of acid-fast bacilli or caseating granulomas while awaiting culture reports.
- Diagnostic laparoscopy demonstrated tuberculous peritonitis with 95 % accuracy in one series in select patients.
- Anorectal involvement results in ulceration and stricture formation, often mimicking malignancy.
- Stool cultures for viable Mycobacterium organisms rarely demonstrate growth but may be more likely positive in active cases of pulmonary tuberculosis.
- Serology tests have been developed and demonstrate sensitivity for intestinal tubercular disease of over 80 %, though still are difficult in differentiating from Crohn's disease.
- Treatment is usually medical with multidrug regimens. Isoniazid and rifampin are first-line treatment, with pyrazinamide and streptomycin or ethambutol often required until sensitivity analysis can be determined in the immunocompromised host.

Fig. 34.1 Endoscopic appearance of gonococcal proctitis. Notice the mucopurulent discharge

- Obstruction of the bowel secondary to sclerosing lesions or fistulous disease may require surgical intervention; however, a medical trial should be attempted as many patients will improve and resolve without surgery.

Neisseria Gonorrhea

- Neisseria gonorrhea, a gram-negative diplococcus, remains the second most common sexually transmitted infection in the United States and Europe.
- Gonococcus can lead to genital or extragenital infections, particularly the pharynx and the rectum, occurring more commonly in men having sex with men (MSM).
- Anorectal gonorrheal infections typically occur among men who engage in anoreceptive intercourse. Symptoms of proctitis start 5–7 days after exposure and include a mucopurulent rectal discharge, tenesmus, constipation, and classically coexistent moderate to severe pain, although infection may infrequently be asymptomatic.
- Physical examination may reveal edema, erythema, or fissuring of the anorectal mucosa (Fig. 34.1). A mucopurulent discharge is the most common finding.
- Culture for N. gonorrhoeae requires a Thayer–Martin chocolate agar and remains the “gold standard” for diagnosis.

- Antimicrobial treatment must consider not only drug resistance but co-pathogens such as Chlamydia trachomatis as well. Third-generation cephalosporins (single dose 125 mg ceftriaxone, intramuscularly) are considered first-line therapy. Based on susceptibility, sulfonamides, penicillin, tetracycline, and fluoroquinolones are no longer recommended for the treatment of gonorrhoeae in the United States due to resistance patterns.
- Coinfection with C. trachomatis should be treated empirically with either doxycycline (100 mg BID for 7 days) or azithromycin (1 g in a single dose). Patients should also alert their sexual partners for evaluation and treatment, to prevent disease spread or continued reinfection.

Lymphogranuloma Venereum

- Lymphogranuloma venereum (LGV) has become an increasingly common cause of proctitis in Western Europe and the United States, particularly among MSM (mainly in HIV-infected patients undertaking high-risk sexual activities).
- LGV is caused by C. trachomatis serovars L1, L2, and L3.
- LGV is primarily a disease of the lymphatics as infection extends from the primary inoculation site to the draining lymph nodes, producing a lymphangitis, with subsequent nodal necrosis and abscess formation.
- The primary lesion of LGV occurs at the site of inoculation 3–30 days after sexual contact in the form of a painless pustule, shallow ulcer, or erosion. A secondary stage can occur 3–6 months after exposure and manifests as acute proctitis and inguinal lymphadenopathy that can suppurate and ulcerate.
- Excruciating pain helps to distinguish it from many other forms of proctitis.
- Lymphedema and genital elephantiasis, with persistent suppuration and pyoderma, can also be seen.
- The anal findings include ulcers, fistulas, and strictures, which, along with endoscopic findings, closely resemble Crohn's disease.
- Specific LGV-associated serovars of chlamydia can be detected in those with positive PCR by genotyping.
- Diagnosis is usually initially based on clinical findings in association with a positive rectal chlamydia culture as genotyping results are not readily or immediately available.
- The preferred treatment is doxycycline 100 mg twice daily for 3 weeks, with erythromycin used as an alternative.

Syphilis

- Treponema pallidum is a spirochete that invades subcutaneous tissues through abrasions caused during sexual intercourse.

Fig. 34.2 Painless posterior-lateral ulceration (chancre) of anal syphilis

Fig. 34.3 Suppurative inguinal lymphadenopathy of syphilis

- A painless ulcer (chancre) forms and then the draining lymph nodes (Figs. 34.2 and 34.3).
- Widespread dissemination of spirochetes occurs early leading to subsequent clinical manifestations of secondary or tertiary syphilis in untreated patients.
- Weeks to a few months later, approximately 25 % of individuals with untreated infection develop a systemic illness that represents secondary syphilis, with symptoms including a rash on the palms, soles, and mucosal surfaces; fever; headache; malaise; anorexia; and diffuse lymphadenopathy.

- Untreated patients are at risk for the manifestations of late or tertiary syphilis, including central nervous system, cardiovascular, and gummatous syphilis. Condylomata lata occurring in the perianal region appear as moist wartlike lesions that may be confused for human papilloma virus infection.
- Serologic testing is the mainstay of diagnosis, traditionally involving a nonspecific nontreponemal antibody test followed by a more specific treponemal test for diagnostic confirmation.
- Long-acting penicillin preparations are the preferred drugs for the treatment of all stages of syphilis. A single dose of benzathine penicillin G (2.4 million units intramuscularly) remains the standard therapy for primary, secondary, or early latent syphilis.
- Late latent syphilis or latent syphilis of unknown duration requires three doses of 2.4 million units intramuscularly each at 1-week intervals.
- Options for the treatment of syphilis in penicillin allergic patients include tetracyclines, macrolides, or ceftriaxone.

Brucellosis

- Brucellosis is a bacterium that is transmitted through unpasteurized goats' milk or cheese, contact with infected animals, or inhalation of aerosols.
- The constellation of symptoms is similar to the flu and may include fever, sweats, headaches, back pains, and weakness. Symptoms are that of a nonspecific colitis.
- Cultures of the exudate will reveal the organism and are required for confirmation.
- Endoscopic examination reveals nonspecific inflammatory changes.
- Serologic tests are available to aid in early diagnosis and installation of treatment.
- 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 IM q 12–24 h for 14 days are preferred. A more recent meta-analysis suggests that triple therapy by adding an aminoglycoside may result in lower failure rates.

Actinomycosis

- Actinomycosis is an uncommon, chronic granulomatous disease caused by *Actinomyces israelii*, an anaerobic gram-positive bacterium.
- Infection in the cervicofacial area is most common (~50 %), but abdominal actinomycosis typically involves the appendix and ileocecal region.
- It may mimic more common conditions such as malignancy, Crohn's disease, and tuberculosis.
- Colonoscopic findings can include thickened appearing mucosa, colitis, ulceration, nodularity, and a button-like elevation of an inverted appendiceal orifice.

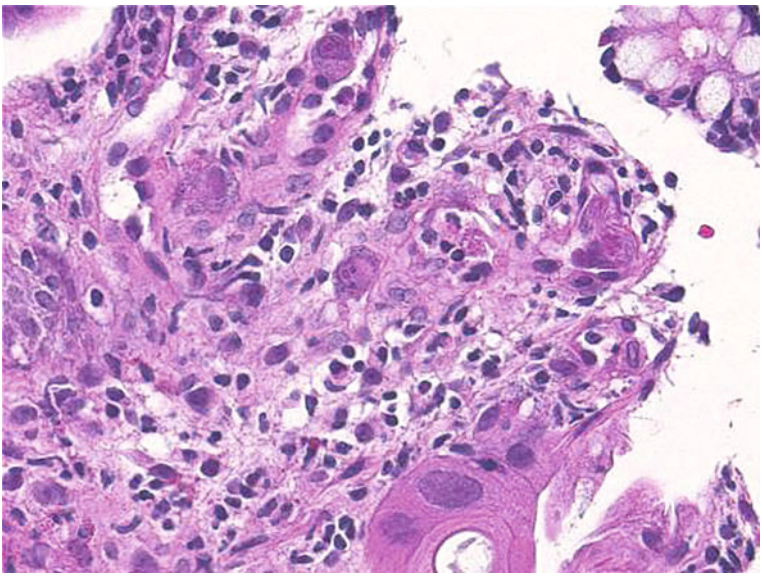

Fig. 34.4 Cytomegalovirus colitis. Infected cells are enlarged with eosinophilic intranuclear and intracytoplasmic inclusions (Courtesy of Jeanette R. Burgess, MD)

- Diagnosis is confirmed upon histological identification of characteristic yellow sulfur granules and/or culture of *A. israelii*.
- Medical treatment consists of a prolonged course of penicillin, intravenously for 4–6 weeks, followed by oral therapy for 6–12 months to prevent relapse.
- Surgical options are most often for disease complications such as resection of an obstructive segment or abscess drainage, which occur most often prior to a confirmative diagnosis.

Viral Enteritis/Colitis

Cytomegalovirus

- Cytomegalovirus (CMV) is a member of the herpes virus family and is considered an opportunistic infection in immunocompromised hosts.
- Infection typically occurs late in the course of HIV infection when CD4 cell counts plummet or in immunosuppressed transplant patients.
- Involvement is most common in the colon, although concomitant disease may occur in the proximal gastrointestinal tract.
- The clinical manifestations of CMV colitis vary greatly, from asymptomatic carriers to fulminate life-threatening infections. Symptoms include fever, weight loss, abdominal pain, and diarrhea, which may be bloody. As the disease progresses, frank ulceration, toxic megacolon, and perforation may occur.
- Biopsies should be obtained for histopathologic examination to evaluate for the characteristic inclusion bodies (Fig. 34.4).

- Currently, there are several agents available for the systemic therapy of CMV infection, including ganciclovir, valganciclovir, foscarnet, and cidofovir. Surgical therapy is generally relegated to complications such as bleeding and perforation, where a subtotal colectomy with ileostomy is often required.

Herpes Simplex Virus Proctitis

- Most colorectal infections are as a result of herpes simplex virus (HSV) type 2. HSV 1 is not common, accounting for 13 % of rectal HSV infections, though most likely represents oroanal transmission. Patients are more commonly HIV positive.
- Presenting symptoms include anorectal pain, discharge, tenesmus, and rectal bleeding as well as difficulty in urinating, temporary impotence, fecal incontinence, and sacral paresthesias.
- The diagnosis is established by a suggestive history and physical examination findings including herpetic vesicles, pustules, and ulcerations that affect the perianal skin and anal canal.
- Sigmoidoscopic exam demonstrates an acute proctitis.
- Laboratory evaluation of rectal samples allows the virus to be isolated by culture. A variety of immunoassays currently exist to aid in diagnosis.
- Oral acyclovir has been demonstrated to be effective in alleviating symptoms although other formulations may allow for twice or once daily dosing regimens. Immunocompromised patients should be treated with intravenous acyclovir followed by chronic suppressive therapy.

Parasitic Enteritis/Colitis

Amebiasis

- Entamoeba histolytica is highly prevalent worldwide with approximately 40–50 million cases annually, accounting for 40,000 deaths.
- This protozoan exists in either the cyst or trophozoite stages. Cysts are ingested in contaminated food or water, or via fecal-oral sexual transmission, and become trophozoites in the small intestine. Upon reaching the colon, they adhere to a specific lectin on the epithelial cell and penetrate the mucosa causing colitis and bloody diarrhea.
- Approximately 90 % of E. histolytica infections are asymptomatic, with invasive disease depending on host genetic susceptibility, age, and immunocompetence.
- Symptoms range from mild diarrhea to severe dysentery. Cases of fulminant colitis with bowel necrosis, perforation, and peritonitis occur in ~0.5 % but are associated with a mortality rate of more than 40 %.
- Localized colonic infection may also occur that results in a mass of granulation tissue, or an ameboma.
- The diagnosis can be aided via antigen testing or serology tests.

- Colonoscopy classically demonstrates characteristic flask-shaped amebic ulcers and scrapings or biopsy specimens can be taken.
- Treatment consists of oral metronidazole.

Balantidiasis

- *Balantidium coli* is the largest and least common protozoal pathogen affecting humans and is the only ciliate that produces important human disease.
- *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 to produce intense mucosal inflammation and ulceration.
- Diarrhea with blood and mucus is accompanied by nausea, abdominal discomfort, and weight loss is common.
- It can develop into fatal fulminant colitis with peritonitis and colonic perforation.
- The diagnosis is made by the identification of trophozoites excreted in the stool or from the margin of rectal ulcers associated with infection.
- The most commonly used treatment is tetracycline 500 mg four times daily for 10 days.

Cryptosporidiosis

- Cryptosporidium is an intracellular protozoan parasite that infects and the epithelial cells of the digestive or respiratory tracts, causing a secretory diarrhea that can be associated with malabsorption, and biliary tract disease (i.e., stricturing and cholangitis).
- Cryptosporidiosis presents in one of three main settings: (1) sporadic, often water-related outbreaks of self-limited diarrhea in immunocompetent hosts; (2) chronic, life-threatening illness in immunocompromised patients (i.e., HIV infection); and (3) diarrhea with malnutrition in young children in developing countries.
- Transmission of Cryptosporidium occurs via spread from an infected person or animal or from a fecal-contaminated food or water source.
- The pathogenesis of Cryptosporidium infection involves ingestion of oocysts, excyst to sporozoites in the small bowel lumen, and invasion of the epithelial cells.
- Clinically, this may result in an asymptomatic carrier state, mild diarrhea, or severe enteritis.
- The illness usually resolves without therapy in 10–14 days in immunologically healthy people, yet excretion of oocysts can continue for prolonged periods.
- In immunocompromised AIDS patients, a number of other clinical manifestations have been described, including cholecystitis, cholangitis, hepatitis, pancreatitis, and respiratory tract involvement. Biliary tract

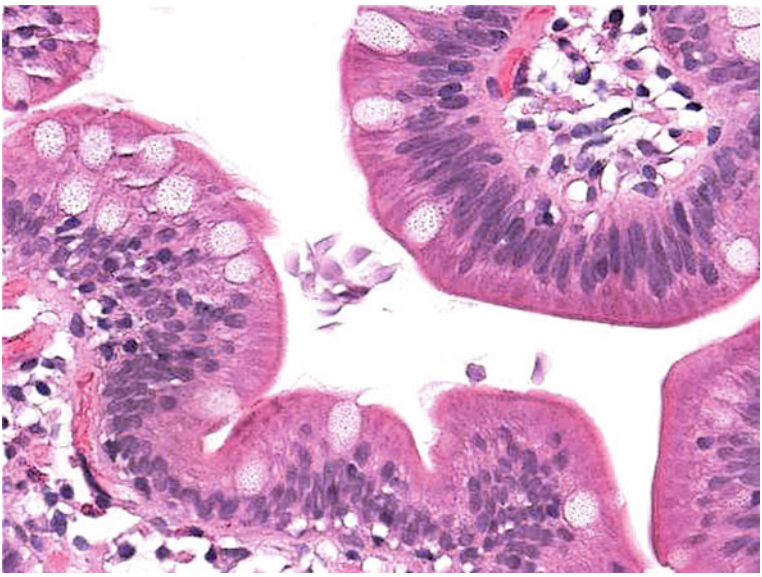

Fig. 34.5 Duodenal giardiasis. *Pale pink* organisms are identified in the lumen. No architectural distortion or inflammation is seen (Courtesy of Jeanette R. Burgess, MD)

involvement most commonly with acalculous cholecystitis or sclerosing cholangitis affects 10–30 % of these patients with underlying AIDS.

- The diagnosis of cryptosporidiosis is made by microscopic identification of the oocysts in stool or tissue, via microscopy, histopathology, ELISA, and PCR.
- Immunocompetent hosts generally recover within 2 weeks without antimicrobial therapy, only requiring simple supportive treatment. Treatment with nitazoxanide has been shown to speed clinical improvement and clear posttreatment Cryptosporidium oocysts from stool samples.
- For HIV-infected patients, it is essential to initiate appropriate HAART treatment. In addition, nitazoxanide is recommended when CD4 counts are less than 100 cells/μL.

Giardiasis

- Giardia lamblia is a flagellated protozoan gastrointestinal parasite that is commonly encountered in the United States.
- This is a common cause of water-borne and food-borne diarrhea encountered in day-care center outbreaks, internationally adopted children, and diarrhea in international travelers.
- Ingested Giardia cysts excyst in the upper small bowel and release trophozoites which absorb to the mucosal surface of the jejunum but do not invade the epithelium (Fig. 34.5).

- The mechanism how this leads to diarrhea and malabsorption is poorly understood.
- Transmission occurs via person-to-person (infectious cysts in stool), in uncooked foods, and contaminated water supplies (common in hikers and bikers who drink from mountain lakes).
- The clinical presentation of infection varies greatly, ranging from asymptomatic infection in up to 60 % to a self-limited acute or long-lasting chronic infection.
- Classic symptoms of an acute infection include a prolonged 2-to-4-week course of diarrhea along with weight loss.
- Chronic infection can occur in up to 30–50 % of symptomatic patients, resulting in loose stools, significant malabsorption, weight loss, and fatigue.
- Proper identification involves stool samples for ova and parasite (O and P), which reveals trophozoites and cysts in 50–70 % of cases with a single specimen and approximately 90 % after three specimens.
- Immunoassays with antibodies directed against either cyst or trophozoite antigens can confirm the diagnosis.
- Symptomatic patients are given antimicrobial therapy with metronidazole as the first-line therapy.

Trypanosomiasis

- Trypanosoma cruzi is the organism responsible for Chagas' disease or trypanosomiasis.
- Chagas' disease is transmitted via the bite of the reduviid bug, also known as the "kissing bug."
- Clinical syndromes present in two stages – acute and chronic. Most patients infected with T. cruzi are asymptomatic during the acute stage of infection, while others develop a wide range of symptoms including fever, swollen face or eyelids (Romana's sign), peripheral edema, conjunctivitis, hepatosplenomegaly, lymphadenopathy, and less commonly, myocarditis and meningoencephalitis.
- Organ damage during the acute phase is due to both high-grade parasitemia and direct tissue parasitism.
- Approximately 50 % of infected individuals develop chronic disease leading to cardiomyopathy, megaesophagus, and megacolon.
- All patients with acute infection and all immunosuppressed individuals should be treated with either nifurtimox or benznidazole.

Ascariasis

- Ascaris lumbricoides is one of the most common helminthic human infections worldwide. Transmission typically occurs via ingestion of contaminated water or food. The life cycle entails the ova hatching in the small intestine and releasing larvae, which penetrate the intestinal wall and migrate hematogenously or via lymphatics.

- The mature worms are generally found in the jejunum, although they can live anywhere from esophagus to rectum.
- Adult worms live 1–2 years, and one person can carry anywhere from 100 to 1,000 worms, depending on egg exposure.
- Although most patients are asymptomatic, large worm loads are responsible for the development of symptoms, primarily obstruction.
- Additionally, symptoms have been attributed to the immunologic response to the foreign body.
- Diagnosis is typically made by stool microscopy.
- The mainstays for treatment are mebendazole and albendazole, typically administered as a single dose.

Schistosomiasis

- Schistosomiasis is caused by infection with parasitic blood flukes/trematode known as schistosomes.
- Their life cycle is complex, beginning with infection via contaminated fresh water and subsequent hematogenous spread, where they survive for many years.
- The eggs invade tissues, release toxins, and provoke an immune response. In the bowel, granulomatous inflammation around the invading eggs can result in intestinal schistosomiasis characterized by ulceration and scarring.
- Regarding intestinal schistosomiasis, most patients present with intermittent abdominal pain, poor appetite, and diarrhea. Intestinal polyps, ulcers, and strictures can also arise due to granulomatous inflammation surrounding eggs that are deposited in the bowel wall.
- The diagnosis is made by microscopy with egg identification, serology radiological findings in the appropriate clinical scenario.
- All infected patients should be treated, regardless of symptomatology, as the adult worms can live for years. Praziquantel paralyzes worms by altering permeability of calcium channels, causing the worms dislodge from the intestines, and are ultimately passed by peristalsis.

Strongyloidiasis

- Strongyloides stercoralis infection results in a wide range of clinical presentations, from a peripheral eosinophilia to septic shock, depending on host immune status.
- Contact with contaminated soil allows the filariform larvae to penetrate the skin and spread hematogenously to the lungs, where they penetrate the alveolae, travel up the tracheobronchial tree, and are swallowed, similar to Ascaris.
- Clinical manifestations include peripheral eosinophilia, cutaneous rashes (entry site most commonly sole of foot), gastrointestinal disturbances including duodenitis, enterocolitis, malabsorption, pulmonary, and hyperinfection syndrome that involve massive hematogenous dissemination (particularly in the immunosuppressed host) to the lungs, liver, heart, central nervous system, and endocrine glands.

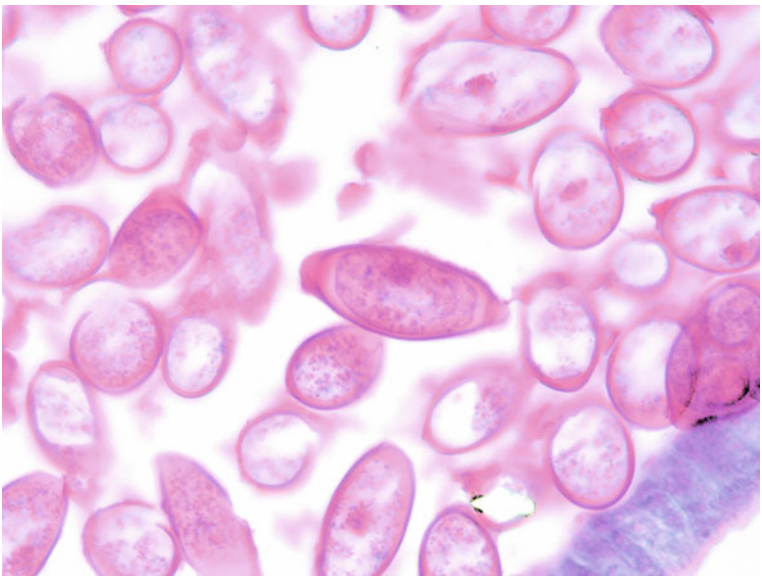

Fig. 34.6 Characteristic microscopic appearance of T. trichiura (whipworm) egg

- The diagnosis of strongyloidiasis is made either by detecting rhabditiform larvae in the stool or via serologic testing. Ivermectin is the treatment of choice for strongyloidiasis, while albendazole is a less reliable option.

Trichuriasis

- Trichuriasis is a common intestinal helminthic infection, seen particularly in warm, moist climates.
- Trichuris trichiura is also called "whipworm" because the adult worm is shaped like a whip.
- Eggs are ingested orally and release larvae that mature into adult worms in the intestinal tract where they attach to the bowel mucosa (Fig. 34.6).
- Most infections are asymptomatic, although heavy worm loads can result in diarrhea with blood, mucous, and rectal prolapse.
- The diagnosis is made by seeing the characteristic barrel-shaped eggs harvested from stool samples or visualizing the adult worms endoscopically (Fig. 34.7).
- Mebendazole is the treatment of choice, administered in a dose of 100 mg twice daily for 3 days.

Enterobiasis

- Enterobius is a common nematode that is found worldwide. Otherwise known as "pinworm," infection occurs most frequently in school children aged 5–10 years.

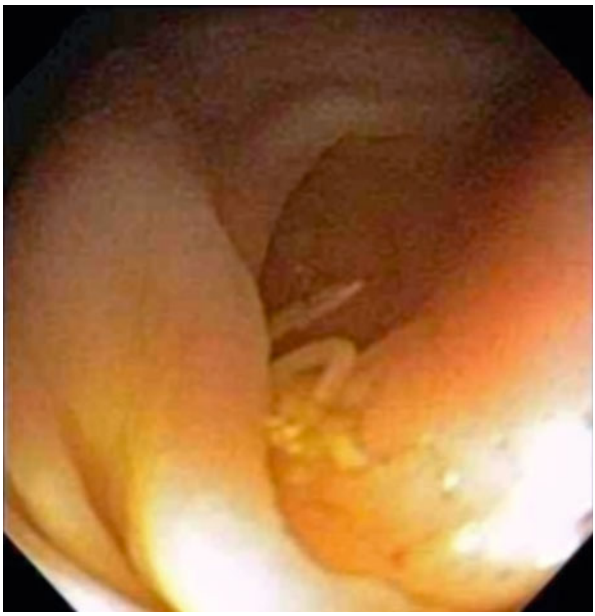

Fig. 34.7 Endoscopic photograph of T. trichiura (whipworm) at appendiceal orifice (Courtesy of Jean M. Houghton MD, PhD and Arumugam Velayudham, MD)

- The worms migrate out through the rectum onto the perianal skin at night to deposit eggs.
- They cause local symptoms of pruritus ani.
- The diagnosis of enterobiasis is best made using a "scotch tape" test, as adhesive tape will capture the eggs, which can be visualized under a microscope with their characteristic "bean-shaped" appearance.
- Both mebendazole and albendazole are equally efficacious in curing 95 % of patients, either with a single dose or repeated dose 1 week later aimed at treating reinfection.
- Pyrantel pamoate is recommended for symptomatic pinworm infections in pregnant women again to the teratogenic effects of the former two medications.

Anisakiasis

- Anisakis is a roundworm that uses marine mammals as their natural hosts.
- The larvae enter the intestinal mucosa where they die, resulting in an inflammatory reaction and abscess formation.
- Patients usually present with relatively acute onset of epigastric or abdominal pain, nausea, and vomiting and subsequent bloody diarrhea. Intestinal complications include obstruction and perforation, along with eosinophilic enterocolitis.

- Diagnosis is made by visualizing the worm at the base of intestinal ulcerations, contrast studies with wormlike filling defects, or via serologic testing.
- Surgical treatment is typically reserved for complications such as perforation or obstruction.

Tapeworm

- A number of adult tapeworms are classified as hermaphroditic flatworm parasites and consist of a head, neck, and segmented body.
- Infection is acquired through the ingestion of raw or inadequately cooked infected flesh of the intermediate host.
- The clinical symptoms of all tapeworm species are variable and include abdominal discomfort, nausea, vomiting, cutaneous sensitivity, headache, and malaise.
- Diphyllobothrium latum is the fish tapeworm that results from the ingestion of raw fish and causes B12 deficiency.
- *Taenia solium* is the pork tapeworm acquired by eating inadequately cooked pork.
- Cysticercosis occurs when humans ingest the egg of *T. solium* and may present with a variety of neurological symptoms.
- *Taenia saginata* is the organisms responsible for beef tapeworm, which is found throughout the world and can achieve many meters in length.
- Finding the ova in fecal samples makes the diagnosis of tapeworm infection.
- Treatment for all tapeworms is with either niclosamide or praziquantel. Until all eggs and scolex portions of the tapeworm are eliminated.

Fungal Enteritis/Colitis

- Fungal colitides may occur but are highly unusual in an immunologically normal patient.
- Clinical settings in which true fungal infection must be considered include human immunodeficiency virus (HIV) infections; immunocompromised states such as postsplenectomy, transplant patients, chronic liver disease, chronic steroid therapy, as well as in debilitated patients being treated with broad-spectrum antibiotics.
- The major pathogens in this category include Candida species, Histoplasma capsulatum, and Cryptococcus neoformans.

Candida

- Certain conditions can promote the involvement of the lower GI tract by Candida species, including age (i.e., extremes of infancy and elderly), HIV infection, neoplasms, diabetes, endocrinopathies, and localized lesions of the GI tract.
- Candida colitis is found predominantly in patients in the intensive care unit.

- Endoscopic findings include small creamy-white, curd-like patches on the surface of edematous and inflamed mucosa.
- Stool cultures coupled with endoscopic biopsies are diagnostic when typical spores, yeast, or pseudomycelia are demonstrated.
- Medical treatment is first-line therapy in the absence of peritonitis.
- Mild candidiasis may only require oral nystatin 500,000–1,000,000 units four times daily. Yet, typically sicker patients need Diflucan or ketoconazole 200–400 mg daily. For extremely ill patients or those with multiresistant disease, amphotericin B (0.3–0.6 mg/kg) or caspofungin (50 mg daily) can be administered intravenously.

Histoplasmosis

- H. capsulatum is found endemically throughout the Midwestern United States. While principally being a pathogen of the reticuloendothelial system, like other fungal infections, it can cause systemic infection in the immunocompromised host. Pulmonary disease is most common, yet ileocolitis does occur as a granulomatous process.
- Skip areas, pseudopolyps, ulcerations, and plaque-like lesions may be seen, although biopsies will reveal intracellular budding yeasts within the mucosa when this organism is present.
- Serologic tests and fungal cultures may also confirm the diagnosis.
- Intravenous amphotericin B may be indicated in severe cases, while ketoconazole has been used effectively in more mild disease and long-term to prevent relapse.

Cryptococcus

- Cryptococcosis most commonly affects the central nervous system when C. neoformans is acquired via inhalation of soil.
- Colitis with perforation can occur spontaneously or following endoscopic biopsy, therefore, surgical intervention is generally reserved to manage life-threatening complications.
- 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 stool culture.
- Similar to other fungal infections, ketoconazole is effective in mild disease forms, while amphotericin B is standard therapy in severely ill or immunocompromised patients.

AIDS Diarrhea

- Diarrhea in the AIDS or HIV-positive patient can be the result of many causes but is often a source of significant morbidity.

- It should be noted that diarrheal disease in HIV-infected individuals is frequently caused by infectious agents but may also be due to medications or infiltrative diseases such as lymphoma, Kaposi's sarcoma, or GI tract infection of the HIV itself.
- Diagnostic work-up is broad-based, with the goal of finding a treatable source of infection. Stool studies including ova and parasites, C. difficile toxin assay, and bacterial culture, and with blood cultures, and endoscopy may all be required.

Clostridium difficile

- C. difficile (CD) is a gram-positive rod bacterium that resides naturally within the human colon but overgrows following antibiotic treatment.
- Symptoms vary from abdominal pain, distention and diarrhea, to outright sepsis with toxic megacolon.
- CD colitis rose 200 % between 2000 and 2005 in the United States.
- Increased virulence of particular strains such as B1/NAP/027 has shown capacity for hypersporulation, increased resistance to fluoroquinolones, a 16-to-23-fold increase in toxin production, and a severe disease pattern leading more frequently to fulminant CD colitis.
- All antibiotics have been associated with C. difficile infection and recurrence.
- CD infection relates to two major bacterial toxins. Toxin A, acts as a chemoattractant for neutrophils and causes inflammation and fluid secretion of the colonic mucosa.
- Toxin A also causes the release of PGE2, which activates the Fas–Fas ligand system causing enterocyte and colonocyte apoptosis. Both toxins A and B activate inflammatory cytokine release from monocytes. Continued toxin production leads to connective tissue degradation causing colitis, watery diarrhea, and a pseudomembrane formation.
- Clinically, C. difficile colitis results in copious gastrointestinal output.
- A small percentage of patients go on to develop fulminant colitis with high fever, severe abdominal pain, and have diffuse peritonitis on abdominal examination. While hypotension, oliguria, sepsis, and toxic megacolon may be seen in this critically ill stage, the diarrhea may be paradoxically absent when the disease reaches its peak.
- Diagnosis may be made clinically by endoscopic examination and/or biopsy with the characteristic presence of pseudomembranes, inflammatory mucosal changes, and erythema (Figs. 34.8 and 34.9).
- Diagnosis is often confirmed by sending stool for C. difficile cytotoxin and antigen assays.
- The most effective and commonly used antibiotics against C. difficile are metronidazole and vancomycin, with cure rates of 76 and 97 %, and recurrence in 14 and 15 %, respectively. Other agents that may be useful are teicoplanin and fusidic acid with clinical cure rates of 96 and 93 %, respectively. Bacitracin, when rarely used, has been shown to be as

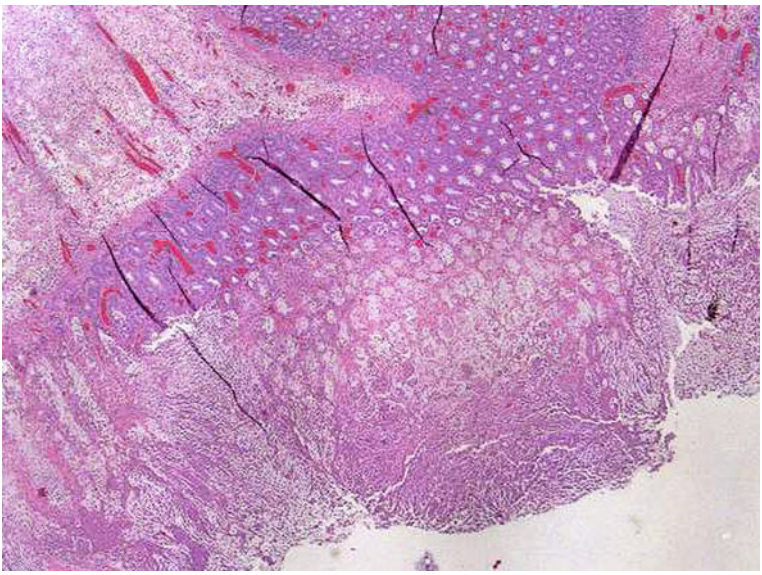

Fig. 34.8 Low power view of pseudomembranous colitis. A thick pseudomembrane adheres to the colonic mucosa (Courtesy of Jeanette R. Burgess, MD)

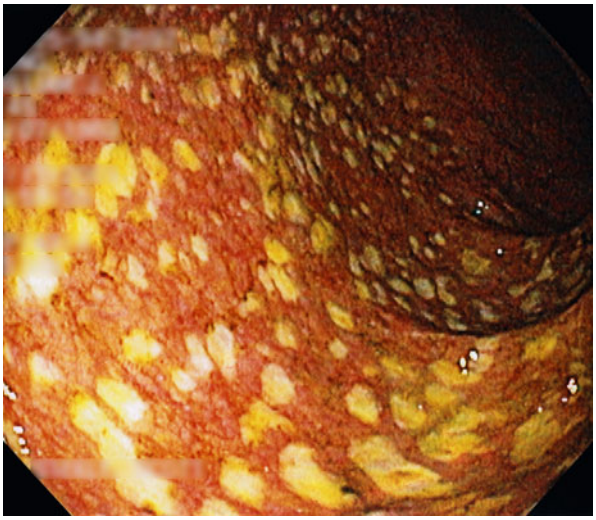

Fig. 34.9 Classic pseudomembranous appearance of C. difficile on endoscopy

effective treatment as vancomycin when 20,000–25,000 units are used four times daily for 7 days.

- Indications for surgical management of CD colitis include severe disease refractory to medical management and the development of life-threatening complications such as perforation or toxic megacolon.

- Data suggests total abdominal colectomy with end ileostomy before onset of multisystem organ failure resulting from CD colitis is associated with improved morbidity and mortality.
- Recurrence of C. difficile infection occurs in 13–28 % of patients and is associated with multiple patient and therapeutic factors.

Other Conditions

Ischemic Colitis

- Gangrenous alterations to the colon were initially described following high ligation of the inferior mesenteric artery during abdominal aortic aneurysm repair as well as with colectomy for carcinoma.
- Currently, ischemic colitis is the most common form of gastrointestinal ischemia, accounting for 50–60 % of all cases, approximately 1 in 2,000 hospital admissions.
- Regardless of its etiology, patient outcome rests on the severity, extent, and rapidity of the ischemic insult and is strongly influenced by prompt diagnosis and appropriate clinical management.
- Nonocclusive ischemia occurs following a precipitating event such as hypotension, medication-induced vasoconstriction, shock, cardiac failure, hemorrhage, or sepsis that results in a low-flow state.
- Although any area of the colon may be affected by inadequate flow, the watershed areas of the rectosigmoid (Sudeck's point) and splenic flexure (Griffith's point) are commonly involved due to frequent incomplete anastomoses of the marginal artery.
- The diagnosis of ischemic colitis is accomplished by the combination of early and repeated clinical evaluations, radiological studies, and colonoscopic visualization.
- Ischemia arising in the left colon and rectum tends produce referred pain to the left lower quadrant and flank areas, followed by an urge to defecate and subsequent passage of either bright red blood or maroon blood mixed with stool, typically within 24 h of onset.
- Laboratory examination is noteworthy for a leukocytosis and metabolic acidosis.
- Colonoscopy remains the most sensitive and specific study available for diagnosis of ischemic colitis (Table 34.1).
- These lesions create the characteristic thumbprinting sign on radiographic studies, which often disappear within days as the submucosal hemorrhages are either resorbed or evacuated into the colon when the overlying mucosa ulcerates and sloughs.
- Computed tomographic (CT) imaging has been used to diagnose ischemic colitis, with associated changes in the bowel wall more often offering clues to the diagnosis (Fig. 34.10).
- In general, angiography does not help in patients with acute ischemic changes.

Table 34.1 Endoscopic findings of ischemic colitis

Stage	Endoscopic findings
Acute	Hyperemia, edema, friable mucosa, superficial ulcerations, petechial hemorrhage, gangrene[a]
Subacute	Edema, exudate, ulceration
Chronic	Stricture, mass, segmental involvement

[a]Irreversible damage characterized by gray, green, or black appearance

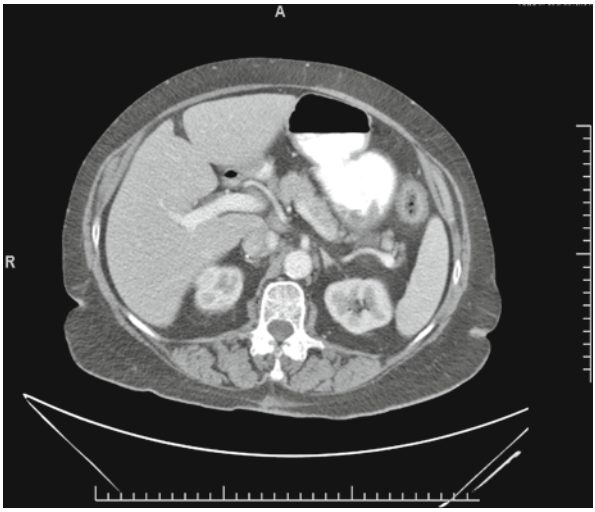

Fig. 34.10 CT image of splenic flexure ischemic colitis demonstrating bowel wall thickening and peri-colonic fat stranding

- Finally, color Doppler and duplex ultrasound determine whether an arterial signal or color Doppler flow can be detected.
- The mainstay of therapy for ischemic colitis remains supportive therapy with adequate fluid hydration and blood pressure support.
- All patients with evidence of bowel infarction or perforation require surgical therapy and exploration should rapidly follow.
- Patients treated operatively in the acute setting have mortality rates as high as 40 %.
- In most cases of ischemic colitis, the signs and symptoms of disease disappear within 24–48 h, with more severe insults result in a future stenosis or stricture of the colon. A follow-up colonoscopy is advisable to confirm complete resolution.

Radiation Colitis

- Radiation therapy causes changes via two major mechanisms: (1) direct damage to DNA and (2) production of oxygen-free radicals.
- In the acute phase, changes within the bowel occur during the course of radiotherapy or shortly thereafter.

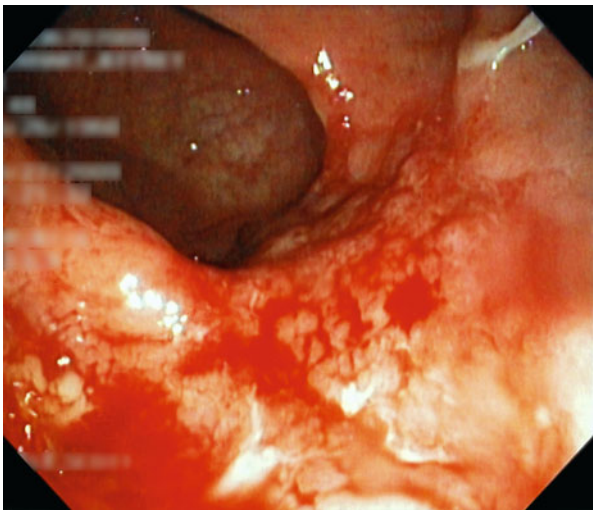

Fig. 34.11 Endoscopic view of radiation colitis

- Patients will experience atrophy of the villi, degeneration of the mucosal lining, diarrhea, mucous discharge, tenesmus, bleeding, and even incontinence.
- Chronic radiation injury appears most often at 6–12 months following radiation and is secondary to a progressive fibrosis of the microvasculature (i.e., obliterative arteritis). Clinically, this may manifest in a wide spectrum of findings including nonhealing ulcerations and telangiectasias of the bowel wall (Fig. 34.11).
- The Radiation Therapy Oncology Group (RTOG) classification system is shown below in Table 34.2.
- While the majority of symptoms are self-limiting, overall rates remain high, ranging from 41 to 57 % for acute grade 2 symptoms and 1–5 % for acute grade 3 symptoms.
- Treatments for hemorrhagic proctitis include the following: electrocautery, mesalamine, steroid, Carafate enemas, Nd:YAG and argon lasers through an endoscope, instillation of topical 4 % formalin, and topical dab with 10 % formalin have demonstrated successful cessation of bleeding in up to 70–90 %
- Patients with significant diarrhea use antimotility agents, such as loperamide or octreotide, and a low residual diet.
- Operative indications include refractory disease (i.e., bleeding, nonhealing ulcer), septic complications (i.e., fistula, perineal sepsis), bowel obstruction or stricture, and secondary malignancies.

Table 34.2 Acute and late complications according to the RTOG and RTOG/EORTC morbidity scales for radiation toxicity

	Grade 2	Grade 3	Grade 4
Acute GI toxicity	Diarrhea requiring medications, rectal pain requiring analgesics, *rectal bleeding requiring topical medications*	Diarrhea requiring parenteral support, severe mucous, or bloody discharge requiring pads, abdominal distension, *bleeding requiring multiple cauteries, or surgery.* Watery diarrhea, obstruction requiring surgery; bleeding requiring surgery or >2 cauteries and/or transfusions	Obstruction, fistula, or perforation. Abdominal pain or tenesmus requiring decompression or diversion
Late GI toxicity (>12 weeks)	Moderate diarrhea, intermittent, severe cramping; bowel movements >5 per day. Frequent bleeding, requiring single-cautery treatment and/or transfusion	Watery diarrhea, obstruction requiring surgery; bleeding requiring surgery or ≥2 cauteries and/or transfusions	Necrosis, perforation, abdominal pain, or tenesmus requiring decompression or diversion

Modifications in italics. Adapted from Peeters ST, et al. Int J Rad Biol Phys. 2005;61(4):1019–34
RTOG Radiation Therapy Oncology Group, *EORTC* European Organization for the Research and Treatment of Cancer, *GI* gastrointestinal

- A study of 5,719 patients undergoing EBRT or BT found a 0.2 % incidence of surgical therapy for late rectourethral fistulae and intractable bleeding.
- Rectovaginal fistulas have been reported in up to 18 % at 3 years following radiation therapy for advanced gynecological malignancy and often require diversion or nonirradiated tissue flaps (i.e., gracilis or Martius).
- Proximal diversion for more distal lesions plays a prominent role. In the case of radiation-induced intestinal stenosis or obstruction, the same surgical considerations apply.
- Where feasible, resection and anastomosis to normal appearing bowel is preferred.

Microscopic Colitis: Collagenous and Lymphocytic Colitis

- Microscopic colitis is responsible for up to 20 % of patients referred for colonoscopy with nonbloody chronic diarrhea.
- Microscopic colitis encompasses both lymphocytic and collagenous colitis, with roughly half of patients in each group.

Fig. 34.12 Lymphocytic colitis. A significant increase in the intraepithelial lymphocyte is present particularly in the surface epithelium

- The hallmark of each is the characteristic histological changes identified in the setting of normal colonic mucosa on endoscopy.
- The majority of patients are older than 50 years of age at disease onset, with a female predominance (especially in collagenous colitis).
- Like many of these "benign" colorectal diseases, patients may present across a spectrum of courses, from mild abdominal pain and diarrhea, to severe volume depletion, electrolyte abnormalities, and protein-losing enteropathy.
- The mainstay of diagnosis is endoscopy with multiple colonic mucosal biopsies. Clinically the mucosa of the colon appears normal, thus random biopsies are required for diagnosis.
- Both collagenous colitis and lymphocytic colitis demonstrate a lymphocytic proliferation and infiltration of the lamina propria and epithelium of the bowel wall. In fact, the histologic criteria for lymphocytic colitis require more than 10 lymphocytes per 100 epithelial cells in the colon (Fig. 34.12).
- Collagenous colitis is diagnosed by the presence of marked thickening of subepithelial collagen layer (Fig. 34.13).
- Treatment options include dietary modifications with elimination of caffeine, dairy, alcohol, and artificial sweeteners; antidiarrheal therapy with loperamide and diphenoxylate/atropine; bile-acid-binding agents such as cholestyramine and budesonide (9 mg daily for 6 weeks);

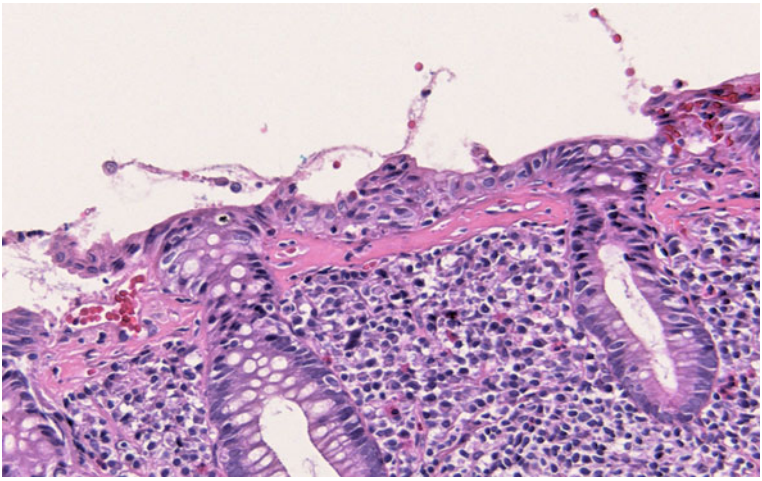

Fig. 34.13 Collagenous colitis. Note the *thick band of pink* collagen beneath the surface epithelium (H and E stain)

and immunomodulatory and anti-inflammatory drugs such as 5-aminosalicylic acid products, steroids, azathioprine, 6-mercaptopurine, methotrexate, probiotics, and octreotide.

Eosinophilic Colitis

- Eosinophilic colitis is the least common component of eosinophilic gastrointestinal disease (EGD).
- All subtypes of EGD are characterized by eosinophilic infiltration of the involved tissues and elevated eosinophil counts in peripheral blood.
- Eosinophilic colitis has a bimodal age distribution affecting neonates as well as young adults, with equal gender distribution.
- Patients most frequently present with nonspecific symptoms that include abdominal pain, nausea, vomiting, diarrhea, and weight loss.
- The diagnosis of eosinophilic colitis is generally made by the trilogy of peripheral eosinophilia (5–35 %), gastrointestinal symptoms, and greater than 20 eosinophils per high-power field on histological examination of endoscopic biopsies – all with no other defined source for the eosinophilic manifestations.
- Colonoscopic findings may range from normal in appearance to diffuse edema.
- Multiple medications have also been associated with this condition to include gold, NSAIDs, rifampin, and tacrolimus.
- Corticosteroids are the first-line therapy for eosinophilic colitis.

Gastrointestinal Manifestations of Vasculitis and Connective Tissue Disorders

- Vasculitis can involve the gastrointestinal tract, resulting in mesenteric ischemia.
- Patients generally present with abdominal pain, nausea, vomiting, diarrhea, and gastrointestinal bleeding.

Polyarteritis Nodosa

- Polyarteritis nodosa (PAN) is a focal segmental vasculitis that affects small and medium-sized arteries. Antigen–antibody complexes are deposited in the vessel walls, causing local inflammation and eventual necrosis ("fibroid necrosis") that result in stenosis, thrombosis, aneurismal dilatation, and rupture.
- (HBV) in approximately 7 % of cases. Overall, gastrointestinal involvement occurs in 14–65 % of patients with PAN.
- Most patients have concomitant systemic symptoms, such as hypertension, renal insufficiency, neurological dysfunction, myalgias, and cutaneous disease.
- The small bowel and gallbladder are the most commonly affected areas in the GI tract.
- Clinical presentation depends on whether ischemia is transmural, varying from postprandial abdominal pain and weight loss or superficial ulcerations to perforation with peritonitis.
- The Churg–Strauss syndrome is a variant of PAN, where GI involvement caused by eosinophilic infiltration causes abdominal pain, bloody stools, and diarrhea.
- Arteriography is a primary modality used to diagnose PAN, revealing focal and segmental saccular aneurysms or stenosis, particularly at areas of bifurcation.
- Tissue biopsy may confirm the diagnosis, and common biopsy sites include sural nerve, muscle, and skin lesions that may be present.
- The mainstay of treatment is 1 year of corticosteroid therapy, resulting in remission in 50 % of cases. Cyclophosphamide for 6 months of duration can be added to improve response rates.

Henoch–Schonlein Purpura

- Henoch–Schonlein purpura (HSP), the most common systemic vasculitis in childhood, is a small-vessel inflammatory disease that classically results in lower extremity purpura, arthritis, and hematuria.
- The gastrointestinal tract is affected in up to 50 % of patients.
- The underlying cause of HSP remains unknown.
- IgA deposits in the arterial wall result in extravasation of erythrocytes and infiltration of tissue with neutrophils, creating the picture of leukocytoclastic vasculitis.

- Abdominal pain, associated with nausea, vomiting, or bleeding, occurs in 51–74 % of patients.
- The small intestine is the most frequently involved site in the GI tract.
- Diagnostic tools include ultrasound, CT scan, upper and lower endoscopy, and video capsule endoscopy.
- The ideal method of diagnosis is to identify leukocytoclastic vasculitis with IgA on tissue biopsy (whether from the skin, kidney, or GI tract) coupled with classic clinical manifestations.
- The natural history of the disease is spontaneous resolution.

Systemic Lupus Erythematosis

- Systemic lupus erythematosis (SLE) is a chronic multisystem inflammatory disease of unknown cause that can affect any organ system of the body.
- Disturbances within the immune system result in the formation of immune complexes in the microvasculature leading to complement activation and inflammation.
- Patients with SLE can develop a small and medium-sized vessel vasculitis that involves the GI tract in approximately 25–40 % of patients.
- Similar to Crohn's disease, SLE can affect any portion of the GI tract.
- The development of abdominal pain is often intermittent and insidious in onset, typically associated with nausea, vomiting, fever, and diarrhea.
- However, patients may also present acutely with mesenteric vasculitis and infarction in a septic picture.
- Diagnosis generally involves CT scan, though arteriography may prove helpful.
- Treatment options include broad-spectrum intravenous antibiotics and systemic corticosteroids.
- Surgical intervention is indicated for failure to respond to aggressive resuscitation or signs of perforation.
- Early treatment with high-dose corticosteroids is efficacious, while other treatment options include immunosuppressive medications (azathioprine, cyclosporin A, and cyclophosphamide).

Behcet's Disease

- Behcet's disease is a chronic, relapsing, inflammatory disease mainly affecting young men in the Middle East and women in Japan and Korea.
- Classically, it causes painful oral and genital aphthous ulcerations, uveitis, arthritis, and skin lesions.
- 15–60 % may also experience gastrointestinal manifestations.
- This vasculitis is unique as it involves blood vessels of all sizes – small, medium, and large – and affects both the arterial and venous systems.
- Behcet's disease typically has a waxing and waning course characterized by exacerbations and remissions.

- Ulcerations may be superficial or transmural and are most often seen in the terminal ileum, cecum, and ascending colon.
- Endoscopically, these ulcerations appear round and deep with discrete margins. When located in the ileocecal location (96 %), they are often single (67 %) and tend to be larger than 1 cm (76 %).
- It is often difficult to distinguish between Behcet's and inflammatory bowel disease, due to the similarity in intestinal symptoms including GI ulcerations, inflammatory masses, anorectal pathology, and rectovaginal fistulas.
- In addition, both have extraintestinal symptoms such as oral ulceration, erythema nodosum, uveitis, and arthritis.
- While nonspecific serum markers of inflammation may be elevated, there are no pathognomonic laboratory tests in Behcet's disease.
- Therefore, the diagnosis is often one of the exclusion and made purely on the basis of the clinical spectrum.
- Treatment is dictated both by the type of organ system involved and by the severity of disease. Due to a paucity of reliable data, medical options remain controversial, though most often include corticosteroids and a variety of immunosuppressive medications.
- Surgery is generally reserved for the management of complications. Long-term, the rate of recurrence after surgery has been reported to be 40–56 % and typically occurs at the anastomotic site.

Scleroderma

- Systemic sclerosis (scleroderma) is a multisystem fibrotic disease secondary to alterations of the microvasculature, the autonomic nervous system, and the immune system.
- Nearly 90 % of patients with systemic sclerosis have GI involvement.
- While the entire GI tract can be affected, esophageal disease is the most common site.
- Patients develop malabsorption as a result of intestinal stasis, bowel dilation, and bacterial overgrowth – often resulting in malnutrition.
- Pseudo-obstruction and small bowel dysmotility are challenging to treat.
- Surgical resection is rarely beneficial due to the diffuse nature of GI involvement and risk for short bowel syndrome with extended resections.
- Collagen is deposited in the mucosa and submucosa of the colon while the muscularis externa undergoes atrophy. Wide-mouthed diverticula can be visible protruding through the weakened wall on the antimesenteric border.
- Clinically, both constipation, due to dysmotility and pseudo-obstruction, and fecal incontinence are common problems.
- Constipation can be managed with bulking agents or PEG, although this may paradoxically worsen proximal dysmotility.

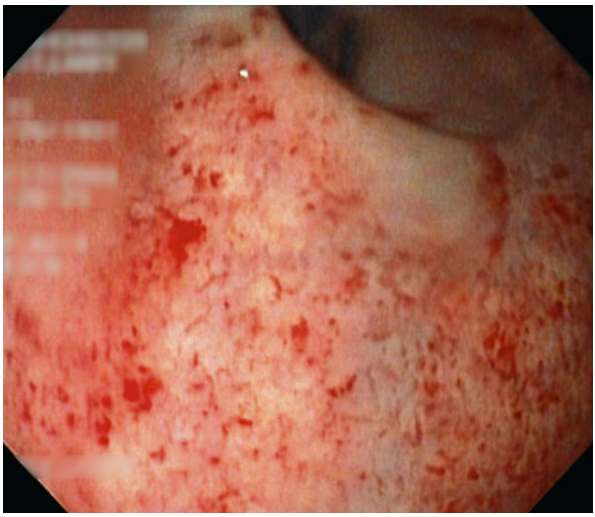

Fig. 34.14 Diversion colitis. Notice the erythematous, friable mucosa

Miscellaneous Colitis

Diversion Colitis

- Fecal diversion may result in clinically evident disease, particularly following extended periods in which the colorectal mucosa is devoid of fecal matter.
- The defunctionalized colon and rectum develops a nonspecific inflammation that is felt to be secondary to a lack of short-chain fatty acids – the primary colonocyte nutrient.
- Patients most often present with symptoms of abdominal and/or pelvic pain, tenesmus, bright red blood per rectum, and mucus discharge.
- Endoscopy commonly reveals erythema, friable mucosa, contact bleeding, and mucus plugs (Fig. 34.14).
- It is often difficult to differentiate the clinical appearance from inflammatory bowel disease.
- Most often patients are asymptomatic and do not require treatment. For those patients with a temporary stoma, resolution of symptoms is the norm once intestinal continuity is restored, while failure to improve should prompt an evaluation for other underlying pathology.
- In symptomatic patients in whom the diversion is permanent or not ready for stomal reversal, treatment regimens including 5-aminosalicylate, sucralfate, and steroid enemas have demonstrated moderate success for symptom control.
- In addition, there is good evidence that twice-daily irrigation of short-chain fatty acid enemas will lead to resolution of symptoms.

Neutropenic Enterocolitis

- Neutropenic enterocolitis, or typhlitis, is a potentially fatal complication of cytotoxic chemotherapy for malignancy, most commonly seen with leukemia or lymphoma.
- Additionally, immunosuppressed patients from other causes such as following transplantation, aplastic anemia, or AIDS may present with a similar clinical picture. One consistent factor is that most patients having absolute neutrophil counts less than 500/mm.
- The process has a predilection for the terminal ileum and cecum.
- During the course of chemotherapy, patients often present with watery diarrhea, vomiting, fever, and abdominal pain, while more severe forms result in perforation and sepsis.
- Computed tomography is the most widely used method of diagnosis, with characteristic right-sided colonic and ileal wall thickening with or without adjacent fat stranding and free fluid.
- Pneumatosis has been reported in up to 21 % of patients. Due to the patients' underlying condition, the mainstay of therapy remains supportive with broad-spectrum antibiotics.
- Surgical therapy is generally reserved for patients with signs of nonviable bowel, perforation, or sepsis.

Disinfectant Colitis

- Endoscopic disinfectants commonly use hydrogen peroxide bases or glutaraldehyde can produce plaque resembling pseudomembranous colitis, and often appears on withdrawal of the scope in regions, which appeared relatively normal on introduction.
- Patients may have a variety of nonspecific complaints ranging from mild cramping abdominal pain to fever, bloody diarrhea, and significant tenderness starting approximately 24–48 h following endoscopy.
- The vast majority of patients will have complete symptom resolution without need for therapy.

Corrosive Colitis

- Specific formulations, such as previously described glutaraldehyde and formalin preparations that are used in a variety of medical capacities may result in an iatrogenic corrosive colitis.
- In addition, self-induced agents per rectum such as household bleach, coffee enemas, colas, and other potentially hazardous liquids and gels may result in varying degrees of bowel wall injury.
- Similar to disinfectant colitis, most patients develop a self-limiting symptom complex of abdominal pain, mucous discharge, diarrhea, and rectal bleeding within hours to a few days depending on the extent of exposure and chemical composition of the offending corrosive agent.

- Treatment typically remains supportive with bowel rest, intravenous fluids, and occasional topical medications (i.e., mesalamine, steroids) as needed, though anecdotal reports exist of full-thickness rectal injury and need for diversion and/or proctectomy with severe cases.

NSAIDs and Salicylate-Induced Colitis

- NSAID use has been postulated to play a role in the pathogenesis of chronic colitis or colonic ulcer formation.
- These drugs have also been associated with causing a reactivation of previously quiescent inflammatory bowel disease (especially ulcerative colitis) via lowering levels of prostaglandins by dual inhibition of the cyclooxygenase (COX) enzymes.
- Presenting symptoms are often diarrhea, rectal bleeding, and abdominal pain, coupled with a history of NSAID usage.
- Endoscopic findings include patchy erythema and ulcerations, and in many cases the colonic mucosa appearance will mimic inflammatory or idiopathic colitis.
- Treatment involves discontinuing NSAID and salicylate use as well as administering topical or steroid preparations.

Toxic Epidermal Necrolysis

- Toxic epidermal necrolysis (TEN), also known as Stevens–Johnson syndrome, is a severe dermatological disease that is characterized by extensive epidermal and mucocutaneous necrosis and exfoliation.
- Whereas the primary manifestation is the appearance of an erythematous confluent eruption that rapidly evolves into necrosis and exfoliation of the skin at the dermal–epidermal junction, it is also been occasionally associated with disseminated mucosal erosions throughout the gastrointestinal tract.
- This appears to be immune-complex mediated and often occurs as an idiosyncratic reaction to a drug or chemical agent.
- The disease has an extremely high mortality rate and manifests with sepsis, gastrointestinal hemorrhage, diarrhea, high fevers, leukopenia, fluid/electrolyte imbalance, and renal insufficiency.
- The ulceration is not limited to the colon, with diffuse ulceration anywhere from mouth to anus.
- Radiographically, the colon may appear stenotic or even “lead-pipe”-like, similar to chronic ulcerative colitis.
- Endoscopically, the colon may resemble severe ulcerative or pseudomembranous colitis; however, biopsies show extensive necrosis and lymphocytic infiltration without crypt abscesses or neutrophils and pathologically the muscular layers remain intact.
- Patients are critically ill and require aggressive surgical resection along with multisystem intensive care support including extensive skin care that is often only available in burn units.

35. Advanced Laparoscopic Colorectal Surgery

Tonia M. Young-Fadok

Introduction

- All laparoscopic colorectal procedures are considered advanced procedures.

Learning Curve

- There continues to be relatively slow adoption of laparoscopic colectomy into practice. Laparoscopic colorectal surgery faces challenges due to the need to work in multiple quadrants of the abdomen, a greater need for understanding of depth perception and proprioception, a coordinated team, and a long learning curve.
- The estimated learning curve for laparoscopic colectomy is 20 or more cases.
- In the UK "CLASICC" trial, despite the surgeon's prior experience, the rate of conversion dropped from 38 to 16 % over the course of the study, suggesting an ongoing "learning curve."
- In the European COLOR trial, the median operative time for high-volume (>10 cases/year) hospitals was 188 min compared to 241 min for low-volume (<5 cases/year) hospitals, and likewise conversion rates were 9 % vs. 24 % for the two groups. High-volume groups also had more lymph nodes in the resected specimens, fewer complications, and shortened hospital stay.

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- Laparoscopic training has been incorporated into most, if not all, of the accredited colorectal training programs, providing graduates with laparoscopic skills.

Conversion

- Conversion rates vary widely in the literature, from 0 % to as high as 48 %, depending on multiple factors such as date of publication, disease process, patient factors, and of course, surgeon experience and ability.
- Patient- and disease-related factors such as obesity (defined as a body mass index greater than 30 kg/m^2), prior abdominal surgery (a marker for adhesions), acuity of inflammation (i.e., abscess and fistula formation), tumor bulk or contiguous involvement, and disease location may also affect the rate of conversion.
- For inflammatory conditions such as Crohn's disease and diverticulitis, the presence of an abscess or fistula may result in the need for conversion in up to 50 % of cases, with reports from experienced centers suggesting a conversion rate of 25–35 % for enteric fistulae.
- 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 open resection should *not* be viewed as a failure of the surgeon but as a sign of mature surgical judgment.
- Delayed conversion, occurring only after a complication has occurred, may in some cases reflect poor judgment or little experience.
- 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, which occurred due to adverse conditions and that could have been avoided.

Outcomes

- In comparison with conventional colectomy, laparoscopic colectomy benefits may include shorter duration of postoperative ileus, less postoperative pain and concomitant reduction in the need for analgesics, earlier tolerance of diet, shortened hospital stay, earlier 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.
- Conclusions regarding outcomes, therefore, often come from the repetitiveness of the results rather than the superiority of study design. For any one study, the evidence is weak, but collectively, due to the reproducibility of results by a large number of institutions, even with different operative techniques and postoperative management parameters, the preponderance of evidence favors a minimally invasive

approach with respect to postoperative outcomes. Also, the prospective randomized studies, which are available, corroborate the findings demonstrated in nonrandomized studies.

Operative Time

- Most studies demonstrate a longer operative time associated with a laparoscopic procedure. In prospective randomized trials, the procedure was roughly 40–60 min longer in the laparoscopic groups. As the surgeon and team gain experience with laparoscopic colectomy, operating times do reliably fall, but rarely does it return to the comparable time for a conventional approach.

Return of Bowel Activity and Resumption of Diet

- Most studies comparing open and laparoscopic colectomy have shown a statistically significant reduction (1–2 days) in the time to passage of flatus and stool.
- Psychological conditioning of the patient preoperatively may interfere with an objective assessment of bowel activity postoperatively.
- Both canine and porcine models have confirmed an earlier return of intestinal myoelectric activity following laparoscopic resection.
- A dog study demonstrated an earlier return to preoperative motility, utilizing radionucleotide techniques in animals subjected to laparoscopic resection.
- With shorter postoperative ileus, tolerance of both liquids and solid food is1–2 days sooner following laparoscopic resection.

Postoperative Pain and Recovery of Pulmonary Function

- Analog pain scales and narcotic requirements have demonstrated a significant reduction in pain following minimally invasive surgery.
- Adequate pain management allows the patient to inspire more deeply. A randomized trial from Cleveland Clinic showed an 80 % recovery of baseline forced vital capacity (FVC) and forced expiratory volume in 1 s (FEV_1). The median recovery for the laparoscopic group was half the recovery (6 days) seen in the conventional group.

Length of Stay

- More rapid resolution of ileus, earlier resumption of diet, and reduced postoperative pain result in a shortened length of stay.
- Recovery after open operation has also been shortened by fast-track practices, but this is not consistent throughout the literature.

- In most studies, the length of hospitalization is 1–6 days less for the laparoscopic group.

Quality of Life and Return to Work

- Psaila et al. found that hand-grip strength, as a measure of protein loss, recovered more rapidly after laparoscopic surgery, and in six of eight areas, the SF-36 questionnaire showed less impairment of health following laparoscopic colectomy. By 4 months postoperatively, this trend persisted but to a lesser degree.
- Quality of life measurements in the COST study found that patients who had a laparoscopically completed procedure were improved compared with open procedures and with laparoscopic patients who required a conversion to open surgery, although this did not achieve significance.
- In a nonrandomized study, patients undergoing laparoscopy returned to full activities and work sooner than matched patients undergoing conventional resection (mean – 4.2 weeks vs. 10.5 weeks, 3.8 weeks vs. 7.5 weeks, respectively ($P < 0.01$ for all)).

Hospital Costs

- A case–control study from the Mayo Clinic looked at total costs following laparoscopic and open ileocolic resection for Crohn's disease. Sixty-six patients underwent laparoscopic ($n = 33$) or conventional ($n = 33$) ileocolic resection during the same time period (10/95 to 7/99) and were well matched. Patients in the laparoscopic group had less postoperative pain, tolerated a regular diet sooner by 1–2 days, and had a shorter length of stay (4.0 days vs. 7.0 days). In their cost analysis, despite higher operative cost, the overall mean costs were $3,273 less in the laparoscopic group.
- Other studies by Dupree et al. and Shore et al. have confirmed these findings with a mean reduction of $438 in costs and $7,465 in hospital charges, respectively, in patients undergoing laparoscopic compared to conventional ileocolic resection.
- The results are similar for elective sigmoid diverticular resection with a mean cost savings of $700–$800 (and there are additional examples in the disease-specific section).

Disease-Specific Outcomes

Crohn's Disease

- In Crohn's disease, there may be inflammatory changes, difficulty in assessing bowel involvement, and associated abscess and fistulous disease.
- Table 35.1 demonstrates an increasing laparoscopic experience with Crohn's disease.

Table 35.1 Studies of laparoscopic resection for Crohn's disease: ileocolic resection

		No. of patients		OP time (min)		LOS (day)		Morbidity (%)		
Author	Year	LAP	Open	LAP	Open	LAP	Open	LAP	Open	Comment
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 % vs. 35 %
Huilgol et al.	2004	21	19	136	120	6.4	8.2	19	16	
Rosman et al.	2005			26.8 min longer		2.62 days less		OR 0.62		Meta-analysis, SBO reduced in LAP cases
Tilney et al.	2006	338	445	29.6 min longer						Meta-analysis, conversion 6.8 %
Tan et al.	2007			26 min longer		1.82 days less		12.8	20.2	Meta-analysis, conversion 11.2 %
Lesperance et al.	2009	2,826 (6 %)	46,783			6.0	9.0	8	16	Nationwide Inpatient Sample
Soop et al.	2009	109		150		4.0		11		Conversion 6 %
Nguyen et al.	2009	335		177		5.0		13		Largest series, conversion rate 2 %

Table 35.2 Early descriptive studies of laparoscopic colectomy for ulcerative colitis

Author	Year	No. of patients	Comment
Meijerink et al.	1999	10	Feasible, 7 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

- The majority of studies are retrospective case–control series and report conversion rates from 10 to 20 %, which increases to 40–50 % with complex cases (abscess, fistula, or reoperative surgery).
- Without tactile sensation, one of the concerns of laparoscopic surgery in the patient with Crohn's is missing an isolated proximal ileal lesion, but this has not been reported.
- Crohn's recurrence rates after laparoscopy are similar to conventional procedures.
- Laparoscopic resection for Crohn's disease appears to be safe.

Ulcerative Colitis

- Studies of laparoscopic proctocolectomy for ulcerative are summarized in Tables 35.2 and 35.3.
- Recent reports demonstrate that laparoscopic total colectomy and proctocolectomy with and without ileal pouch-anal anastomosis is technically feasible and shares the same advantages as seen with segmental colonic resection.
- Indar et al. showed that adhesions are reduced with laparoscopic pouch procedures, in a series of 34 patients (21 females).

Diverticulitis

- There are now a large number of studies evaluating laparoscopic surgery for diverticulitis (Tables 35.4 and 35.5).
- Most series report an operative time of 2–3 h with a conversion rate of 10–20 % for larger series.

Table 35.3 Comparative studies of laparoscopic resection for ulcerative colitis

		No. of patients		OP time (min)		LOS (day)		Morbidity (%)		
Author	Year	LAP	Open	LAP	Open	LAP	Open	LAP	Open	Comment
Maartense et al.	2004	30	30	210	133	10	11	20	17	SF-36 and GIQLI scores similar
Larson et al.	2006	100	200	333	230	4	7	33	37	LAP faster than hand assisted (320 min vs. 372 min)
Zhang et al.	2007	21	25	325	220	9	11	25	28	
Benavente-Chenhalls	2008	16	16	500	382	25	44	5.3	9.9	UC and primary sclerosing cholangitis
Ahmed Ali et al.	2009	253	354	91 min longer		2.7 days less		38–47	42–53	Cochrane review
Fichera et al.	2009	73	106	335	322	8.3	7.4			Incisional hernia repair 7.8 % open vs. 0 % LAP
Chung et al.	2009	37	44	223	140	4.9	8.5	9/37	21/44	1st of 3 stage procedure, 2nd stage earlier in LAP

Table 35.4 Descriptive series of laparoscopic resection for diverticulitis

Study	Year	*N*	Mortality (%)	Morbidity (%)	Conversion (%)	OR time (min) [a]	Resume diet (day)[a]	Flatus/BM (day)[a]	LOS (day)[a]
Eijsbouts et al.	1997	41	0	18	15	195	NA	NA	6.5
Stevenson et al.	1998	100	0	21	8	180	2	2	4
Tuech et al.	2000	77	0	17	14	NA	NA	NA	NA
Trebuchet et al.	2002	170	0	8.2	4.1	141	3.4	NA	8.5
Bouillot et al.	2002	179	0	15	14	223	3.3	2.5	9.3
Pugliese et al.	2004	103	0	8	3	190	NA	4	9.7
Schneidbach et al.	2004	1,545	0.4	17	6.1	169	NA	NA	NA
Pessaux et al.	2004	582	1.2	25	NA	NA	NA	NA	NA
Schwandner et al.	2005	363	0.6	22	6.6	192	2.8	4.0	11.8
Jones et al.	2008	500	0.2	11	8–1.5	120	NA	NA	4

OR operating room, *BM* bowel movement, *LOS* length of stay, *NA* not available
[a]Median or mean values listed

Table 35.5 Case–control studies of laparoscopic resection for diverticulitis

Study	Year	No. of patients		Mortality (%)		Morbidity (%)		Convert (%)	OR time (min)[a]		Resume diet (day)		Flatus/BM (day)		LOS (day)		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		9.2	6.3[b]	P 13,400	11,500
Bruce et al.	1996	17	25	0	0	23	16	12	115	397[b]	5.7	3.2[b]	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 8,975	7,185[b]
Senagore et al.	2002	71	61	0	1.6	30	8[b]	7	101	107	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		8.8	4.8[b]	$14,863	13,953[b]
Lawrence et a1.	2003	215	56	1.6	1	27	9[b]	7	140	170[b]	NA		NA		9.1	4.1[b]	$25,700	17,414[b]
Gonzalez et al.	2004	80	95	4	1	31	19[b]	NA	156	170	NA		3.7	2.8	12	7[b]	NA	
Alves et al.	2005	169	163			31.4	16.0	15.3										
Lee et al.	2006	21	21						171	197					18	10		
Shapiro et al.	2008	166	80	0	0	7.8	6.3	12.5	153	185					4	8		

OR operating room, *BM* bowel movement, *LOS* length of stay, *CON* conventional surgery, *LAP* laparoscopic surgery, *NA* not available, *P* pounds, *DM* Deutsche marks

[a]Median or mean values listed

[b]Statistically significant difference

[c]Results of nonconverted laparoscopic cases given

[d]Minilaparotomy

- The largest series of diverticular resection comes from a German multi-institutional study of 1,545 patients accumulated over 7 years at 52 institutions. The study demonstrated a low morbidity and mortality with an overall conversion rate of 6.1 %.
- Nearly all of the comparative studies related to laparoscopic vs. open sigmoid resection demonstrate a benefit for the laparoscopic approach including a shorter duration of ileus and shortened length of stay, but as in other studies, with a longer operative time.
- Recent studies have demonstrated a cost saving with the laparoscopic approach.
- Less experienced surgeons should consider an early conversion of complicated diverticular resection or potentially an alteration in the approach to a hybrid approach where the difficult pelvic dissection can be guided by the hand laparoscopically or by conventional means through the open wound.
- Laparoscopic lavage and placement of drains for purulent peritonitis secondary to perforated diverticulitis has been reported.
- Myers et al. concluded that laparoscopic management of perforated diverticulitis with generalized (purulent) peritonitis is feasible, with a low recurrence risk in the short term.
- Alamili et al. performed a review of the literature, which included eight studies, none randomized, reporting 213 patients with acute complicated diverticulitis managed by laparoscopic lavage. Mean age was 59 years and most patients had Hinchey stage III disease. Conversion to laparotomy occurred on 6 patients (3 %) and the complication rate was 10 %. Mean hospital stay was 9 days. After mean follow-up of 38 months, 38 % underwent elective sigmoid resection. Potential benefits were acknowledged, but larger studies were recommended.

Rectal Prolapse

- Laparoscopic fixation and sigmoid resection and rectopexy have been used to treat rectal prolapse (Table 35.6).
- Laparoscopic studies have shown a longer operative time (45–60 min) and shortened length of stay (2–3 days). Functional results following surgery were similar and the majority of patients reporting an improvement in incontinence and constipation.
- The majority of reports on laparoscopic surgery for rectal prolapse have limited follow-up (less than 3 years), and the reported recurrence rates ranges from 0 to 6 % (Table 35.6).
- Recently, however, there have been two studies with a mean follow-up of 5 years.
- In a study of 42 patients by D'Hoore et al., with a mean follow-up of 61 months, the rate of recurrent prolapse was 4.8 %.

Table 35.6 Laparoscopy for rectal prolapse

Study	Year	No. of patients	Follow-up (month)	Procedure	Operative time (min) LR/LRR	LOS (day)	Recurrence (%)	Comment
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
Stevenson et al.	1998	34	18	LR/LRR	185	5	0	7 % mucosal prolapse, no recurrence
Bruch et al.	1999	57	30	LR/LRR	227/257	15	0	Constipation improved in 76 %
Boccasanta et al.	1999	10						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 a1.	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
Heemskerk et al.	2007	33		LR	39 min longer			OR time longer for robotic vs. LAP, more expensive

Adapted from: Heemskerk J, de Hoog DE, van Gemert WG, Baeten CG, Greve JW, Bouvy ND. Robot-assisted vs. conventional laparoscopic rectopexy for rectal prolapse: a comparative study on costs and time. Dis Colon Rectum 2007;50:1825–30

RR resection rectopexy, *PFR* pelvic floor repair, *AR* anterior resection, *FRM* full rectal mobilization without fixation, *LRR* laparoscopic resection rectopexy, *LR* laparoscopic rectopexy, *FT* full thickness, *MP* mucosal prolapse, *NS* not specified

- In the largest study of laparoscopic surgery for rectal prolapse by Ashari et al., with 117 patients over a 10-year period and a mean follow-up of 62 months, the rate of recurrent full-thickness prolapse was only 2.5 %. They also noted an 18 % rate of mucosal prolapse, which is somewhat concerning.
- Further long-term follow-up of these patients is needed to ensure that the rate of recurrence remains acceptable.

Colorectal Cancer

- Prior to 2004, fewer than 5 % of resections for colon and rectal cancer were being performed laparoscopically.
- There are no good sources for estimating current figures although approximately 30 % of candidates for recertification for the American Board of Colon and Rectal Surgery (ABCRS) denote that they perform "some" laparoscopy.
- Data from randomized controlled trials, however, have laid to rest these controversial aspects of the minimally invasive approach for colon cancer, especially with respect to early concerns.
- Lacy and colleagues published the first large single-center randomized controlled trial in 2002. With median follow-up of 39 months, he and his colleagues reported higher cancer-related survival for the laparoscopic arm. Specifically, he showed no difference between arms for stage II cancers, but an improved survival for the laparoscopic approach in stage III cancers where the outcome was similar to that of stage II patients.
- This was followed in 2004 by 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, no differences were found in overall survival nor disease-free survival. Further reassurance was provided in finding that there were only two wound recurrences in the laparoscopic group and one in the open arm.
- The "CLASICC" trial from the UK included both colon and rectal cancers. The findings were similar, except for a rather spectacularly high rate of conversion, at 29 %. Those results were updated more recently in 2007.
- Concerning issues from that trial were the very high conversion rate, the rate of positive radial margins in patients undergoing resection for rectal cancer (in both the laparoscopic *and* the open arms), and the 20 % reduction in survival in patients undergoing abdominoperineal resection compared with low anterior resection. This raises very realistic concerns regarding technical issues.
- The COLOR (colon cancer laparoscopic or open resection) trial was performed as a multicenter randomized trial at 37 centers throughout Europe. The study accrued patients from 1997 to 2003, and there were several interim reports regarding accrual and outcomes compared with operative volumes, but the long-term oncologic outcomes were not reported until 2009, and even then only 3-year outcomes were reported.
- The results of these four trials are summarized in Table 35.7.

Table 35.7 Prospective, randomized trials comparing laparoscopic and conventional surgery for colorectal cancer

	Lacy et al. 2002	COST 2004	CLASICC 2005	COLOR 2009
Baseline characteristics	LAP vs. open	LAP vs. open	LAP vs. open	LAP vs. open
No. assigned	111:108	435:437	526:268	627:621
No. completed (dead or no data)	105:101	435:428	452:231 (74:37)	534:542 (83:70)
Age	68:71	70:69	69:69	71:71
Gender (F)	55:58	49 %:51 %	44 %:46 %	48 %:47 %
Previous surgery	40:47	43 %:46 %		38 %:38 %
BMI				24.5:24.9
Operative findings				
Procedure				
Right	49:49	54 %:54 %	24 %:24 %	48 %:47 %
Left	4:1	7 %:7 %	7 %:9 %	11 %:11 %
Sigmoid	52:46	38 %:38 %	13 %:12 %	38 %:39 %
AR/LAR	3:9		37 %:36 %	
			12 %:13 %	
Other	3:3		4 %:3 %	4 %:4 %
TNM stage				
0		5 %:8 %	Not given	
I	27:18	35 %:26 %		24 %:25 %
II	42:48	31 %:34 %		43 %:41 %
III	37:36	26 %:28 %		33 %:34 %
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	19 %:N/A
OR time (min)	142:118[a]	150:95[a]	180:135 (anesthesia time)	
Incision length (cm)		6:18[a]	10:22	

(continued)

Table 35.7 (continued)

	Lacy et al. 2002	COST 2004	CLASICC 2005		COLOR 2009
Short-term outcomes					
Oral intake (h)	54:85[a]				
(day)			6:6		
Hospital stay (day)	5.2:7.9[a]	5:6[a]	9:11		
30-day mortality		<1 %:1 %	4 %:5 %		
Postoperative complications	12:31[a]	19 %:19 %	33 %:32 %		21 %:20 %
			Colon	Rectum	
Wound infection	8:18		5 %:5 %	13 %:12 %	4 %:3 %
Pneumonia	0:0		7 %:4 %	10 %:4 %	1 %:2 %
Ileus	3:9				
Leak	0:2		2 %:0 %	10 %:7 %	3 %:2 %
Duration of oral analgesics (day)		1:2[a]			
Duration of parenteral analgesics (day)		3:4[a]			
Cancer outcomes					
Tumor recurrence	18:28	76:84			
Distant	7:9				56:54
Locoregional	7:14				26:26
Peritoneal seedling	3:5				
Port site	1:0	2:1	9 (2.5 %):1 (0.6 %)		7 (1.3 %):2 (0.4 %)
5-year overall survival[b]	82 %:74 %	79 %:78 %	3-year reported 68.4 %:66.7 %		3-year reported 81.8 %:84.2 %
I	85 %:94 %	84 %:94 %	No graphs by TNM stage		84 %:82 %
II	75 %:77 %	78 %:81 %	No graphs by TNM stage		78 %:82 %
III	72 %:45 %	60 %:63 %	No graphs by TNM stage		62 %:57 %

5-year disease-free survival[b]		78 %:80 %	3-year reported 66.3 %:67.7 %	3-year reported 74.2 %:76.2 %
I	90 %:88 %	92 %:96 %	No graphs by TNM stage	80 %:77 %
II	80 %:76 %	82 %:88 %	No graphs by TNM stage	70 %:75 %
III	70 %:45 %	62 %:60 %	No graphs by TNM stage	58 %:55 %
Cancer-related survival[b]	91 %:79%[a]			
I	100 %:99 %			
II	88 %:85 %			
III	84 %:50%[a]			

[a]Statistically significant difference
[b]Extrapolated from graphs in manuscript

- The results of these trials (Table 35.7) have demonstrated that similar oncologic resections can be achieved by experienced surgeons performing laparoscopic colon resections. After publication of the COST study results, ASCRS and SAGES copublished an approved statement that laparoscopic colectomy for cancer appeared to produce similar oncologic outcomes but emphasized that these procedures should only be attempted by surgeons experienced with laparoscopic techniques.

Outcomes for Rectal Cancer

- Surgical resection of rectal cancer has the potential to achieve a curative result. Total mesorectal excision (TME) is currently the standard of care, minimizing the risk of local recurrence and providing accurate information regarding staging, that affects prognosis and subsequent therapy.
- Early prospective studies, from experienced surgeons, suggested that laparoscopic resection did not worsen survival or disease control in patients with rectal cancer compared with open resection.
- An early study by Leung et al. evaluated laparoscopic vs. open resection for rectosigmoid cancer, so this was not a trial of TME. A total of 403 patients were accrued between 1993 and 2002, 203 in the laparoscopic arm and 200 open. The probability of survival at 5 years for the laparoscopic and open resection groups were 76.1 and 72.9 %, respectively. Five-year disease-free survival rates were 75.3 and 78.3 %, respectively. The operative time for the laparoscopic group was significantly longer, whereas postoperative recovery was significantly better than for the open resection group. These benefits, however, were at the expense of higher direct cost. Reassuringly, the distal margin, the number of lymph nodes found in the resected specimen, overall morbidity, and operative mortality did not differ between groups.
- The CLASICC randomized controlled trial in the UK differed from its contemporaneous trials (COST, COLOR) in that patients with both colon cancer and rectal cancer were included. The study enrolled 268 patients to the open arm, of whom 128 (48 %) had rectal cancer, and 526 patients to the laparoscopic arm, of whom 253 (48 %) had rectal cancer. The conversion rate for the study overall was 29 %, with a 25 % conversion rate for colon cancer and 34 % for rectal cancer. The conversion rate dropped by year of the study, from 38 % in year 1 to 16 % in year 6 of the study. Operative time was longer for the laparoscopic rectal resections (180 min vs. 135 min), time to bowel movement shorter (5 days vs. 6 days), time to regular diet the same (6 days), and hospital stay shorter (11 days vs. 13 days). It was noted that the rate of positive circumferential resection margins (CRM) was the same between the two groups, but a closer look at the data is very disturbing. The CRM was positive in 14 % of open patients and 16 % of laparoscopic patients ($P = 0.8$). Admittedly, these are not significantly different, but the fact they are not different is not reassuring as

the rate in the open group is hardly acceptable! In the low anterior resection group, it was noted that there was a nonsignificant trend toward a higher positive CRM rate in the laparoscopic group (12 % vs. 6 %, $P=0.19$). It was noted that no difference was seen in CRM positivity in the abdominoperineal group, but again the actual figures are far from reassuring with a 20 % (10/49) positive rate in the open group vs. 26 % (7/27) in the laparoscopic group.

- Thus although the reports of the randomized controlled trials for colon cancer were reassuring, the CLASICC trial raised concerns regarding the application of laparoscopic techniques for rectal cancer. The fact that there were also high rates of CRM positivity in the open cases raised the issue of technical competence in the CLASICC trial and deflected some of the attention away from the laparoscopic technique itself. Fortunately, overall, there were no differences in the long-term outcomes in the follow-up report of oncologic outcomes. There was no statistically significant difference in 3-year overall survival for patients undergoing anterior resection (AR) or abdominoperineal resection (APR) in either technique group (AR, open 66.7 %, laparoscopic 74.6 %; APR, open 57.7 %, laparoscopic 65.2 %). The higher positivity of the circumferential resection margin reported after laparoscopic anterior resection did not translate into an increased incidence of local recurrence. There was no difference in 3-year local recurrence rates after anterior resection of rectal cancer (7 % open, 7.8 % laparoscopic) or abdominoperineal resection of rectal cancer (21 % open, 15 % laparoscopic).
- Numerous single-institution prospective case series have since supported the safety and efficacy of laparoscopic resection of rectal cancer in experienced centers and experienced hands.
- Ng et al. reported short-term outcomes and long-term survival in a large single-institution series of 579 patients undergoing laparoscopic resection for rectosigmoid and rectal cancer. Rectosigmoid and upper rectal cancers (12–18 cm from the anal verge), both undergoing low anterior resection, were grouped together for the subsequent analysis. Patients with tumors in the mid-rectum (7–12 cm from the anal verge) underwent sphincter-preserving TME. Patients with low-rectal tumors (<7 cm from the anal verge) underwent either TME or APR. Over a 15-year period, there were 316 laparoscopic anterior resections, 152 sphincter-preserving TME, and 92 laparoscopic APRs. Median follow-up was 56 months. Overall, early and late operative morbidity rates were 18.8 and 9.7 %, respectively. The anastomotic leak rate was 3.5 % ($n=20$). Conversion occurred in 31 patients (5.4 %). Port site recurrence was seen in 0.4 % of patients (1 laparoscopic anterior resection, 1 laparoscopic TME) and locoregional recurrence in 7.4 % of patients. Microscopic resection margin involvement was identified in 6 laparoscopic TME and in 2 laparoscopic APR. Overall 5- and 10-year survival rates were 70 and 45.5 %, and cancer-specific 5- and 10-year survival rates were 75 and 56 %, respectively. Of note, patients in

the anterior resection group were not stratified by tumor location, so the number of patients with rectosigmoid vs. upper rectal cancer is unclear. The authors concluded that laparoscopic resection for rectal cancer is safe and offers long-term oncologic outcomes equivalent to those of open resection.

- In a retrospective study of 421 patients comparing outcome between open (310 patients) and laparoscopic (111) resection for stage II and stage III rectal cancer, Law et al. reported 5-year actuarial survival rates of 71.1 % vs. 59.3 % in the laparoscopic vs. open arms, respectively ($P=0.029$), after a median follow-up of 34 months. There was no difference in local recurrence. Laparoscopic resection was associated with decreased blood loss (200 ml vs. 350 ml, $P<0.001$) and shorter hospital stay (7 days vs. 9 days, $P<0.001$). The conversion rate was 12.5 %. On multivariate analysis, laparoscopic resection was an independent factor associated with improved survival ($P=0.03$, hazards ratio 0.558 [95 % confidence interval, 0.339–0.969]). There was, however, no breakdown of the number of stage II vs. stage III rectal cancer patients. The study concluded that compared to open resection, laparoscopic resection for locally advanced rectal cancer is associated with more favorable overall survival.
- Thus in these large retrospective and prospective single-institution studies, the data consistently demonstrate improved early postoperative outcomes with no negative impact on oncologic outcomes and even improved oncologic outcomes in some series.
- Interestingly, the potential for improved TME specimens has been demonstrated in an elegant study by Gouvas et al., in 39 open and 33 laparoscopic proctectomies.
- A more recent single-institution randomized controlled trial was reported by Lujan et al. After neoadjuvant chemoradiation, 204 patients with mid- and low-rectal cancer were randomized to open (103) or laparoscopic resection (101). Sphincter preservation rates were not different, 78.6 and 76.2 % in the open and laparoscopic group, respectively. Complication rates and involvement of CRM rates were similar, but the lymph node retrieval rates were greater in the laparoscopic group (mean 13.6 vs. 11.6). There were no differences in oncologic outcomes in terms of local recurrence, disease-free, or overall survival.
- Concerns still remained regarding the applicability of laparoscopic techniques for rectal cancer outside highly specialized, high-volume institutions. For this reason, there are several multicenter randomized trials in various stages of accrual.
- In the USA, a prospective, multicenter randomized trial was established to determine the feasibility, reproducibility, and oncologic applicability of minimally invasive techniques in the resection of rectal cancer. This study is currently accruing patients under the auspices of the ACOSOG Study AZ6051. The primary objective of the trial is to test the hypothesis that laparoscopic resection of rectal cancer is not inferior to open resection.

Outcomes being measured are based on a composite primary endpoint of oncologic factors, which are considered to indicate a safe and feasible operation. These parameters are circumferential margin >1 mm, distal resected margin >2 cm (or >1 cm with clear frozen section in the low rectum), and completeness of TME, defined by careful evaluation by an experienced pathologist. Secondary objectives are to assess patient-related benefit of laparoscopic-assisted vs. open rectal resection (blood loss, length of stay, pain medicine utilization), to assess disease-free survival and local pelvic recurrence at 2 years, and to assess quality of life, sexual function, bowel, and stoma function.

- The UK MRC CLASICC trial is close to reporting its mature 5-year data. The Japan Clinical Oncology Group (JCOG) Study 0404, which has been evaluating laparoscopic surgery for colorectal cancer, was activated in October 2004 and is also close to reporting its long-term data.
- At present, the European Colon Cancer Laparoscopic or Open Resection (COLOR) II trial is a randomized, international, multicenter study comparing the outcomes of laparoscopic and conventional resection of rectal carcinoma with curative intent. Prior to its start, a feasibility study is to be performed with the objective of controlling for quality of laparoscopic TME. The primary endpoint is locoregional recurrence at 3 years. Secondary endpoints are recurrence-free and overall survival at 3, 5, and 7 years, rate of distant metastases, port site and wound site recurrences, microscopic evaluation of the resected specimen, 8-week morbidity and mortality, quality of life, and cost.
- Given limited prospective data, laparoscopic resection for rectal cancer remains investigational in the USA. Although it is performed in some specialist centers by experienced surgeons, open surgical resection is still the standard of care in most hands, and the role of laparoscopy is yet to be confirmed. Studies consistently show improved short-term outcomes, such as quicker recovery times, shorter hospital stays, and reduced analgesic requirements, but these are at the price of longer operative times and higher overall costs. Careful patient and tumor selection are essential. Mature 5-year data are pending from the MRC CLASICC and the JCOG 0404 trials. The European COLOR II trial and the ACOSOG-Z6051 trial, specifically comparing outcomes of laparoscopic-assisted and open resection for rectal cancer, are under way but far from reporting results.

Laparoscopic Resection of Colon and Rectal Cancer

- The following description regarding the safe performance of laparoscopic resection for curable colon and rectal cancer is based on current literature, experience, and an understanding that patients are treated by experienced surgeons whose minimally invasive skills fulfill the Credentialing Recommendations endorsed jointly by ASCRS and SAGES.

General Considerations

- Following 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 when a laparoscopic approach is considered: (1) site of the tumor is important, as right and sigmoid colectomy are generally less technically demanding than, for example, low anterior resection; (2) extensive adhesions; (3) obesity, and particularly the distribution of abdominal fat, may preclude laparoscopic resection, especially in the case of a rectal cancer in an obese male patient with a narrow pelvis; (4) the patient should be informed of both laparoscopic and open alternatives and the possible need for conversion; and (5) the surgeon must have adequate experience prior to embarking on resection for a potentially curable malignancy.

Tumor Localization

- A laparoscopic approach requires accurate localization of the tumor to a specific segment of the colon, as even a known cancer may not be visualized from the serosal aspect of the bowel during laparoscopy. The wrong segment of colon may be removed if accurate localization has not been performed.
- A variety of other options are available to localize a lesion including, preoperative colonoscopic marking with ink tattoo or metallic clips, barium enema, or intraoperative endoscopy. The area adjacent to a cancer or polyp may be marked either by endoscopic clips or by submucosal India ink injection. If clips are placed, immediate abdominal X-ray films should be taken; otherwise, intraoperative imaging with laparoscopic ultrasound or fluoroscopy is necessary to localize the clip's location. This procedure is not commonly employed since it requires an experienced radiologist and/or endoscopist.
- Preoperative endoscopic tattooing is a common method of tumor localization. India ink is a nonabsorbable marker, which 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 cm^3 per site). During diagnostic laparoscopy the ink marking can be identified even at the flexures or transverse colon. India ink injection appears to be safe with few reported complications.
- Intraoperative endoscopy is hampered by persistent bowel distention, prolongation of operative times, and need for equipment and endoscopist intraoperatively. More recent studies have evaluated CO2 colonoscopy, which allows for more rapid absorption of the intracolonic gas which may facilitate its use during laparoscopic procedures.

- Preoperative staging and perioperative preparation are similar to open resections.

Operative Issues

- Oncologic principles must not be compromised by a laparoscopic resection. For colon cancer surgery: proximal and distal resection margins (based upon 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.
- For rectal cancer surgery: 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.

Contiguous Organ Attachment

- En bloc resection is recommended for locally advanced adherent colorectal tumors. A bulky tumor invasive into an adjacent organ may be detected by preoperative imaging, such as CT scan, and guide the recommendation for an open resection.
- A known T4 colonic cancer will prompt an open approach in the vast majority of cases, although some experienced surgeons may complete en bloc resection of involved small bowel or abdominal wall laparoscopically.

Prevention of Wound Implants

- Port site recurrences, or wound implants, have been reported at both extraction site and trocar site incisions, which prompted extensive investigation. Current consensus is that wound implants should be kept at a rate less than 1 % by correct oncologic technique and experience.
- In vitro and in vivo animal models have generated most recommendations for avoidance of wound implants.
- Gasless laparoscopy has shown mixed results.
- 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.
- Helium decreases tumor implants but is not easily adapted to the clinical setting.
- Wound excision may either decrease or increase the rate of tumor implants.
- Gas leakage along loosely fixed trocars (the “chimney effect”) may be associated with increased cancer wound implantation.
- An expert panel convened by the European Association of Endoscopic Surgery (EAES) reported that half the members irrigated the port sites and

all members protected the extraction site and/or extracted the specimen in a bag.

- The most important development in the issue of wound implants is experience and the refinement of laparoscopic techniques and equipment that permit a true oncologic resection to be performed.
- Early reports of implant rates of 2–21 % have not been reproduced in large retrospective series by experienced surgeons, who reported rates of 1 % or less (similar to the incisional recurrence rate for open colorectal cancer resection).

Training and Credentialing in Laparoscopic Colorectal Surgery

- Early studies estimated the learning curve for laparoscopic colectomy to be 20–50 cases.
- The following is the approved statement from ASCRS and SAGES:

> Laparoscopic colectomy for curable cancer results in equivalent cancer related survival to open colectomy when performed by experienced surgeons. Adherence to standard cancer resection techniques including but not limited to complete exploration of the abdomen, adequate proximal and distal margins, ligation of the major vessels at their respective origins, containment and careful tissue handling, and en bloc resection with negative tumor margins using the laparoscopic approach will result in acceptable outcomes. Based upon the COST trial, prerequisite experience should include at least 20 laparoscopic colorectal resections with anastomosis for benign disease or metastatic colon cancer before using the technique to treat curable cancer. Hospitals may base credentialing for laparoscopic colectomy for cancer on experience gained by formal graduate medical educational training or advanced laparoscopic experience, participation in hands-on training courses and outcomes.

- The issue of defining numbers for credentialing purposes is a source of considerable controversy.
- For perspective, a resident completing a General Surgery Residency Program in 2003 and entering practice had performed a mean of 120 cases on the large intestine (mode 106, Residency Review Committee for Surgery, Reporting Period 2002–2003). Of these, an average of 50 cases required resection and anastomosis. Thus the guideline for 20 laparoscopic cases is not excessive or unreasonable in terms of attaining comparable experience prior to independent practice.

Alternative Approaches

Hand-Assisted Laparoscopy

- Hand-assisted laparoscopic colectomy is an alternative to straight laparoscopic techniques.

- A hand-assisted laparoscopic colectomy may be easier to adopt than a straight laparoscopic approach.
- Studies have demonstrated that hand-assisted colectomy provides similar functional results to straight laparoscopic resection with fewer conversions.
- Operative times appear shorter than traditional laparoscopy in the majority of studies but length of stay has been similar.

Robotic Colorectal Surgery

- The robotic device allows for precise control of movement, restoration of all the "degrees of freedom" provided by the human wrist, magnification, and three-dimensional images. The most convincing application to date has been in the field of urology, where the device has allowed for intracorporeal suturing of the bladder to urethra anastomosis. Even this has been challenged recently.
- In the field of colorectal surgery, the use of the device remains controversial. It is hard to justify its use in colectomies. Even those who have used it for right and left colectomy have demonstrated increased operative times and increased costs.
- It may potentially have a greater role in the resection of rectal cancer.
- However, consensus has not been reached. It is salutary to read the editorial of Cadeddu et al. on robotic prostatectomy. He reflects upon the issue that marketing of the robotic device has reached such heights that opinion has "reached the level of surgical dogma among patients and physicians at the expense of objective data." The robotic device fascinates surgeons and patients alike. It is a wonderful tool. But it remains just that – a tool. Many surgeons who are currently performing advanced laparoscopic colorectal procedures have skills such that they do not require a robot. The robot may facilitate dissection in the pelvis for rectal cancer, especially for surgeons who might not otherwise be able to complete a pelvic dissection laparoscopically, but it remains to be seen if the current economic climate will continue to support expensive technology to support lack of acquisition of operative skills.

Single-Incision Colectomy

- This development of single-incision colectomy is still in its seminal stages. Initial publications are primarily case reports or press releases. Reports have expanded from the original cholecystectomy to include appendectomy, sleeve gastrectomy, adrenalectomy, and colectomy.
- There is growing data about the safety of single port in skilled hands, but incremental benefits may be very difficult to confirm.

NOTES Colectomy

- Natural orifice transluminal endoscopic surgery (NOTES) became a focus of intellectual and surgical creativity after the pairing of a surgeon

and a gastroenterologist in India led to the release of a video of an appendectomy performed via a gastrotomy with flexible endoscopic instruments, with extraction of the specimen transorally. After 5 years and millions of dollars of research and development money later, yet the approach is still seeking what Jeff Ponsky has referred to as the "Killer App" or the application that transcends obstacles to its use (personal communication). Although surgeons see this approach as potentially being the same quantum leap in surgical technique that laparoscopy was compared with laparotomy, there are different barriers.

- The transvaginal approach has been used primarily, as the majority of patients requiring cholecystectomy are female, and this approach affords greater confidence in the quality of the preparation. The transrectal approach does have its merits, however, and transrectal endoscopic microsurgery (TEMS) has illustrated that this path of access can be adequately prepped.
- Second, and likely least pertinent, the rectum has been used as a means of obtaining access to the peritoneal cavity with a flexible instrument that is then used to perform dissection and resection of a segment of colon. Transgastric and bidirectional approaches with both transgastric and transrectal approaches have been described. These are tours de force of technique but not immediately relevant to clinical practice.
- The third area of research has focused on use of the TEMS device as a means of access. This makes sense that the planned anastomotic site becomes the means of access to the abdominal cavity and has implications for sigmoidorectal surgery (and also for bariatric surgery with upper endoscopy using the planned anastomotic site). Several groups have described using the TEMS device to make a circumferential incision in the rectum at the planned level of anastomosis and then continuing the dissection in the presacral space and the left retroperitoneum. The technique does not reliably allow for mobilization of the splenic flexure, so again, applications are limited at this point with current instrumentation.

Future Considerations

- It is actually quite fascinating to see how slowly laparoscopic techniques for colorectal surgery have been adopted. The procedures are likely similar in terms of technical difficulty to bariatric procedures, yet the vast majority of bariatric procedures are performed laparoscopically as opposed to less than 30 % of colorectal procedures. One wonders if market forces are implicated, as many bariatric procedures are not covered by insurance and the patient pays out of pocket. Over the next few years, the field of colorectal surgery may become quite divergent, especially within the subspecialist field of minimally invasive procedures. Surgeons who have adopted hand-assisted techniques may not be able to adopt single-incision

techniques, if the latter prove to have benefits. The realm of NOTES is still undetermined, but there will likely be considerable cross-fertilization with the techniques and instrumentation used for single-incision procedures.

- Bemelman phrased this upcoming period best: when fast-track protocols make it difficult to differentiate laparoscopic from open approaches, then the long-term implications of a laparoscopic approach carry far more weight than such short-term benefits as time to bowel function and time in the hospital. More important are long-term outcomes such as rates of bowel obstruction and preservation of fertility. This is an exciting time for this field, not least for our patients who will hopefully continue to benefit from the extensive efforts being expended in making these major procedures less invasive.

36. Polyps

Paul E. Wise

- Polyps are defined as pathologic epithelial elevations of the aerodigestive and genitourinary tracts. This term describes any of the types of abnormal growths identified on or involving the colonic mucosa that protrude into the bowel lumen.
- Polyps are of concern to clinicians due to their malignant potential depending on the histologic type of the polyp identified.
- The primary histology of colonic polyps includes the following: adenomas, serrated polyps [including hyperplastic polyps and sessile serrated adenomas (SSAs)], hamartomas, and inflammatory polyps.
- As some are neoplastic, they are the target of screening modalities (including colonoscopy, computed tomography (CT) colonography) to remove them prior to their malignant degeneration. Other polyp-like lesions, usually submucosal rather than mucosal in nature, such as carcinoids, leiomyomas, and lipomas, will be described and discussed in Chap. 49.

Adenomas

Definition and Pathology

- Adenomas are the most common neoplastic colonic polyps (50–67 % of all polyps) and are thought to be the precursor lesion to the majority of colorectal cancers (and therefore the target of screening programs).
- They are by definition a low-grade dysplastic lesion with the potential for progression of the dysplasia to an invasive malignancy.

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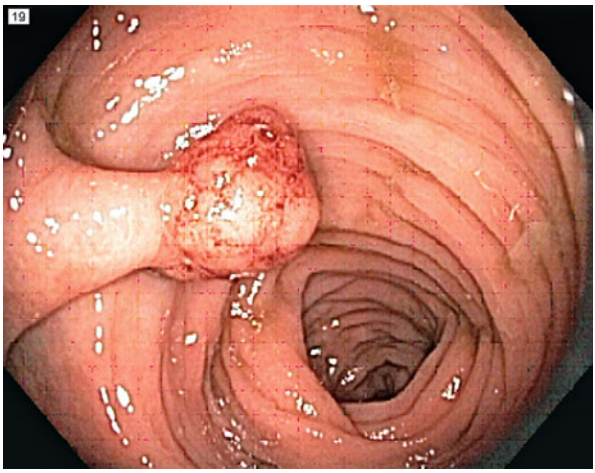

Fig. 36.1 Endoscopic appearance of a pedunculated adenoma

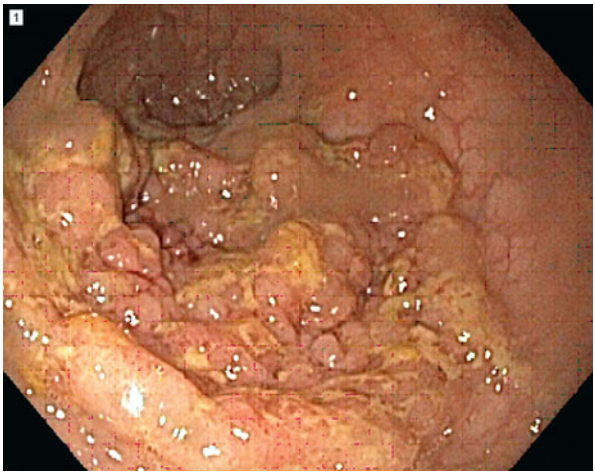

Fig. 36.2 Endoscopic appearance of a sessile adenoma (Courtesy of Roberta L. Muldoon)

- Grossly, these lesions can be pedunculated (mushroomlike on a stalk of submucosa lined by normal mucosa, Fig. 36.1) or sessile with a broader base (Fig. 36.2), can occur singly or as multiple lesions, and can vary greatly in size and extent.
- Adenomas are classified as tubular, villous, or tubulovillous. The former lesions comprise approximately 75–87 % of all adenomas identified in the colon and contain uniform-sized tubules and glands. As the tubules become more elongated with less stroma between glands, they assume a more villous character. For pathologists, tubular adenomas (Fig. 36.3) can consist of up to 20–25 % villous features and still be considered a "tubular

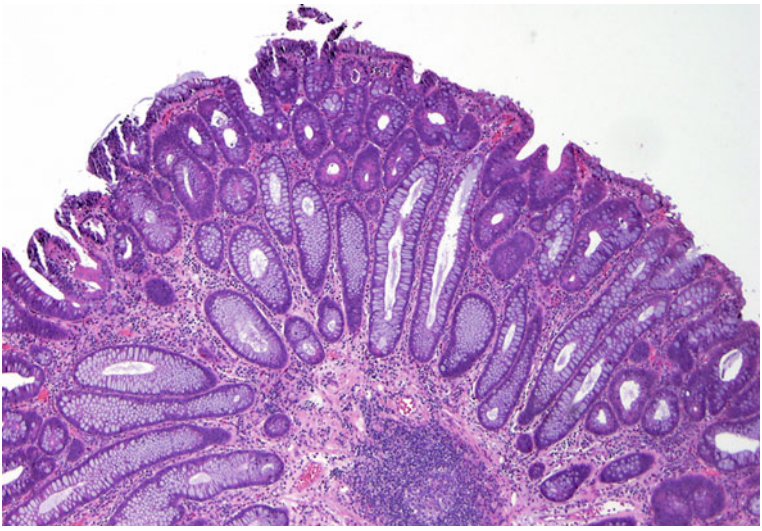

Fig. 36.3 Microscopic view of a tubular adenoma (Courtesy of William Chopp, MD)

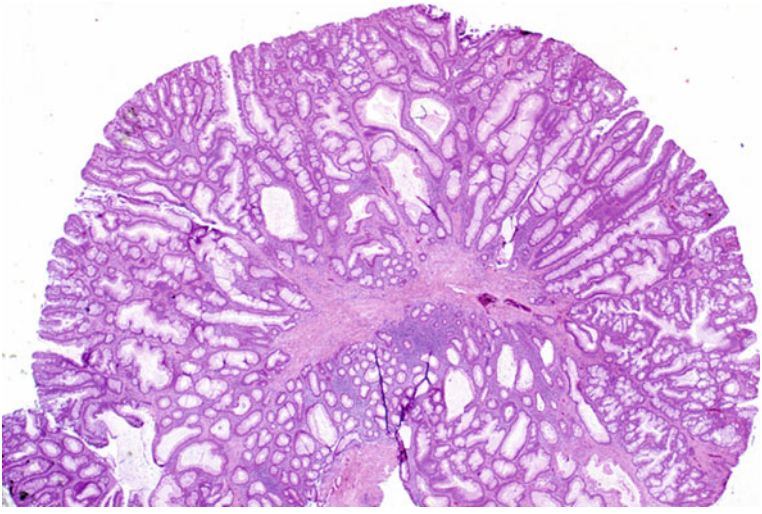

Fig. 36.4 Microscopic view of a tubulovillous adenoma (Courtesy of M. Kay Washington, MD, PhD)

adenoma," while villous adenomas (5–10 % of all adenomas) contain more than 50–75 % villous features, making tubulovillous adenomas (8–15 % of all adenomas, Fig. 36.4) those polyps in between. While the likelihood of a polyp to harbor malignancy may be impacted by this classification, the treatment for the three classes of adenomas remains the same and thus has little true clinical significance.

- Adenomas are differentiated from hyperplastic polyps in that they display cellular atypia with lack of differentiation into specialized cell types. The epithelial lining will show increasing mitoses and some degree of hyperchromasia (darker hematoxylin and eosin staining) depending on the degree of dysplasia. In adenomas, the normal process of cellular maturation and differentiation from the base of the crypt to the surface does not occur.
- Adenomas can be graded by the degree to which epithelial growth is disturbed. Mild or low-grade dysplasia is characterized by tubules, which are lined from top to bottom by epithelium, which is morphologically similar to the normal basal proliferative zone. The nuclei are enlarged, oval, and hyperchromatic and have normal orientation. There is a slight excess of mitotic figures, but the architecture is not disrupted.
- By definition, all adenomas show at least low-grade dysplasia. In moderate dysplasia, the nuclear features are more advanced, cellular polarity is less preserved, there is nuclear stratification, and the glands are more crowded. In severe or high-grade 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 both numerous 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. The terms "carcinoma in situ" and "intramucosal carcinoma" are often used to describe these high-grade dysplastic adenomas, but these terms are potentially misleading as these lesions do not have metastatic potential.

Presentation and Diagnosis

- Most adenomas are asymptomatic and are therefore found with screening studies or incidentally diagnosed through investigations of symptoms unrelated to the adenoma.
- Larger adenomas may display overt hematochezia or anemia secondary to occult or overt blood loss. Adenomas in the rectum may cause rectal bleeding, mucoid discharge, tenesmus, and/or fecal urgency. Very large adenomas may rarely cause electrolyte abnormalities or diarrhea or may lead to intussusception of the colon or prolapse through the anus.
- Adenomas are often multifocal and can be identified anywhere in the colon and rectum but tend to be more prevalent distally.
- In one large prospective study (US National Polyp Study), the distribution of adenomas was as follows: cecum 8 %, ascending colon 9 %, hepatic flexure 5 %, transverse colon 10 %, splenic flexure 4 %, descending colon 14 %, sigmoid 43 %, and rectum 8 %.
- Other studies have also documented that 24–31 % of adenomas are proximal to the splenic flexure in colonoscopies in higher-risk or symptomatic patients.

- In addition, when a sporadic adenoma is identified in the colon or rectum, the likelihood of a synchronous adenoma elsewhere in the colon ranges from 31 to 40 %. Therefore, when a distal adenoma is found, a complete colonic assessment is necessary because of this high rate of synchronous neoplasms.
- Most, but not all, studies of screening flexible sigmoidoscopy suggest that patients with no distal polyps, distal hyperplastic polyps, or a single small tubular adenoma have a low risk of proximal advanced adenomas (0–4 %). Multiple other studies, however, support the recommendation that villous adenomas (regardless of size) and any adenoma >1 cm are important markers for the presence of advanced adenomas and even carcinoma in the proximal colon.
- The fact that adenomas are often asymptomatic precursor neoplasms justifies the use of screening to identify and remove these lesions before they become clinically recognizable, thus halting the adenoma to carcinoma sequence (discussed below).
- Colonoscopy is the most accurate test for polyps, especially when compared to double-contrast barium enema (DCBE) as shown by the US National Polyp Study.
- DCBE alone has been repeatedly shown to be less sensitive than colonoscopy (even for polyps >10 mm with a miss rate of 52 %), offers no therapeutic benefit, and has not been shown to reduce cancer incidence or mortality.
- Colonoscopy, on the other hand, decreases the risk of colorectal cancer incidence by 76–90 % and has been indirectly shown to reduce cancer mortality.
- Flexible sigmoidoscopy has also been shown to lead to a decrease in distal colon cancer mortality as much as 80 % (45 % for all colorectal cancers) but does not show a reduction in deaths from more proximal cancers.
- More recently, CT colonography or "virtual colonoscopy" has been supported as a potential screening modality.
- Three meta-analyses (between 1,300 and 6,400 patients in each analysis) have shown sensitivities and specificities for detecting polyps ≥10 mm to be in the 85–95 % and 95–97 % ranges, respectively. Medium-sized polyps (6–9 mm) had lower sensitivities and specificities of 70–86 and 86–93 %, respectively.
- Newer screening modalities such as chromoendoscopy or dye-spray endoscopy, narrowband imaging, magnification endoscopy, and pill colonoscopy have not been established as effective means for surveillance or screening for all patients and are not equivalent in the hands of all providers.

Epidemiology

- Colonoscopy-determined prevalence rates in asymptomatic, average-risk individuals ≥50 years range from 24 to 50 %, with the prevalence

of advanced adenomas (≥1 cm in size, with villous features, and/or with high-grade dysplasia) varying from 3.4 to 9.5 % depending on age and gender.

- Prevalence rates have been shown to increase with age, even doubling between ages 50 and 60.
- Higher adenoma prevalence rates have been identified in men, with a relative risk of 1.5–2.0 compared to age-matched women.
- Interestingly, however, in one study of screening colonoscopies performed on 1,463 asymptomatic women ≥40 years old, 20.4 % were diagnosed with an adenoma and 4.9 % with an advanced adenoma. When these women were compared to a matched group of men (8.6 % of whom had advanced adenomas on screening colonoscopy), almost 65 % had their advanced adenomas in the proximal colon versus 34 % of the men, suggesting that gender differences may lead to changes in adenoma location as well as overall prevalence.
- In terms of family history risk, a multicenter screening colonoscopy study examining the risk of colorectal adenomas in a cohort of individuals with one affected first-degree relative with sporadic colorectal cancer 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 (see below).
- The prevalence of adenomas and advanced 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.
- Adenoma prevalence rates determined by colonoscopy are roughly double the rates determined by flexible sigmoidoscopy.
- The prevalence of a proximal synchronous adenoma in a patient with a distal adenoma (or even hyperplastic polyps in some studies) is such that proximal colonic assessment is warranted if a distal lesion is found on screening.
- The incidence of adenomas is the rate at which individuals develop colorectal adenomas over a specified time interval.
- The incidence of adenomas at intervals ranging from 6 months to 5 years in post-polypectomy surveillance colonoscopy studies varies from 20 to 50 %.
- Most incident polyps are small, and a higher incidence has been associated with multiple adenomas at the index colonoscopy, larger size of the index adenoma, older age, and a family history of a parent with colorectal cancer.
- The incidence rate of colorectal adenomas after a clearing colonoscopy is actually the sum of the true incidence rate of new adenoma formation plus the miss rate at the initial colonoscopy plus the recurrence rate of incompletely removed polyps.
- Judging 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 it is approximately 10 %, and for adenomas ≤5 mm it approaches 30 %.

- These high miss rates for small lesions suggest that many adenomas detected on surveillance colonoscopy are actually lesions that were missed during the index examination.
- Incident polyps are distributed more proximally, consistent with the observation that miss rates for adenomas are higher in the proximal colon.
- The incidence rate for advanced adenomas ranges from 6 to 9 % and is closely related to the findings at initial colonoscopy.
- Based on a pooled analysis of more than 9,000 patients in North America, of which 11.2 % had advanced neoplasia (adenoma or cancer) on subsequent colonoscopy, a greater number of adenomas at initial colonoscopy, histologic features (villous architecture) of the excised adenoma, larger adenoma size, proximal adenoma location (odds ratio [OR] 1.68; 95 % confidence interval [CI], 1.43–1.98), and male gender (OR 1.40; 95 % CI, 1.19–1.65) were all attributed to increased risk of development of advanced neoplasia.
- Three or more polyps at the initial colonoscopy have been shown to increase the risk of subsequent advanced adenomas, and in the US 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 US 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 years of follow-up.
- The 5-year incidence of advanced adenomas in individuals with a previously negative colonoscopy is also <1 %.
- Similarly, post-polypectomy surveillance studies have shown that cancer incidence is also low, and in the US National Polyp Study, colonoscopic surveillance was associated with a 76–90 % reduction in the cancer incidence compared to reference populations.
- The rare appearance of incident cancers at short intervals in patients who have had a clearing colonoscopy suggests that either the neoplasm was initially missed or incompletely treated (27–31 % of incident cancers may be due to “ineffective” polypectomy) or the cancer developed rapidly.
- Based on long-term follow-up from the Polyp Prevention Trial, these interval cancers are even more common in those patients with a previous history of advanced adenoma.
- Despite the initial colonoscopy miss rates, however, modeling shows that >90 % of the reduced incidence of colorectal cancer over the first 5–6 years after screening colonoscopy is the result of the initial polypectomy rather than removal of adenomas at subsequent surveillance.

Adenoma to Carcinoma Sequence

- The idea that an adenoma would progress into a carcinoma has been based primarily on observational epidemiologic studies, clinical studies, pathologic findings, and molecular genetic studies, and therefore the evidence, while extensive, is truly circumstantial.
- Given the high prevalence of sporadic adenomas in the general population but the relatively low lifetime risk of developing colorectal cancer in Western countries (6 % by age 85), it appears that only a few adenomas become adenocarcinomas.
- While not all adenomas develop into colorectal cancer, it appears that most sporadic colorectal cancers (80–85 %) develop from adenomas, although there is evidence for rare de novo colorectal cancer development as well as other less-rare carcinoma sequences.
- Adenoma size seems to be important in the likelihood for malignant degeneration, and the likelihood that a diminutive tubular adenoma will progress to become an adenocarcinoma is likely very low.
- 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 as follows: <5 mm, 3.4 %; 5–10 mm, 13.5 %; and >10 mm, 38.5 %. No invasive cancer was found in polyps ≤5 mm. Villous change, left-sided lesions, and age ≥60 years were also associated with advanced histologic features.
- One longitudinal study showed that over a 3–5-year period, only 4 % of 213 adenomas measuring 2–15 mm increased in size.
- 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 depending on size and histologic factors such as the conversion rate for polyps >1 cm (3 %), for villous adenomas (17 %), and for adenomas with high-grade dysplasia (37 %).
- Gender does not appear to affect the rate of transition from advanced adenoma to carcinoma, but age clearly impacts malignant degeneration (ranging from 2.6 % at age <60 to >5 % annually at age >80 years for both men and women).
- On a molecular level, the “traditional” pathway from adenoma to adenocarcinoma (also known as the “loss of heterozygosity” (LOH) or “chromosomal instability” (CIN) pathway), thought to account for the development of 80–85 % of sporadic colorectal cancers, was elucidated from studies on patients with familial adenomatous polyposis (FAP).

- The process starts with a single colorectal epithelial cell undergoing a series of genetic alterations leading to the inactivation of both copies of the tumor suppressor adenomatous polyposis coli (*APC*) gene on chromosome 5q that regulates cell growth and apoptosis. This appears to occur very early in the process of the normal epithelial cell transitioning into adenomatous tissue or low-grade dysplasia by leading to increased cell proliferation.
- The next alteration in the pathway is thought to occur with *k-ras*, an oncogene involved in signal transduction from the cell membrane to the nucleus. Mutation of this gene (seen in 50 % of colorectal cancers) in the setting of the *APC* mutation appears to lead to exophytic growth and transition to an "intermediate" adenoma.
- Important to the transition from intermediate to advanced adenoma is mutation of the deleted in colon cancer (*DCC*) gene that is important for encoding an adhesion molecule and facilitating apoptosis and therefore tumor suppression.
- The final step to the development of invasive adenocarcinoma (found in 75 % of colorectal adenocarcinomas) is a mutation in the p53 gene, which regulates the cell cycle after DNA injury to allow for DNA repair.
- The accumulation of some or all of these molecular abnormalities is therefore associated with the development of invasive colorectal cancer.
- The "serrated neoplasia" pathway (see below) is thought to account for the other 10–15 % of sporadic colorectal cancers. This pathway is characterized by cancers showing microsatellite instability (MSI), likely due to hypermethylation of the *hMLH1* mismatch repair gene promoter leading to its inactivation, likely occurring after *BRAF* (a serine–threonine kinase involved in the *k-ras* pathway) gene mutations. These cancers are morphologically and pathologically similar to the MSI cancers that are associated with the germline mismatch repair gene mutations seen in hereditary nonpolyposis colorectal cancer (HNPCC)/Lynch syndrome (see Chap. 37). While these cancers do appear to develop through an adenoma–carcinoma sequence, the adenomas are not considered the traditional adenomas seen in the *APC* adenoma–carcinoma sequence and are more likely the SSAs discussed below. See Chap. 38 for a more detailed review on the molecular basis of carcinogenesis.

Management

- All adenomas or apparent adenomas should be completely removed for confirmation of the diagnosis and to exclude a concurrent malignancy and the potential need for further intervention.
- The majority of adenomas are amenable to endoscopic removal by various means including "cold" (without electrocautery) or "hot" (with electrocautery) biopsy forceps or loops/snares.

- Complications of polypectomy, primarily bleeding and perforation, can be limited through the appropriate use of these standard techniques.
- Because of the concern for perforations related to the use of cautery, recommendations include limiting the use of hot forceps to small polyps (<5 mm) while tenting the mucosa and somewhat deflating the colon.
- The majority of these smaller polyps are usually amenable to single-bite or piecemeal excision with cold forceps that will eliminate the cautery risks.
- Large pedunculated polyps can often be removed with snare cautery techniques (although bleeding is uncommon after removal of these). The important aspect of removal of these types of polyps is to ensure that the blood supply through a thick stalk (>1 cm), which may contain substantial vasculature, is controlled prior to the polypectomy. Alternatively, metal clips or endoloops can be placed at the base, or the stalk can be injected with epinephrine to provide hemostasis. The base of the stalk may be tattooed with ink or carbon agents to allow for subsequent identification (endoscopically or surgically) if the polyp has a concerning appearance for malignancy. At times, piecemeal resection of the polyp head is necessary before a large snare can even get around the polyp to reach the stalk.
- Larger sessile polyps (>15–20 mm) will usually require piecemeal resection with a large snare cautery. Safe polypectomy while avoiding injury to surrounding normal tissues may also be facilitated by saline lift as described below. When performing a standard piecemeal polypectomy, starting on the proximal aspect of the polyp with or without using a spike-tip snare (allows the snare to be anchored so that pushing the sheath causes the snare loop to widen for more effective placement around the polyp) will allow for easier and more complete polyp resection. While the piecemeal technique is an effective means of removal, it requires meticulous removal of the entire polyp and capture of the pieces. This technique ensures that pathologic examination of the polyp will be complete, although the margins will be unclear when the specimen is resected in this fashion. Larger pieces might require basket retrieval and division of the larger pieces with the cold snare or may necessitate multiple insertions and withdrawals of the colonoscope to remove them.
- Careful coagulation of the base and edge of the polypectomy defect with the argon plasma coagulator or other electrocautery device has been shown to decrease the incidence of residual polyp.
- It is also advisable to utilize endoscopic tattooing techniques to identify the area again for subsequent examinations of the site as well as potential surgical resection if invasive cancer is identified.
- Any remaining polyp tissue should be treated with argon plasma coagulation or other coagulation techniques as noted above and has been shown to be effective in decreasing recurrence of the polyp.
- It has been repeatedly shown in retrospective studies that endoscopic resection of large polyps can be performed safely with low risk of

perforation (rare and often treatable nonoperatively, although 5 % can be fatal) or bleeding (2–24 %, treatable medically or endoscopically).

- If a polyp is too large for a safe polypectomy (piecemeal or otherwise) to be performed, a conventional oncologic surgical resection should be done.
- Submucosal injection of various agents has been utilized to elevate and more safely facilitate endoscopic resection of large sessile polyps in the colon and rectum by elevating the submucosa and thus increasing the distance between the mucosa and the muscularis propria. This operation not only decreases the risk of perforation but also increases the potential for complete excision.
- Agents that are useful include saline with or without methylene blue (to distinguish the layers) and with or without epinephrine.
- Other agents used to slow absorption of the fluid and prolong the elevation effect during the polypectomy include 0.5 % sodium hyaluronate and 0.83 % hydroxypropyl methylcellulose.
- Carbon/ink solutions can also be used to both tattoo the area for subsequent identification and elevate the polyp. The volume of the agent to use is not standardized, but injection of 1–4 mL at a time to create swelling of the submucosa and up to 20–30 mL or greater may be needed for larger polyps.
- Injection distal to a polyp (along the front edge on retrograde view) may obscure the view and make polypectomy more difficult. Therefore, starting with proximal injections (far edge of the polyp) may facilitate the lateral and distal injections and thus the ability to view the polyp and allow for its subsequent removal.
- Failure of the polyp to elevate at the time of submucosal injection despite appropriate swelling of the submucosa ("nonlifting sign") is concerning for invasion of the polyp into the submucosa or deeper and should therefore indicate need for surgical resection.
- The nonlifting sign may be falsely positive if a previous biopsy of the polyp has caused scarring in the area.
- If a complex polypectomy is to be performed, the patient must understand that repeat procedures may be necessary to completely remove the polyp. Of note, polyps that occupy greater than one-third the circumference of the colon, encompass two or more haustral folds, or involve a diverticulum or the base of the appendix are rarely amenable to endoscopic removal.
- At the time of surgical resection for an endoscopically challenging polyp, intraoperative colonoscopy is a technique useful for localizing nonpalpable or softer polyps, which have not been preoperatively tattooed. This technically can complicate a surgical resection, however, due to insufflation of the colon and potentially the small bowel.
- Use of carbon dioxide insufflation rather than room air can help in this regard based on its quick resorption and resulting colonic decompression.

- Hybrid minimally invasive and endoscopic procedures have been shown to be safe with long-term success in removing large colonic polyps. This technique utilizes intraoperative colonoscopic polypectomy in conjunction with laparoscopic confirmation of complete polypectomy while assessing for colonic perforation or uses endoscopic assistance with a laparoscopic wedge resection of the polyp. These procedures are also best performed in combination with the use of carbon dioxide as the endoscopic gas. While the endoscopist identifies the mass, the surgeon performs diagnostic laparoscopy to examine the affected area of the colon as well as the remainder of the abdomen for other pathology.
- Any invasive cancer or concerning features may warrant immediate laparoscopic colectomy, which would be discussed with preoperatively and consented to by the patient.

Surveillance

- Improvements in colorectal cancer incidence and mortality rates are attributed to prevention through adenoma removal with screening and surveillance endoscopy, as well as risk factor modifications and improved therapies.
- Patients with adenomas are at increased risk for metachronous adenomas and have been shown to have a decreased incidence of subsequent cancer with follow-up surveillance.
- Surveillance recommendations after colonoscopic polypectomy, therefore, are based on the estimated risk of metachronous neoplasia.
- After polypectomy of large (≥1 cm) or multiple adenomas (three or more) or advanced adenomas, cancer risk is increased three- to fivefold.
- The risk of subsequent cancer is not measurably increased in patients with only one or two small tubular adenomas.
- The US National Polyp Study determined that colonoscopy performed 3 years after initial polypectomy protects patients just as well as more frequent examinations.
- Currently, no other modalities other than colonoscopy are advocated for post-polypectomy surveillance (although CT colonography has had some support as a surveillance option for patients with <1 cm adenomas who refuse or are not candidates for colonoscopy). In fact, utilizing other surveillance modalities such as fecal occult blood testing (positive predictive value in surveillance of <30 %) has been ineffective at best and is currently discouraged for those patients having undergone screening colonoscopy.
- Current recommendations for colonoscopic surveillance based on the ASCRS Practice Parameters and the joint guidelines from the American Cancer Society, the US Multi-Society Task Force on Colorectal Cancer, and the American College of Radiology are as follows (see also

Table 36.1 Colonoscopy surveillance guidelines[a]

Screening colonoscopy finding	Recommended follow-up	Comments
No polyps	10-year colonoscopy or standard screening recommendations	Assumes no familial colorectal cancer history
Small distal hyperplastic polyps	10-year colonoscopy or standard screening recommendations	Assumes no hyperplastic polyposis or familial colorectal cancer history
≤2 small (<1 cm) tubular adenomas	5–10-year colonoscopy	Timing based on clinical factors (e.g., family history, patient preference, physician judgment)
3–10 adenomas or 1 adenoma >1 cm or any adenoma with villous features or high-grade dysplasia	3-year colonoscopy	All lesions completely removed. If follow-up scope shows only 1–2 small tubular adenomas, repeat colonoscopy in 5 years
>10 adenomas	<3 years colonoscopy	Consider polyp syndrome
Sessile adenoma(s) removed piecemeal	2–6 months colonoscopy to ensure complete excision	Once complete removal confirmed, subsequent follow-up is based on clinical factors as above

Adapted from Winawer SJ, Fletcher RH, Miller L, et al. Colorectal cancer screening: clinical guidelines and rationale. Gastroenterology. 1997;112:594–642

[a]Assumes a full colonoscopy to the cecum in a well-prepared colon by an experienced endoscopist with a withdrawal time of 6–10 min from the cecum

Table 36.1): Patients with one to two <1 cm tubular adenomas should have a repeat in 5–10 years, depending on personal and family history. Patients with advanced adenomas or cancer in a completely resected polyp or patients with 3–10 adenomas all completely removed should have a repeat colonoscopy in 3 years, assuming a complete colonoscopy in a well-prepared colon. If they have more than ten polyps, or an incomplete or poorly prepared colon, they should have a repeat in <3 years. After the follow-up colonoscopy for these conditions is clear, a repeat examination every 5 years is warranted if the repeat is normal and well prepared.

- Due to a high recurrence rate after endoscopic polypectomy, patients with large, sessile adenomas that are resected piecemeal should undergo repeat in 2–6 months to verify complete removal. Follow-up examinations reveal residual or recurrent polyp in approximately 14–55 % of patients.
- Most patients with hyperplastic polyps except those with hyperplastic polyposis are considered average risk depending on family and personal history otherwise and should continue routine screening.
- Patients with a strong family history of colorectal cancer concerning for a hereditary predisposition (e.g., HNPCC/Lynch syndrome, familial polyposis) warrant more frequent surveillance (see Chap. 37).

Adenoma Prevention

- Observational studies looking at the effect of diet initially suggested that excess dietary fat and limited dietary fiber lead to increased incidence of colorectal cancer, but prospective trials on fiber supplements (e.g., Nurses' Health Study) as well as dietary fat intake did not show any decrease in adenoma development.
- Certain foods, especially certain fruit and vegetable types, have been shown in case-controlled trials to decrease colorectal cancer risk between 13 and 40 %, but long-term follow-up in large prospective trials such as the Polyp Prevention Trial and the Women's Health Initiative has shown no difference in colon cancer incidence with dietary alterations.
- Increased body mass index, decreased physical activity levels, red meat intake, smoking, and alcohol intake have all been lifestyle issues that have been associated with increased colorectal cancer risk, but alterations in these factors have not been studied in relation to the possible improvement in adenoma or colorectal cancer development.
- Folate was thought to be an effective colorectal cancer preventative agent in observational trials, but prospective trials have shown weaker effects leading to low enthusiasm for its use as a chemoprevention agent.
- Chemoprevention methods that have been shown repetitively to lead to decreased adenoma development, however, include the intake of aspirin (relative risk between 0.65 and 0.96 for adenoma formation compared to that of controls), calcium (15 % decline in adenoma risk), selenium, and cyclooxygenase-2 (cox-2) inhibitors (e.g., celecoxib).
- Given the variable efficacy of these agents for preventing colon cancer, not all are recommended for institution as standard chemoprevention.
- Of course, the cox-2 inhibitors have been the subject of controversy due to their association with cardiovascular toxicity that was identified during adenoma prevention trials. These agents were shown conclusively to decrease the development of advanced adenomas in high-risk individuals between 28 and 66 % after 3 years of use, but the longevity of these affects was variable once the agents were discontinued due to the concerns about the cardiovascular side effects.

Special Adenomas

Rectal Adenomas

- Rectal adenomas when larger may not be amenable to endoscopic polypectomy, and therefore, transanal excision or transabdominal radical resection may be necessary to ensure complete extirpation of the polyp as well as accurate pathologic assessment. For lesions in the lower half of the rectum, transanal excision is generally performed and can be facilitated with submucosal injection of saline or epinephrine under the lesion and use of any of the multitude of hemostasis devices that are available.

- Other operative options include transsacral (Kraske or York–Mason) or transperineal approaches.
- For more proximal rectal lesions, transanal endoscopic microsurgery (TEM) or transanal minimally invasive (TAMIS) may be appropriate.
- Larger lesions that extend too proximally for transanal excision will usually be best managed by anterior resection. The technical aspects of TEM and the other noted procedures are discussed in more detail in Chap. 43.
- Resection of difficult sessile rectal polyps (lower and middle third of the rectum, primarily) is best performed after full evaluation/staging for underlying malignancy using endorectal ultrasound or other staging procedure (e.g., MRI with endorectal coil). Endorectal ultrasound may offer some guidance for therapy after endoscopic polypectomy of a malignant polyp.
- In general, however, endorectal ultrasound of these lesions is notoriously inaccurate after polypectomy due to the postprocedure inflammatory response of the local site and local lymph nodes, making accurate determination of the polyp stage difficult prior to neoadjuvant therapy or resection.

Malignant Polyps

- Malignant polyps are defined as pedunculated or sessile polyps with cancer cells penetrating the lamina propria and muscularis mucosa into the submucosa. These polyps (T1 lesions by definition) account for 2–12 % of polyps in colonoscopic polypectomy series.
- They may appear benign on gross endoscopic appearance and are therefore usually noted to harbor an invasive malignancy only once they are excised and examined histologically.
- These differ from polyps with high-grade dysplasia (also called carcinoma in situ) in that dysplastic polyps have their malignant component superficial to the lamina propria and muscularis mucosa and therefore have no chance of metastatic spread.
- The risk of a malignant polyp increases with patient age, degree of dysplasia noted in the polyp, and polyp size. One study noted the risk of cancer in an adenoma to be 1.3 % in polyps <1 cm, 9.5 % in polyps between 1 and 2 cm, and 46 % in polyps ≥2 cm. The risk of malignancy in another series was 2 % for adenomas 0.6–1.5 cm, 19 % for polyps 1.6–2.5 cm, 43 % for polyps 2.6–3.5 cm, and 76 % for polyps >3.5 cm.
- The clinical decision to proceed with further treatment after polypectomy for a malignant polyp, such as surgical resection or local excision, depends on the patient's general condition and the depth of invasion of the cancer (which offers a surrogate for the estimated risk of lymph node metastasis).
- Haggitt's classification system of malignant polyps is based on the level of invasion into the stalk of a pedunculated polyp (or the submucosa underlying a sessile polyp) (Fig. 36.5):
  - Level 0 – noninvasive (high-grade dysplasia).
  - Level 1 – cancer invading through the muscularis mucosa but limited to the head of a pedunculated polyp.

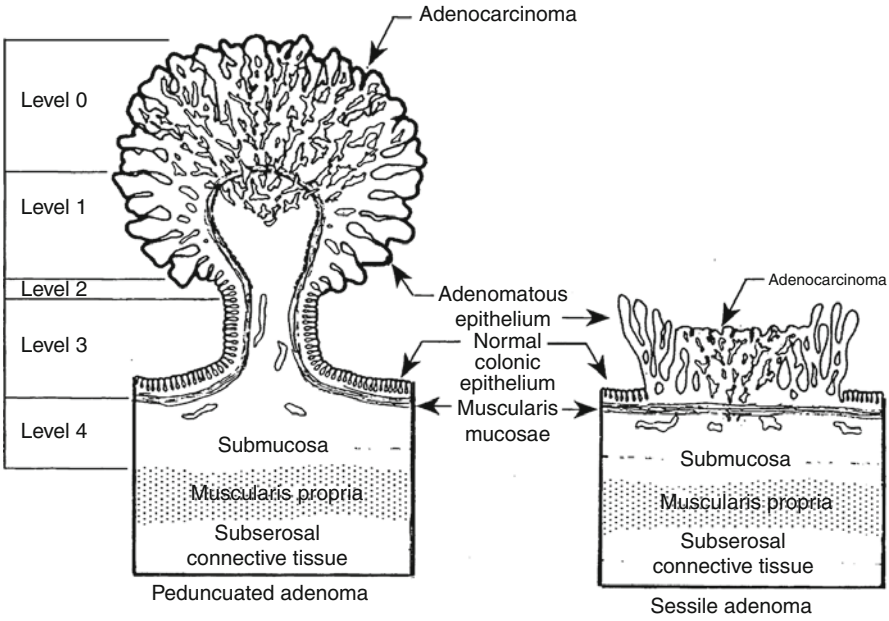

Fig. 36.5 Anatomic landmarks of pedunculated and sessile malignant polyps (Reprinted from Haggitt RC, Glotzbach RE, Soffer EE, et al. Prognostic factors in colorectal carcinomas arising in adenomas: implications for lesions removed by endoscopic polypectomy. Gastroenterology. 1985;89:328–36. With permission from the American Gastroenterological Society)

  - 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.
- A line drawn at the junction of normal and adenomatous epithelium is the transition between the stalk and the head of the polyp, also called the neck (level 2).
- The risk of lymph node metastasis is <1 % for pedunculated polyps with Haggitt level 1, 2, or 3 invasion.
- The risk of lymph node metastasis for Haggitt level 4 lesions, pedunculated or sessile, ranges from 12 to 25 %.
- Kudo further stratified the depth of submucosal invasion into three levels (Fig. 36.6):
  - SM_1 – invasion into the upper third of the submucosa.
  - SM_2 – invasion into the middle third of the submucosa.
  - SM_3 – invasion into the lower third of the submucosa.
- Haggitt levels 1, 2, and 3 are all considered equivalent to SM_1, while Haggitt level 4 may be SM_1, SM_2, or SM_3.

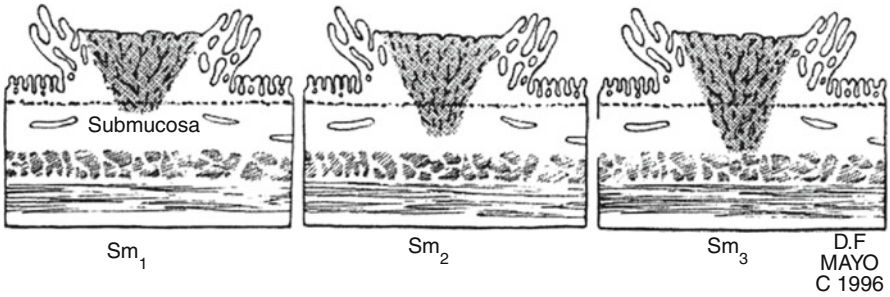

Fig. 36.6 Depth of submucosal invasion in sessile malignant polyps. *Sm_1* invasion into the upper third, *Sm_2* invasion into the middle third, *Sm_3* invasion into the lower third (Reprinted with permission from Nivatvongs S. Surgical management of early colorectal cancer. Surg Clin North Am. 2000;8:1052–5)

- SM_3 level of invasion seems to have the greatest impact on likelihood of nodal metastases relative to SM_1 or SM_2.
- Other factors reported to be associated with an increased risk of lymph node metastases include lymphovascular invasion (LVI), poor differentiation, gender, extensive budding, microacinar structure, and flat or depressed lesions.
- In a series of 353 T1 sessile colorectal cancers, the risk factors for lymph node metastasis that were statistically significant on multivariate analysis included SM_3 level of invasion, LVI, and location in the lower third of the rectum.
- In another study, only SM_3 invasion was an independent risk factor for lymph node metastases.
- A positive polypectomy margin, regarded as inadequate treatment for a malignant polyp, has not been shown to be associated with increased nodal metastasis in some but not all studies, but it is associated with increased local recurrence, distant metastases, and cancer-related death.
- A distance of 2 mm beyond the deepest level of invasion is needed to consider the margin of polyp resection clear, although there is debate as to how to define a positive margin.
- 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 following full-thickness local excision of T1 lesions of the distal rectum.
- Current NCCN guidelines for the treatment of rectal cancer recommend at least full-thickness transanal excision of T1 rectal cancers.
- In view of the very low risk of lymph node metastases with pedunculated polyps with invasion to Haggitt levels 1–3, these can be safely treated by margin-negative snare polypectomy.
- Level 4 pedunculated lesions are treated as sessile adenomas.

- Sessile lesions that are snared in one piece and have a margin of at least 2 mm are considered adequately treated.
- High-risk sessile lesions, such as those with SM_3, a resection margin of <2 mm, LVI, and/or poor differentiation, should undergo appropriate oncologic resection.
- For rectal lesions that are well to moderately differentiated, <3 cm in size, <30 % of the circumference of the bowel wall, mobile, and nonfixed, within 8 cm of the anal verge, without LVI or perineural invasion, and without evidence of nodal metastases on preoperative imaging, full-thickness transanal excision with or without consideration of the use of TEM or TAMIS is acceptable based on NCCN guidelines.
- Transanal excision of these lesions with adjuvant chemoradiation is an alternative approach but not considered the standard of care. See also section "Rectal adenomas".
- Close endoscopic follow-up is required after polypectomy for a malignant polyp due to the concern for local recurrence of these lesions. A reasonable schedule is to examine the polypectomy site in 2–3 months and then every 6–12 months for the first 2 years with a complete colonoscopy done in the third year and then at 3–5-year intervals depending on other findings and family history. For further discussion about the management of colorectal malignancies, see Chaps. 41 and 43.

Flat and Depressed Adenomas

- Some adenomas display a flat or depressed growth pattern and are therefore not considered "true" polyps since they are not elevated above the mucosal surface.
- They are defined in some classification systems as being elevated <2.5 mm off the surface of the colon ("flat" or "nonpolypoid") or depressed into the surface <2.5 mm ("depressed").
- These are concerning in that they have a greater tendency to grow laterally or, in the case of the depressed lesions especially, into the wall of the colon rather than into the lumen.
- This makes their identification and potential for harboring malignancy concerning (between 27 and 36 % of depressed cancers invade the submucosa versus <3 % of cancers in polypoid lesions).
- These lesions are recognized macroscopically by color and textural changes and by interruption of the capillary network pattern of the colonic wall.
- They are most readily identified by chromoendoscopy with indigo carmine or other dye-spray techniques.
- The pathogenesis of these lesions is thought to arise through different mechanisms than the traditional adenoma–carcinoma sequence, with a low level of *k-ras* and *APC* mutations in these lesions, a higher level of p53 mutations, and greater prevalence of MSI noted.
- In addition, these lesions appear to be more frequently associated with de novo adenocarcinomas, thus apparently bypassing the adenoma–carcinoma sequence entirely.

- The prevalence of flat and depressed adenomas in three Western population studies was approximately 20 %, and these lesions contained cancer more often than polypoid adenomas.
- One US series showed that <2 % of lesions were depressed, and reassessment of the original US National Polyp Study polyp classification showed that 31.4 % of the polyps in the original study would have been considered "flat."
- Large Japanese series have also shown up to 42 % of all the identified lesions to be of the nonpolypoid variety with <5 % being depressed.
- In a large UK study of 1,000 patients in which chromoendoscopy was used to search for small flat lesions, 36 % of the 321 detected adenomas were flat or depressed.
- The overall risk of a polypoid lesion containing early cancer was 8 % but was 14 % for the flat lesions.
- Flat or depressed lesions that were >1 cm were about twice as likely as polypoid lesions of a similar size to contain high-grade dysplasia or cancer.
- Twenty-nine percent of flat lesions >1 cm contained either high-grade dysplasia or cancer.
- Because of the risk of cancer, these lesions (except in rare cases with a normal overlying mucosal pattern in a <1 cm nonpolypoid lesions) should be removed, either by endoscopic polypectomy or by operative resection. It has been suggested that using special dyes and magnifying colonoscopy should be incorporated into general endoscopic practice to better identify these lesions.

Serrated Polyps

- Serrated polyps were all categorized as hyperplastic polyps, but further research and closer histologic assessment revealed subsets of serrated polyps distinct from the benign hyperplastic polyps.
- Serrated polyps include at least hyperplastic polyps and SSAs.
- Debate continues over the semantics and pathologic features of other subtypes of these polyps such as "sessile adenomas," "traditional sessile adenomas," and "sessile serrated polyps" (with interobserver variability as high as 40 % among "expert" pathologists).
- For the purpose of this review, the term "sessile serrated adenoma" will be used to describe those sessile polyps that are dysplastic and are clearly distinct from nondysplastic hyperplastic polyps.

Hyperplastic Polyps

- Hyperplastic polyps are considered metaplastic, nonneoplastic epithelial elevations with well-formed glands and crypts with frequent goblet cells (unlike adenomas with few goblet cells), although mucin-poor and microvesicular variants exist.
- Because of the goblet cells, hyperplastic polyps are frequently coated with a layer of mucous (again, unlike adenomas), and they don't show the

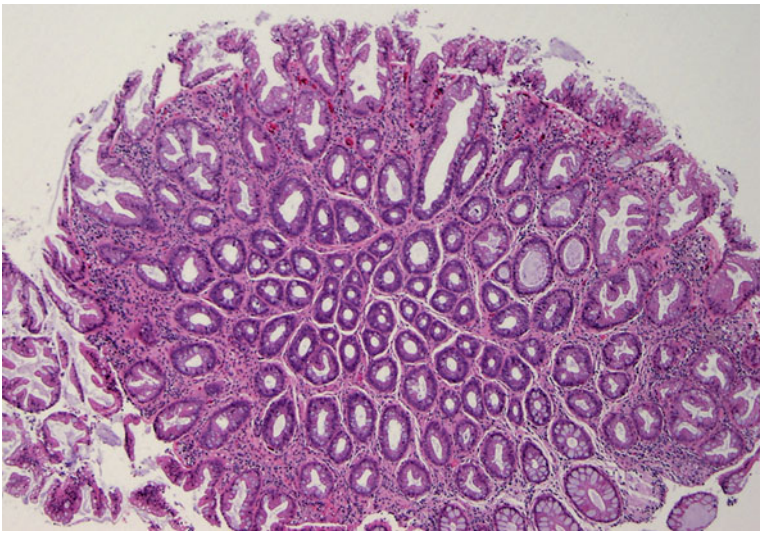

Fig. 36.7 Microscopic view of a hyperplastic polyp (Courtesy of William Chopp, MD)

papillary infoldings or more prominent vasculature of adenomas, so this can facilitate their gross identification endoscopically.

- These polyps develop when epithelial cells from the base of the crypts differentiate and mature normally, but the cells accumulate on the mucosal surface leading to crowding of the epithelium and infoldings of the mucosa giving them a saw-toothed appearance histologically without dysplasia (Fig. 36.7). This crowding is thought to be due to delayed shedding of the epithelial cells on the surface of the polyp and a failure of programmed cell death.
- Endoscopic diagnosis based on visual appearance alone with standard colonoscopy has a sensitivity of 80 % and specificity of 71 %.
- Chromoendoscopy can improve the ability to distinguish hyperplastic from adenomatous polyps. Hyperplastic polyps have a characteristic star-like pit pattern when stained with indigo carmine and assessed with magnifying colonoscopy. The sensitivity and specificity of this technique in discriminating between adenomatous and nonadenomatous polyps was found to be 93 and 95 %, respectively.
- Hyperplastic polyps have a prevalence of 10–15 % in adults in Western populations and represent 25 % of all endoscopically excised polyps. They are usually small (<5 mm), sessile, and often are present in multiples. They are found primarily in the distal colon and rectum, although larger or more proximal lesions are described.
- In a study of 1964 diminutive (≤5 mm) polyps on sigmoidoscopy, 41 % were adenomas, 37 % hyperplastic polyps, and 18 % nonneoplastic.
- Hyperplastic polyps are found more commonly in patients who smoke, consume alcohol, and have low dietary folate intake.

- The US National Polyp Study found no association between left-sided hyperplastic polyps and synchronous adenomas.
- 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.
- Multiple professional societies state that hyperplastic polyps found on flexible sigmoidoscopy are not an indication for colonoscopy and that small, distal hyperplastic polyps on colonoscopy do not warrant more frequent surveillance.
- The risk of cancer developing in small, distal hyperplastic polyps is small, but lesions >1 cm and those identified in the proximal colon should be excised.
- The rare hereditary syndrome of hyperplastic polyposis facilitated the identification of the serrated neoplasia pathway once it was appreciated that this syndrome was not without cancer risk.
- This syndrome is characterized by either ≥30 hyperplastic polyps regardless of size or location or by five large (at least one or two being >1 cm) proximal hyperplastic polyps or by any number of hyperplastic polyps with a positive family history of hyperplastic polyposis.
- The more diffuse variety is thought to have a low malignant potential and be associated with *k-ras* mutations, while the type with larger more proximal lesions (more likely SSAs than true hyperplastic polyps) is thought to have greater malignant potential through the *BRAF*/MSI-related serrated neoplasia pathway.
- Reports of patients with hyperplastic polyposis syndrome showed an average age of 52 years, >100 polyps in half the cases, and an average polyp diameter of 16 mm (range 5–45 mm), and more than half of the patients had a cancer present (half of these in the right colon).
- Management of this syndrome includes endoscopic removal of all polyps >5 mm and consideration of total abdominal colectomy and ileorectal anastomosis (lifelong distal endoscopy still required) for those patients who wish to avoid repeat colonoscopy or if their lesions are not endoscopically treatable due to polyp size, number, or presence of malignancy. Genetic counseling and familial assessment is recommended despite the lack of a clear gene for testing. Surveillance colonoscopy is recommended every 1–2 years with consideration for the use of chromoendoscopy to facilitate identification of the polyps.

Sessile Serrated Adenomas (SSAs)

- SSAs are uncommon polyps accounting for approximately 0.2–9 % (usually <2 %) of colorectal polyps, depending on the definition used.
- The SSA has exaggerated serrated crypts that are longer and broader than in hyperplastic polyps but still has a similar serrated or saw-toothed epithelial appearance.

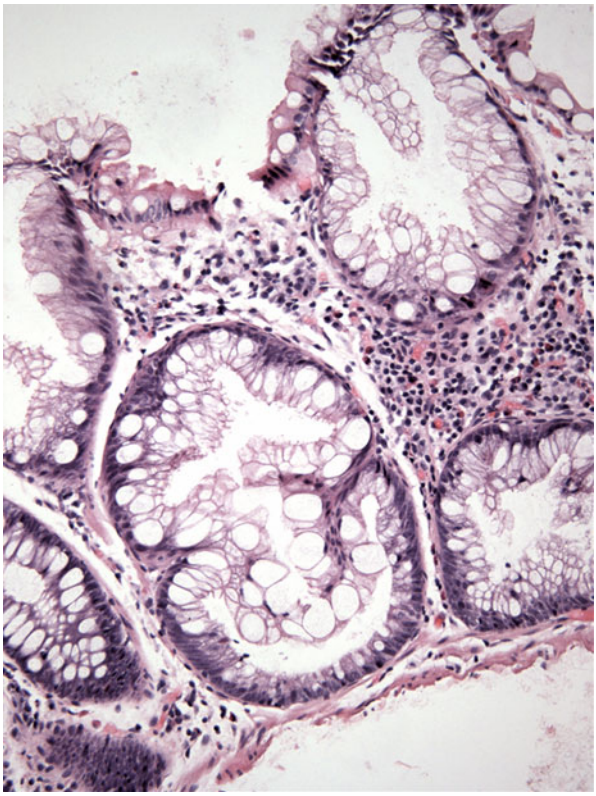

Fig. 36.8 Microscopic view of a sessile serrated adenoma (Courtesy of M. Kay Washington, MD, PhD)

- The SSA crypts contain cells with slight cytologic atypia like enlarged hyperchromatic and stratified nuclei (as in adenomas) as well as cells with normally arranged, small, basal nuclei (as in hyperplastic polyps).
- They are also characterized by dilated crypts and crypt branching as well as hypermucinous epithelium (Fig. 36.8).
- Endoscopically, many SSAs grossly appear like hyperplastic polyps with pale, slightly protruding lesions, and most are in the range of 0.2–7.5 mm in diameter (Fig. 36.9).
- Some SSAs are larger, however, and may resemble villous adenomas grossly.
- Unlike hyperplastic polyps, SSAs are more often found in the proximal colon and cecum. It is unclear whether SSAs develop in association with hyperplastic polyps or develop de novo, but it appears that the former is more likely based on molecular and pathologic studies.
- In one report, 5.8 % of colorectal cancers were associated with an adjacent SSA, and up to 37 % of SSAs harbored dysplasia.
- One review concluded that the risk of high-grade dysplasia was the same in SSAs as in the more common adenomatous phenotypes.

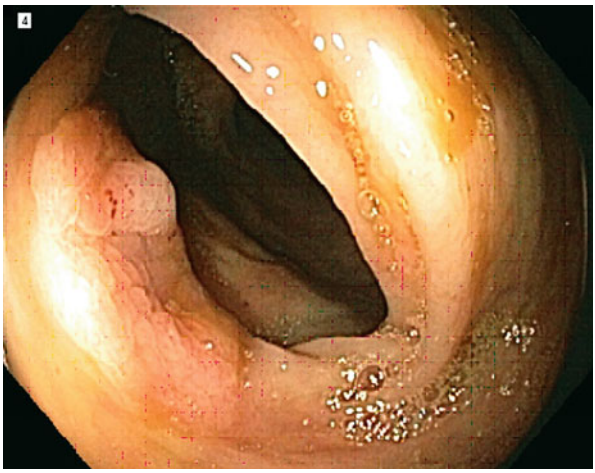

Fig. 36.9 Endoscopic appearance of a sessile serrated adenoma

- In addition, the association of cancer with hyperplastic polyposis syndrome (when the syndrome is characterized by the SSA-predominant type of polyps) seems to make the link between SSAs and cancer development more conclusive.
- The relative rarity of SSAs being identified at the time of malignant transformation may be due to a rapid transition from dysplasia to malignancy in these lesions.
- This may be similar to the quick malignant transformation in HNPCC-associated cancers due to germline mismatch repair deficiency.
- The serrated neoplasia pathway is believed to be characterized by initial loss of *BRAF* with subsequent hypermethylation of promoter regions of a number of genes including the *hMLH1* mismatch repair gene leading to MSI phenotype cancers.
- When SSAs are found concomitantly with a cancer, their molecular characteristics are often similar, including loss of the *hMLH1* protein, further supporting the serrated neoplasia theory.
- Individuals with sporadic colorectal cancer with high-level MSI (MSI-H) cancers are four times more likely to harbor at least one serrated polyp than individuals with low MSI cancers.
- Sporadic adenocarcinomas arising through the serrated neoplasia pathway occur in older patients (>70 years), have a female gender bias, and are predominantly located in the right colon, similar to SSAs.

Hamartomas

- The term hamartoma was originally coined by Albrecht in 1904 to refer to abnormally arranged but nondysplastic architecture of any of the layers of the normal lining of the colon (or other tissues).
- These polyps are usually considered nonneoplastic except when associated with rare hereditary disorders that have been linked to an increased

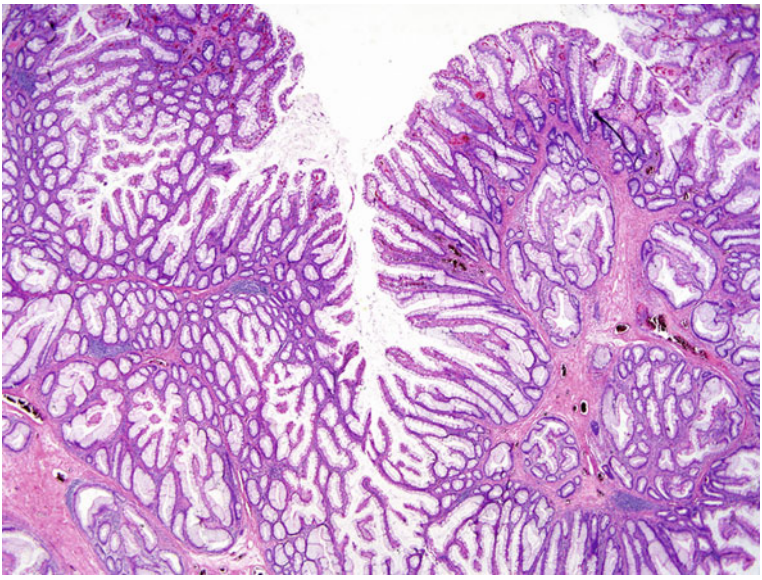

Fig. 36.10 Microscopic view of a hamartomatous Peutz–Jeghers polyp (Courtesy of Tonia Zuluaga Toro, MD)

risk of colorectal cancer and include the following: familial juvenile polyposis syndrome (JPS), Peutz–Jeghers syndrome (PJS), PTEN hamartoma tumor syndrome (PHTS), multiple endocrine neoplasia syndrome 2B, hereditary mixed polyposis syndrome, Cronkhite–Canada syndrome, basal cell nevus syndrome, and neurofibromatosis 1 (some of which are discussed in Chap. 37).

- These conditions represent the etiology of <1 % of all gastrointestinal malignancies.
- There are two primary hamartoma types described in the colon: juvenile (or retention) polyps and Peutz–Jeghers-type polyps. The former term was introduced in the late 1950s by Horrilleno after a review of pediatric colorectal polyps, but they are named based on their histology and not the age of presentation as they can occur at any age. Juvenile polyps are characterized by three classic histologic features including dilated mucous-filled glands/retention cysts lined by columnar epithelium, an expanded and abundant lamina propria, and infiltration of inflammatory cells, often eosinophils. The muscularis is not usually part of the structure of these polyps. They are usually round with a smooth, often shiny appearance and are frequently pedunculated. Juvenile polyps can reach several centimeters in diameter.
- These are differentiated from the Peutz–Jeghers-type polyps which are grossly more red and lobulated with their histology characterized by arborizing smooth muscle proliferation from the muscularis mucosa that is then lined by normal colonic epithelium with extensive goblet cells (Fig. 36.10).

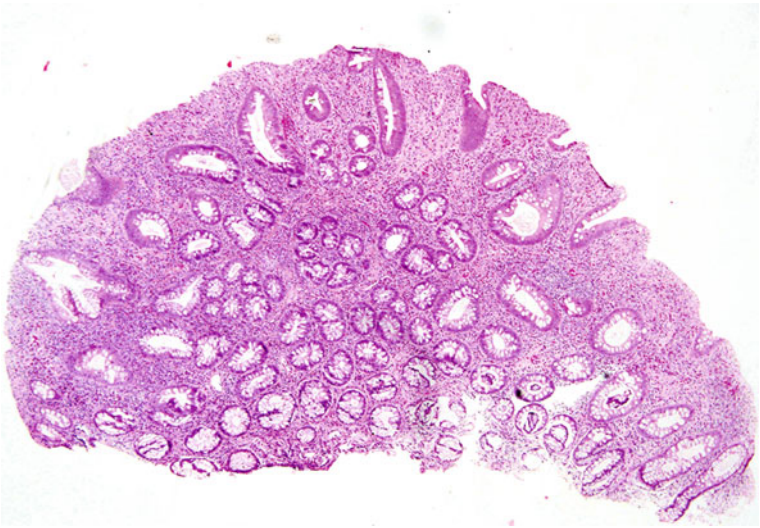

Fig. 36.11 Microscopic view of an inflammatory polyp (Courtesy of Tania Zuluaga Toro, MD)

- Neither of these polyp types is characterized by abnormal mucosal lining or increase in mitoses to suggest premalignancy.
- The majority of isolated colorectal hamartomas present as juvenile polyps before the age of 10 with a peak presentation around the age of 5 years and are diagnosed with endoscopic assessment and biopsy/excision.
- Sporadic hamartomas represent <1 % of polyps identified in adults and are usually larger than 1 cm and pedunculated at the time of diagnosis.
- The majority of these isolated polyps in adults and children are found in the sigmoid colon and rectum and present with symptoms of rectal bleeding and/or polyp prolapse, but patients may present with anemia, diarrhea, and/or mucoid stools.
- Colonic intussusception is rarely associated with more proximal polyps. These polyps can autoamputate when they become larger due to their long stalks, and they can therefore be passed in the stool.
- Treatment of hamartomas is usually endoscopic but may require resection if the polyp is too large to be removed endoscopically or if there is evidence of malignancy within the polyp.
- Malignant degeneration of solitary colorectal hamartomas appears to be a very rare phenomenon, so much so that some authors feel that this is purely "coincidental."

Inflammatory Polyps

- Inflammatory polyps are islands or elevations of normal or near-normal colonic mucosa and submucosa surrounded by denuded or abnormal colonic lining and therefore are not considered true "polyps" (Fig. 36.11).

- They are usually associated with a chronic inflammatory process of the colon, especially with inflammatory colitis (Crohn's and ulcerative colitis), but can also be due to regeneration of the colonic lining in inflammatory, infectious, or ischemic conditions.
- Symptoms from the polyps including bleeding and diarrhea can be difficult to differentiate from the symptoms of the underlying condition leading to the development of these polyps. Rarely, obstruction or intussusception can occur if the inflammatory polyps become very large ("giant inflammatory polyposis"). Treatment is focused on the underlying disease causing the chronic inflammation or ischemia. Inflammatory polyps are not neoplastic but can make screening for neoplasia in chronic inflammatory conditions of the colon difficult due to their concerning appearance with endoscopic surveillance and their potential to mask an underlying malignancy.

37. Hereditary Colorectal Cancer

James Church

Introduction

- Colorectal cancer is both a genetic and epigenetic disease.
- The classes of genes primarily involved are largely those concerned with regulation of cell growth, tumor suppressor genes and proto-oncogenes, and the average sporadic colorectal cancer has accumulated 90 different mutations.
- Most mutations occur because of the environment and about one third of colorectal cancers have a hereditary component.
- Hereditary colorectal cancer is important because members of affected families can be identified as high risk and be advised to have early, intensive surveillance or even prophylactic surgery.
- Hereditary colorectal cancer can be broadly divided into non-syndromic and syndromic conditions (Fig. 37.1).
- Non-syndromic hereditary colorectal cancer refers to familial clustering that does not fit criteria for the definition of a syndrome and no germ line mutation is found.
- Syndromic hereditary colorectal cancer is more important, however, because of the extremely high level of risk associated with it and because it is relatively easier to identify.

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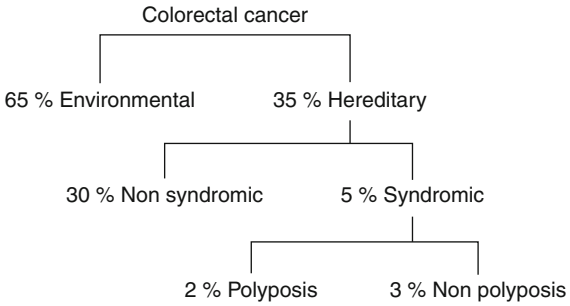

Fig. 37.1 Colorectal cancer viewed broadly

Syndromic Hereditary Colorectal Cancer

- A syndrome is a condition characterized by a constellation of symptoms, signs, and associations that go together so that the presence of one feature may alert the clinician to the presence of others.
- Hereditary colorectal cancer syndromes can be broadly separated into those that are associated with multiple polyps (the hereditary polyposis syndromes) and those that are not (hereditary nonpolyposis colorectal cancer (HNPCC)). These syndromes and their definitions are listed in Table 37.1.
- All of them confer an enhanced risk of colorectal and extracolonic cancers on affected patients and demand a sophisticated knowledge of genetics and medical and surgical treatment from caregivers.

The Polyposis Syndromes

The Adenomatous Polyposes

Familial Adenomatous Polyposis

- Familial adenomatous polyposis (FAP) is an autosomal, dominantly inherited condition due to a germ line mutation of *APC*, which occurs with a frequency of about 1:10,000 live births.
- About 22 % of germ line *APC* mutations occur "de novo," meaning that there is no family history of the syndrome.
- Inactivating mutations of this tumor suppressor gene result in a generalized disorder of growth regulation with a range of clinical manifestations, principally the formation of multiple gastrointestinal adenomas and carcinomas.
- FAP is thought to account for between 0.05 and 1 % of all colorectal cancers.
- Patients with a diagnosis of FAP and their family should be referred to a polyposis registry.

Table 37.1 Hereditary colorectal cancer syndromes

Polyposis syndromes	Phenotypic definition	Genotype
Familial adenomatous polyposis	Attenuated: <100 synchronous adenomas Mild: <1,000 synchronous adenomas Severe/profuse: >1,000 synchronous adenomas	Dominant inheritance of germ line mutation in *APC*
MYH-associated polyposis	Attenuated/mild polyposis	Recessive inheritance: biallelic mutations of *hMUTYH*
Hyperplastic polyposis	>20 hyperplastic polyps of any size or location >50 hyperplastic polyps proximal to sigmoid, 2 >10 mm Any number of hyperplastic polyps with a family history of hyperplastic polyposis	Unknown
Hamartomatous polyposes	Two of the following criteria:	
1. Peutz–Jeghers syndrome	Mucocutaneous pigmentation Gastrointestinal Peutz–Jeghers polyps Family history of Peutz–Jeghers polyposis	Dominant inheritance of germ line mutation in *STK11*
2. Juvenile polyposis coli	>4 juvenile polyps in the colorectum Any number of juvenile polyps and a family history of juvenile polyposis	Dominant inheritance of germ line mutation in *SMAD4* or *BMPR1*
3. PTEN tumor hamartoma syndromes		Dominant inheritance of a germ line mutation in *PTEN*
(a) Cowden's syndrome	International Cowden Consortium Criteria	
(b) Bannayan–Riley–Ruvalcaba syndrome		
(c) Proteus syndrome		
Nonpolyposis colorectal cancer		
Lynch syndrome	Dominant family history, microsatellite-unstable (high) colorectal cancer, young age of onset	Dominantly inherited germ line mutation of DNA mismatch repair gene: *hMLH1*, *hMSH2*, *hPMS2*, *hMSH6*
Familial Colorectal Cancer Type X	Dominant family history, microsatellite-stable tumor	Unknown

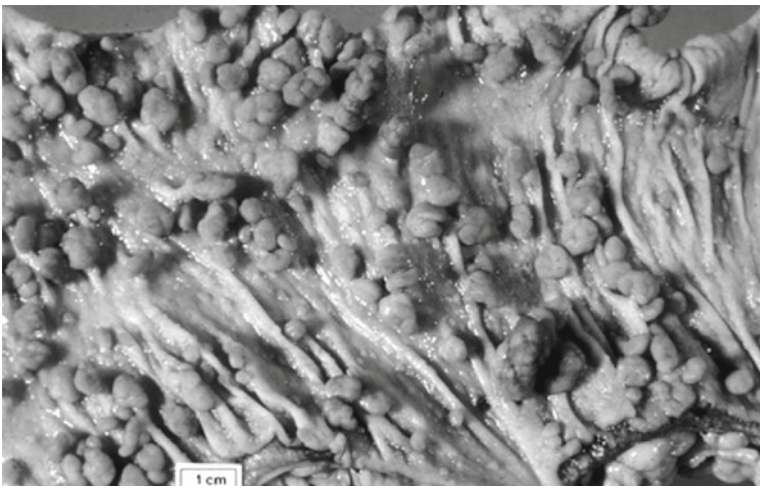

Fig. 37.2 The large bowel in classical familial adenomatous polyposis

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 genetic testing and clinical surveillance.
- Those shown to be affected can be offered prophylactic surgery.
- Some registries also coordinate postoperative surveillance and provide a focal point for education, audit, and research.
- Observational studies suggest that the introduction of registries, together with the use of prophylactic surgery, has led to increased life expectancy and a dramatic reduction in the incidence of colorectal cancer in FAP.

Features of FAP

- The Large Bowel. The cardinal manifestation of FAP is the development of over 100 colorectal adenomatous polyps, one or more of which inevitably progress to carcinoma if not removed (Fig. 37.2).
- Polyps usually appear in adolescence, with colorectal cancer diagnosed at an average age of about 40 years.
- The severity of the colorectal polyposis is an important determinant of treatment and is used to define the pattern of FAP.
- Patients with less than 100 adenomas are classified as having attenuated FAP, and this phenotype overlaps significantly that of *MYH*-associated polyposis (MAP).
- Patients with 100–1,000 adenomas have classical FAP, while those with >1,000 adenomas have profuse FAP.

- Polyposis severity is partly a reflection of the location of the *APC* mutation and partly due to unidentified modifying factors. The "hotspot" mutation at *APC* codon 1309 is reliably associated with profuse polyposis.

Genetics

- The *APC* Gene. *APC* is a large gene on chromosome 5q21 (q = the long arm).
- It is a key (gatekeeper) gene in colorectal carcinogenesis and is mutated in a majority of sporadic colorectal cancers.
- Over 820 different germ line *APC* mutations causing FAP have been identified, almost all resulting in truncation of the APC protein. Mutations have been found between codons 168 (exon 4) and 2839 (exon 15), but most are between codons 168 and 1640 (exon 15) in the 5′ half of the coding region, with a particular concentration at two "hotspots," codons 1061 and 1309.
- The *APC* Protein. *APC* is expressed in all organs, but the mRNA is found at particularly high levels in normal colonic mucosa.
- In many epithelia, APC 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. It plays a central role in the highly conserved Wnt signaling pathway, which is involved in the normal development of three-dimensional structures and is abnormally activated in some malignancies.
- *APC* binds and downregulates cytoplasmic β-catenin, preventing its translocation to the nucleus. Abnormal *APC* 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 cell proliferation.

Genotype–Phenotype Correlation in FAP

- There is evidence of correlation between the position of the germ line *APC* mutation (genotype) and some aspects of phenotype (Fig. 37.3).
- Mutation at codon 1309 is associated with profuse polyposis and between codons 1250 and 1464 with earlier onset of, and death from, colorectal cancer.
- Mutations located 5′ of codon 160 and 3′ of codon 1597 are associated with mild or attenuated colonic polyposis, accounting for about 10 % of those affected.
- Some extracolonic manifestations have also been associated with mutations at certain sites, although not upper gastrointestinal polyposis.
- Congenital hypertrophy of the retinal pigmented epithelium (CHRPE) occurs only with mutations between codons 450 (exon 9) and 1444.

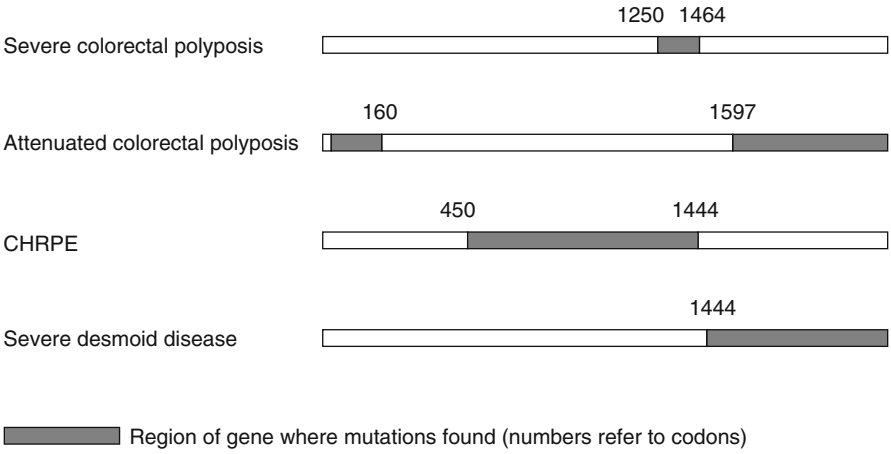

Fig. 37.3 Schematic representation of the APC gene showing genotype–phenotype correlations

Table 37.2 Extracolonic features of familial adenomatous polyposis

System	Feature	Frequency (%)
Upper gastrointestinal tract	Upper gastrointestinal adenom	95
	Upper gastrointestinal carcinoma	5
	Fundic gland polyps	40
Connective tissue	Osteomas (especially jaw)	80
	Desmoid tumor	15
Dental	Unerupted 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	Congenital hypertrophy of the retinal pigmented epithelium (CHRPE)	75
	Tumors (especially medulloblastoma)	<1

- The association of desmoid disease with germ line *APC* mutations 3′ of codon 1444 can be clinically important, although identical *APC* mutations may be associated with diverse phenotypes, suggesting that other genetic modifiers are involved.

Clinical Variations of FAP

Extracolonic Manifestations

- The extracolonic manifestations of FAP are shown in Table 37.2.
- Two of these, duodenal cancer and desmoid disease, are major sources of morbidity and mortality (Fig. 37.3).

- Other features may be a useful clue in diagnosis. CHRPE are hyper- or hypopigmented spots seen on retinal examination. They have no effect on vision but act as markers of FAP in the 66 % of families that have a total of at least four CHRPEs in both eyes.

Attenuated Familial Adenomatous Polyposis

- A group of patients have been described who develop fewer than 100 colorectal adenomas (oligopolyposis) at a greater age (34–44 years) than in "classical" FAP, but who are at high risk of colorectal cancer, may exhibit extracolonic manifestations, and carry a germ line *APC* mutation.
- The colorectal cancers have a later age of onset than with classical or profuse FAP (mean age 56 years).
- 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.
- The genotype of this group of patients may be one of the three: germ line *APC* mutation, biallelic *MYH* mutations, and germ line DNA mismatch repair (MMR) gene mutations.
- *APC* mutations associated with attenuated familial adenomatous polyposis (AFAP) are either at in exons 3 and 4; at the 5′ end of the gene; or at the 3′ end of exon 15.
- Fundic gland polyps (FGPs) and duodenal adenomas are frequent, but CHRPEs are not found in there patients.
- Desmoid disease is rare in those with a 5′ mutation, but families with 3′ mutations (beyond about codon 1444) have a high risk of desmoid disease together with attenuated polyposis.
- The missense *APC* mutation I1307K has been identified in Ashkenazi Jews with multiple adenomas, and E1317Q has also been found in association with AFAP.
- When *APC* is normal, up to 30 % of patients with oligopolyposis have biallelic *MYH* mutations.
- It is can be difficult to recognize AFAP clinically, leading to the clinical situation of an obstructing transverse colon cancer where right-sided polyposis is only found when the specimen is opened.
- Because the polyps in AFAP are predominantly right sided, screening and work-up must include a full colonoscopy.
- Genetic testing for germ line *APC* and *MYH* mutations has a relatively low yield, partially because of technical difficulties in detection of abnormalities that may be present and partly because gene expression may be lost for reasons other than a mutation.
- 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 (MSI)

and MMR immunohistochemistry (IHC) (to exclude Lynch syndrome) may be helpful.

- Genetic testing for a germ line *APC*/*MYH* mutation should be pursued in patients with a total of ten or more colorectal adenomas, especially if there is a positive family history for colorectal adenomas or cancers.
- A positive result has implication for family screening, but the patient is managed in the same way regardless of the result.
- If the polyps are controllable endoscopically, then yearly colonoscopy is reasonable. If the adenoma burden is uncontrollable or dangerous, colectomy with ileorectal anastomosis (IRA) should be performed.

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 later used to describe colorectal adenomatous polyposis occurring with these extracolonic manifestations.
- Gardner's syndrome is genetically the same as FAP, and systematic examination has revealed that most patients with FAP have at least one extraintestinal feature.
- Though it is of historical interest, the term "Gardner's syndrome" is no longer considered genetic or clinically useful and should be regarded as obsolete.

Turcot's Syndrome

- This is the association between colorectal adenomatous polyposis and central nervous system tumors. Recent molecular genetic investigation has shown that about two thirds of families have mutations in *APC*, with cerebellar medulloblastoma as the predominant brain tumor. Most of the other third, including Turcot's original family, appear to be variants of hereditary nonpolyposis colorectal cancer (HNPCC) with glioblastoma as the predominant brain tumor and multiple (but fewer than 100) colorectal adenomas.

Presentation

- Patients with FAP present either with or without symptoms (on screening).
- There is a significant difference in cancer incidence between these two groups, with over 60 % of unscreened, symptomatic patients having colorectal cancer at presentation.

Screening

- Clinical FAP screening begins at puberty because the risk of colorectal cancer under the age of 12 years is very small.
- Genetic testing of at-risk family members in a family with a known mutation usually starts when endoscopic surveillance would start, at ages 12–14.

- When a relative is identified as a mutation carrier, full colonoscopy is performed. EGD screening usually begins at age 20 years. Thyroid screening with ultrasound should also start then.
- If genetic testing is uninformative or cannot be done in a family with classical FAP, endoscopic screening starts at age 12–14 with flexible sigmoidoscopy. Polyps are biopsied to prove they are adenomas.
- An alternative would be to do retinal examinations for CHRPE or look for other extracolonic examinations with a skull X-ray or panorex examination of the jaw.
- If a marker of FAP is found, full colonoscopy follows. The polyp burden is documented endoscopically and histologically and a decision made regarding the timing and type of surgery.

Symptoms

- About 22 % of FAP patients have no family history. Clinical symptoms are often related to colorectal cancers, and should be investigated immediately.

Diagnosis

Genetic Testing

- Genetic testing should be preceded by counseling, ideally by a genetic counselor. Counseling includes the provision of written information about the process and its consequences, after which informed consent is documented. The implications of genetic testing with respect to confidentiality, employment, insurance, and other financial issues vary from country to country but must be discussed prior to testing. In the USA, the Genetic Information Nondiscrimination Act (GINA) that became law in 2008 offers protection against genetic discrimination in Health and Life insurance. Posttest counseling deals with the implications of the genetic test results and may include psychological help to deal with emotional reactions, such as guilt (in an unaffected person), anxiety (in an affected person), and the effect of the results on family relationships.
- DNA from an individual with clinically obvious FAP is sequenced to identify a mutation in *APC*, a process which is successful in about 80 % of cases. Failure to detect an *APC* mutation does not exclude a diagnosis of FAP and may occur for a variety of reasons, including the presence of large deletions or missense mutations. Such results have been misinterpreted as ruling out the diagnosis of FAP, with potentially serious consequences.
- If a deleterious mutation is found in an affected family member, at-risk family members can be offered predictive testing with a high degree of accuracy. This is generally done between the ages of 12 and 15 years, when the individual is old enough to take part in genetic counseling.
- When an individual does not carry the family mutation, that person can be discharged from further surveillance and be reassured that they do not have FAP.

- A positive test result allows surveillance and prophylaxis to be targeted to those who need it, and knowledge of the site of mutation can aid decision making with regard to prophylactic surgery.
- If no mutation can be found in an affected patient, then the family must be managed without genetic testing.
- The negative result does not mean that the family does not have FAP; it means that the genetic cause of the FAP has not been found.

Management of the Large Bowel

- Aims of Treatment. While the prevention of cancer remains an important priority in the management of patients with hereditary colorectal cancer, maintaining the quality of life is also important. This is especially the case in young, asymptomatic patients who have been diagnosed by screening. Where options exist for the timing and type of surgery, those with the least impact on social, academic, and vocational activities should be chosen. After all, surgery will not cure FAP.
- Prophylactic Surgery. Patients with FAP, if untreated, are almost guaranteed to develop colorectal cancer.
- Prevention of cancer by endoscopic control of the polyposis is not usually possible, and so colectomy or proctocolectomy is necessary to prevent cancer.
- Timing. Patients with severe polyposis (over 1,000 colonic or over 20 rectal polyps), or those who are symptomatic, should have surgery as soon as possible.
- In asymptomatic patients with mild disease (100–1,000 adenomas, all <1 cm, none with severe dysplasia), surgery can usually be delayed until the patient reaches appropriate physical and intellectual maturity.
- An important reason for delay is the concern for the development of desmoid disease. Affected women with a family history of desmoid disease, extracolonic manifestations of Gardner's syndrome, and a 3′ *APC* mutation are at highest risk.
- As long as surgery is delayed, annual colonoscopy is recommended to monitor the polyps. Most patients with classical polyposis have surgery between the ages of 16 and 20, which is well before cancer usually develops.
- Choice of Operation. The colorectal surgical options for the management of FAP are proctocolectomy with end ileostomy (with or without Koch pouch), colectomy with IRA, and proctocolectomy with ileoanal pouch (IPAA). Few patients desire a permanent ileostomy, and so proctocolectomy with ileostomy is rarely done.
- IRA is more straightforward to perform than IPAA and requires only one procedure, with a shorter hospital stay and fewer complications. The risks of erectile and ejaculatory dysfunction caused by nerve damage during pelvic dissection are minimized, as is the significant reduction in

fecundity observed in women after IPAA. In addition, bowel frequency and soiling are less, and no temporary stoma is necessary.

- Polyp counts are a reliable way to identify a low-risk rectum, but patients still need yearly surveillance proctoscopy.
- Any polyps over 5 mm should be removed, and polyps with high-grade dysplasia are relative indications for completion proctectomy.
- Compared to an IRA, IPAA has the advantage of removing the entire colon and rectum. Although complication rates and functional results have improved with experience, they are still worse than those associated with IRA.
- There has been controversy over the need for mucosectomy to remove the anorectal transition zone, which theoretically prevents cuff neoplasia, but causes more complications and perhaps poorer function. Dysplasia in the transition zone occurs after both double-stapled and mucosectomy techniques and the latter is probably only indicated in individuals with severe low rectal polyposis. The indications and contraindications and advantages and disadvantages of each surgical option are summarized in Table 37.3.
- In summary, IRA is reasonable and safe in mildly affected patients, particularly if there are fewer than five rectal polyps.
- Most individuals presenting with severe polyposis or those known to carry a mutation in codon 1309 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 may be compromised.

Postoperative Surveillance

- After IRA the retained rectum should be examined using a flexible sigmoidoscope, with a basic interval of 12 months or shorter, depending on the severity of disease. Polyps over 5 mm should be removed cleanly with a snare. Repeated polyp fulguration can result in rectal scarring, making future surveillance difficult and unreliable. In patients with chronically scarred rectal mucosa, random biopsy is recommended to detect invisible dysplasia. If severe dysplasia or uncontrolled polyposis develops, completion proctectomy with or without ileoanal pouch formation is indicated.
- Surveillance of ileoanal pouches at several centers has shown adenomas in up to 53 % and even some cancers. Treatment of pouch adenomas depends on their number and size. Polyps over 5 mm should be removed by snare excision, while multiple small polyps respond to sulindac (150 mg by mouth twice daily).
- Anal transition zone (ATZ) adenomas occur commonly after both stapled and hand-sewn IPAA, although they are twice as common in the former as the latter.

Table 37.3 Surgical options for familial adenomatous polyposis

Surgical option	Indication	Advantages	Disadvantages
Colectomy and ileorectal anastomosis (leave 15 cm rectum)	<20 rectal adenomas <1000 colon adenomas	Low complication rate No stoma Close to normal bowel function	Risk of rectal cancer
Proctocolectomy and ileal pouch anal anastomosis (stapled)	>20 rectal adenomas >1000 colon adenomas	Minimizes risk of rectal cancer	Complex surgery
	Large rectal adenoma	Avoids permanent stoma	Often needs stoma
	Rectal adenoma with severe dysplasia	Bowel function better than with mucosectomy and hand-sewn anastomosis	Bowel function unpredictable but may be quite abnormal
	Sparing of low rectum		Risk of damage to pelvic nerves and decreased the ability of women to conceive Risk of pouch and anal transitional adenomas and cancer
Proctocolectomy and ileal pouch anal anastomosis (hand sewn)	As above but with adenomas to dentate line	Minimizes risk of rectal cancer Avoids permanent stoma	As above but bowel function is worse than with stapled anastomosis
Proctocolectomy with end ileostomy	Low rectal cancer Poor anal sphincters	Simple operation with lower complication rate and minimal chance of reoperation	Permanent stoma

- Several case reports of cancer in the ATZ underline the difficulty in following this critical area.
- Adenomas in the ATZ can be excised individually (under anesthesia), or the entire ATZ can be stripped. If stripping is chosen because of the extent of the polyposis, the procedure should be performed in two stages to avoid stenosis.

Adenoma Chemoprevention

- A range of chemopreventive agents have been studied in FAP, in part because of the problems of managing the retained rectum after IRA, but also because this disease provides a useful experimental model of colorectal carcinogenesis. In placebo-controlled trials, both the nonsteroidal anti-inflammatory drugs (NSAIDs) sulindac and the COX-2 inhibitor celecoxib have reduced the number and size of colorectal adenomas.

- Chemoprevention, however, is not an alternative to prophylactic surgery, as no benefit in terms of cancer reduction has been demonstrated, and there have been reports of rectal carcinoma occurring in patients on sulindac despite reduction in polyp number and size.

Upper Gastrointestinal Polyposis

- Fundic gland polyps (FGPs), made up of areas of cystic hyperplasia,[42] are found in the stomach of about 80–90 % of individuals with FAP. These are benign but a recent prospective survey showed that low-grade dysplasia was present in FGP in 41 % of patients.
- Three percent of patients had high-grade dysplasia in FGP. This is concerning as some patients have profuse FGP, impossible to survey.
- Current practice is to biopsy representative FGPs during regular surveillance, but not to try and treat all.
- Gastric adenomas can be found, usually in the antrum, in 10 % of patients in western series. It is likely that these give rise to the very rare gastric cancers in western patients.
- The incidence of gastric cancers in FAP patients in Japan is seven times that in the West, and for Korea, three times.
- An excess of gall bladder and bile duct adenomas and carcinoma has also been reported.
- Prospective studies have demonstrated that over 95 % of individuals with FAP have duodenal adenomas, which tend to occur about 15 years later than large bowel polyps.
- Duodenal cancers are the second most common cause of death in patients with FAP because although they are relatively rare (5 %), they are highly lethal. Average age at diagnosis is 50 years.
- The highest density of adenomas is on and around the ampulla of Vater, testimony to the tumorigenic effect of bile.
- Fifty percent of normal-appearing ampullae are dysplastic on biopsy.
- Adenomas can also be found throughout the small intestine, and early studies of capsule endoscopy show that incidence of jejunal and ileal adenomas is higher in patients with severe duodenal polyposis (Spigelman stages III and IV).
- Occasional cases of small bowel adenocarcinoma occur, but routine small bowel screening is not recommended.
- Surveillance of the Duodenum. Duodenal adenomas are flat, white mucosal patches, completely different in appearance to colorectal adenomas.
- The Spigelman staging system allows an objective assessment of the severity of duodenal polyposis in FAP (Table 37.4).
- 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. Several carcinomas were missed on endoscopy, and all of those who developed cancer died as a result, despite surgery.

Table 37.4 Scoring of polyp features in Spigelman staging for duodenal adenomas

Points allocated	Number 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 37.5 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	Consider duodenectomy. If not, rescope in 6 months

- Regular endoscopic surveillance of the stomach and duodenum is recommended so that individuals at high risk of developing carcinoma can be identified and offered intervention (although there is currently no evidence that this approach decreases the rate of invasive disease). Table 37.5 shows recommended surveillance intervals according to the severity of duodenal polyposis. Duodenal polyps are sampled for histology and even a normal-appearing ampulla is biopsied.
- Management. Management of severe duodenal polyposis is difficult, but once invasive carcinoma has developed, the outcome is poor.
- Duodenectomy and open polypectomy is associated with 100 % recurrence a year after surgery.
- Endoscopic mucosal resection seems a more attractive option but is made difficult by the frequently plaque-like morphology of the polyps and involvement of the ampulla.
- The use of chemoprevention to prevent progression of earlier-stage disease has attracted great interest. Sulindac can result in regression of small polyps but has little effect on larger ones.
- A randomized trial of the COX-2 inhibitor celecoxib showed significant improvement in the Spigelman stage for those with mild to moderate disease.
- Duodeotomy, whether by 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, preemptive duodenectomy should be seriously considered for Spigelman IV disease. Pancreas-preserving duodenectomy provides satisfactory control with reasonably low morbidity.
- When cancer is suspected, a Whipple's procedure is the better choice but carries a high rate of complications.

Desmoid Disease

- Desmoids are locally invasive, non-metastasizing clonal proliferations of myofibroblasts that are rare in the general population but can be found in 30 % of patients with FAP.
- Their etiology, pathogenesis, and natural history are not clearly understood.
- Desmoid disease is the third most common cause of death in FAP patients overall, after colorectal cancer and duodenal cancer.
- Overall desmoid-related 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.
- Desmoid disease is a spectrum from white, sheetlike plaques to large rapidly growing tumors.
- When found within the abdomen, desmoid disease can be seen to pucker and distort adjacent tissues, causing obstruction in tubular organs.
- Ten to fifteen percent of patients with FAP develop desmoid tumors, while another 15 % develop the plaques.
- The peak incidence is around 30 years of age, 2–3 years after surgery. While 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 (50 %), especially in the small bowel mesentery, and in the abdominal wall (45 %), although many extra-abdominal sites have been described.
- Mesenteric desmoids (Fig. 37.4) encase or compress mesenteric blood vessels. Rarely, this can result in ischemia and perforation of the bowel, but it always makes resection hazardous.
- Trauma (particularly in the form of surgery) and estrogens have both been identified as causes of desmoids, although they can occur spontaneously.
- There is evidence for some degree of genotype–phenotype correlation in that desmoids have been reported to occur more frequently in patients with 3′ germ line *APC* mutations. However many patients with desmoid disease have mutations in the 5′ half of the gene so modifier genes may well also play a part.
- Recent publication of a “desmoid risk factor” score underlines the importance of female gender, the presence of extracolonic manifestations (especially Gardner’s syndrome), and most importantly a family history of desmoids, in alerting surgeons to the likelihood of desmoid disease in their patients.
- Abdominal surgery in patients at high risk of desmoid disease should be delayed as long as possible and, when performed, should preferably be a laparoscopic ileorectal anastomosis.

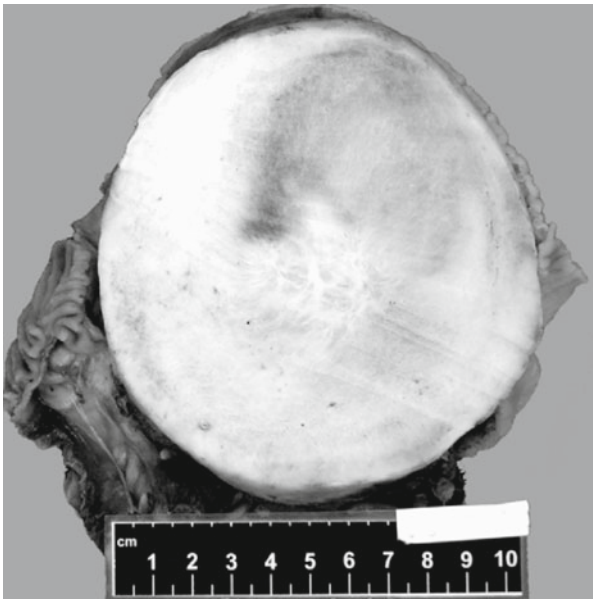

Fig. 37.4 Desmoid tumor arising in the small bowel mesentery

Presentation

- Asymptomatic desmoid disease can be found incidentally, on physical examination, on CT scan, or at laparotomy.
- Symptomatic desmoids cause pain and bowel or ureteric obstruction or are apparent as a mass.

Investigation

- CT or MRI scans are the mainstays of investigation and follow-up (Fig. 37.5). There is some evidence that MRI, T2-weighted signal intensity correlates with subsequent growth.

Management

- The treatment of desmoids is controversial, often empirical and difficult.
- The natural history of desmoid disease in FAP is variable, with about 10 % resolving spontaneously, 10 % growing rapidly and relentlessly, and the remainder either showing cycles of growth and resolution or remaining stable.
- A desmoid staging system has been proposed that allows separation of desmoid tumors by prognosis and sets the stage for a more rational approach to treatment.

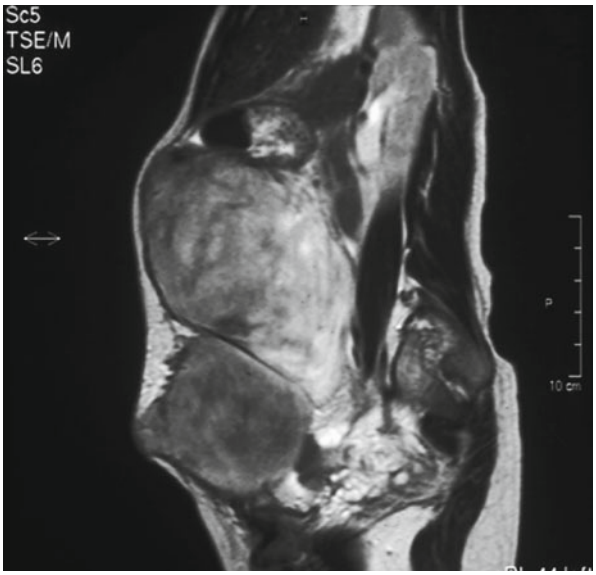

Fig. 37.5 MRI scan showing intra-abdominal desmoid tumor

- Surgery is widely accepted as the first-line treatment for troublesome extra-abdominal and abdominal wall desmoids. Recurrence is common (20–50 %), but complications are few.
- Within the abdomen the situation is very different, as the majority of desmoids develop in the small bowel mesentery. When the tumors are at the root of the mesentery, encasing the mesenteric vessels, surgery is a last resort and may mean small bowel transplant.
- Even after R0 resections, however, recurrence rates are in the order of 50 %.
- Attempts at resection of desmoids in the mesenteric root may lead to perioperative mortality (usually from hemorrhage) and substantial morbidity, particularly due to extensive loss of small bowel.
- Ureteric obstruction is best managed with stents, although even stents may be poorly tolerated due to pain or sepsis.
- Ureterolysis is rarely effective and may lead to nephrectomy. Renal autotransplant has proven effective, however, when medical treatments do not resolve the ureteric obstruction.
- Nonresective surgery may be needed to treat the complications of desmoid disease. Various medical treatments for desmoid disease have been reported, the most widely used being NSAIDs (particularly sulindac) and antiestrogens (raloxifene, tamoxifen, or toremifene). There have been no prospective controlled trials, and particularly in view of the unpredictable and variable behavior of desmoids, the small retrospective series are difficult to interpret. Cytotoxic chemotherapy has been used in

Table 37.6 Staging system for abdominal desmoid tumors

Stage	Definition
I	Size <10 cm, not growing, asymptomatic
II	Size <10 cm, mildly symptomatic, slow growing[a]
III	Size 10–20 cm, moderate symptoms (bowel obstruction, ureteric obstruction), slow growing
IV	Size >20 cm or rapid growth[b] or severe symptoms (abscess, fistula, hemorrhage)

[a]Slow growth = <50 % increase in maximum diameter in 6 months
[b]Rapid growth = >50 % increase in maximum diameter in 6 months

irresectable or aggressive desmoid disease, and objective remissions have been noted with a variety of different agents. There have been a number of encouraging reports of an antisarcoma regimen consisting of doxorubicin and dacarbazine in the treatment of life-threatening intra-abdominal desmoid disease, and more recently the better-tolerated liposomal doxorubicin has shown benefit. A less toxic combination of vinblastine and methotrexate has also produced some responses.

- A treatment regimen can be proposed that uses the staging system outlined in Table 37.6. Stage I tumors may receive either no treatment or sulindac, 150–200 mg twice daily. Stage II tumors are treated with sulindac and an estrogen-modifying agent (tamoxifen or raloxifene 120 mg per day). Stages III and IV require chemotherapy. Liposomal doxorubicin is a reasonable agent to use, with methotrexate/vinorelbine as an alternative. If a septic complication precludes chemotherapy or if the maximum safe dose of Adriamycin has been reached, agents such as Gleevec, bevacizumab, or Erbitux can be tried.

MYH-Associated Polyposis

- MAP is an autosomal recessive form of familial adenomatous polyposis, due to mutations in the human MutY homolog (*hMUTYH*) gene.
- Many of the individuals identified with biallelic *hMUTYH* mutations have fewer than 100 polyps; some have many hundreds and thus appear as if they are a genuine clinical case of FAP.
- Colonic microadenomas and duodenal adenomas, desmoids and fundic gland polyps, sessile serrated polyps, and a variety of extracolonic cancers have also been reported in this group.
- MAP can mimic many of the other hereditary forms of colorectal cancer, from sporadic cancer to FAP, from Lynch syndrome to serrated polyposis (SPS).
- MAP has major implications for genetic counseling as, for the first time, an autosomal recessive form of FAP has been identified.
- This diagnosis should be considered in patients where no *APC* mutation has been identified, the mode of inheritance is not clearly autosomal dominant, or polyp numbers are low.

- Genetics. Base excision repair corrects the sequelae of oxidative damage to the DNA. Oxidation changes the pattern of guanine coupling from G=C to G^{o}=T. In subsequent cell division, an uncorrected G^{o}=T becomes A=T, creating a "G=C to A=T transversion." This change, when uncorrected, produces mutations in several genes, including *APC* and *KRAS*. The effect on *APC* is enough to produce adenomatous polyposis, and serrated polyps harboring similar mutations in *KRAS* have been reported in patients with MAP.
- The locations of the pathogenic *hMUTYH* mutations vary according to ethnicity. The common mutations in the USA are Y179C and G396D, and these are screened for in Caucasian patients. There is some evidence that the Y179C mutation is associated with a more severe phenotype.
- Clinical. Patients usually present with oligopolyposis (<100 adenomas), although some cases with hundreds of polyps have been reported. Patients may present with young age onset colon cancer.
- Prior to awareness of these syndromes, patients with MAP were sometimes diagnosed as having attenuated FAP. Although some affected individuals have a very few adenomas, the presence of ten or more synchronous adenomas should trigger a referral for genetic counseling and testing, regardless of family history of colorectal neoplasia. The presence of serrated polyps with multiple adenomas should also stimulate a referral for genetic testing.
- Once the genotype of MAP is confirmed, full colonoscopy and EGD are performed. The syndrome has not been known for long enough to have an accurate list of all extracolonic manifestations.
- Treatment of the large bowel depends on whether the adenomas can be controlled endoscopically. If this can be done, surgery may be avoided. However, surgery is often necessary, usually colectomy with ileorectal anastomosis.
- Genetic Testing. MAP generally follows an autosomal recessive pattern of inheritance, although monoallelic mutations (carriers) have a mildly increased risk of colorectal cancer. There has been a report of MAP with a dominant pattern of inheritance.
- However, recessive inheritance means that both parents of a proband are likely to be unaffected carriers, with the risk to siblings being 25 %.
- Carriers should have enhanced colonoscopic surveillance, beginning 10 years before any cancer in the family and continuing at least 5 yearly. If the spouse is a carrier, then the inheritance pattern within that family becomes dominant, with each child at 50 % risk of having MAP. In addition, antecedents on both sides of the family must be alerted to the possibility that they are carriers or affected.
- In a study screening 9,268 colorectal cancer patients for the two commonly mutated alleles, Lubbe et al. found biallelic hMutYH mutations in 0.3 % of cases. This conferred a 28-fold increase in colorectal cancer risk and was associated with proximal tumors and synchronous adenomas. Monoallelic mutations were not associated with an increase in colorectal cancer risk.

The Hamartomatous Polyposes

Peutz–Jeghers Syndrome

- Peutz–Jeghers syndrome (PJS) is a dominantly inherited cancer syndrome defined by the presence of two of the following three characteristics: perioral, buccal, and occasionally genital melanin pigmentation; gastrointestinal hamartomatous (Peutz–Jeghers) polyposis; and a family history of PJS. The 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 20s. 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 in the submucosa. Adenomatous change with dysplasia and progression to invasive adenocarcinoma has been observed. PJS has an incidence of 1 in 200,000.

Inheritance

- Peutz–Jeghers polyposis is autosomal, dominantly inherited with high penetrance, and is caused by mutation of *LKB1* (also known as *STK11*) on chromosome 19 p13.3. The gene encodes a serine–threonine kinase. Mutation of *LKB1* is only found in about 60–70 % of cases and has been formally excluded in some, suggesting that either other genes are responsible or *LKB1* may be inactivated by epigenetic mechanisms. While a family history is common, de novo mutations are responsible for a significant number of cases.

Clinical Issues

- Polyp-Related Complications. The most common clinical problems in PJS are anemia due to chronic blood loss from large polyps and small bowel obstruction due to intussusception with a polyp at the apex. Repeated emergency bowel resections can lead to increasing operative difficulty and even short-bowel syndrome.
- 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. Approximately half of all patients in one series had died of cancer by age 57, with 50 % being GI. The lifetime risk of any cancer in affected patients is over 90 %. 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), and ovarian sex-cord tumors (10 % of females); feminizing Sertoli cell testicular tumors in prepubertal boys; and pulmonary and cervical malignancies.

Management

- Probands usually present at a young age with complications of their small bowel polyposis. This often involves laparotomy for intussusception or bleeding. A symptom-focused approach predisposes to frequent laparotomies as untreated polyps enlarge to cause a new set of symptoms. The technique of laparotomy with intraoperative enteroscopy was introduced to reduce the number of repeat emergency laparotomies and small bowel resections. During laparotomy a colonoscope is passed from below through the colon and, with the assistance of the surgeon, into the small bowel for as far as it will go. The most proximal site of insertion is marked with a suture or tape. Then, the colonoscope is withdrawn in a darkened operating room and the sites of polyps marked as it is withdrawn. The procedure is repeated with an enteroscope inserted through the stomach and encouraged to pass distally. The mucosa between the limits of endoscopy can usually be examined through an enterotomy. In most patients, the intussusception is obvious and even if it is reduced, a serosal dimple can be seen at the site of the polyp. The bowel is palpated, and at the site of palpable polyp, an enterotomy is made. The polyps are removed and the bowel intussuscepted through the incision up and down as far as possible. All visible lesions are either removed or cauterized. The enterotomies are closed. Polypectomy is best done by ligating the stalk and excising the polyp with cautery distal to the tie. Otherwise, the stalk may bleed copiously. The fourth part of the duodenum and proximal jejunum is typically a difficult part of the bowel to palpate and to operate.
- Using this "clean sweep" technique, the entire small bowel is cleared of all macroscopic lesions, minimizing the number of laparotomies in subsequent years. The recent availability of capsule endoscopy and double/single balloon enteroscopy offers the potential for endoscopic diagnosis and treatment of the polyps; however, the vascularity of the polyps makes endoscopic treatment in the mid small bowel worrisome. There is a role for capsule endoscopy, however, in surveillance of asymptomatic patients. Colonic polyps can usually be controlled colonoscopically.
- Gastrointestinal Surveillance. Surveillance intervals depend on polyp number, size, histology, and location. A near normal examination can be followed 2 or 3 years later by repeat EGD, capsule endoscopy, and colonoscopy. Hemoglobin should be checked annually. Small bowel polyps causing symptoms or anemia, or measuring over 1.5 cm, should be removed, either endoscopically or at laparotomy with intraoperative enteroscopy.
- 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. While in some centers regular ultrasound scanning of the pancreas and ovaries are performed, there is no evidence that such measures have any impact on prognosis.

Juvenile Polyposis

- Juvenile polyps are hamartomas, which lack smooth muscle histologically, having poor anchorage to the bowel wall. Solitary juvenile polyps are the commonest colorectal lesion in children, being found in up to 2 %. They have little or no malignant potential. Juvenile polyposis (JPS) is defined as the presence of five or more juvenile polyps in the large bowel or any number of juvenile polyps in a patient with a family history of JPS. Although the colorectum is always affected, the stomach (and perhaps small intestine) is also affected in about 50 %. Most affected individuals develop 50–200 polyps, but some have very few.
- JPS is rare with a frequency of about 1 per 100,000. It presents with rectal bleeding, anemia, or polyp prolapse, at an average age of about 9 years. The polyps are hamartomas, with a characteristic hyperplastic stroma, abundant lamina propria, cystic glands, and inflammation. Adenomatous dysplasia occurs in up to half, which may then progress to adenocarcinoma.
- Other morphologic abnormalities, including macrocephaly, mental retardation, cleft lip or palate, congenital heart disease, genitourinary malformations, and malrotations, are found in 10–20 %. Some patients with JPS have a familial pattern of disease, while in others there is no family history. In those with familial disease, the chances of finding a causative mutation are relatively high (>60 %).

Genetics

- This syndrome is genetically heterogeneous, with three separate genes currently implicated. Mutations in *SMAD4* have been identified in affected individuals. *SMAD4* is a tumor suppressor gene on chromosome 18q21 and is implicated in sporadic colorectal carcinogenesis. It codes for a protein involved in the TGFp signaling pathway. Germ line mutations have been found in 35–60 % of juvenile polyposis patients in the USA, but rather fewer (3–28 %) in Europe.
- Germ line mutations in a second gene, *BMPR1A* on 10q22, have been found in a further 15 % of cases. *BMPR1A* encodes a protein involved in the same signaling pathway.
- *PTEN* mutations have also been reported in so-called juvenile polyposis, but it is as yet unclear whether these cases have Cowden's syndrome or whether they represent a variant of juvenile polyposis.
- Patients with JPS due to a *SMAD4* mutation have a high likelihood of also having hereditary hemorrhagic telangiectasia (HHT). Such patients need a vascular assessment to diagnose or exclude this potentially dangerous condition.

Cancer Risk and Management

- The cumulative risk of colorectal cancer in patients with JPS has been estimated at 30–50 % and that of upper gastrointestinal cancer at 10–20 %. First-degree relatives of affected individuals should be screened by

colonoscopy from around the age of 12 years if asymptomatic and, if normal, 5 yearly thereafter. In many 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 where polyps are either too numerous or too large to be managed in this way, or when patients are symptomatic with diarrhea, mucus, bleeding, and cramps, colectomy with IRA or restorative proctocolectomy is advised.

- It is not clear whether endoscopic surveillance and polypectomy is adequate to prevent malignancy, but there are insufficient data to justify purely prophylactic colectomy. Affected individuals should also undergo upper gastrointestinal surveillance from the age of 25 years.

PTEN Tumor Hamartoma Syndromes

- *PTEN* is an important tumor suppressor gene with key roles in the mTOR/AKT pathway.

Cowden's Syndrome

- This autosomal dominantly inherited syndrome is characterized by macrocephaly (30 %), trichilemmomas (which are considered pathognomonic), and both benign and malignant neoplasms of the thyroid, breast, uterus, and skin. Hamartomas occur in the mouth as well as other parts of the gastrointestinal tract, resulting in a nodular appearance of the buccal mucosa. The International Cowden's Syndrome Group has described a set of major and minor criteria by which to diagnose the syndrome.
- In CS patients, the colon is affected with a variety of polyps, the histology of which includes hamartomas, lipomas, fibromas, neurofibromas, ganglioneuromas, and adenomas.
- Although CS has not been considered a high risk for colorectal cancer, recent data seems to suggest otherwise.
- Certainly, it is safe to start colonoscopic screening when patients are in their 30s and to continue it at least every 3 years, or more often if findings indicate.
- Prophylactic colectomy is indicated when polyposis cannot be controlled endoscopically.

Bannayan–Riley–Ruvalcaba Syndrome

- Here, the colorectal hamartomas (50 %) are associated with characteristic pigmented penile macules, macrocephaly, mental retardation (50 %), lipomatosis, and hemangiomas. It seems likely that as Cowden's and Bannayan–Riley–Ruvalcaba syndromes are caused by mutations of the same gene, they are slightly different forms of the same disorder, and families have been identified in which both phenotypes are evident. There is no evidence to suggest an increased risk of colorectal cancer in this syndrome.

Serrated Polyposis

- Serrated polyps are lesions of the large bowel that were until recently thought to have no premalignant potential. A new nomenclature has arisen wherein serrated polyps with abnormal proliferation are termed sessile serrated polyps (or sessile serrated adenomas) and are now known to be premalignant precursors in a serrated polyp to cancer pathway.
- This pathway is linked genetically to *BRAF* mutations and DNA hypermethylation, particularly when it leads to loss of expression of *hMLH1*.
- The WHO definition for serrated polyposis is any one of the following: 20 or more serrated polyps of any size and location; more than 5 serrated polyps proximal to the sigmoid color, of which 2 are larger than 10 mm; and any number or size of serrated polyps with a family history of SPP.
- No germ line mutation has been identified as the cause of serrated polyposis, and the pattern of inheritance is still not clear. Occasionally patients with a genuine mutation in a DNA mismatch repair gene (i.e. Lynch syndrome) may present with multiple serrated polyps. Fulfiling the cetena for serrated polyps. The presence of multiple synchronous-serrated polyps has, however, been shown to confer a very high risk of colorectal cancer, approaching 50 %.

Treatment

- Treatment of patients with SPP is either endoscopic or surgical. Colonoscopy must be careful as serrated polyps can be difficult to recognize and are likely to be easier to miss than adenomas.
- Yearly, colonoscopy is necessary to prevent cancer.
- If the polyps are not controllable endoscopically, colectomy with IRA is indicated.
- First-degree relatives of patients with SPP are candidates for early screening colonoscopy (10 years prior to the earliest age at diagnosis of a neoplastic lesion in the family).

Hereditary Nonpolyposis Colorectal Cancer

Introduction

- HNPCC refers to a dominant pattern of inheritance of colorectal cancer predisposition without an association with unusual numbers of colorectal polyps.
- Multiple diagnostic criteria have been proposed for the identification of HNPCC families. The most widely used are the Amsterdam I and II criteria, originally proposed to facilitate research but almost immediately adapted for clinical use (see Table 37.7).

Table 37.7 Amsterdam criteria

Amsterdam criteria
At least 3 family members with colorectal cancer, one of whom is first-degree relative of the other 2
At least 2 generations with colorectal cancer
At least 1 individual <50 years at diagnosis of colorectal cancer
Amsterdam criteria II
At least 3 family members with HNPCC-related cancer, one of whom is first-degree relative of the other 2
At least 2 generations with HNPCC-related cancer
At least 1 individual <50 years at diagnosis of HNPCC-related cancer Modified Amsterdam criteria
Two first-degree relatives with CRC involving 2 generations
At least one case diagnosed before 55 years
Two first-degree relatives with CRC and a third-degree relative with endometrial cancer or another HNPCC-related cancer.

Modified from Chung DC, Rustgi AK. The hereditary nonpolyposis colorectal cancer syndrome: genetics and clinical implications. Ann Intern Med. 2003;138:560–70

- Subsequent research has shown that Amsterdam I patients can be divided into two broad subgroups: those whose tumors are microsatellite unstable evidence of defective mismatch repair and presumably (Lynch syndrome) and those whose tumors are microsatellite stable (Familial Colorectal Cancer Type X). Type families are likely to be a heterogeneous group of colorectal cancer predisposition states.
- Type families have a significantly lower risk of colorectal cancer than that found with Lynch syndrome, and they do not have the same array of extracolonic cancers.

Lynch Syndrome

Definition

- Lynch syndrome is hereditary DNA MMR deficiency associated with the early onset of colorectal and other cancers (mean age for colorectal cancer, 45 years).
- Multiple generations are affected with a pattern suggesting dominant inheritance.
- Colorectal cancers tend to be proximal to the splenic flexure, and there is an increased frequency of synchronous and metachronous cancers.
- There is also a high risk of extracolonic cancers, including endometrial, ovarian, gastric, small bowel, hepatobiliary, and transitional cell carcinomas.
- The lifetime risk of cancer is up to 80 %, with colon cancer being the most commonly diagnosed.

History

- By the mid-1980s, two patterns of disease became apparent; Lynch I (colorectal cancer only) and Lynch II (colorectal and other malignancies).
- Concurrent observations showed that the number of colorectal adenomas in these patients was no greater than that in the general population and that there was considerable overlap between Lynch I and II syndromes. Terminology has now come full circle with Lynch syndrome, now a genetic diagnosis, referring to families with a germ line mutation in a MMR gene.
- A set of diagnostic guidelines was agreed upon that would allow researchers to gather homogeneous populations to be studied (Amsterdam I criteria, see Table 37.7).
- Tumors from affected patients show multiple mismatched nucleotides in areas of genes called "microsatellites" described by the term "microsatellite instability."

Genetics

DNA Microsatellites

- 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 (MSI)."
- It is assessed using a panel of microsatellite markers. Over 40 % instability in termed MSI-high and is a strong indication of defective DNA mismatch repair.

DNA Mismatch Repair

- DNA mismatches occur during cell division when one strand slips on the other as a new DNA molecule is reconstituted. This is especially likely to happen in DNA microsatellites that can be thought of as "slippery" parts of the DNA.
- Unrepaired mismatches are seen as MSI (Fig. 37.6). The mismatch repair genes are *hMLH1*, *hPMS1*, *hPMS2*, *hMSH2*, *hMSH3*, and *hMSH6*. Both *MSH3* and *MSH6* must be abnormal to have complete loss of hMSH2-dependent mismatch repair.
- MLH1 and PMS2 bind to form a second heteroduplex that interacts with the MutS duplex, stimulating excision and resynthesis. When an inactivating mutation silences expression of an MMR gene, the microsatellite mismatches go unrepaired and are propagated into lines of daughter cells as mutations. This so-called mutator phenotype of Lynch syndrome is characterized by an increased genome-wide mutation rate. When tumor suppressor genes contain a microsatellite, they are vulnerable to loss of expression in the mutator phenotype. Examples of such genes are *MSH3*, *MSH6*, *TCF4*, *BLM*, *caspase-5*, *TGFβRII*, *IGFRII*, *BAX*, *PTEN*, and *APC*, many of which are involved in control of colonocyte growth.
- The most commonly mutated genes in Lynch syndrome families are *MLH1* (33 % of families) and *MLH2* (31 %). Recently, a meta-analysis

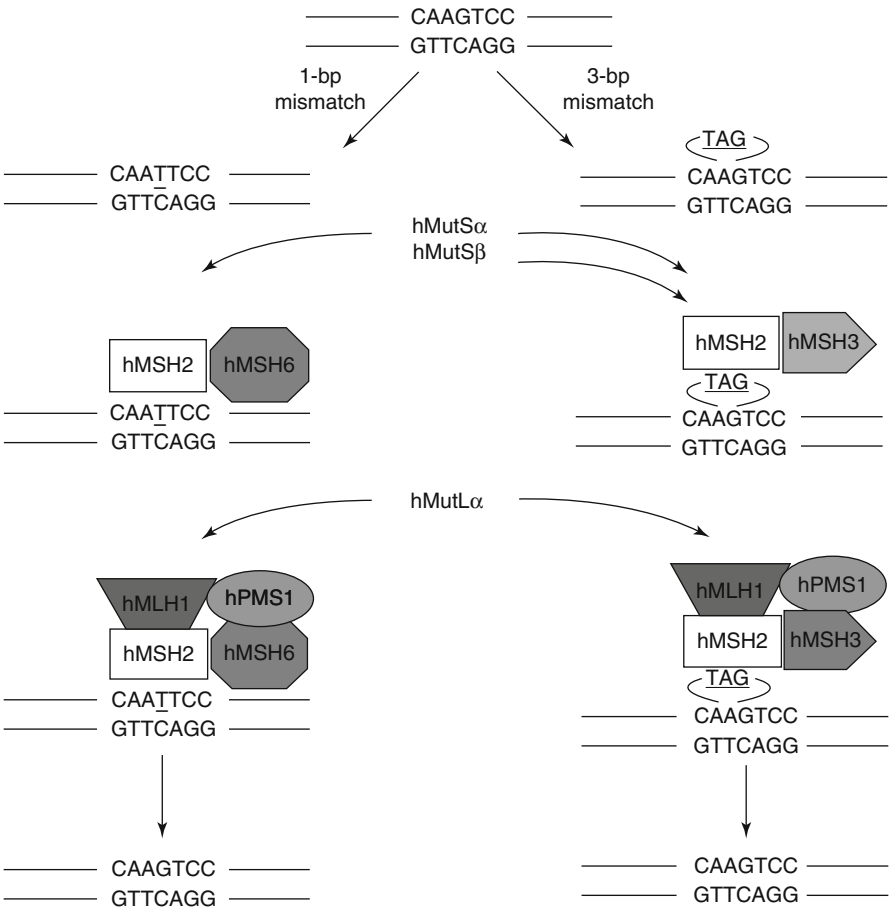

Fig. 37.6 The DNA mismatch repair system can correct either single base-pair mismatches or larger loops of mismatched DNA. hMSH2 serves as the "scout" that recognizes mismatched DNA. It forms a complex with either hMSH6 or hMSH3, depending on the number of mismatched nucleotides. A second heterodimeric complex (hMLH1/hPMSI) is then recruited to excise the mispaired nucleotides. hMUTSα = hMSH2/hMSH6; hMuTSβ = hMSH2/hMSH3; hMutLα = hMLH1/hPMS1. *bp* base pair (Reprinted with permission from Chung DC, Rustgi AK. The hereditary non-polyposis colorectal cancer syndrome: genetics and clinical implications. Ann Intern Med. 2003;138:560–70)

of index families fulfilling the Amsterdam criteria revealed that a mutation in *MLH1* is found in 25.5–29.6 % of families and *MSH2* is found in 14.8–21.6 % of the families.

Pathology

- Some pathologic features can be seen in tumors associated with the mutator phenotype and MSI. These include mucinous differentiation with signet ring cells, the presence of tumor-infiltrating lymphocytes

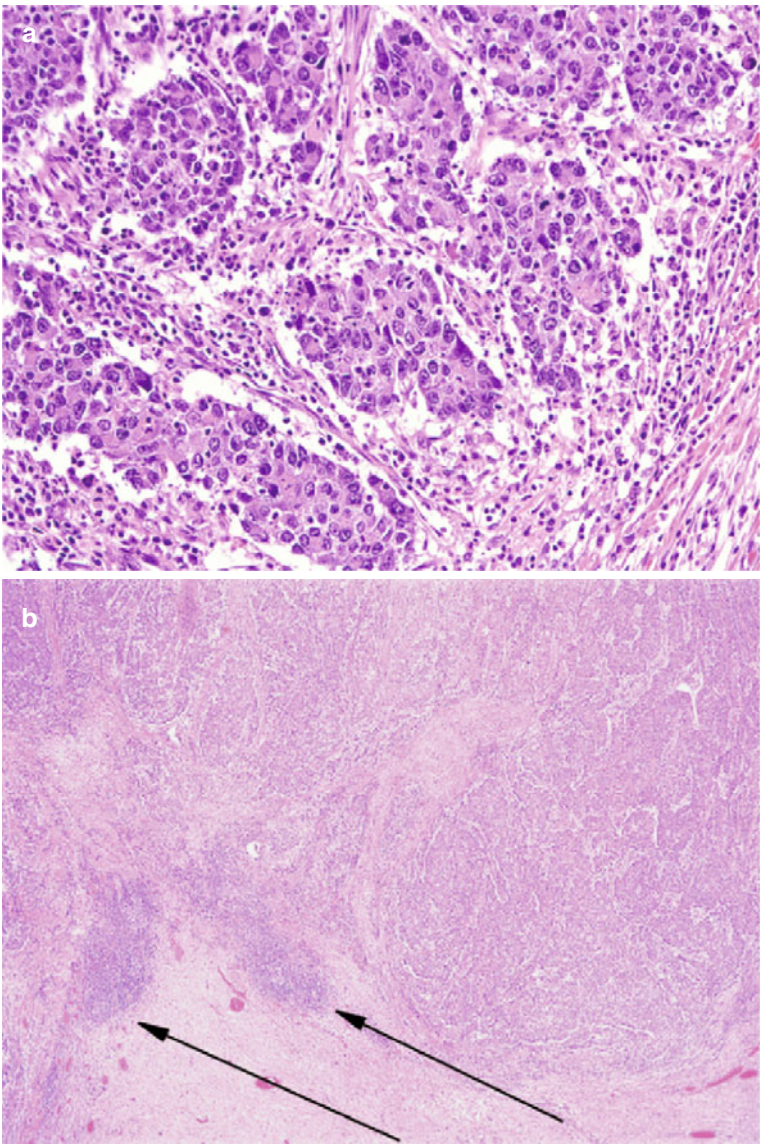

Fig. 37.7 (**a**) Medullary carcinoma-type pattern with peritumoral lymphocytic infiltrate. (**b**) MSI-H cancer with *marked* peritumoral lymphocytic infiltrate (*black arrows*) (Crohn's-like reaction), ×20 magnification (Courtesy of Robert E. Petras, MD, National Director Gastrointestinal Pathology Services, Ameripath Inc., Oakwood Village, OH and Associate Professor of Pathology, Northeastern Ohio University College of Medicine)

(Fig. 37.7a), a Crohn's-like reaction (Fig. 37.7b), and the absence of dirty necrosis. Despite what appears to be unfavorable histology, the incidence of metastatic tumor in lymph nodes is less than that found with sporadic colon cancer.

Table 37.8 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

Adapted from Chung DC, Rustgi AK. The hereditary nonpolyposis colorectal cancer syndrome: genetics and clinical implications. Ann Intern Med. 2003; 138:560–70

- Most Lynch syndrome tumors are diploid compared to sporadic chromosomal unstable tumors which are frequently aneuploid, where tumorigenesis is related to sporadic mutations and loss of heterozygosity (LOH).

Clinical Features

- Patients with Lynch syndrome have an increased lifetime risk of colon cancer and other extracolonic cancers (see Table 37.8).
- Colon cancer is the most frequently diagnosed cancer (80 %).
- Endometrial cancer is the most frequent extracolonic cancer (50–60 %).
- Colorectal cancers in Lynch syndrome are usually proximal to the splenic flexure (68 % vs. 49 % of sporadic cancers), more likely to have associated synchronous cancers (7 % vs. 1 % sporadic colon cancer), and have increased metachronous cancers at 10 years (29 % vs. 5 % sporadic cancers).
- Similarly, women with Lynch syndrome-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.
- In Lynch syndrome, an adenoma is the precursor lesion for cancer. Adenomas are located in the proximal colon and 70 % of the polyps have an absent MMR protein on immunohistochemistry. It is estimated that malignant transformation occurs in 1 to 3 years in Lynch syndrome 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 Lynch syndrome cancers. Flat adenomas are found proximally in up to 50 % of Lynch syndrome patients (Fig. 37.8a, b). About 20 % of flat adenomas show MSI-H and have a mutation in the *TGFβRII* gene. These polyps are difficult to detect during

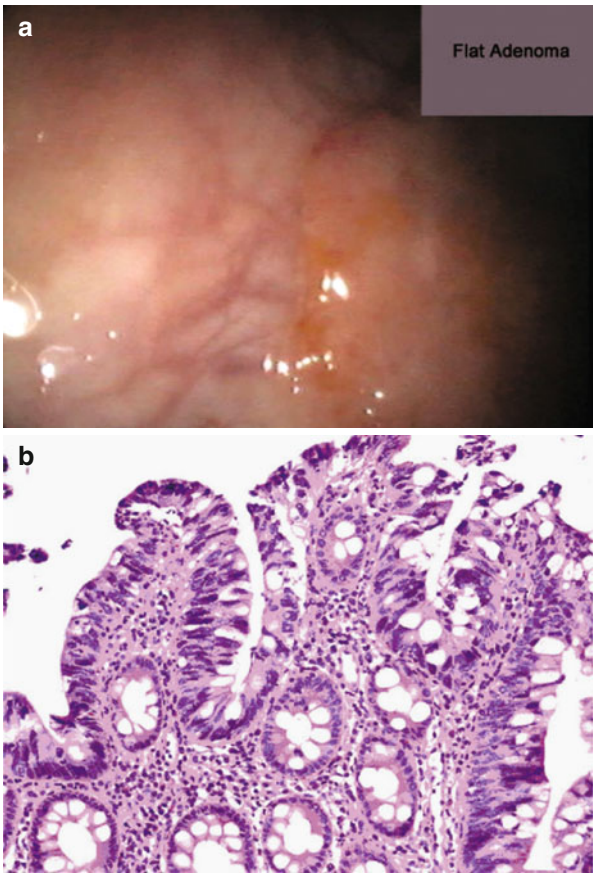

Fig. 37.8 (**a**) Colonoscopic view of a flat adenoma in the cecum that could easily be overlooked. Such polyps are more easily seen using dye-spraying techniques. (**b**) Microscopic view of same polyp following endoscopic removal, showing severe dysplasia, ×100 magnification (Courtesy of Dr. Robert E. Petras, MD, National Director Gastrointestinal Pathology Services, Ameripath Inc., Oakwood Village, OH and Associate Professor of Pathology, Northeastern Ohio University College of Medicine)

colonoscopy, and flat adenomas with advanced histology (high-grade dysplasia or cancer) are significantly smaller (10.7 mm) than comparable polypoid lesions (20 mm).

Genotype–Phenotype Relationships

- *MSH2* mutation appears to be associated with a later age of onset of rectal cancer and more extracolonic cancers than in the *MLH1* mutation-positive group.
- Germ line *MSH6* mutations are uncommon and associated with a particularly high risk of uterine cancer, which is more common than colon cancer in affected women.

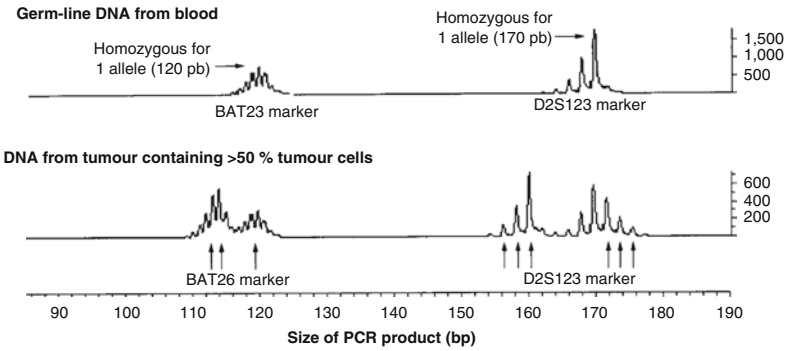

Fig. 37.9 Detection of microsatellite instability with the use of fluorescent labeling of polymerase chain reaction (*PCR*) products analyzed in an automatic sequencer. Two markers are analyzed in the same track: the mononucleotide repeat marker BAT26 is shown on the *left*, and the dinucleotide marker D2S123 is shown on the *right*. The *upper* tracking is from germ line 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, germ line 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, germ line DNA is homozygous, whereas tumor DNA shows two new alleles (*triple arrows*), one with a loss of approximately 10 nucleotides (*left*) and one with a gain of two nucleotides (*right*). Thus, the tumor shows microsatellite instability 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;348:919–32. Copyright © 2003 Massachusetts Medicine Society. All rights reserved)

- Over 30 potentially pathogenic *MSH6* mutations exist, and 35 % involve only one amino acid.
- Colorectal cancers are more frequently left sided in *MSH6* carriers (Figs. 37.9, 37.10, and 37.11).

Muir–Torre Syndrome

- The Muir–Torre syndrome is the combination of Lynch syndrome and sebaceous adenomas, sebaceous carcinomas, and keratoacanthomas.
- Colorectal cancers are most commonly found (51 %) and are often proximal to the splenic flexure (60 %).
- Although only 25 % of Muir–Torre patients develop a polyp, 90 % of patients who develop polyps develop colon cancer.
- The second most frequent tumors are genitourinary (24 %).
- Germ line mutations in *MLH1* and *MSH2* have been identified, and many of the tumors exhibit MSI.
- The median age of diagnosis is 55 years and only 60 % has a positive family history.

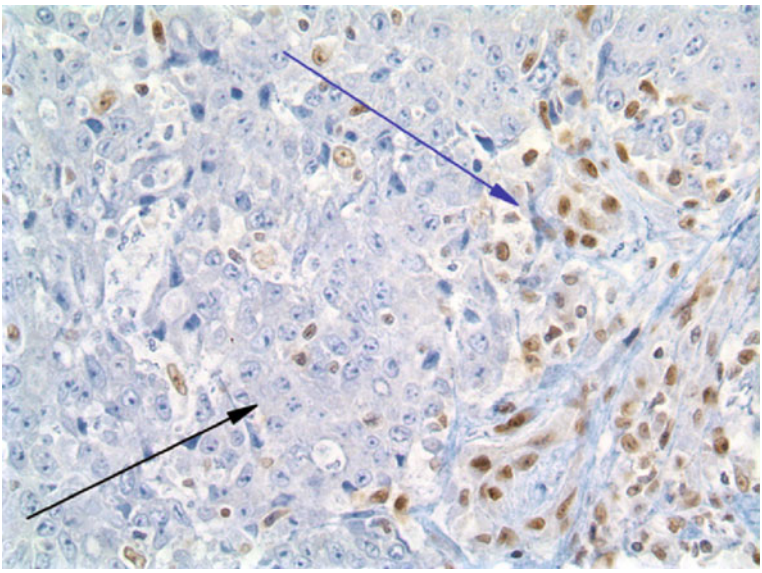

Fig. 37.10 hMLH1 immunohistochemistry. *Blue arrow* indicates positive nuclear staining for the presence of hMLH1 protein within an inflammatory cell. *Black arrow* demonstrates the absence of protein within cancer cells, ×400 magnification (Courtesy of Robert E. Petras, MD, National Director Gastrointestinal Pathology Services, Ameripath Inc., Oakwood Village, OH, and Associate Professor of Pathology, Northeastern Ohio University College of Medicine)

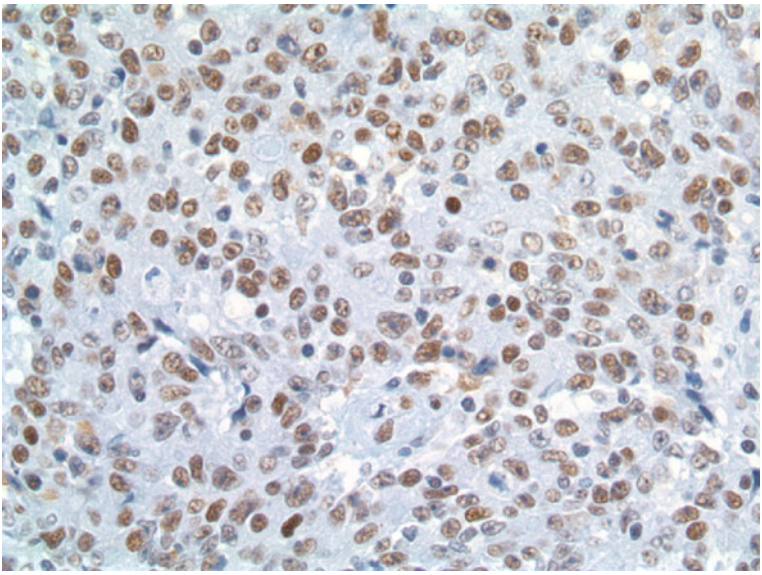

Fig. 37.11 hMSH2 immunohistochemistry. Positive nuclear staining demonstrates the normal presence of hMSH2 protein, ×400 magnification (Courtesy of Robert E. Petras, MD, National Director Gastrointestinal Pathology Services, Ameripath Inc., Oakwood Village, OH, and Associate Professor of Pathology, Northeastern Ohio University College of Medicine)

Table 37.9 Modified Bethesda guidelines

Patient with 2 HNPCC-related tumors
Patient with CRC with first-degree relative with HNPCC-related cancer; one of the cancers at <50 years or adenoma at <40 years
Patient with CRC or endometrial cancer at <50 years
Patient with right-sided, undifferentiated CRC at <50 years
Patient with signet ring CRC at <50 years
Patient with adenoma at <40 years

Modified from Rodriguez-Bigas MA, Boland CR, Hamilton SR, Henson DE, Jass JR, Khan PM, Lynch H, Perucho M, Smyrk T, Sobin L, Srivastava S. A National Cancer Institute Workshop on hereditary nonpolyposis colorectal cancer syndrome: meeting highlights and Bethesda guidelines. J Natl Cancer Inst. 1997;89:1758–62

Diagnosis

Amsterdam Criteria

- The key to the diagnosis of Lynch syndrome is a high index of suspicion and an awareness of some of the subtle phenotypic clues. The easiest clue to detect is a strong family history of colorectal and Lynch syndrome cancers. The first Amsterdam criteria (I) (Table 37.7) were created to identify patients with a high probability of having HNPCC. However, the Amsterdam I criteria were faulted for not including extracolonic cancers, and so Amsterdam II criteria were published to correct this (Table 37.7). A third set of Amsterdam criteria (Amsterdam-like) have been used, where an advanced adenoma is allowed to qualify one of the three affected individuals, accounting for the phenotype attenuation caused by increasingly widespread screening. However Hampel et al. have shown that when Lynch syndrome was diagnosed by MSI-directed mutational testing, 22 % of families did not meet Amsterdam criteria and 10/23 probands were older than 50 years. Therefore, although Amsterdam criteria are still useful, on their own they have a high false-negative rate. The “false-positive” rate of Amsterdam criteria for MMR gene mutation carriers (Lynch syndrome) represents Familial Colorectal Cancer Type X.

Bethesda Criteria

- In 1996, a National Cancer Institute workshop on MSI produced a set of criteria to identify patients whose cancers are likely to be microsatellite unstable. These Bethesda criteria and their revision (Table 37.9) include family history as well as tumor characteristics, such as histology and site. The Bethesda criteria are a useful screen for triaging colorectal cancers for MSI testing but were never intended as diagnostic criteria for Lynch syndrome.

Tumor Testing with MSI and Immunohistochemistry

- MSI testing is being used as a screening test to detect Lynch syndrome although 15 % of sporadic colorectal cancers are unstable due to promoter methylation of *hMLH1*. If *hMSH2* is not expressed, this is good evidence for Lynch syndrome. If *hMLH1* is not expressed, the clinical situation (i.e., family history, age, and site of the cancer) may give a clue as to the existence of Lynch syndrome. The tumor can also be tested for a *BRAF* mutation which, if present, suggests a sporadic, hypermethylated cancer rather than Lynch. After tumor triage by MSI and IHC testing, patients can be selected for genetic testing for a germ line mutation.

Histology

- Pathologists may recognize cancers that have arisen due to the mutator phenotype by the presence of tumor-infiltrating lymphocytes, a Crohn's-like reaction, mucinous differentiation, signet ring cells, and the absence of dirty necrosis.

Predictive Models

- Jenkins et al. using tumor-infiltrating lymphocytes, tumor location (proximal vs. distal), mucinous histology, poor differentiation, Crohn's-like reaction, and diagnosis before age 50 years had a sensitivity of 93 % and a specificity of 55 % for MSI-high.
- MMRpro was devised by Chen et al. to predict the probability that a patient carries a deleterious mutation of *MLH1*, *MSH2*, or *MSH6* and the chances of developing colorectal or endometrial cancer in the future. It includes family history, endometrial cancer status, and current age or age at last follow-up (in years) if unaffected. The formula had a concordance index of 0.83 and a ratio of observed to predicted cases of 0.94. It is available online at http://www4.utsouthwestern.edu/breasthealth/cagene/.
- Barnetson et al. produced a predictive formula to calculate the risk of carrying a germ line MMR gene mutation. It is as follows: $\mathrm{Pr}/(1-\mathrm{Pr}) = 1.39 \times 0.89$ age at diagnosis $\times 2.57$ gender (male = 1, female = 0.57) $\times 4.45$ (site of tumor, proximal = 1, distal = 0) $\times 9.53$ synchronous or metachronous tumor (yes = 1, no = 0) $\times 46.26$ family history of colorectal cancer (youngest < 50) $\times 7.04$ family history of colorectal cancer (youngest > 50 years of age) (yes = 1, no = 0) $\times 59.36$ family history of endometrial cancer <50 years of age (yes = 1, no = 0). This model provided a subset of patients in whom preoperative tumor biopsies could be subjected to IHC, and the combination has a positive predictive value of 80 % for mutation carriers.

Table 37.10 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

Adapted and reproduced from Syngal S, Fox EA, Eng C, Kolodner RD, Garber JE. Sensitivity and specificity of clinical criteria for hereditary non-polyposis colorectal cancer associated mutations in MSH2 and MLH1. J Med Genet. 2000;37:641–45

Genetic Testing for a Germ Line MMR Gene Mutation

Indications

- Patients whose families fulfill Amsterdam I, II, and like criteria; patients fulfilling revised Bethesda criteria; patients with MSI-high tumors with wild-type *BRAF* or loss of expression of an MMR protein are candidates for genetic testing (Table 37.10).

Procedure

- Genetic counseling is routine.
- Sequencing of *MSH2*, *MLH1*, *PMS2*, and *hMSH6* is now commercially available. The cost of this testing is usually covered by the patient's health insurance. Once the pathologic mutation in the family has been found, screening of at-risk relatives is considerably cheaper. A data bank of known mutations is kept by the International Society for Gastrointestinal Hereditary Tumors (InSiGHT).

Strategy of Genetic Testing

- Testing should begin with an affected individual (in whom a Lynch syndrome cancer has been diagnosed). When the proband has a negative or a noninformative test (including variant of unknown significance), genetic testing of at-risk family members is not helpful and all at-risk family members require intensive surveillance.
- When the proband has a pathologic mutation, at-risk family members can be offered genetic screening.

Surveillance

- Colorectal cancers in Lynch syndrome can occur in very young patients and develop within a year of a negative colonoscopy.
- Adenomas occur earlier and are more likely to be villous.

- The adenoma to carcinoma transition occurs early and small cancers can be missed.
- Most guidelines suggest beginning colonoscopy at age 21, or 10 years younger than the youngest affected relative's age at diagnosis (whichever is younger).
- Colonoscopies continue every 2 years until age 40 when they are every year. If an adenoma is found, colonoscopy is every year thereafter.
- The value of screening colonoscopy in Lynch syndrome was demonstrated by Jārvinen and colleagues who studied a group of 252 individuals belonging to 22 HNPCC families. Colorectal cancer developed in 8 % of the screened family members, compared to 16 % of those who refused screening. In those individuals who were known to have a DNA MMR gene mutation (Lynch syndrome), the rate of colorectal cancer in those who underwent screening was 18 % compared to 41 % in those who did not undergo screening.
- Due to the high risk of endometrial cancer in women, annual pelvic ultrasound to examine the endometrium is recommended beginning between ages 25 and 35 years as the increased risk for gynecological cancer in these patients begins at age 25.
- Prophylactic colectomy and hysterectomy is the most effective way to prevent cancer in Lynch syndrome patients. Although prophylactic colectomy is not commonly performed in unaffected mutation carriers, its benefits must be discussed.

Treatment

Surgery

- The surgical options for colon cancer in a Lynch syndrome patient are a standard right, left, or sigmoid colectomy or a colectomy and ileorectal anastomosis. Oncologically, IRA is the operation of choice for colon cancer. It minimizes cancer risk, preserves anal sphincter function, and retains the reservoir capacity of the rectum. The estimated risk of rectal cancer after colectomy and IRA is 12 % at 12 years. The risk for a metachronous colon cancer in HNPCC is 45 % with only segmental colectomy.
- In women undergoing colectomy, strong consideration should be given to performing a hysterectomy and bilateral salpingo-oophorectomy if their family is complete, due to the increased risk of both endometrial and ovarian carcinoma.

Prognosis

- The survival rate in Lynch syndrome patients with colorectal cancer is better than that of patients with sporadic colorectal cancer when matched for stage and age of onset. There is also evidence that patients with stage II or III microsatellite-unstable colorectal cancers do not benefit from 5-fluorouracil-based adjuvant therapy and may even do worse with it.

Chemoprevention

- Data exist to support the efficacy of NSAIDs in reducing the risk of colorectal cancer in the general population, and a recent study suggests the same benefits as high dose aspirin in patients with Lynch syndrome.
- This recent CAPP II trial was a controlled, randomized trial of colorectal polyp and cancer prevention using aspirin and resistant starch in carriers of a germ line MMR gene mutation. Its first report described no impact of this chemoprevention on the development of adenomas but a reduction in the rate of cancers of all types.
- Calcium and vitamin D intake have been associated with a decreased risk of sporadic colorectal cancer.

Familial Colorectal Cancer Type X

- This collection of families, where the history of colorectal cancer is strong enough to comply with Amsterdam criteria but where tumors are microsatellite stable, is poorly defined.
- A local registry can be found by accessing the Collaborative Group of the Americas on Inherited Colorectal Cancer at http://www.cgaicc.com.

38. Colorectal Cancer: Epidemiology, Etiology, and Molecular Basis

Harvey G. Moore, Nancy N. Baxter, and Jose G. Guillem

Epidemiology

- Colorectal cancer (CRC) is a disease with a major worldwide burden. It is the fourth most frequently diagnosed malignancy in men and third most common in women, with almost one million people developing CRC annually. It was estimated that 147,000 cases were diagnosed in the USA in 2009 and that there were 50,000 deaths from the disease.
- The worldwide incidence of CRC is increasing; in 1975, the worldwide incidence of CRC was only 500,000.
- In the time period 1998–2005, the rate of decline accelerated; –2.8 % per year in men and 2.3 % per year in women (Fig. 38.1).
- CRC in the USA over a lifetime is 5.5 % in men and 5.1 % in women.
- The risk of CRC continues to increase with age (Fig. 38.2).
- Overall, the incidence of CRC in men is 61 per 100,000 males as compared to 45 per 100,000 females.
- In addition, the ratio of colon to rectal cancer differs by sex; the ratio of colon to rectal cases for women is 3:1 as compared to 2:1 for males.

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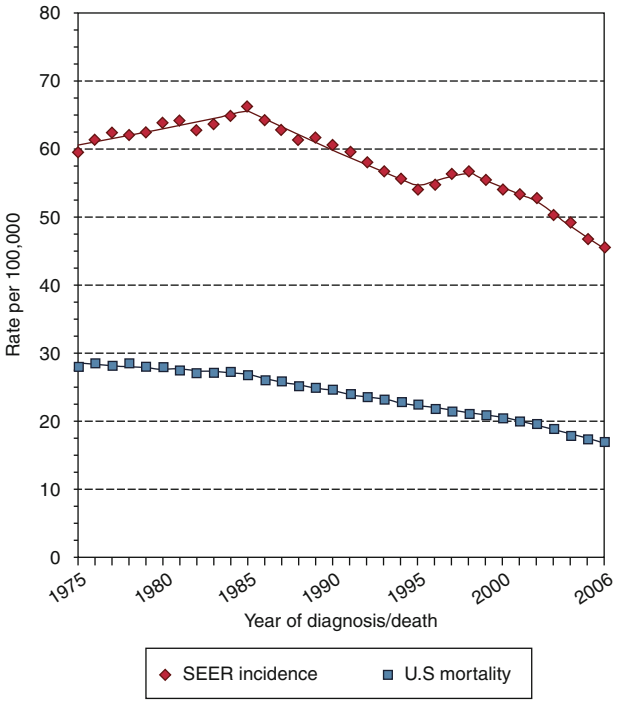

Fig. 38.1 Age-adjusted colorectal cancer incidence and death rates in the USA 1975–2006

- Ashkenazi Jewish individuals appear to be at a slightly increased risk of CRC. At least part of this increased incidence may be due to a higher prevalence of the I1307K mutation of the adenomatous polyposis gene (APC), a mutation that confers an increased risk of CRC development (18–30 % lifetime risk).
- In the USA, the incidence of CRC is higher in African Americans of either sex as compared to white Americans. Asian American/Pacific Islanders, Native Americans, and Hispanic Americans experience a lower incidence of CRC than Caucasians (Table 38.1).
- According to the American Cancer Society, between 1996 and 2004 for all patients diagnosed with CRC, 40 % of patients were diagnosed with localized disease, 36 % with regional disease, and 19 % with metastatic disease. Five percent of patients were not staged. As a proportion of total cases, African Americans were more likely to present with advanced disease; 24 % of African Americans have metastatic disease at presentation (Table 38.2).
- 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. 38.3).
- Environmental factors (most prominently dietary factors) are still considered to have a major role in this disease.
- Interestingly, there is less variation in the incidence of rectal cancer between countries as compared to the incidence of colon cancer.

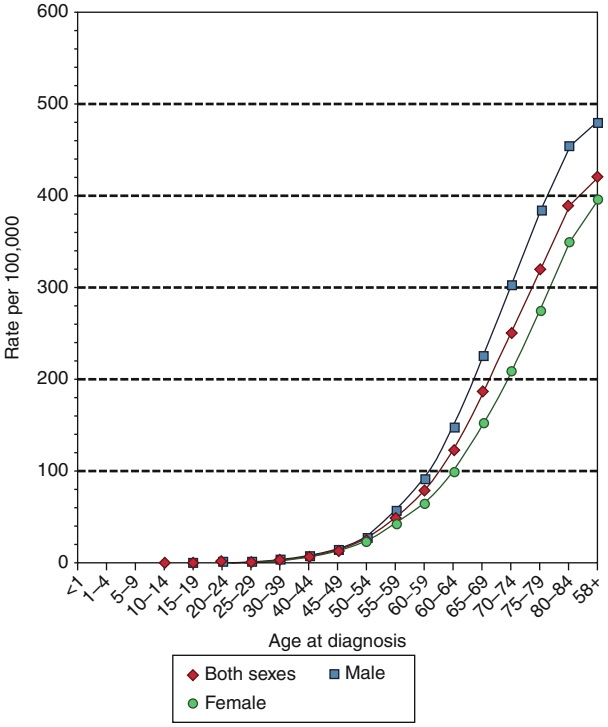

Fig. 38.2 Age-specific SEER incidence rates in the USA 1992–2006

Table 38.1 Incidence and mortality rates for CRC by site, race, and ethnicity, USA 2001–2005

		White	African American	Asian American and Pacific Islander	American Indian/Alaska Native	Hispanic/ Latino
Incidence	Male	58.9	71.2	48.0	46.0	47.3
	Female	43.2	54.5	35.4	41.2	32.8
Mortality	Male	22.1	31.8	14.4	20.5	16.5
	Female	15.3	22.4	10.2	14.2	10.8

Adapted from Jemal A, Siegal R, Ward E, Hao Y, Xu J, Ward E, and Thun MJ; American Cancer Society. Cancer statistics, 2009. CA Cancer J Clin. 2009;59:225–249. Table 11 DOI:10.1007/_11. Incidence and mortality rates for by site, race and ethnicity, USA, 2001–2005. Pg 242
Incidence and mortality rates per 100,000 age-adjusted to the 2000 US standard population

Table 38.2 Stage at diagnosis (USA 1996–2004)

	Whites (%)	African Americans (%)
Localized	40	35
Regional	36	34
Distant	19	24
Unstaged	5	7

Adapted from Jemal A, Siegal R, Ward E, Hao Y, Xu J, Ward E, and Thun MJ; American Cancer Society. Cancer statistics, 2009. CA Cancer J Clin. 2009;59:225–249. Figure 9. Incidence and mortality rates for by site, race and ethnicity, USA, 2001–2005. Pg 246

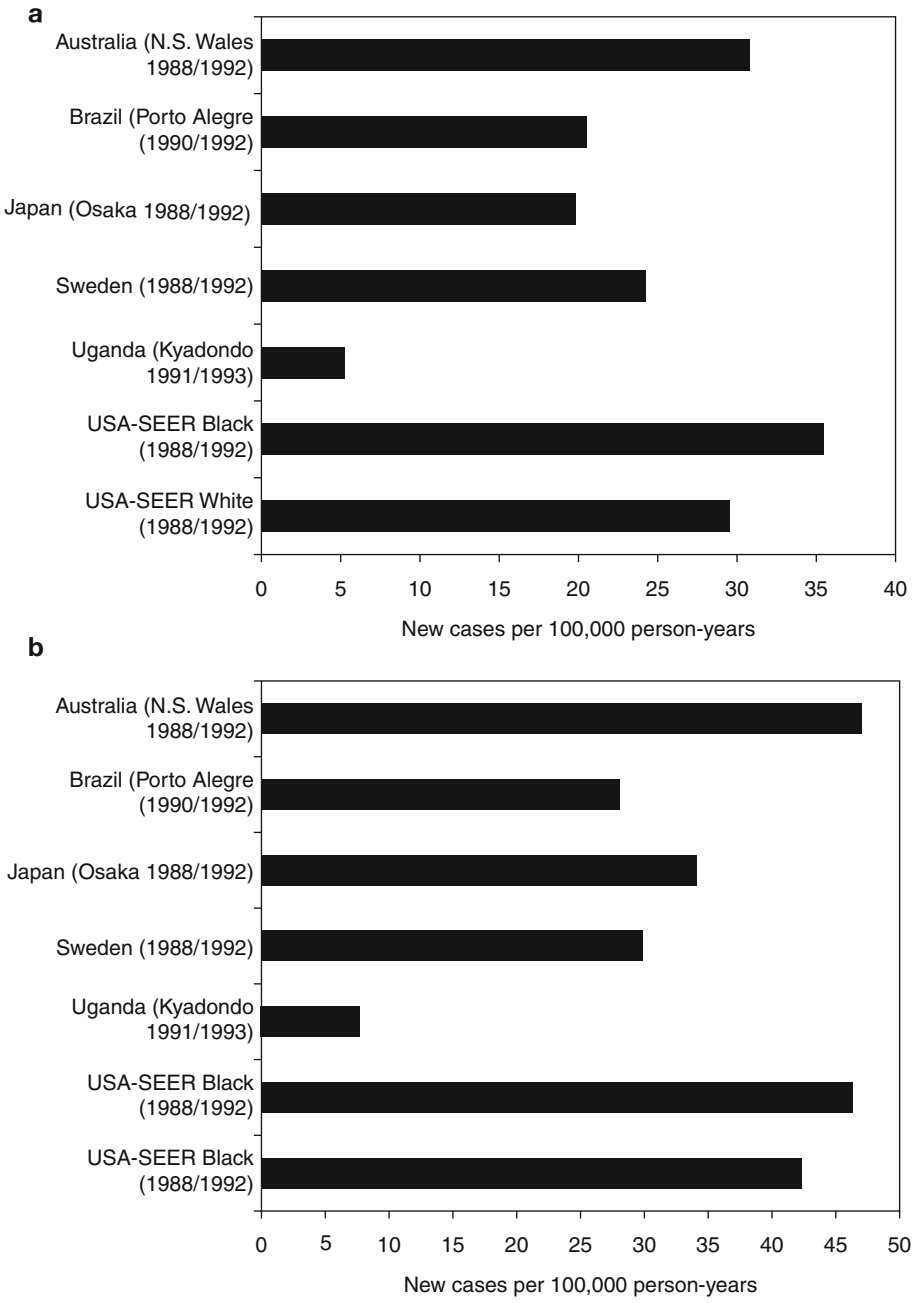

Fig. 38.3 (**a**) Age-standardized (to the world population) incidence rates of cancer of the large bowel among females. (**b**) Age-standardized (to the world population) incidence rates of cancer of the large bowel among males

- Mortality from CRC is declining in the USA (Fig. 38.1 and Table 38.1).
- However, for those who develop CRC, no improvement in case fatality has been identified since 1986 indicating that the trends in mortality are likely complex.
- African Americans suffer the highest mortality rate from CRC in the USA (Table 38.1).
- Because CRC is a survivable cancer, with a 5-year survival rates adjusted for life expectancy of 64 %, the prevalence of people living with a diagnosis of CRC in the population is substantial. In total, over one million Americans alive in 2006 have had a diagnosis of CRC.

Etiology

Dietary Constituents and Supplements

- The relationship between diet and CRC risk is at best unclear.

Dietary Fat

- Dietary fat, particularly saturated animal fat, has been implicated in carcinogenesis of the colon and rectum.
- Countries with populations eating a high-fat diet had higher CRC rates than countries with populations eating a lower fat diet, making ecological comparisons between countries subject to a substantial risk of confounding.
- Over 13 case–control studies evaluating the relationship between dietary fat intake and the risk of CRC were quantitatively summarized by Howe et al. and include 5,287 cases with CRC and 10,470 controls.
- Overall, there was no evidence for any association of total dietary fat intake and development of CRC.
- In addition, at least six cohort studies have been conducted to evaluate the relationship between dietary fat and CRC.

Red Meat

- Red meat is high in iron, a pro-oxidant. Dietary iron may increase free-radical production in the colon, and these free radicals may cause chronic mucosal damage or promote other carcinogens.
- Alternatively, dietary heme, present in red meat, may have a cytotoxic effect on colonic surface epithelium, resulting in rebound inhibition of apoptosis and crypt hyperplasia.
- A large number of epidemiologic studies and three meta-analyses have been published. The pooled estimate for the increase in the risk of CRC due to red meat consumption was similar; odds of development of CRC in the highest meat consuming groups as compared to the lowest was

1.14–1.28. It is therefore difficult to rule out the possibility that the apparent effect of red meat on the development of CRC may be confounded or modified by other dietary or lifestyle factors.

- Genetics may also play a role. In the Fukuoka Colorectal Cancer Study, colon cancer risk was increased in relation to red meat intake only in individuals with a specific polymorphism of Cytochrome P450 2E1 (CYP2E1).

Fruit and Vegetable Intake

- Fruits and vegetables are a source of antioxidants, including carotenoids and ascorbate.
- Results from 22 case–control studies and four prospective cohort studies have provided substantial support for the hypothesis that vegetable intake reduces the risk of CRC while intake of fruit did not seem to have an effect.
- Other studies, however, did not demonstrate a convincing link between vegetable or fruit intake and a reduced risk of CRC.
- In four large prospective cohort studies (the Nurse's Health Study of 121,700 women, the Health Professionals Follow-up Study of 51,529 men, the Netherlands Cohort Study on Diet and Cancer including 120,852 men and women, and the Cancer Prevention Study II Nutrition Cohort, including 133,163 men and women), fruit and vegetable intake was not statistically significantly associated with a reduced risk of CRC.
- More recent studies have reported conflicting results. A pooled analysis of 14 cohort studies, including 756,217 men and women followed between 6 and 20 years also did not find a significantly reduced risk of CRC in the highest consumers of total fruits and vegetables, total vegetables, or total fruits.
- Finally, the recently reported European Prospective Investigation into Cancer and Nutrition (EPIC) study, involving a cohort of 452,755 men and women followed an average of 8.8 years, reported a significant inverse relationship between total fruit and vegetable consumption and the risk of colon cancer (RR = 0.76; 95 % CI, 0.63–0.91).
- The Polyp Prevention Trial randomized 2,079 people with a history of colorectal adenomas to either intensive dietary counseling with assignment to a diet low in fat and high in fruits, vegetables, and fiber, or to a control group (no dietary change). No difference in adenoma recurrence rate was found in the intervention group as compared to the control group. However, follow-up of 34,467 women participating in the Nurses' Health Study found an inverse relationship for total consumption of fruit, but not vegetables, on the risk of colorectal adenomas.
- Overall, the evidence for an association between fruit and vegetable intake and the risk of CRC is inconsistent.

Fiber

- Dietary fiber was one of the first dietary components thought to have a protective role in carcinogenesis.

- A number of 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, or fiber may dilute or absorb various potential carcinogens, particularly bile salts.
- Surprisingly, two large American cohort studies, the Nurses' Health study and the Health Professionals' Follow-up Study found no evidence of benefit of fiber on CRC risk.
- However, more recent studies have reopened the debate. In the PLCO Cancer Screening Trial, a nested case–control study of over 37,508 people undergoing flexible sigmoidoscopy was performed using food frequency questionnaires. People who reported the highest amounts of fiber in their diets had the lowest risk of colorectal adenomas – 27 % risk reduction compared to people who ate the least amount of fiber.
- A meta-analysis in which the data from 13 prospective cohort studies were reanalyzed. Although dietary fiber intake was inversely associated with the risk of CRC in age-adjusted analyses, this association did not hold when adjusted for other dietary risk factors.
- A meta-analysis has evaluated the effect of five intervention trials. These studies randomized a total of 4,349 individuals to some form of fiber supplementation or high-fiber dietary intervention. When the data were combined, there was no difference between the intervention and control groups for the number of subjects developing at least one adenoma (RR = 1.04; 95 % CI, 0.95–1.13). The authors concluded that there is currently no evidence from randomized studies to suggest that increased dietary fiber intake reduces the incidence or recurrence of adenomatous polyps within a 2–4-year period.

Calcium and Vitamin D

- Calcium has the capacity to bind and precipitate bile acids and may directly influence mucosal cell proliferation.
- Two randomized, double-blind, placebo-controlled intervention trials of calcium for the prevention of adenoma recurrence that included a total of 1,346 subjects have demonstrated that the use of calcium supplementation (1,200 mg daily for a mean duration of 4 years or 2,000 mg daily for a mean duration of 3 years) was associated with a reduction in the recurrence of colorectal adenoma, although only one study achieved statistical significance.
- In a meta-analysis of the two studies, the relative risk of developing recurrent adenomas was 0.74 for patients randomized to receive calcium as compared to placebo.
- A meta-analysis of available studies conducted in 1996 concluded that the evidence to support the benefit of calcium intake on reduction of colorectal neoplasia was not consistent with a substantial effect.
- Vitamin D alone may also have a chemopreventative effect via modulation of calcium absorption and gene expression.

- A large epidemiological study found a 29 % reduction in CRC risk in individuals with the highest vitamin D intake.
- In a case–control study nested within the Multiethnic Cohort Study, plasma 25 (OH) D levels were measured using a chemiluminescence assay in 229 patients with CRC and 434 matched controls. An inverse trend was observed between vitamin D level and the risk of CRC (OR, per doubling of 25(OH)D = 0.68; 95 % CI, 0.51–0.92).
- A recent meta-analysis investigated the relationship between circulating 25(OH)D levels and vitamin D intake on the incidence of colorectal adenomas. Circulating 25(OH)D was inversely correlated with the incidence of adenomas (OR = 0.70; 95 % CI, 0.56–0.87) for the high versus low circulating 25(OH) D groups.
- A meta-analysis of ten cohort studies involving 2,813 cancer cases reported that vitamin D intake was associated with only a nonsignificant 6 % reduction on CRC risk (RR = 0.94; 95 % CI, 0.83–1.06).

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.
- In 15 retrospective epidemiologic studies evaluating the association between folate and CRC risk, most demonstrate a statistically significant or trend toward a significant relationship between higher intake of folate and a reduced risk of CRC or adenoma formation.
- However, recently, results of two randomized, double-blind, placebo-controlled intervention trials have been published that do not support a protective effect of folate supplementation. Taken together, these studies demonstrate that folate supplementation is unlikely to be of benefit as secondary prevention in patients with a history of colorectal adenomas and may actually be detrimental.
- Consistent with this data, one recent observation suggests folate supplementation may actually increase the risk of CRC.

Alcohol

- Alcohol ingestion has a possible role in colorectal carcinogenesis. Alcohol may alter folate absorption, increasing CRC through the reduction of folate bioavailability. Acetaldehyde, a product of alcohol metabolism may have a role, and alcohol may also contribute to abnormal DNA methylation directly.
- A meta-analysis of five follow-up studies and 22 case–control studies published in 1990 demonstrated only a weak association between alcohol and CRC, although the effect was stronger when only rectal cancer was considered.

- Two more recent meta-analyses of 16 and 5 cohort studies demonstrate a strong association between alcohol consumption and development of CRC.
- The EPIC trial, a prospective cohort trial involving 478,732 subjects, looked at both baseline and lifetime intake of alcohol as risk factors. Lifetime alcohol intake was significantly correlated with increased CRC risk (RR = 1.08; 95 % CI, 1.04–1.12 for 15 g/day increase).
- In a prospective cohort study involving 1,009 Stage III CRC patients enrolled in a randomized adjuvant chemotherapy trial, food frequency questionnaires were administered during and for 6 months after adjuvant chemotherapy. At a median follow-up of 5.3 years, patients in the highest quintile of Western dietary intake had a significantly worse disease-free (adjusted hazard ratio (AHR) 3.25; 95 % CI, 2.04–5.19) and overall survival (AHR 2.32; 95 % CI, 1.36–3.96) compared to those in the lowest quintile of Western dietary pattern.

Aspirin and Nonsteroidal Anti-inflammatory Drugs

- 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 involved.
- At least 30 observational studies have been conducted to evaluate the influence of NSAID (primarily aspirin) use on the development of CRC and colorectal adenoma.
- A consistent reduction in the risk of colorectal neoplasia in NSAID users is identified in these studies of various designs.
- In a pooled analysis of the effect of aspirin and NSAIDs on CRC risk, the results were virtually the same. Overall, the data evaluating the effect of nonaspirin NSAIDs is more limited than that for aspirin.
- The authors of a meta-analysis reviewed one population-based prevention trial (including 22,071 people), three secondary prevention trials in patients with sporadic polyps (including 2,028 patients), and four trials in 150 patients with familial adenomatous polyposis. The authors conclude based on data from these high-quality trials that there is some evidence for the effectiveness of intervention strategies using NSAIDs for the prevention of colorectal adenoma.
- However, the single primary prevention trial reviewed did not demonstrate a decreased incidence of CRC in the intervention group.
- NSAIDs and aspirin may play an important role in secondary chemoprevention of colorectal adenomas and cancer.
- Baron et al. randomized 2,587 to either the COX-2 inhibitor rofecoxib 25 mg/day versus placebo. Adenoma recurrence was less frequent for rofecoxib subjects than for those randomized to placebo (41 % vs. 55 %; $P < 0.0001$; RR = 0.76; 95 % CI, 0.69–0.83).
- Prolonged use of NSAIDs may have additional benefits. Long-term follow-up of the Aspirin/Folate Polyp Prevention Study revealed that

patients who used regular NSAIDs in the 4 years following the study intervention (3 years of 81 mg aspirin/day) had a persistent reduction in the development of adenoma versus patients who were infrequent post-study NSAID users (RR = 0.62; 95 % CI, 0.39–0.98).
- In a prospective cohort study involving 1,279 patients previously treated for Stage I–III colorectal cancer, regular aspirin users had a significantly reduced risk of CRC-specific mortality versus nonusers (RR = 0.71; 95 % CI, 0.53–0.95).

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 meta-analysis of 18 observational studies of postmenopausal HRT demonstrated a 20 % reduction in incidence of CRC in women who had taken HRT as compared to those that had never taken HRT.
- Overall, there appears 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.

Obesity

- Obesity appears to increase the risk of colon cancer in men and premenopausal women.
- Case–control studies and cohort studies have demonstrated a strong association between a high body mass index (BMI) and incidence of CRC, with an up to twofold increased risk of CRC found in the obese.
- A more accurate predictor than BMI may be the waist–hip ratio, a measure of abdominal obesity. A recent meta-analysis of 30 prospective studies revealed an increasing risk of colon cancer with increasing waist–hip ratio (per 0.1 unit) in men (RR = 1.43; 95 % CI, 1.19–1.71) and women (RR = 1.20; 95 % CI, 1.08–1.33).
- 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 insulin growth factor (IGF) peptides. High IGF-1 levels are associated with cell proliferation and may increase the risk of colonic neoplasia.
- In the past, most studies have demonstrated a stronger association between obesity and CRC risk in men than in women.

- In postmenopausal women, the increased estrogen production associated with obesity was thought to mitigate the risk. Of note, not all studies have confirmed this relationship.
- Obesity is also a risk factor for the development of colorectal adenomas, although like the risk of CRC, the effect appears to be stronger in men than in women.
- In a pooled analysis of six prospective trials involving 8,213 participants, obesity was statistically significantly associated with the risk of metachronous adenoma in men (OR = 1.36; 95 % CI, 1.17–1.58) but not in women (OR = 1.10; 95 % CI, 0.89–1.37).

Physical Activity

- Over 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, recreational, or total activity) is associated with a reduced risk of CRC.

Smoking

- Consistent with a 35–40 year time lag between exposure and induction of cancer, early studies did not demonstrate an association between cigarette smoking and colorectal neoplasia.
- Twenty-seven epidemiologic studies that demonstrate an association between tobacco and the risk of CRC have been conducted. Most demonstrate an association between heavy smoking and increased CRC risk. The majority of studies demonstrate an effect at relatively high levels of smoking (20 or more cigarettes per day).
- A meta-analysis of 106 studies revealed a positive dose–response relationship between increasing cigarette consumption and CRC risk. The risk increased by 7.8 % for every additional 10 cigarettes per day or by 4.4 % for every additional 10 pack-years. The incidence of CRC was 65.5 per 100,000 in smokers and 54.7 per 100,000 in nonsmokers.

Cholecystectomy

- Abnormal bile acid metabolism may predispose both to CRC and cholelithiasis.
- After cholecystectomy, increased quantities of secondary bile acids have been detected in the feces and may have a role in colonic carcinogenesis.
- A meta-analysis of studies evaluating the effect of cholecystectomy on CRC risk published in 1993 demonstrated conflicting results. Analysis of the 33 case–control studies generated a pooled relative risk of CRC after cholecystectomy of 1.34 (95 % CI, 1.14–1.57), limited to the proximal

colon. However, no significant effect was found when the results of six cohort studies were evaluated.

- In the Nurses' Health Study, a significant positive association between cholecystectomy and the risk of CRC was found (RR = 1.21; 95 % CI, 1.01–1.46 after adjusting for important CRC risk factors, including diet, family history, calcium intake, BMI, and the use of HRT). In this study, the risk of CRC after cholecystectomy was elevated both for proximal bowel and rectal cancers.
- Prior cholecystectomy does not seem to affect the risk of adenoma formation. In the Nurses' Health Study, no elevation in the risk of colorectal adenoma was identified in those patients having had a cholecystectomy.
- Similarly, in a study involving data from three large randomized adenoma chemoprevention trials, no increased risk for adenomas was observed for patients who had undergone cholecystectomy (RR = 1.02; 95 % CI, 0.88–1.18).

Inflammatory Bowel Disease

- Patients with long-standing inflammatory bowel disease (IBD) are known to be at an elevated risk of CRC, although it is difficult to precisely estimate the risk.
- A meta-analysis of 116 studies evaluating the risk of CRC in UC patients found the overall prevalence of CRC in UC patients was 3.7 % (95 % CI, 3.2–4.2 %). In 19 of the studies reviewed, the duration of colitis was reported by decade.
- A cumulative probability of CRC of 2 % after 10 years of disease, 8 % after 20 years, and 18 % after 30 years. The risk of CRC varied geographically and was higher in studies conducted in the USA. The meta-analysis did not evaluate the extent of disease (pancolitis vs. left-sided disease vs. proctitis).
- Two recent population-based studies from Denmark and the Mayo Clinic failed to demonstrate any increased risk of CRC in ulcerative colitis patients. This may be impacted by better medical therapy and earlier selection of IPAA in the modern era.
- Denmark followed a median of 19 years. The observed number of CRC cases was almost identical to the expected number (13 vs. 12.42, SIR = 1.05; 95 % CI, 0.56–1.79).
- The extent of disease does appear 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.
- Other factors that may modify the risk of CRC in patients with UC include the coexistence of primary sclerosing cholangitis (PSC), presence of inflammatory pseudopolyps, and severity of inflammation.
- The relationship between Crohn's disease and the development of CRC has been less consistently demonstrated. In studies using data from

referral-based practices, the risk of development of CRC appears to be significantly increased in patients with extensive Crohn's colitis.

- In a Canadian population-based cohort study, the risk of CRC in 2,857 patients with Crohn's disease was compared to a randomly selected group of controls matched 10:1 for age, sex, and geographic location. Patients with Crohn's disease were found to have an elevated risk of colon cancer (incidence rate ratio (IRR) = 2.6; 95 % CI, 1.69–4.12) but not rectal cancer (IRR = 1.08; 95 % CI, 0.43–2.70). Patients with Crohn's disease also had an elevated risk of cancer of the small intestine (IRR = 17.4; 95 % CI, 4.16–72.9) and lymphoma (IRR = 2.40; 95 % CI, 1.17–4.97).
- In summary, it appears that the risk of CRC in patients with Crohn's disease is elevated, but the exact magnitude of increased risk remains unclear and requires further investigation.

Family History

- Individuals with a family history of CRC are at an increased risk of themselves developing CRC.
- In a recent meta-analysis involving 59 studies, the relative risk of developing CRC with one affected first-degree relative was 2.24 (95 % CI, 2.06–2.43) and 3.97 if more than two first-degree relatives were affected. This corresponds to a pooled lifetime risk of a 50-year-old of 1.8 % with no family history, 3.4 % with one affected first-degree relative, and 6.9 % with two or more first-degree relatives.
- Some of the increased risk attributed to family history is due to inheritance of known susceptibility genes, such as mutations in the APC gene, p53 gene, or in MMR genes, particularly MSH2, MLH1, and MSH6; these are discussed in detail elsewhere in this text.

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. Close observation may be required for survivors of childhood pelvic tumors treated with radiation therapy, as secondary colorectal malignancies may develop decades later.

Ureterosigmoidostomy

- Formation of a ureterosigmoidostomy has been associated with an increased risk of carcinoma in the area of the ureterosigmoid anastomosis.
- 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 develop neoplasia at the anastomosis.

- The average latency period from the formation of the ureterosigmoidostomy to the development of malignancy is 26 years.

Acromegaly

- Acromegaly, a rare endocrine syndrome resulting from the secretion of excess growth hormone from a pituitary neoplasm, has been found to be associated with an increased risk of CRC in a number of studies. The magnitude of the risk is unclear, with reports ranging from nonsignificant increases in the risk to a relative risk of 18.3.
- Patients with acromegaly also have an increased incidence of adenomatous polyps.

Molecular Basis

- All cancer has a genetic basis. Carcinogenesis is a multistep process, requiring an accumulation of inherited and acquired genetic alterations.
- Hanahan and Wienberg have described the following six alterations in regulatory mechanisms that appear constant in most cancers from the several hundred genetic mutations that have been identified in cancer cells Fig. 38.4.
- 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, where as others tend to occur later and are termed promoters.
- 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 the development of critical alterations in the mechanisms of cell regulation. Mutations causing such expression behave in a dominant fashion, 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 colorectal cancers. The K-ras proto-oncogene, located on the short arm of chromosome 12 (12p) is mutated in approximately half of all CRC.
- The K-ras gene product appears 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. Patients with mutant K-ras may have a poor response to the chemotherapeutic agent Erbitux.

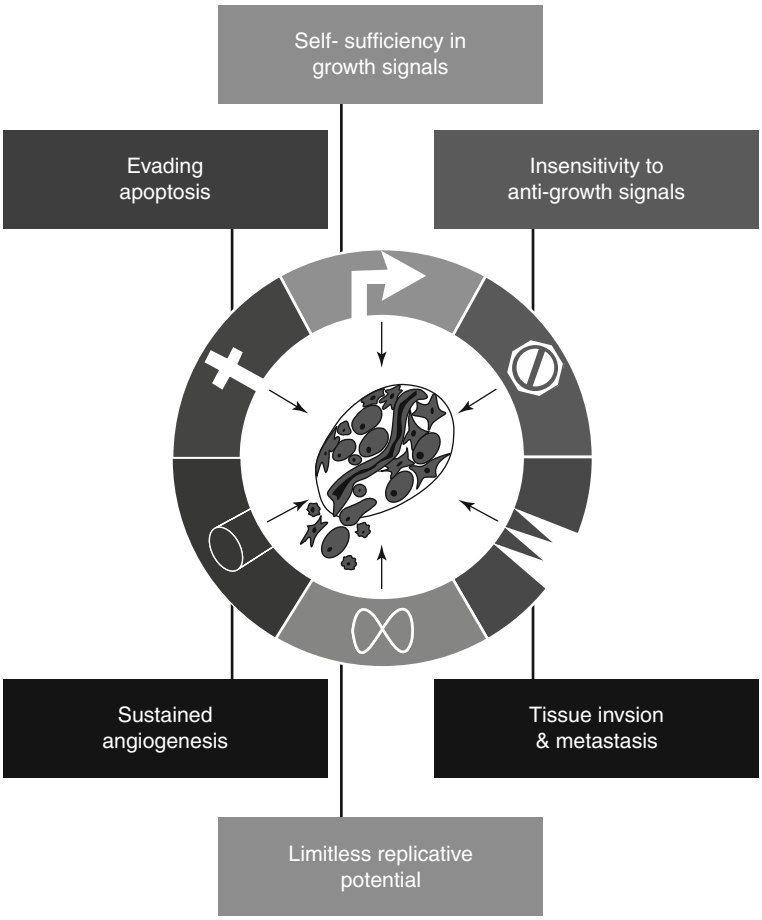

Fig. 38.4 Alterations in regulatory mechanisms important for carcinogenesis

- Other oncogenes that are frequently identified in sporadic CRC include c-myc and c-erbB2.
- Tumor suppressor genes normally inhibit cellular proliferation or promote apoptosis. When gene expression is lost, there is a 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 2-hit theory of carcinogenesis, Fig. 38.5) either through inherited mutation, somatic mutations, or both. There are a number of tumor suppressor genes that have been found to play an important role in CRC carcinogenesis, including the APC, DCC, p53, and MCC genes.
- The 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 appear to be initiators of disease. Mutations in the APC gene

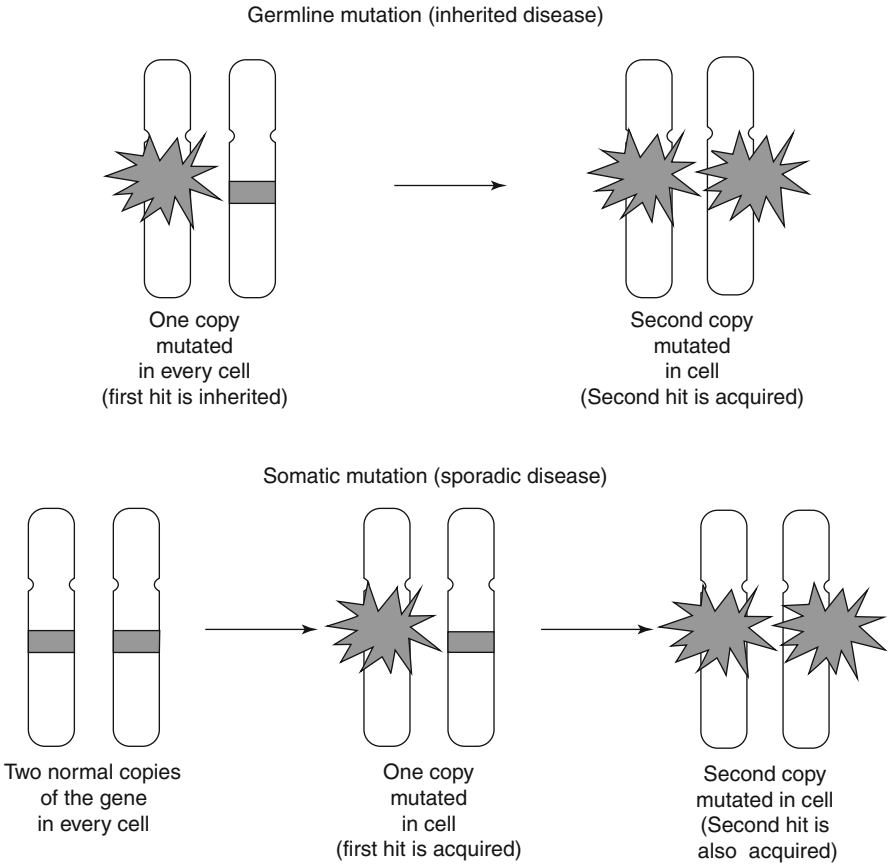

Fig. 38.5 Loss of suppressor-gene function

have been found in 50 % of sporadic adenomas and in 75 % of sporadic cases of CRC.

- Familial adenomatous polyposis (FAP), discussed in detail in Chap. 37, 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 the formation of a truncated or shortened protein product that affects the function of the protein.
- 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 result in 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 commonly mutated gene in human cancers.
- Normally, by slowing the cell cycle, p53 facilitates DNA repair during replication and when repair is not feasible, p53 induces apoptosis. Inactivation of p53 is found in up to 75 % of sporadic colorectal tumors; however, the mutation appears to occur late in the tumorigenic sequence.
- Patients with Li–Fraumeni syndrome (an inherited defect in p53) do not have an increased risk of CRC.
- 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 to 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) in 1989. Mutations in this gene have been found in the majority of CRC. 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.
- Located in close proximity to the DCC gene, mutations in a group of genes terms SMADs (SMAD2 and SMAD4) have been reported in colorectal cancers. The protein products of these genes are components of the transforming growth factor-b (TGF-p) signaling pathway, which mediates growth inhibitory signals from cell surface to nucleus.
- 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 of errors in DNA replication, increasing the probability that a mutation in an important gene in cell regulation occurs and carcinogenesis is thus initiated or promoted. Defects in the MMR system are identified by the detection of microsatellite instability.
- 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 demonstrate MSI.

- MSI-H tumors are more likely to be high-grade, right-sided, and 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) (discussed elsewhere in the text), while approximately 5–10 % of HNPCC cases are due to mutations in the MSH6 gene.
- Germline mutations in other MMR genes are rare.
- MMR defects in these tumors lead to genetic mutations in key cell regulator genes, particularly the TGF-β pathway.
- Sporadic tumors that demonstrate an MSI-H phenotype generally have a loss of MLH1 function, not due to mutation but due to aberrant methylation of the promoter region of the MLH1 gene (see below).
- MYH is an additional DNA repair gene specifically active for adenine-guanine mismatches. This gene has been found to be responsible for some cases of APC mutation-negative FAP. This defect is inherited in an autosomal recessive fashion, i.e., defects must be inherited from both parents to result in phenotypic expression of the disease. Biallelic carriers have a 53-fold increased risk of CRC with a cumulative risk by age 70 of 80 %. Monoallelic carriers may also be at increased risk to develop CRC; relative risk estimates for monoallelic carriers have ranged between 1.4 and 3.0.
- In their landmark article, Vogelstein and Fearon (Fig. 38.6) described the pathogenesis of colon cancer as one that follows a predictable sequence of events, from adenoma to carcinoma. 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.
- Although MSI-H tumors may arise from adenomas, there is increasing evidence that sporadic MSI-H tumors also arise from serrated lesions (hyperplastic polyps, serrated adenomas, and sessile serrated adenomas).
- As only 70 % of colorectal carcinomas are believed to arise from classic adenomas, serrated lesions may be the precursor lesion for a substantial number of cancers. The serrated adenoma-carcinoma pathway is believed to be initiated by hypermethylation of the promoter region of various genes and is associated with increasing age.
- Methylation of cytosines in cytosine-guanosine dinucleotide repeats (termed CpG islands) results in the silencing of transcription, without an actual change in the nucleotide sequence of the gene.

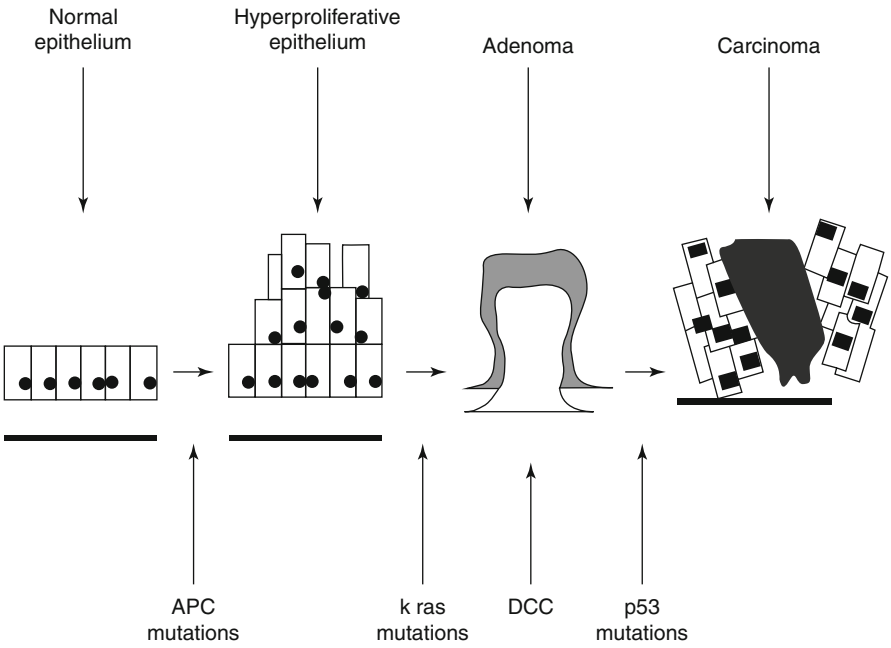

Fig. 38.6 The adenoma to carcinoma sequence of colorectal carcinogenesis

- Tumors exhibiting this phenomenon are referred to as CpG island methylator phenotype (CIMP).
- Although the MLH1 gene is often involved (resulting in sporadic, MSI-H CRC), it need not be, and thus approximately 50 % of CIMP tumors do not exhibit microsatellite instability. Accumulating evidence indicates that activating somatic mutations in the BRAF gene may be responsible for promoter methylation. The MCC gene may also play a key role in this pathway.
- Hyperplastic polyposis (HPP) syndrome is characterized by multiple hyperplastic polyps and other serrated lesions and may be familial. There may be an autosomal recessive pattern of inheritance, and the familial HPP-serrated lesions show a similar frequency of CIMP and BRAF mutations compared to sporadic serrated polyps.

39. Colorectal Cancer Screening

Jason F. Hall and Thomas E. Read

Introduction

- Without undergoing screening or preventive action, approximately 1 in every 17 people in this country will develop colorectal cancer at some point in life.
- There is clear evidence that colorectal adenocarcinoma can be prevented by detecting and removing adenomatous polyps and that detecting early-stage cancers reduces mortality.
- Both polyps and early-stage cancers are usually asymptomatic; cancers that have grown large enough to cause symptoms have a much worse prognosis.
- In 1996, the federal Agency for Health Care Policy and Research (AHCPR) convened a collaborative group of experts to develop appropriate clinical practice guidelines.
- The AHCPR guidelines have provided the framework for colorectal cancer screening.
- Most people will be of average risk and require screening for colorectal cancer and polyps beginning at age 50. People with increased risk (inherited predisposition) may need screening or treatment as early as puberty.

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Table 39.1 Patients with colorectal cancer

75 %	Average risk (sporadic)
15–20 %	Family history of colorectal cancer
3–8 %	Hereditary nonpolyposis colorectal cancer
1 %	Familial adenomatous polyposis
1 %	Ulcerative colitis

Classification of Risk and Screening Recommendations

- Appropriate recommendations for screening depend on determining a patient's risk of development of colorectal cancer.
- The cornerstone of risk is a family history.

Average Risk

- The majority of patients who develop colorectal cancer have no identifiable risk factors (Table 39.1).
- 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.
- In October 2008, the US Preventive Task Force recommended that average-risk persons should undergo one of the following screening regimens, beginning at age 50 and continuing until age 75 (Table 39.2):
  - High-sensitivity fecal occult blood testing (FOBT) annually
  - Flexible sigmoidoscopy every 5 years with high-sensitivity FOBT every 3 years
  - Colonoscopy every 10 years
- The American College of Gastroenterology guidelines (updated in 2008) outline a "preferred" strategy for colorectal cancer screening suggests that patient compliance increased when there is a "preferred" strategy rather than a "menu" of options. Preferred screening recommendations for average-risk persons beginning at age 50 included one of the following (screening should begin at age 45 in black patients):
  - Colonoscopy every 10 years
  - Annual fecal immunochemical test (FIT) for blood
  - Alternative prevention tests
  - Flexible sigmoidoscopy every 5–10 years
  - CT colonography every 5 years
  - Alterative cancer detection tests
  - Annual Hemoccult SENSA
  - Fecal DNA testing every 3 years

Table 39.2 Screening for colorectal cancer and polyps

Risk category	Screening method	Age to begin screening
Average risk	Choose one of the following: 1. High-sensitivity FOBT annually[a] 2. Flexible sigmoidoscopy every 5 years combined with high-sensitivity FOBT every 3 years[a] 3. Colonoscopy every 10 years	50 years
Family history	Choose one of the following: 1. Colonoscopy every 10 years 2. Colonoscopy every 5 years if diagnosis of colorectal cancer was made before age 60 3. Air-contrast barium enema every 5 years[b]	40 or 10 years prior to diagnosis of the youngest affected family member, whichever is earliest
Lynch syndrome	Colonoscopy every 1–3 years Genetic counseling Consider genetic testing	21 years
Familial adenomatous polyposis	Flexible sigmoidoscopy or colonoscopy every 1–2 years Genetic counseling Consider genetic testing	Puberty
Inflammatory bowel disease (ulcerative colitis and Crohn's colitis)	Colonoscopy with random biopsies for dysplasia every 1–2 years	7–8 years after the onset of pancolitis; 12–15 years after the onset of left-sided colitis

FOBT fecal occult blood test

[a]The American Cancer Society recommends the combination of yearly FOBT and flexible sigmoidoscopy is preferable to either examination alone

[b]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

Fecal Screening Tests

- Several large randomized controlled trials as well as high-quality systematic reviews have shown that annual or biannual 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.
- Testing of three samples is more sensitive than testing of a single sample.
- An alternative method of FOBT is the fecal immunochemical test which employs antibodies specific to blood components.
- A major drawback to using stool testing 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 that in the research environment.

- The steps necessary for adequate sample collection, combined with dietary restrictions to avoid agents that can cause false-positive and false-negative results may also hinder compliance with FOBT.
- Proper performance of FOBT involves the sampling of atraumatically obtained stool from three consecutive bowel movements in a patient who has not ingested red meat, aspirin, nonsteroidal inflammatory medications, turnips, melons, salmon, sardines, horseradish, or vitamin C for the 2 days preceding the test and throughout the test period.
- FOBT should not be confused with random stool guaiac testing, which is the analysis of stool found on digital rectal exam for blood. The lack of adequate diet and medication restriction prior to 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.
- In the future, immunochemical techniques or genetic analysis of cellular material in stool may prove to be more effective than current FOBT technology.
- In 2004, the Colorectal Cancer Study Group compared Hemoccult II with fecal DNA testing (21 mutations) in 5,486 patients who subsequently underwent a colonoscopy. The sensitivity of the fecal DNA test for advanced neoplasms (cancer, adenomas with villous or dysplastic histology, adenomas $\geq$10 mm) was 18 % in comparison to Hemoccult II, which was 11 %. The specificities were 94 and 95 %, respectively. Other studies have been less convincing and it remains unclear whether there are adequate data to support widespread use of fecal DNA tests as a viable colorectal cancer screening strategy.

Sigmoidoscopy

- 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 Prostate, Lung, Colon, and Ovary Trial supported by the National Cancer Institute evaluated flexible sigmoidoscopy in a randomized, controlled setting and found that incidence was decreased by 21 % and death was decreased by 26 % over an average of almost 12 years.
- In this trial, wide variability in polyp detection rate was observed between endoscopists, which raises concern regarding adequacy of the examination in the hands of inexperienced endoscopists.
- Flexible sigmoidoscopy alone will fail to detect neoplasms in the proximal colon unless adenomatous polyps or cancer are found in the distal colon that prompt colonoscopy. For this reason, the American Cancer Society recommends combining flexible sigmoidoscopy every 5 years

with annual FOBT, rather than utilizing flexible sigmoidoscopy alone as a screening method.

- Although this combined approach may detect more proximal neoplasms than flexible sigmoidoscopy alone, 15–30 % of patients with negative flexible sigmoidoscopy and negative FOBT will have neoplastic lesions in the proximal colon at colonoscopy.

Contrast Enema

- 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 reduce the incidence and mortality from colorectal cancer.
- Single-column barium enema is less sensitive and should be combined with flexible sigmoidoscopy, if used as a screening tool.
- Proctoscopy should be considered as an adjunct exam because the balloon on the enema catheter often prevents adequate imaging of the distal rectum.
- Another major limitation of barium enema is the requirement of colonoscopy if lesions are detected.

Colonoscopy

- 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.
- Although its effectiveness depends on the skill and experience of the endoscopist to both reach the cecum and identify small lesions, it remains the gold standard to evaluate the colonic mucosa. The ability of colonoscopy to reduce colorectal cancer mortality has been recently confirmed by a long-term prospective observational study published in 2012 in the NEJM. In the study, CRC mortality was reduced by 53 %. Compliance with screening colonoscopy may be superior to that of other methods because no confirmatory exams are required, and thus, patients are subjected to a single cathartic bowel preparation.

Virtual Colonoscopy or MR

- CT colonography (virtual colonoscopy) was developed in an attempt to increase compliance with colorectal cancer screening, based on the impression that people would be more inclined to have a “scan” than a “scope.”
- The technique involves thin-section computed tomography (CT) or magnetic resonance (MR) with three-dimensional computer reconstructions to examine the colonic mucosa.

- Although the technique has the advantages of being considered "noninvasive" and not requiring sedation, a vigorous oral cathartic laxative preparation is required, because adherent stool cannot be reliably differentiated from neoplasia on CT. In addition, a rectal catheter and air insufflation is utilized to distend the colon.
- Recent improvements in technology and experience with interpretation have resulted in improved performance of the test.
- The sensitivity for the detection of polyps 10 mm or larger can be up to 90 % with a specificity of 86 % in the hands of interested radiologists. Polyps that are 6 mm or larger have detection rate of up to 78 % with a specificity of 88 %. CT colonography is both less sensitive and less specific in the detection of polyps less than 6 mm in size.
- Controversy exists regarding the size of polyp detected at CT colonography that should prompt optical colonoscopy.
- Regardless of its accuracy, CT colonography suffers (as does contrast enema) from the disadvantage that biopsies cannot be obtained and positive findings require endoscopic confirmation.
- It is estimated that 27–69 % of patients who have CT colonography will have at least one potentially pathologic finding in an organ outside of the colon.
- For all these reasons, CT colonography is not utilized at most centers as the preferred initial screening test.
- CT colonography is an excellent choice: for the evaluation of a patient who has just had an incomplete colonoscopy (the colon is already prepared and it is distended by air) and for patients who must remain on anticoagulants.

Cost and Reimbursement

- In 2001, CMS authorized reimbursement for screening colonoscopy for average-risk persons.
- As of January 2010, the CMS guidelines for reimbursement for colorectal cancer screening include the following (excerpted from their website, http://www.cmshhs.gov/ColorectalCancerScreening):
  - Fecal occult blood test (FOBT) – once every year.
  - Flexible sigmoidoscopy – once every 4 years.
  - Colonoscopy – once every 2 years, if the patient is at high risk for colon cancer, and once every 10 years (but not within 47 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.
- The American College of Gastroenterology suggested that screening colonoscopy every 10 years beginning at age 50 is the preferred 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.
- Patients who undergo curative intent 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 US Multi-Society Task Force on Colorectal Cancer and the American Cancer Society updated guidelines for colonoscopy after polypectomy and colorectal cancer resection in 2012. This panel recommended that patients with hyperplastic polyps in the rectum or sigmoid should be considered average risk and therefore screened every 10 years, as with patients with normal colonoscopy. Patients with an adenomatous or sessile serrated polyp greater than 1 cm should have a repeat colonoscopy in 3 years. Patients who have 3 or more tubular adenomas or adenomas with villous features or high-grade dysplasia are also recommended to have a surveillance colonoscopy in 3 years, as are patients with sessile serrated polyps with dysplasia or traditional serrated adenomas. Patients with fewer than three small adenomas may be surveyed every 5–10 years.
- A rational surveillance strategy should take into account the patient's age, comorbid conditions, life expectancy, completeness of prior examinations, pattern of neoplastic growth, family history, and histologic features of previously resected neoplasms.
- For example, a patient in good health who is found to have adenomas that are multiple, large, sessile, dysplastic, or removed in a piecemeal fashion 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 may not benefit from surveillance examinations, because removal of premalignant lesions will probably not alter lifespan or quality of life.

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 familial adenomatous polyposis (FAP).

- As a greater understanding of the molecular genetics of colorectal cancer is gained, many patients with familial colorectal cancer may eventually be categorized as having distinct inherited syndromes.

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 prior to the age at diagnosis of the affected relative, whichever is earliest.
- Those patients whose first-degree relatives developed colorectal cancer prior to 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.
- More recently, the American College of Gastroenterology recommended that patients with a single first-degree relative (<60 years) with colorectal cancer or an adenoma >1 cm or an adenoma with villous features or high-grade dysplasia begin screening at age 40 or 10 years before the diagnosis in the youngest affected relative. This recommendation emphasizes that an increased level of screening is not recommended for a history of adenomas without adverse features in a first-degree relative.

Lynch Syndrome

- Lynch syndrome (formerly hereditary nonpolyposis colorectal cancer syndrome) is an inherited disorder that predisposes patients to the development of colorectal cancer, with up to 75 % of patients developing colorectal cancer by age 65. Lynch syndrome is inherited in an autosomal dominant fashion and is thought to be the result of germline mutations in mismatch repair genes (genes that code for proteins responsible for correcting errors during DNA replication).
- Patients with Lynch syndrome typically develop cancer between age 40 and 50 and most tumors occur proximal to the splenic flexure.
- "Nonpolyposis" in the term "hereditary nonpolyposis colorectal cancer" refers to the distinction between Lynch syndrome and FAP (in which patients have hundreds of polyps) but is somewhat misleading as patients with Lynch syndrome will develop adenomatous polyps.
- The major distinction is that progression from adenoma to carcinoma appears to be accelerated in Lynch syndrome patients as compared to patients with sporadic cancers and FAP, and there is a tendency to develop multiple colorectal cancers in Lynch syndrome.

- Patients with Lynch syndrome have germline mutations and are also at high risk for the development of other cancers including endometrial, ovarian, gastric, transitional cell, small bowel, and hepatobiliary neoplasms.
- 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 %).
- The Amsterdam I 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 prior to age 50) are the most stringent criteria and have the highest concordance with known mismatch repair gene mutations.
- However, they fail to identify patients who may be affected with Lynch syndrome 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 Lynch syndrome.
- The Bethesda criteria were developed to acknowledge the shortcomings of the Amsterdam I criteria as clinical guidelines and to expand the clinical suspicion of Lynch syndrome to a broader range of patients.
- Microsatellite instability has been reported in 85–90 % of Lynch syndrome 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.
- Patients who satisfy the Bethesda criteria should have immunohistochemistry staining for mismatch repair proteins or microsatellite testing of their, or an afflicted family member's, neoplasm.
- Germline mutational analysis can then be performed.
- If a proband tests positive, the appropriate family members can be offered screening.
- 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.
- The American College of Gastroenterology recommends that persons who are members of a family that fits clinical criteria for Lynch syndrome undergo colonoscopy at age 20–25 and repeat colonoscopy every 2 years until age 40.
- The panel recommends that patients should have annual colonoscopies after age 40.
- Patients and at-risk family members should be referred for genetic counseling.

Familial Adenomatous Polyposis

- Familial adenomatous polyposis (FAP) is caused by a germline defect in the adenomatous polyposis coli gene, which is inherited in autosomal dominant fashion.
- 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 extracolonic 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.
- At present, germline mutational analysis is the preferred method of confirmation of the disease. If patients suspected of having FAP are not found to have an APC mutation, then MYH polyposis should be considered.
- Patients with a family history of FAP should undergo flexible sigmoidoscopy or colonoscopy at puberty.
- Lower endoscopy should be repeated every 1–2 years.
- Patients with FAP should undergo upper endoscopic surveillance every 1–3 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 genetic 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.

Inflammatory Bowel Disease

- Patients with ulcerative colitis have an increased risk of developing colorectal cancer, due to the chronic effects of inflammation on the mucosa, leading to malignant degeneration.
- The altered appearance of the mucosa often makes carcinomas difficult to identify endoscopically.
- Frequent colonoscopy with random biopsy is recommended, in an attempt to identify early-stage carcinomas or premalignant change (dysplasia) that would predict the presence of occult carcinoma or predict the subsequent development of carcinoma. Proctocolectomy could then be performed for cure or prophylaxis.

- The risk of colorectal cancer in patients with Crohn's disease is now considered to be similar to that of patients with ulcerative colitis and therefore they should be screened in similar fashion.
- Patients with inflammatory bowel disease are recommended to undergo screening colonoscopy with multiple random biopsies looking for dysplasia every 1–2 years, beginning 7–8 years after disease onset in patients with pancolitis and 12–15 years after disease onset in patients with left-sided colitis.
- Definitive evidence that surveillance colonoscopy with random biopsies reduces mortality, or is better than timing a colectomy according to extent and duration of disease, is lacking.

Future Directions

- Much energy and expense are devoted to the cure of advanced or recurrent colorectal cancer in the USA, while little is devoted to screening for polyps and early-stage cancers.
- In 2012, the US General Accounting Office found that colorectal cancer screening is the least utilized preventive health benefit available to Medicare beneficiaries (General Accounting Office, Medicare – Beneficiary Use of Clinical Preventive Services, Report No. GAO-12-81; January 2012).
- Recent data suggest that among Medicare beneficiaries aged 65–80, colonoscopy rates have increased while FOBT rates decreased. Both health care professionals and the public need to become more aware of the potential benefits of colorectal cancer screening.

40. Colon Cancer Evaluation and Staging

Eric G. Weiss

Introduction

- Colorectal cancer is the third most common cancer affecting persons in the USA. In 2008, there were an estimated 148,810 new cases of colon and rectal cancer with colon cancer making up the majority of new cases at 107,143 and the remaining 28 % arising in the rectum.
- Overall, approximately one-third of newly diagnosed patients with colorectal cancer in the USA will die of their disease.

Clinical Presentation

- Colon cancers diagnosed in patients who are asymptomatic and undergoing screening or surveillance have a very favorable prognosis.
- The most common presenting symptoms are abdominal pain, change in bowel habits, rectal bleeding, and occult blood in the stool.
- Abdominal pain is the most common presenting symptom of colon cancer.
- A change in bowel habits is the second most common symptom and entails narrowing of the stool, irregular shape, and typically looser or diarrheal stool. Symptoms depend on the location of the tumor.
- Symptoms are more frequently associated with a more advanced tumor.
- Larger masses cause obstruction with crampy, colicky pain, associated with or after meals.

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- Rectal bleeding may be present in as many as 25 % of patients with colon cancer. The bleeding may be of varying intensity and color. Bright red rectal bleeding is more consistent with a more distal location of a cancer.
- 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.
- Most patients regardless of age who present with rectal bleeding should undergo colonoscopic evaluation or a minimum flexible sigmoidoscopy depending on patient age and characteristics of the bleeding.
- 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.

Staging and Prognostic Factors

Evolution of Staging Systems

- The original staging system for colorectal cancer was reported by Cuthbert Dukes (a British pathologist) in 1930 and then revised by him in 1932. Subsequently others have made modifications.
- The TMN staging system is the current preferred method of colorectal cancer staging.

Current Staging Systems

- Staging is important for treatment planning and prognosis.
- The TNM classification was developed by the American Joint Committee on Cancer (AJCC) and the International Union Against Cancer (UICC) (Table 40.1). It utilizes three descriptors: 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 most recent AJCC/UICC definitions were published in 2010.
- The T stage can be divided into categories based on the depth of invasion. Tis, carcinoma in situ, represents a nonmalignant 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), T4a has penetration to the surface of the visceral peritoneum, and T4b has invasion of other organs or structures.
- The N stage can also be divided into categories: N0, with no lymph node involvement; N1, with one to three lymph nodes involved (N1a, one node involved; N1b with two to three involved nodes; N1c with tumor deposits in the subserosa mesentery or pericolic tissues); and N2, with four or more lymph nodes involved.

Table 40.1 *AJCC* anatomic stage/prognostic groups

Stage	T	N	M
0	Tis	N 0	M 0
1	T 1–2	N 0	M 0
2 A	T 3	N 0	M 0
2 B	T 4 a	N 0	M 0
2 C	T 4 b	N 0	M 0
3 A	T 1–2	N 1	M 0
3 B	T 3–4	N1	M 0
	T 1–3	N2a	M 0
	T 1–2	N 2b	M 0
3 C	Any T	N2	M 0
	T 4b	N1a-b	M 0
4	Any T	Any N	M 1

From AJCC 7th Ed.

- The M stage is divided into two main categories, either no metastases (M0) or distant metastases (M1). M1 is further divided into M1a and M1b (M1a, metastases confined to one organ or site; M1b, metastases in more than one organ/site).
- The combination of T, N, and M will lead to one of the four stages based on the combination of findings.

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 prior to this age.
- Patients with Lynch syndrome (HNPCC) can present at any age, but tend to have colon cancer between the ages of 40 and 50.
- Younger patients present with worse tumors of more advanced stage and grade. However, stage for stage they have an equivalent or improved 5-year survival.

Presentation

- Obstruction and perforation are poor prognostic signs often associated with advanced disease. In addition, because patients are operated on in an urgent fashion, their operative morbidity and mortality is increased.

- Perforated cancers had a 9 % operative mortality compared to obstructed cancers of 5 %. Overall 5-year survival was 33 % in each group, much lower than the expected rate based on similar stages in noncomplicated cases.

Blood Transfusion

- Blood transfusions can cause immunosuppression in the postoperative 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 (occurs in 5–12 %) can involve any structure or organ adjacent to the primary tumor (T4b).
- For right colon cancers the most commonly involved structures are the liver, duodenum, pancreas, and abdominal wall. Extended resections (en bloc) provide equivalent survival compared to similar T3 tumor.

Histologic/Biochemical/Genetic Factors

Histologic Grade

- Broders classified adenocarcinomas by the degree of differentiation. He originally described four grades.
- Today, 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 to better differentiated tumors.

Tumor Budding

- Tumor budding is now recognized and reported by pathologists and represents an undifferentiated portion of tumors at the leading invasive edge.
- Tumor budding is associated with a high risk of recurrence. In addition, it has been associated as an independent risk factor for local spread, lymph node and distant metastases, and worse survival.

Microsatellite Instability (MSI)

- The most common pathway for the development of colorectal cancer is via the mechanism of chromosomal instability pathway (microsatellite stable or MSS). This pathway is responsible for an estimated 80–85 % of all colorectal cancers.
- The remaining 15–20 % of colorectal cancers occur via a different pathway associated with a high frequency of MSI.
- MSI is associated with HNPCC, although only about 20 % of patients with MSI tumors will be due to HNPCC. MSI is an alteration in mismatch repair genes, which are important to repairing errors in replication. Since there is preexisting loss of one of the two alleles in HNPCC, these patients tend to present earlier in life, with multiple colonic and extracolonic cancers.

Signet-Cell Histology

- Signet-ring or signet-cell tumors have a worse prognosis.
- Patients with signet-ring cancers were younger, had more advanced stages, and had an increased incidence of liver metastases. In addition, the rate of curative resection was lower at 35 % compared to 79 %.

Venous Invasion

- Blood vessel invasion has been linked with poor prognosis both independently as well as with its association with lymph node metastasis.
- Although arterial invasion occurs, most series define and describe vascular invasion based on venous invasion.
- Venous invasion in colon cancer occurs in up to 42 % of patients and increases with increasing grade and stage. Patients with blood vessel invasion had a 74 % survival compared to those without it at 85 %. In those patients with both intramural and extramural vascular invasions, the prognosis was even worse at 32 %.

Perineural Invasion

- The growth of tumor along perineural spaces is known as perineural invasion, and like venous invasion, it increases with increasing grade and stage of the tumor. It occurs in 14–32 % of colorectal cancers and can extend to as far away as 10 cm from the primary tumor.
- Numerous studies have confirmed poorer prognosis when perineural invasion is noted.

Lymph Node Involvement

- Lymph node metastasis is one of if not the most important prognostic factor in colon cancer outcome.

- All currently utilized staging systems rely on the presence or absence of lymph node metastases.
- Scott and Grace reported that at least 13 lymph nodes are required for adequate staging.
- 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 PCR techniques.

Carcinoembryonic Antigen

- Carcinoembryonic antigen (CEA), discovered in 1965, is a glycoprotein absent in normal colonic mucosa, but present in 97 % of patients with colon cancer.
- Patients with disease confined to the colonic mucosa or submucosa will have elevated CEA in only 30–40 % of cases.
- In patients with elevated CEA preoperatively and localized disease that is resectable, the CEA should fall following surgery.
- If the CEA level does not fall, then occult metastases may be present.
- The absolute level of CEA is also important. A CEA of greater than 15 mg/ml predicts an increased risk of metastases in an otherwise apparently curable colon cancer. Even a patient with a normal preoperative CEA may present with a CEA elevated with metastatic disease. Following CEA postoperatively may allow a survival advantage in patients willing to undergo metastasectomy.

Patterns of Spread

- Colon cancer can spread via a variety of pathways. Spread can be local or distant based on these pathways.

Intramural Spread

- Intramural spread refers to tumor spreading along the bowel wall either proximally or distally in one of the bowel wall layers. Both rectal and cancers rarely spread this way.
- In a study of 42 colorectal cancers of which 64 % were colonic, the maximum extent of intramural spread was 2 cm. This 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

- As they advance, colon cancers invade deeper into the colonic wall. This colonic wall invasion is the basis of many of the currently used staging systems including the Dukes and TNM.

- T4 tumors penetrate full thickness through the colonic wall and then by direct extension or adherence and may invade into other structures in proximity to the primary tumor.
- When present, en bloc resection is mandatory for an R0 resection.
- Preoperative evaluation can sometimes predict adjacent organ involvement, but often it is an intraoperative finding.

Radial Margins

- The circumferential margins are important to both colon and rectal cancer, but most series and studies have been confined to rectal cancers. 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. Typically for colon cancer the only radial margin which may be involved in a tumor without adjacent organ invasion are those tumors with serosal involvement. In 279 patients with colon cancer, serosal involvement was not associated with a poorer outcome, and outcome was related only to tumor stage.

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. Most commonly 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 female patients, bilateral oophorectomy should be performed. In a recent series, 86 % of patients with ovarian metastases had transmural extension of the primary colon cancers.

Lymphatic

- Lymphatic spread is the most common path leading to metastatic disease.
- Lymphatics exist within the colonic wall, and lymphatic involvement correlates with the depth of penetration of colon cancers.
- T1 tumors have a risk of lymph node involvement up to 10 %, T2 up to 25 %, and T3 up to 45 %.

Hematogenous

- Hematogenous spread of colon cancer is less common than lymphatic spread. Hematogenous spread may occasionally bypass the liver and allow tumor cells to go peripherally into the systemic circulation (the mechanism for the development of pulmonary metastases).

Metastatic Evaluation

- Once a patient is diagnosed with colon carcinoma, a search for metastatic disease is often performed. This assessment includes a variety of imaging studies, laboratory tests, and endoscopic procedures.

Detection and Management of Synchronous Lesions

- Synchronous polyps and cancers occur frequently 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, CT colonography, intraoperative colonoscopy at the time of resection, or resection of the entire proximal colon.
- Synchronous cancers occur in 6 % or less of patients. When present, it should raise the suspicion of Lynch syndrome, which is associated with synchronous and metachronous colon cancer. When synchronous colon cancer is diagnosed, the treatment may include a subtotal colectomy.

Distant Metastatic Disease

- Distant metastatic disease usually involves the liver or lung.
- Bone, brain, and other organ involvement can occur, but is rare and therefore the search for these metastases in an asymptomatic patient is unwarranted.

Liver Metastases

- Surface ultrasound is available in almost all institutions; however, its accuracy compared to newer modalities is lower in studies comparing it to CT and liver scans.
- CT scan is the most commonly employed method to preoperatively and postoperatively determine the presence or absence of liver metastases associated with colon cancer. Advantages of CT over US 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 greater than 1 cm.
- With modern techniques MRI is also useful for evaluation of liver metastases.

Lung Metastases

- Lung metastases occur in 3.5 % of patients with colon cancer; there are limited data on the utility of plain chest radiographs or CT scans in the initial evaluation of the lungs for metastatic disease.

- 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 prior to surgical intervention, the addition of imaging of the chest via CT seems reasonable and is currently recommended in NCCN Guidelines.

PET Scans

- PET scans involve the IV administration of a glucose analog, 18F-flourodeoxyglucose (FDG). This glucose analog is preferentially taken up and trapped by tumor cells making those areas with trapped FDG show up brightly on PET scanning. Due to the lack of spatial resolution, the specific anatomic locations of the lesion(s) are difficult.
- Therefore combinations of PET with CT allow for precise spatial correlation and location with abnormally identified areas on PET.
- A recent meta-analysis was reported in 2005 using 61 published studies comparing CT, MR, and PET for the diagnosis of liver metastases in colorectal cancer. Comparisons of nonhelical and helical CT, 1.5 T MR, and FDGPET showed sensitivities of 60.2, 64.7, 75.8, and 94.6 %. FDGPET had a significantly higher sensitivity compared to the other studies.

Response to Potential Chemotherapy

- Recent publications and clinical trials have shown that patients with metastatic colorectal cancer benefit from treatment with monoclonal antibodies to EGFR.
- Monoclonal antibodies to EGFR include cetuximab, panitumumab, and the more commonly used bevacizumab.
- Patients with KRAS mutations do not benefit from this therapy.
- Patients without KRAS mutations are known as wild-type KRAS, whereas those with mutations are considered abnormal.
- A recent Provisional Clinical Opinion by the American Society of Clinical Oncology about testing for KRAS gene mutations was published in 2009.
- Other markers that may predict the response to anti-EGFR therapy include mutations of BRAF and PIK3CA or loss of PTEN expression.
- Thymidylate synthase (TS), an enzyme required for DNA synthesis and targeted by competitive inhibition by 5FU-based chemotherapy, can now be measured. Elevated levels of TS in tumor cells are associated with resistance to 5FU-based chemotherapy.

41. Surgical Management of Colon Cancer

Matthew Mutch and Christina Cellini

Introduction

- The two most important prognostic indicators for colon cancer remain the degree of bowel wall invasion and status of the lymph nodes. This supports the importance of adequate locoregional oncological principles when performing curative resections of colon cancer.

Preoperative Preparation

- Localization of the tumor and its histopathology are important in selecting an operative plan and the optimal resection margins.
- Colonoscopy is widely used today and represents the optimal means of detecting a cancer, identifying its location, providing histopathologic material, and tattooing for intraoperative localization when required. Precise localization of the lesion with ink tattooing is paramount in the era of laparoscopy since manual palpation may not be possible.
- The lesion should be inked in three separate areas around the circumference of the colon wall just distal to the lesion.
- Computed tomography (CT) allows the localization of larger lesions and identification of local organ invasion and provides important staging

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information regarding the presence of extracolonic disease, particularly liver involvement.

- Computed tomography is the most widely used imaging modality to screen for liver metastasis because of its availability and relative low cost compared to positron emission tomography (PET).
- However, combined PET/CT imaging appears to provide the most accurate detection of liver metastasis (PET alone 93 %, CT alone 92 %, and PET/CT combined 97 %).
- The PET scan has a role in detecting recurrent disease or extrahepatic disease when evaluating a patient for surgical resection of the local recurrence or liver metastasis.
- Bowel preparation has historically been considered an essential component of the preoperative preparation of the patient.
- More recent prospective randomized studies have questioned the additional benefit of luminal preparation, compared to the use of appropriate intravenous antibiotics administered in a timely manner.
- Slim et al. reported a review and meta-analysis of randomized controlled trials. They found no difference between the groups for anastomotic leak rate and the incidence of pelvic or abdominal abscess. There was a slightly higher risk of deep abdominal abscess with no bowel preparation; however, given that the number needed to have a complication was greater than 300 patients, they concluded that this risk did not seem to be clinically relevant.
- The study did not confirm the harmful effect of mechanical bowel preparation suggested in previous studies.

Surgical Technique

- Surgery remains the mainstay for the treatment of colon cancer. The 2000 National Cancer Institute issued principles of an oncologic resection: a wide mesenteric resection achieved by ligating the feeding artery at its origin with adequate distal and proximal margins and a minimum of 12 lymph nodes should be examined.
- Several studies support a survival benefit for patients who have 12 or more lymph nodes examined after surgical resection.

Right Colectomy

- Keys include clear lateral margins, resection of the locoregional lymph node-bearing mesentery for both cure and staging, and performance of an accurate and well-vascularized anastomosis.
- A right-sided hemicolectomy begins by gaining access to the retroperitoneum.
- This maneuver can be accomplished via four different approaches:
  - First, there is the traditional lateral to medial mobilization begun by incising the lateral peritoneal attachments of the colon.

Fig. 41.1 The drawing demonstrates the incision made at the root of the right colon mesentery just caudal to the third portion of the duodenum to the right of the superior mesenteric artery

  - Second, a posterior approach (Fig. 41.1) enters the retroperitoneum by reflecting the small bowel to the right upper quadrant and incising the peritoneum under the small bowel mesentery from the fourth portion of the duodenum to the cecum.
  - Third, the superior approach enters the retroperitoneum by opening the lesser sac and incising the peritoneum at the hepatic flexure.
  - Finally, with the medial to lateral approach, the ileocolic pedicle is grasped and elevated. The peritoneum on the caudal side of the pedicle is incised and the retroperitoneum is entered.
- Regardless of how the retroperitoneum is accessed, the principles of the resection are the same. The right colon mesentery is elevated off the retroperitoneum and the duodenum is identified. The lateral attachments are incised, and the hepatic flexure is fully mobilized.
- The ileocolic (Fig. 41.2) and right or hepatic branch of the middle colic vessels are ligated at their origins. The terminal ileum should be divided 10–15 cm proximal to the ileocecal valve to allow for good vascular

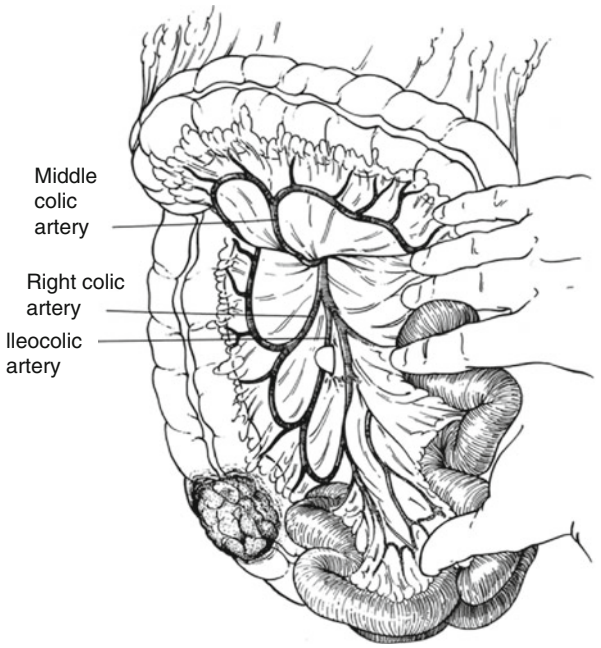

Fig. 41.2 The vessel(s) is elevated off the retroperitoneum, and a proximal ligation is performed at the origin of the superior mesenteric artery. The surgeon's finger is used to demonstrate the vascular origin for accurate placement of the ligation

supply (see Fig. 41.3 for extent of resection). The transverse colon is divided just to the right of the main trunk of the middle colic artery. The ileocolic anastomosis can be fashioned according to the desire of the operating surgeon. The authors prefer to divide the ileum and colon with linear staplers and perform a functional end-to-end anastomosis by anastomosing the antimesenteric surfaces of the bowel segments with a linear stapler and closing the remaining colostomy with a linear stapler or sutures.

Extended Right Colectomy

- An extended right colectomy may be performed for any lesion involving the transverse colon.
- The operation proceeds in similar fashion as the right colectomy described above. However, rather than proceeding through the transverse colon mesentery to ligate and divide the right branch of the middle colic artery, dissection continues in the retroperitoneal plane to identify the main middle colic arterial trunk anterior to the pancreas. This vessel is ligated and divided.
- The splenic flexure is released and the bowel with its mesentery is divided just proximal to the left colic artery, which is preserved for right-sided lesions.

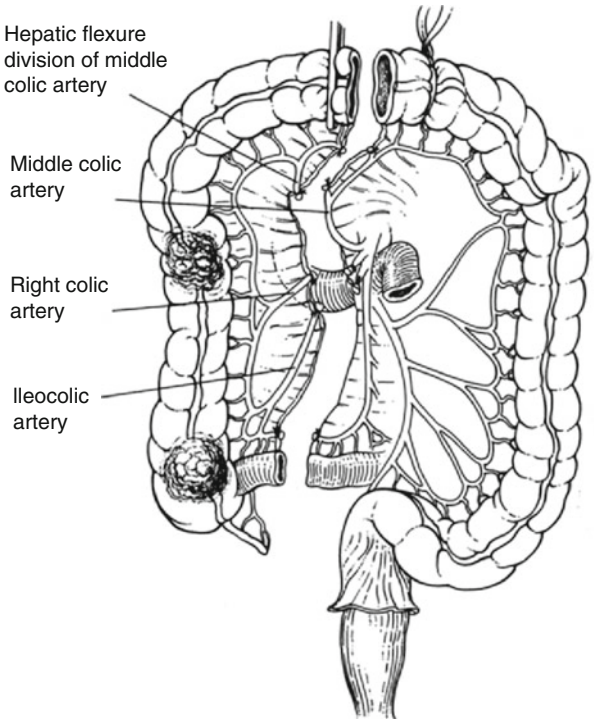

Fig. 41.3 The drawing demonstrates the appropriate levels for vascular ligation and colonic transition for a right hemicolectomy. Notably, the transverse colon is divided just to the right of the main trunk of the MCA, although the right branch of the MCA may be taken, if required. The middle colic vessels 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

- The left colic may be sacrificed for left transverse colon lesions, where a more distal colonic anastomosis is desired.

Left Colectomy

- The left colon can be mobilized in either a lateral to medial or medial to lateral approach.
- Resection of proximal left colon lesions may require division of the middle colic artery to allow the right transverse colon to reach the rectal stump for an anastomosis.
- A subtotal colectomy and ileosigmoid or ileorectal anastomosis may be preferable if there is any concern related to the blood supply. Another alternative is to perform a retroileal right colon to rectum anastomosis if maintenance of the right colon is desired (Fig. 41.4).

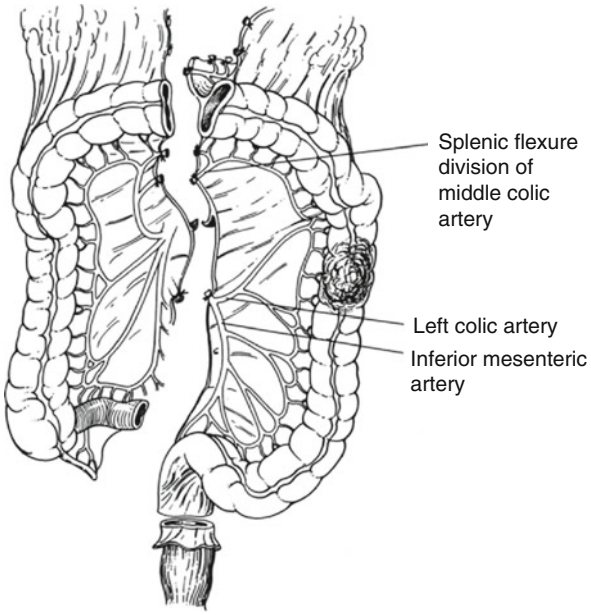

Fig. 41.4 The small bowel mesentery is mobilized to the right upper quadrant to expose the origin of the IMA located just caudal to the third portion of the duodenum. An incision running along the base of the left colic and sigmoid mesentery from the sacral promontory to the ligament of Treitz exposes 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 requires ligation and division for a formal left colectomy

Total Abdominal Colectomy with Ileorectal Anastomosis

- This procedure should be applied in specific circumstances, such as where 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 authors prefer a circular stapled end-to-end anastomotic technique (Fig. 41.5).

Special Circumstances

Acute Obstruction

- Acute colonic obstruction produces dilated bowel with a large amount of fecal loading proximal to the blockage.

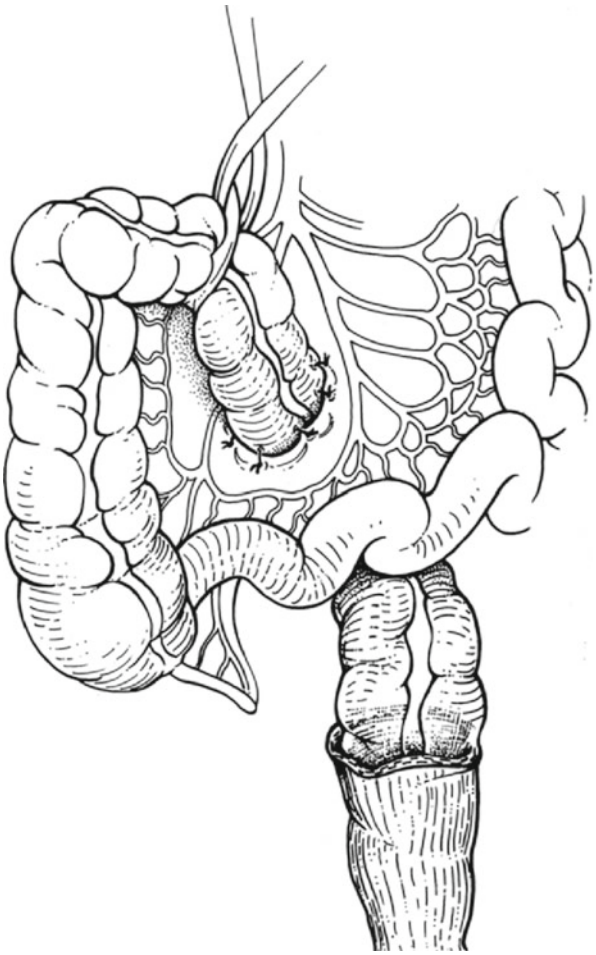

Fig. 41.5 An alternative method of reconstruction that preserves the right colon is a retroileal right colon to rectum anastomosis. This is performed by swinging the fully mobilized colon in a counterclockwise direction down into the pelvis to place the cut edge of the right colon mesentery across the pelvic brim

- The associated bacterial overgrowth coupled with possible impairment of blood flow in the proximal bowel has been the primary factors that have classically dictated resection and proximal diversion.
- On-table colonic lavage has been advocated as an alternative.
- More recently, endoscopically placed self-expanding metal stents have been used to manage patients with malignant large bowel obstruction.
- Colonic stenting can serve as a bridge to elective surgery converting an emergency procedure into an elective one in patients with operable cancers. Recent large reviews have reported technical and clinical success rates of over 90 %.

Prophylactic Oophorectomy

- The debate continues regarding the relative risks and benefits of a prophylactic bilateral oophorectomy.
- The potential benefits are the removal of an ovary seeded by colon cancer cells which manifests as a delayed metastatic site and the reduction in the risk of primary ovarian cancer in this age group.
- The data are limited for both issues. The risk of micrometastatic implants in the ovary increases with tumor stage and approaches 10 %.
- A comparison of cohorts of women with and without prophylactic oophorectomy could not demonstrate a survival advantage, but a 3.2 vs. 0 % risk of primary ovarian cancer in survivors with ovaries not resected was noted.

Colon Cancer and Abdominal Aortic Aneurysm

- The best answer is not available.
- 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.
- The best guidance suggests that any aneurysm >6 cm should be repaired first or synchronously with the removal of a colon cancer to avoid the risk of rupture.
- The advent of endovascular repairs, when feasible, allows the aneurysm and cancer to be addressed in either a staged fashion (endovascular repair followed by colectomy within the next couple of days) or synchronously under a single anesthetic.

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 prove to have more widely metastatic disease in several months.
- The risks of simultaneous colectomy and hepatectomy do not appear to be excessive in select patients operated by expert groups, and long-term survival rates seem to be similar.
- In the situation where liver metastases are unresectable, recent studies suggest that upfront chemotherapy without prophylactic resection of the primary tumor is appropriate. In addition, up to 16 % of previously unresectable patients can be downstaged and eventually undergo curative resection with as high as 40 % 5-year survival.

- The role of resection of the primary tumor in patients with unresectable liver metastases is debatable.
- Studies have shown that resection of primary lesions is safe, provides good local control, and allows the patient to proceed to adjuvant therapy in a timely fashion.
- In addition, some retrospective data suggest that noncurative resection of asymptomatic colorectal primary tumors may prolong survival when compared to nonresected patients.

Sentinel Node Assessment

- Sentinel node assessment was first described as a means of improving staging and treatment for melanoma patients and is currently considered the standard of care for breast cancer patients.
- There are several limitations in colorectal cancer:
  - First, there is no consensus of opinion regarding the prognostic significance of micrometastatic lymph nodes in colorectal cancer, particularly those identified by immunohistochemistry or PCR.
  - Second, the relatively high false-negative rates, and/or lack of node visualization, limit the confidence in restricting microsectioning and the use of special stains to the group with stained nodes.
  - Finally, there is limited data that the technique is sufficiently accurate to alter the extent of surgical resection in a reasonable number of patients.

Outcome of Colectomy for Colon Cancer

- In general, the operative outcome and long-term survival parallels the American Joint Committee on Cancer staging system (I, well above 90 %; II, 65–90 %; III, 45–75 %) which may be modulated by adjuvant chemotherapy.
- The risk of locoregional recurrence following colectomy should be below 5 %.
- The surgeon's experience and the expertise of the institution have 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 improved survival after colectomy for colon cancer.
- Jagoditsch et al. demonstrated the benefits of careful surgical technique which results in a complete resection of all tumors (R0). Their data demonstrated an operative mortality of 1.3 % and a 5-year survival rate of 71.8 % for curative operations in Stage I–III disease.

Summary

- Data clearly supports the benefits of wide mesenteric resection, clear radial margins, and resection of adherent adjacent organs.
- The mesenteric resection is obtained by ligating the feeding vessel at its origin.
- This maximizes the chances that 12 or more lymph nodes are examined to allow for accurate staging.

42. The Preoperative Staging of Rectal Cancer

Susan L. Gearhart and Jonathan E. Efron

Introduction

- The effective evaluation of a newly diagnosed rectal cancer should result in a determination of the need for neoadjuvant therapy, the potential for sphincter preservation, and the expected quality of life following treatment. The currently used system proposed by American Joint Committee on Cancer (AJCC) for staging rectal cancer is listed in Table 40.1.
- The tumor-related factors of prognostic significance, which may be evaluated prior to the treatment of rectal cancer, include the depth of penetration of the tumor through the rectal wall, the presence or absence of metastases to the regional and pelvic lymph nodes, and the presence of distant metastases.
- Clinicians have a variety of diagnostic tools at their disposal that can aid in delineating these aforementioned factors.
- The most commonly used modalities for the preoperative staging of rectal tumors available today are digital rectal examination, computed tomography (CT), endorectal ultrasonography (ERUS), magnetic resonance imaging (MRI), and positron emission tomography combined with computerized tomography (PET/CT).

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Local and Regional Staging

Digital Rectal Examination (DRE)

- Careful digital exam of a rectal tumor may yield valuable information regarding the location and degree of fixation of the tumor to the rectal wall and sphincter muscles (Table 42.1).
- DRE alone is considered inadequate in the staging of rectal cancer.

Rectal Ultrasound

- Endorectal ultrasound (EUS) is an outpatient procedure requiring only enema preparation and often no sedation.
- The accuracy of ERUS is user dependent and variable (Fig. 42.1).
- The Minnesota series, one of the largest series published in 2002 by Garcia-Aguilar et al., describes 1,184 patients with rectal carcinoma or villous adenoma that underwent ERUS. Histopathologic correlation was available for the 545 patients who had no prior radiotherapy.
  - The accuracy of ERUS in assessing the level of penetration was only 69 %, with 18 % overstaged and 13 % understaged.
  - For nodal involvement, the accuracy in the 238 patients who had radical surgery was poor, 64 % with 25 % overstaged and 11 % understaged.
- Limitations to ERUS:
  - A significant learning curve associated with the interpretation of the endorectal ultrasound image.
    - Rafalesen et al. reported that the reader experience had a significant effect on the assessment of penetration of the bowel wall by tumor. When comparing more experienced with less experienced radiologists, the accuracy for bowel wall penetration was 90 % vs. 66 %, respectively.
  - Overstaging of a tumor is common because of the inability of ultrasound to differentiate perirectal inflammation from tumor infiltration in the perirectal fat.
  - ERUS is difficult to perform in near obstructing lesions and those higher up in the rectum.

Table 42.1 Tumor characteristics to assess and record on digital examination

Location
Morphology
Number of quadrants involved
Degree of fixation
Mobility
Extrarectal growths
Direct continuity with other structures (vagina)

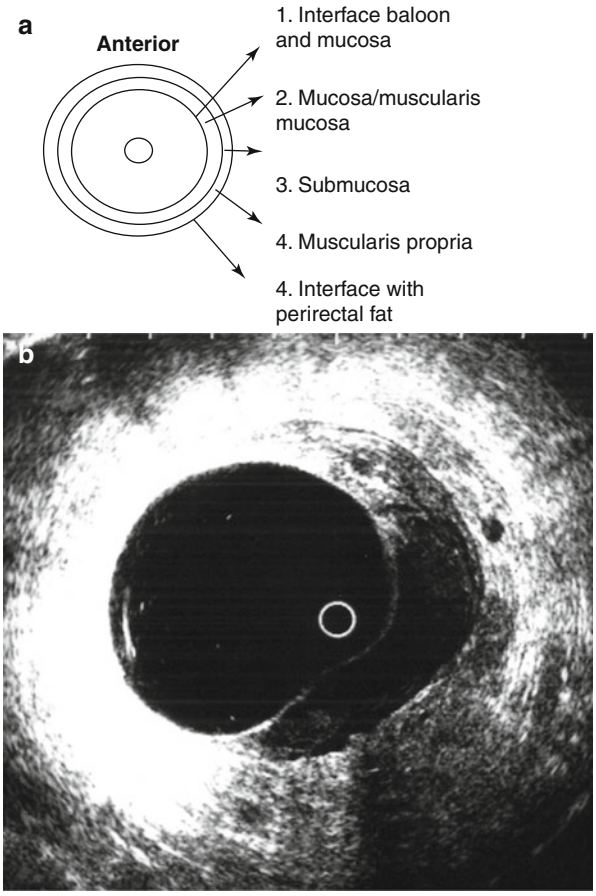

Fig. 42.1 The main concept in the use of MRI to stage rectal cancer is to obtain high-resolution images within small field-of-view thin sections with fast/turbo spin echo (FSE/TSE) T2-weighted axial and coronal views of the rectum. (**a**) EUS demonstrating the five layers of the rectum, (**b**) Standard EUS of a rectal tumor

Magnetic Resonance Imaging

- MRI use in staging rectal cancer was originally described in 1986.
- Kim et al. compared the histopathologic staging with the preoperative staging in 217 rectal cancer patients. The accuracy for the depth of invasion was 81 % and for regional lymph node metastasis was 63 %.
- MRI T staging has been defined (Table 42.2).
- MRI identification of metastatic lymph node involvement has not been standardized.
  - Criteria that are most predictable for determining lymph node metastasis are signal heterogeneity and an irregular border. Size criteria are not adequate. It is important to remember that in patients

Table 42.2 MRI T staging as proposed by Brown et al.

MRI T stage
T1: Low signal in the submucosal layer or replacement of the submucosal layer by abnormal signal not extending into circular muscle layer
T2: Intermediate signal intensity within muscularis propria. Outer muscle coat replaced by tumor of intermediate signal intensity that does not extend beyond the outer rectal muscle into perirectal fat
T3: Broad-based bulge or nodular projection (not fine speculation) of intermediate signal intensity projecting beyond outer muscle coat
T4: Extension of abnormal signal into adjacent organ, extension of tumor signal through the peritoneal reflection

with rectal cancer, approximately 15 % of lymph nodes smaller than 5 mm are positive for metastasis.
  - With the use of ultrasmall superparamagnetic iron oxide (USPIO)-enhanced MRI, recent advances have been made in the evaluation of lymph nodes. The iron oxide nanoparticle is given intravenously and is transported to the lymphatic system where it is picked by macrophages. The nanoparticle causes a decrease in signal intensity, and therefore, inflammatory lymph nodes exhibit less signal intensity.
- Initial results using this technique demonstrate up to 93 % sensitivity and 96 % specificity for perirectal lymph node metastasis. However, larger prospective trials are needed.
- In recent years, tumor involvement of the circumferential resection margin (CRM) has been identified as an important predictor of locoregional recurrence in rectal cancer patients undergoing a radical proctectomy with total mesorectal excision (TME).
- 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 upmost importance in selecting neoadjuvant therapy and planning the surgical resection.
- The fascia propria of the rectum is well visualized by phased-array 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 (Fig. 42.2).

Distant Metastases

- Detection of distant metastasis is of prime importance for the accurate staging.
- The most common metastatic sites include the liver and lung.

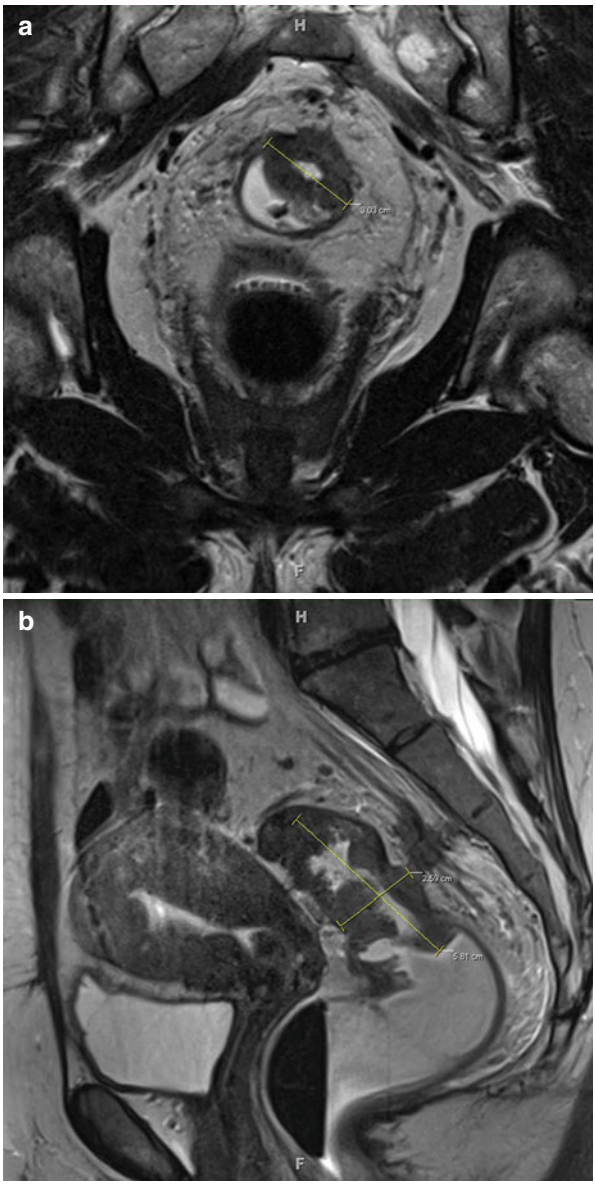

Fig. 42.2 (**a** and **b**). The main concept in the use of MRI to stage rectal cancer is to obtain high-resolution images within small field-of-view thin sections with fast/turbo spin echo (FSE/TSE) T-2-weighted axial and coronal views of the rectum.

- The common imaging modality used today to detect liver metastasis pre-operatively is computerized tomography (CT); however, MRI and PET/CT are being used more frequently (Tables 42.3 and 42.4).

Table 42.3 Sensitivity and specificity for EUS, CT, and MRI in the preoperative staging of rectal cancer

Stage	Imaging modality	Sensitivity % (95 % CI)	Specificity % (95 % CI)
T2	EUS	94 (90–97)	86 (80–90)
	MRI	94 (89–97)	69 (52–82)*
	CT	–	–
T	EUS	90 (88–92)	75 (69–81)
	MRI	82 (74–87)*	76 (65–84)
	CT	79 (74–84)*	78 (73–83)
T4	EUS	70 (62–77)	97 (96–98)
	MRI	74 (63–83)	96 (95–97)
	CT	72 (64–79)	96 (95–97)
Node positive	EUS	67 (60–73)	78 (71–84)
	MRI	66 (54–76)	76 (59–87)
	CT	55 (43–67)	74 (67–80)

Modified from Bipat S, van Leeuwen M, Comans E, Pijil M, Bossuyt P, Zwinderman A, Stoker J. Colorectal liver metastases: CT, MR Imaging, and PET for diagnosis – meta-analysis. Radiology. 2005:237;123–31.29

EUS endorectal ultrasound, *CT* computed tomography, *MRI* magnetic resonance imaging, *CI* confidence interval

*$p < 0.05$ EUS to other

Table 42.4 Accuracy of nodal staging in preoperative evaluation of rectal cancer with MRI pelvic phased-array coil

References	No. of patients	Accuracy (%)
Ferri (2005)	29	59
Matsuoka (2003)	19	89.5
Brown (2003)	60	85
Gagliardi (2002)	26	69
Blomqvist (2000)	47	47
Kim (2000)	217	63
Hadfield (1997)	28	76

Modified from Skandarajah A and Tjandra J. Preoperative loco-regional imaging in rectal cancer. ANZ J Surg. 2006;76:497–504

MRI magnetic resonance imaging

- A recent meta-analysis reported by Bipat et al. that evaluated the use of CT, MRI, or PET found that 18-fluorodeoxyglucose positron emission tomography (FDG-PET) was the more accurate method to detect liver metastasis on a per-patient basis.
  - When evaluating different lesions, MR imaging at 1.5 T and FDG-PET were comparable and significantly more accurate than CT.
  - Sensitivity estimates for all imaging modalities studied for lesions less than 1 cm were much less than for lesions ≥1 cm (11.6–29.3 % vs. 65.7–90.2 %).
  - They reported an accuracy rate of 95 % on the depth of invasion for MDRCT vs. 100 % for MRI, whereas lymph node accuracy was 70 % vs. 61 % for MDRCT and MRI, respectively.

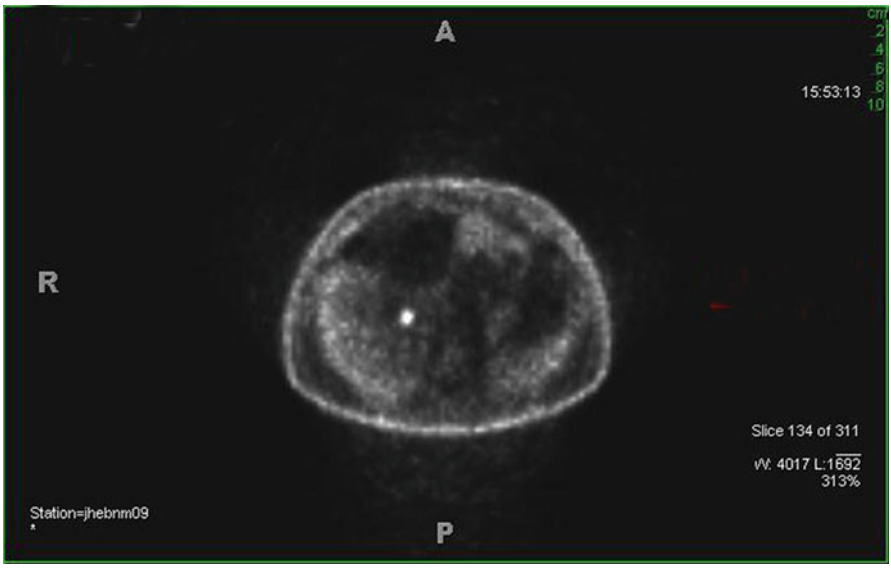

Fig. 42.3 PET scan

- At the present time, FDG-PET is primarily used for the diagnosis of local and distant recurrence after curative surgery for colorectal cancer (Fig. 42.3).
- The impact of FDG-PET and FDG-PET/CT in the preoperative staging and management of rectal cancer patients has been studied by Heriot et al. in a series of 46 patients who were assessed with FDG-PET scans at the time of their initial diagnosis. The surgical management was changed in 17 % of the patients because of positive FDG-PET scan findings that upstaged the disease.
- Furthermore, Gearhart et al. demonstrated in 37 patients that FDG-PET/CT was able to demonstrate additional significant findings in 38 % of patients with a known primary rectal cancer resulting in an alteration in the treatment planning for 27 % of patients. These changes in management included canceling surgery and changing the field of administered radiation.
- Preoperative radiation of rectal cancer causes various degrees of tumor regression resulting in scarring and fibrosis that impairs accurate imaging.
- The value of EUS in restaging rectal cancer following radiation is limited.
- The limitation of MR imaging in rectal cancer has been its inherent inability to differentiate fibrosis from residual tumor following treatment. For this reason, conventional MRI has not been shown to be useful in determining response to therapy.
- However, functional MR imaging has been demonstrated to be useful in the evaluation of the response of rectal cancer to neoadjuvant therapy.

- The components of functional MR include spectroscopy, diffusion, and contrast enhancement.
  - Further studies to validate promising early results are necessary.
- The use of serial FDG-PET/CT in predicting response to neoadjuvant therapy has been evaluated by several investigators.
  - The reported specificity for predicting a near-complete or complete pathologic response to therapy with serial FDG-PET/CT is 60–95 % (Table 42.5).
  - The timing of serial FDG-PET appears to be important in that FDG-PET/CT after 2 weeks of treatment can predict pathologic response with similar specificity to FDG-PET/CT performed at the end of treatment. This earlier time period may be advantageous for determining if the neoadjuvant regimen should be modified in patients that appear not to be responding.

Table 42.5 Specificity of FDG-PET to predict near-complete or complete pathologic response following chemoradiation for primary rectal cancer

Author	Year	*N*	Specificity (%)	Parameter	Endpoint
Guillem	2004	10	80	VRS	pCR (TRG 1)
Amthauer	2004	20	86	RI	R1
Capirci	2004	78	76	VRS	TRG 1–2
Chessin	2005	21	95	VRS	Response
Deneke	2005	23	60	RI	Major response
Melton	2007	21	81	RI	TRG 1–2
Cascini	2006	33	87	RI	TRG 1–2
Caprici	2009	81	80	RI	TRG 1–2

Modified from Capirci C, Rubello D, Pasini F, et al. The role of dual-time combined 18-fluoridedoexyglucose positron emission tomography and computed tomography in the staging and restaging workup of locally advanced rectal cancer, treated with preoperative chemoradiation therapy and radical surgery. Int J Radiation Oncology Biol Phys. 2009;74:1461–69.51
VRS visual response score, *RI* response index, *TRG* tumor regression grade

43. Local Excision of Rectal Cancer

Peter A. Cataldo

Introduction

- The earliest treatment for rectal cancer involved local excision. Transabdominal resections were thought to be too risky due to limitations in anesthesia, surgical instruments, operative techniques, and blood transfusions.
- Local excision, although safe, was associated with high local recurrence rates and poor overall survival, perhaps due to patient selection and inability to remove peritumoral lymph nodes containing regional metastases.
- For these reasons, Sir Ernest Miles expanded the indications for abdominal–perineal resection (APR), originally described by Faget for perianal sepsis, for the treatment of rectal cancer. He believed that excision of regional lymph nodes would improve overall cure rates. Miles' theories were correct, but not without consequences, as seven of his original nine patients died from complications of surgery. Complication concerns following APR continue today with mortality rates ranging from 0 to 6.3 % and complication rates as high as 61 %. In addition, APR is associated with a high rate of sexual dysfunction (up to 67 %) and stoma-related problems (up to 66 %).
- Finally, despite these complications and long-term functional consequences, some early rectal cancers recur despite radical surgery.
- The 5-year survival for Stage I rectal cancer following radical surgery is 73 % as reported by the National Cancer Data Base.

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- For these reasons, many surgeons have sought alternative treatment options for early rectal cancer. These include chemoradiotherapy alone and local excision with or without adjuvant treatment.
- Treatment always begins with patient selection and is dependent upon accurate (preoperative) tumor staging.
- Local staging represents a difficult and important challenge in rectal cancer. Tumor staging must include the depth of penetration of the rectal wall (T-stage) and evaluation of adjacent lymph nodes (N-stage).
- This information helps identify which patients are candidates for local excision (T_1) or prompt surgery (T_2) or who require neoadjuvant chemoradiotherapy (T_3).
- Lymphadenopathy has great impact as patients with metastatic regional lymph nodes (N+) are not candidates for any type of curative local excision.
- Unfortunately, the accuracy of local staging with both pelvic MRI (with or without endorectal coil) and endorectal ultrasound is variable (see Chap. 42).

Treatment Algorithm

- At any stage a patient may be a candidate for *palliative* local excision provided that the lesion is accessible and safe excision (and rectal closure) is technically possible. However, the criteria for *curative* transanal excision (TAE) are much stricter.
- A reasonable patient selection guide and treatment algorithm is as follows:
  - For T_1N_0 lesions without adverse histologic features (lymphovascular invasion, involved margins, or poor differentiation), local excision alone without adjuvant therapy is adequate.
  - For T_1N_0 lesions with adverse histologic features, local excision must be combined with postoperative chemoradiotherapy (histologic features are rarely available on preoperative, endoscopic biopsy).
  - For T_2N_0 tumors, local excision should be combined with preoperative or postoperative chemoradiotherapy.
  - T_3N_0 patients are candidates for local excision only if major comorbidities preclude radical surgery or patients refuse a radical approach.
  - Node positive patients (N_1 or N_2) are not candidates for curative local excision as mesorectal lymph nodes cannot be reliably removed transanally.
- Traditional criteria for local excision (<10 cm from dentate line, <4 cm in diameter, <40 % of rectal circumference) no longer apply due to more sophisticated, yet imperfect, staging and more advanced surgical techniques, such as transanal endoscopic microsurgery (TEM).

Transanal Techniques

- Once the decision to perform local excision has been made, traditional surgical principles apply. The goals are to (1) remove the tumor with negative resection margins, (2) restore normal anatomy to the fullest extent possible, (3) minimize morbidity and mortality, and (4) minimize any impact on long-term function.
- Positive resection margins result from inadequate surgical technique and dramatically increase the risk of local recurrence and treatment failure.
- To perform a successful local excision, there must be good exposure, optimal visualization, and precise surgical technique.
- Four techniques are available:
  - Traditional TAE creates minimal disruption to local anatomic structures but is applicable only to the very distal rectum, and exposure, visualization, and precision are limited.
  - The Kraske, or transcoccygeal, approach provides better exposure but is more destructive (i.e., coccygectomy) and has a high fecal fistula rate.
  - The York–Mason, or transsphincteric, technique again provides better exposure than TAE but, by definition, disrupts the anal sphincters and is associated with high rates of postoperative fecal incontinence.
  - TEM provides excellent exposure and visualization throughout the rectum and offers a precise surgical excision and wound closure. It does, however, require specialized equipment, specialized training, and an adequate volume of cases to become adept.

Transanal Excision

- Local excision via a transanal approach is suitable for the majority of low rectal cancers.
- All patients should receive a full mechanical and antibiotic bowel preparation.
- After the induction of anesthesia, the patient is positioned based on the location of the tumor. For posterior-based tumors, lithotomy position is preferred. For lateral or anterior tumors, the patient is flipped over and placed in the prone-jackknife position, with the buttocks taped apart.
- A pudendal nerve block may be administered, which aids in postoperative pain control and more importantly relaxes the sphincter complex.
- An anal retractor alone or in combination with a retractor with self-retaining hooks is then used to dilate the anus and expose the lesion. Once adequate visualization has been obtained, traction sutures are often placed 1–2 cm caudal to the tumor, and the line of dissection is marked circumferentially on the mucosa using electrocautery. This line of dissection should be approximately 1–2 cm from the border (Fig. 43.1a).

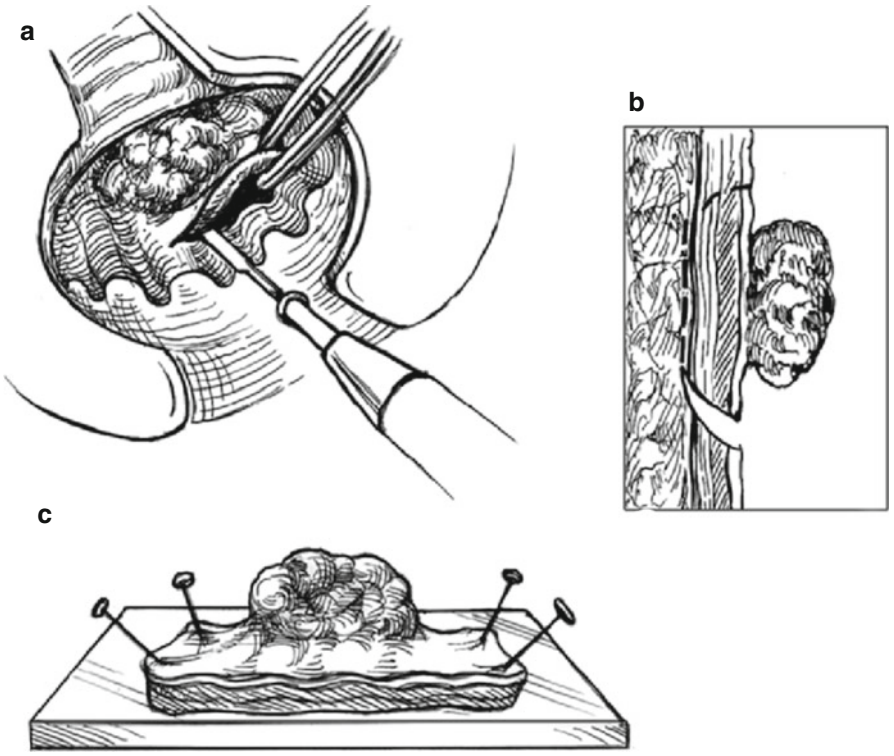

Fig. 43.1 (**a**–**c**) Transanal excision. (**a**) A transanal excision is performed by marking out a 1 cm or greater margin around the tumor. (**b**) A full-thickness excision is then performed to obtain adequate radial as well as lateral margins. (**c**) The specimen is then oriented accurately for the pathologist

- If visualization is not initially adequate, serial traction sutures should be used to prolapse the lesion into the field of view. Next, the electrocautery is used to make a full-thickness incision along the previously marked mucosa, typically starting at the caudal aspect (Fig. 43.1b).
- The specimen is then oriented accurately for the pathologist (Fig. 43.1c). Upon completion of this excision, the perirectal fat should be visible beneath the lesion to confirm a full-thickness excision.
- For anterior lesions, care must be taken not to injure the back wall of the vagina in females or the prostate or membranous urethra in males.
- The defect in the bowel wall is then closed transversely, if possible, using interrupted 2-0 or 3-0 polyglycolic sutures.
- The complications most commonly associated with transanal excisions include urinary retention, urinary tract infections, delayed hemorrhage, infections of the perirectal and ischiorectal space, and fecal impactions. The overall incidence of these complications is quite low, and the mortality rate is 0 % in most series.

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.
- After undergoing a full antibiotic and mechanical bowel preparation, the patient is placed in the prone-jackknife position with the buttocks taped apart after the induction of general anesthesia. The tape is released to facilitate the approximation of the subcutaneous tissues and skin and an incision is made in the posterior midline adjacent to the sacrum and coccyx down to the upper border of the posterior aspect of the external sphincter.
- The coccyx, which along with the anal coccygeal ligament lies immediately deep to the skin and subcutaneous tissue, is removed to improve exposure. In order to do so, the anal coccygeal ligaments and other attachments are cauterized from each side and from the lower edge of the coccyx.
- The dissection then proceeds along the undersurface and anterior edge of the coccyx until a cutting wire can pass through the sacral coccygeal joint. The coccyx is then removed with occasional bleeding from an extension of the middle sacral artery, which is easily controlled with electrocautery.
- The levator ani muscles visible at the base of the wound are separated in the midline, exposing a membrane that resides just outside of the perirectal fat. Division of this membrane allows for complete mobilization of the rectum within the intraperitoneal pelvis.
- For posterior-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. 43.2). The excision is then completed with a 1-cm margin surrounding the lesion.
- For anterior lesions, a posterior proctotomy is made, and then the lesion is approached under direct vision, again excising the lesion down to the perirectal fat with a 1-cm margin (Fig. 43.3).
- Following removal, the specimen is reoriented for the pathologist and all the rectal incisions are closed in either a longitudinal or transverse manner in order to avoid narrowing of the rectum, using an absorbable suture. An air test should be performed, filling the operative field with sterile saline and insufflating air in the rectum in order to check for air leaks in the suture line. Once these air leaks are controlled, the levator ani is reapproximated in the midline. The operation is completed with the closure of the skin and subcutaneous 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.

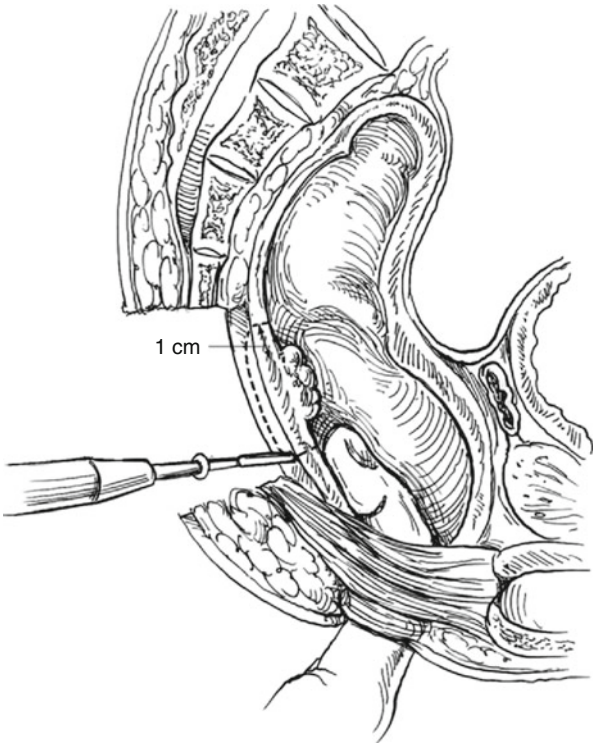

Fig. 43.2 Transcoccygeal excision. For posterior lesions using a transcoccygeal or "Kraske" approach, one can palpate the lower border of the tumor to ensure an adequate distal margin

Transsphincteric Excision

- The transsphincteric approach developed by York and Mason involves the complete division of the sphincters and the posterior wall of the rectum.
- Patients undergo an antibiotic and mechanical bowel preparation on the day before surgery. General anesthesia is chosen for the operation.
- The procedure starts similarly to the Kraske transcoccygeal approach; except the levator ani and the external sphincter muscles are divided in the midline. These muscles are carefully tagged, so matching sutures can be reapproximated exactly at the end of the procedure. Care must be taken to remain in the midline in order to avoid the nerve supply to the sphincters that lie in a posterolateral position bilaterally.
- 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. Since 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.

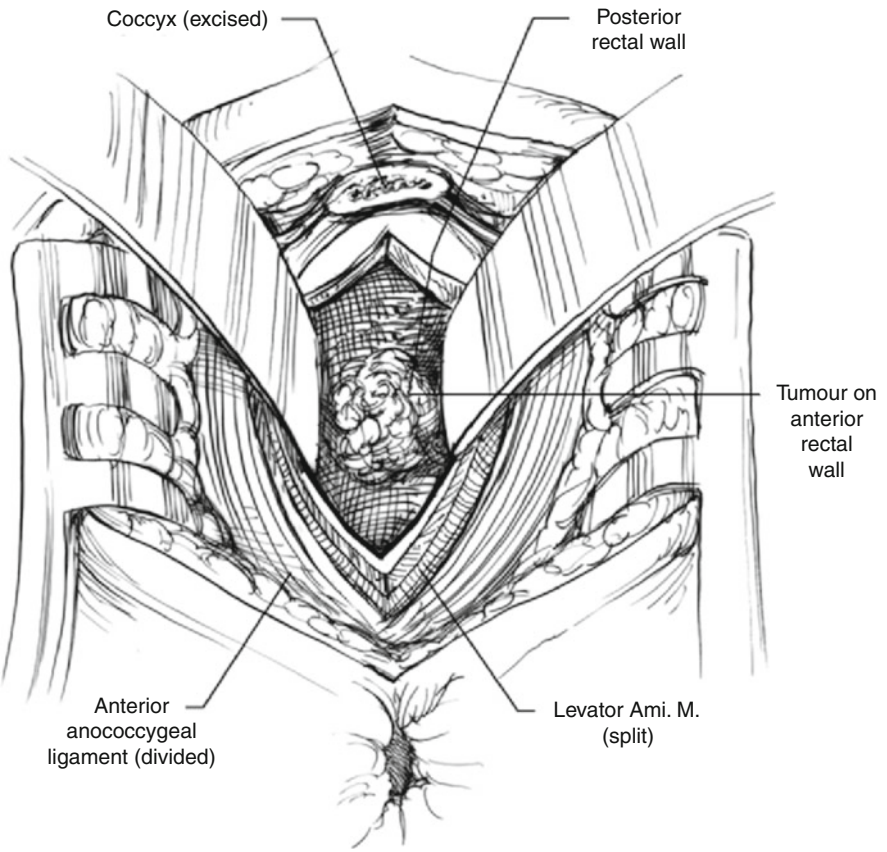

Fig. 43.3 Transcoccygeal excision. Anterior lesions need to be approached by first making a posterior proctotomy and then excising the lesion through the rectum. The anterior and posterior walls of the rectum then need to be repaired, usually in a transverse manner in order to maintain the lumen diameter

Transanal Endoscopic Microsurgery

- TEM was developed by Gerhard Buess and the Richard Wolf Medical Instruments Company in 1983 in Germany. Originally designed for the removal of large rectal polyps beyond the reach of traditional transanal excision, its indications eventually expanded to include the excision of early-stage rectal cancers.
- TEM is essentially the earliest natural orifice transluminal endoscopic surgery (NOTES). It utilizes endoluminal insufflation to create rectal distension and exposure. Access is obtained via a proctoscope 4 cm in diameter and either 12 or 20 cm in length, which allows for resection of lesions anywhere in the rectum. Visualization is provided by a special binocular optic passed through the proctoscope which provides three-dimensional

viewing. In addition, a laparoscopic camera can be attached to a separate optic with the image being viewed on a standard video monitor.

- TEM is a closed system and a faceplate on the end of the proctoscope maintains an airtight seal. Instruments are passed through three-gasket ports, similar to laparoscopy. All instruments are 5 mm in diameter and >30 cm in length and include graspers, cautery, needle holders, suction, scissors, and clip appliers.
- Recently, modifications of TEM have been described, utilizing single-port laparoscopy devices and standardized laparoscopic instrumentation (TAMIS – transanal minimally invasive surgery)
- Briefly, the technique is as follows. The lesion and its location are precisely identified and the patient is positioned on the operating room table with the lesion oriented toward the floor (i.e., prone for anterior lesions, lithotomy for posterior lesions). This is important as the TEM equipment is designed to operate from "the top down."
- The proctoscope is inserted, the lesion is located, and the proctoscope is then fixed in place by attaching it to the "Martin Arm," a three-elbowed gadget that attaches to the OR table, locks in place, and keeps the TEM scope fixed (Fig. 43.4). Lidocaine with epinephrine is instilled underneath the lesion and 1-cm margins (5 mm for benign lesions) are marked with electrocautery surrounding the lesion. Using cautery, the lesion is then excised circumferentially in the full-thickness plane until it has been completely detached from the surrounding rectal wall (Fig. 43.5).
- The defect is then closed transversely to prevent rectal stenosis. The midpoint of the proximal and distal edges of the defect is identified and approximated with a single suture to ensure correct orientation and to facilitate transverse closure. The remaining defect is closed from each corner to the middle. Silver clips or "bbs" are used at the beginning and end of all sutures (usually running) in lieu of tying knots, as this is tedious in the small operative field (Fig. 43.6).
- Complications of TEM are rare but include transient urinary retention, dehiscence of the operative closure, hemorrhage, perirectal or intraperitoneal infection, and rectovaginal fistulae. Rarely reoperation and even temporary fecal diversion are necessary to treat severe complications.

Follow-Up

- Follow-up after resection for rectal cancer is essential as local recurrence, if identified early, can be cured with radical resection. History and physical exam and CEA are performed every 3 months for 2 years and every 6 months for the following 3 years. Flexible sigmoidoscopy is performed at 3 and 9 months following surgery and yearly thereafter. Colonoscopy is scheduled at 1 year and every 3 years regularly. CT scans begin at 1 year postoperatively and are then performed yearly.

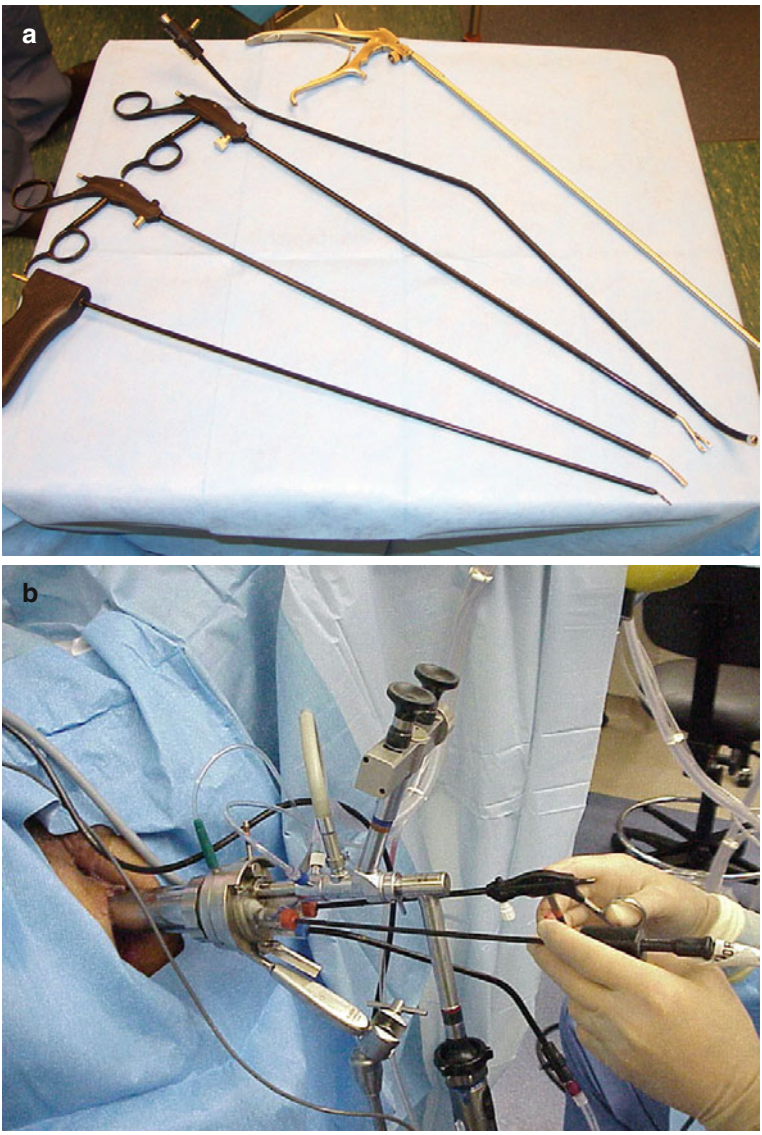

Fig. 43.4 (**a**) Five-millimeter TEM instruments, including needle cautery, graspers, suction, and needle holder. (**b**) External view of assembled TEM equipment in use

Results

- When evaluating results following various treatments for rectal cancer, local recurrence and survival are naturally most important. It is important to also consider surgical morbidity and mortality, functional

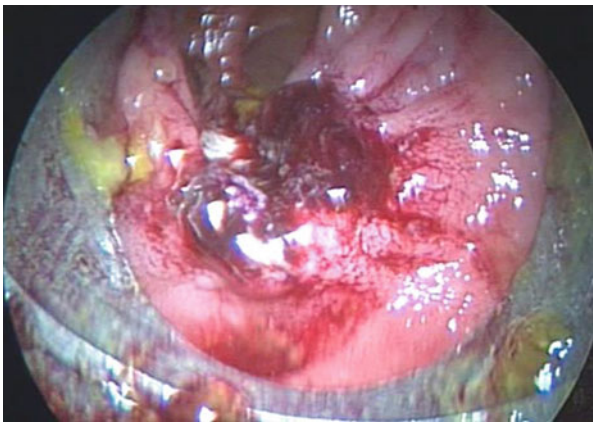

Fig. 43.5 Lesion properly positioned for TEM

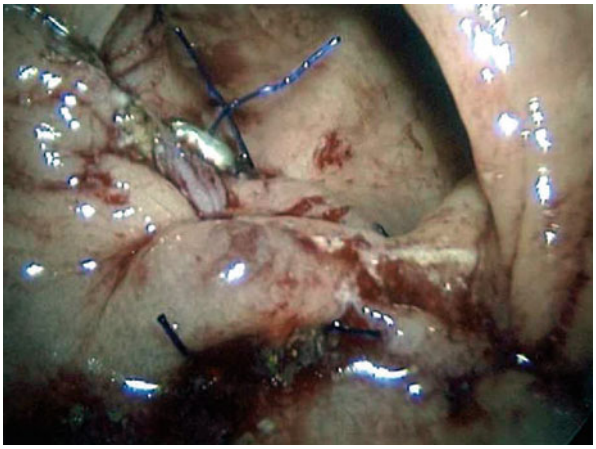

Fig. 43.6 Defect closed in transverse fashion in order to prevent stenosis. Silver "bbs" are used in lieu of tying knots

consequences, and the quality of life. Various local excision techniques can be compared to each other and/or compared to traditional, radical resection.

- Survival following radical resection for rectal cancer as reported by the National Cancer Data Base is 73 % for Stage I, 56 % for Stage II, 47 % for Stage III, and 6 % for Stage IV. As we evaluate survival following local excision, it is essential to remember that not all patients with early-stage rectal cancer are cured by radical resection.
- If a patient undergoes a well-performed, oncologically sound radical resection and then recurs, it is traditionally blamed on tumor biology. If recurrence develops after local excision, we assume that recurrence is due to

inadequate surgery. While that may sometimes be the case, it is certainly not always the case as judged by the survival data following radical resection.

- Many local failures following local excision are thought to arise in undiagnosed metastatic lymph nodes in the mesorectum. If this is in fact the case, then these are truly Stage III rectal cancers, which have been understaged, not Stage I rectal cancers that have recurred. In this situation, the problem lies with under-staging and subsequent inadequate treatment. This only occurs following local excision (as lymph nodes are excised and evaluated with radical resection) and therefore artificially increases local recurrence rates and lowers overall survival following local excision of "early-stage" rectal cancers.
- You et al. performed an extensive study evaluating local excision of early rectal cancers with data obtained from the National Cancer Data Base. They compared standard resection (SR) (abdominoperineal and low anterior resection) to local excision (LE) and looked at operative mortality, local recurrence, disease specific survival (DSS), and overall survival (OS) for both groups for T_1 and T_2 rectal cancers. A total of 2,124 patients treated between 1994 and 1996 were included: LE 765 (T_1 601, T_2 164) and SR 1359 (T_1 493, T_2 866). Overall operative mortality was lower for LE (0.5 % vs. 1.8 %). Thirty-day mortality was also lower for LE (5.6 % vs. 14.6 %). For T_1 tumors, overall survival was similar at 8 years (LE 61.7 % vs. SR 66.3 %, $p=0.09$). However, local recurrence was significantly higher for LE compared with SR (14.3 % vs. 8.5 %, $p=0.007$) at 8 years. Similarly, DSS was worse for LE (93.2 % vs. 97.2 %, $p=0.004$). For T_2 tumors, local recurrence again was higher for LE (22.1 % vs. 15.1 %, $p=0.01$) but DSS was similar for LE and SR (90.2 % vs. 91.7 %, $p=0.95$). OS was worse for LE (67.6 % vs. 76.5 %, $p=0.01$) at 5 years.
- These data suggest that LE is clearly safer than SR but at the cost of inferior oncologic outcomes. Yet when overall survival is evaluated, both groups are similar.
- Despite being a large, exhaustive project, this study has several shortcomings. (1) Many patients included in the LE group did not have R_0 excisions, which would clearly increase the LR rate and decrease the overall survival. In addition, any patient who received adjuvant therapy (chemotherapy or radiation) was excluded from the analysis. Many surgeons would consider chemoradiation a standard component of treatment for any T_2 tumor and selected T_1 tumors treated by LE. Finally, no mention is made of the "stage shift" phenomenon, where a small but significant number of T_1 and T_2 tumors treated by LE (but not by SR) were truly Stage III cancers and had undocumented disease in unresected perirectal lymph nodes.
- Ptok et al. compared local and radical resection for low-risk T_1 rectal cancer. Similar to the large database study by You, morbidity was lower with LE (9.2 % vs. 22.8 %, $p=0.001$), but local recurrence was higher (6 % vs. 2 %, $p=0.049$). However, 5-year tumor-free survival was similar for both groups.

- In evaluating multiple studies of traditional local excision for early rectal cancer, several patterns arise. (1) Morbidity, mortality, and functional outcomes are better with local excision. (2) Local recurrence rates are higher following local excision when compared with radical resection. (3) Salvage radical surgery is possible in 30–50 % of patients developing local recurrence after local excision. (4) Disease-free survival and overall survival are similar following local excision and radical resection for T_1 and T_2 rectal cancers.

Transanal Endoscopic Microsurgery

- TEM has been in use since the early 1980s but only in select centers, particularly in Europe. Over the past 10 years, its role has expanded significantly and its use is now widespread in Europe, Great Britain, and more recently the USA. It has been advocated as technically superior to TAE, and oncologically favorable results have been reported. Few studies, however, directly compare TEM to traditional techniques. Yet, the limited data is encouraging.
- Christforidis et al. at the University of Minnesota retrospectively compared TEM to traditional TAE in 171 patients (42 TEM, 129 TAE). Negative resection margins were obtained in 98 % of the TEM group compared with 84 % of the TAE group. Disease-free survival at 5 years was slightly better for the TEM group (84 % vs. 76 %), but did not reach statistical significance.
- Moore et al. evaluated 171 patients subject to TEM (82) or TAE (89) at the University of Vermont for rectal adenomas and carcinomas. In the group of patients undergoing resection for cancer, TEM, when compared to TAE, provided an intact, nonfragmented specimen more often (100 % vs. 63 %), achieved negative resection margins (98 % vs. 78 %, $p = 0.01$), and was associated with a lower recurrence rate (8 % vs. 24 %). When only curative resections were considered, recurrence rate for TEM was 3 % compared with 22 % for TAE. In this study, TEM was clearly technically and oncologically superior to TAE.
- In another series Guerrieri et al. reviewed 196 patients (51 T_1, 84 T_2, 61 T_3) treated with TEM for rectal cancer. All patients with T_2 or T_3 lesions underwent preoperative radiotherapy, combined with chemotherapy in some instances. All patients achieved negative resection margins (real-time frozen section analysis was used when necessary). Follow-up ranged from 12 to 178 months and local recurrence rates were 0 % for T_1, 6 % for T_2, and 5 % for T_3 lesions. Disease-free survival was 100 % for T_1, 90 % for T_2, and 77 % for T_3 lesions. Downsizing and downstaging were good prognostic indicators and the authors only found local recurrence in patients with lesions deemed “non-responders” to radiation therapy.

- Two prospective, randomized trials have compared TEM to radical surgery for early rectal cancer. Winde et al. randomized 53 patients with ultrasound-staged T_1 rectal cancer to TEM vs. anterior resection (TEM 25; LAR 28). Complication rates were significantly higher for radical resection while 5-year survival was similar for both groups at 96 %.
- Lezoch et al. published 5-year follow-up data from a prospective randomized trial for the treatment of early rectal cancer. Patients with UT_2N_0 biopsy-proven, low-grade rectal cancer underwent preoperative chemoradiotherapy (5,040 rads with continuous infusion of 5-FU) and were then randomized to TEM vs. laparoscopic radical resection (APR vs. LAR). Median follow-up was 84 months. Local recurrence following TEM was 5.7 % (2/35) and 2.8 % after radical resection (1/35). One patient developed distant metastases in each group. The 5-year disease-free survival was 94 % for both groups. The authors concluded that TEM provided equivalent oncologic results to radical resection.
- Experience and outcomes vary significantly from center to center and country to country with regard to TEM in the treatment of early rectal cancer.
- Several clear points emerge from a cloudy picture. TEM appears to be technically superior to traditional TAE in its ability to produce a nonfragmented specimen with tumor-free margins. It is clearly associated with lower morbidity and mortality than radical resection. Patient selection and preoperative staging are essential.
- TEM alone may be justified for select T_1 rectal cancers, but recurrence rates are prohibitive without adjuvant chemoradiotherapy for T_2 (and T_3) tumors.
- When compared to radical resection in a prospective, randomized fashion, TEM, in limited data, compares well to radical resection for T_1 cancers. In addition TEM, combined with preoperative adjuvant therapy, again compares well to radical resection with T_2 rectal cancers.
- In the USA, a multicenter prospective phase II trial ACOSOG Z-6041 has been evaluating local excision (TAE and TEM) for UT_2N_0 rectal cancer following 5,040 Gy combined with 5 FU and oxaliplatin. The preliminary results reveal a high rate of complete pathologic response (PCR) at 44 % and a high rate of negative surgical margins (99 %). The long-term results of this study may help clarify the role of local excision and adjuvant therapy for Stage I rectal cancer.

Predicting Lymph Node Metastases

- The reasons for local recurrence following local excision of rectal cancer are likely multifactorial. Clearly, leaving tumor behind at the site of resection (i.e., positive margins) increases the risk of recurrence and is responsible for many treatment failures. However, many patients with

clear margins ultimately develop local recurrence. These failures may be the result of undiagnosed and untreated metastatic lymph nodes in the mesorectum.

- The incidence of lymph node positivity is directly related to T-stage and is well documented in the literature. Local recurrence rates following local excision for rectal cancer seem to parallel the likelihood of lymph node positivity stage for stage.
- Metastatic lymph nodes are found in 5–10 % of T_1 tumors, 10–20 % of T_2 tumors, and 30–50 % of T_3 tumors. However, many of these lymph nodes are very small making ultrasound or MRI detection difficult.
- Many studies have looked at factors to predict the presence or absence of occult lymph node metastases and local recurrence following local excision of rectal tumors.
- In an insightful study, Read et al. used residual T-stage following chemoradiation in 644 patients who underwent neoadjuvant therapy followed by radical surgery as a predictor for the presence of mesenteric lymph nodes containing tumor. Postradiation T-stage was determined and then correlated with the presence or absence of metastatic lymph nodes. For postradiation T_0 lesions, the risk of positive nodes was 2 %, for T_1 4 %, for T_2 23 %, and for T_3 47 %.
- Further confirmation of the "response to radiation" as a predictor of successful outcomes is provided by the multicenter study authored by Capirci et al. As part of the Gastro-Intestinal Working Group in the Italian Association of Radiation Oncology, data was gathered on 566 patients with complete clinical response following preoperative chemoradiotherapy. Patients underwent low anterior resection (73 %), abdominoperineal resection (22 %), and TEM (5 %). Complete pathologic response following neoadjuvant therapy was associated with a 1.6 % local recurrence rate, disease-free survival of 85 %, overall survival of 90 %, and cancer-specific survival of 94 %.
- Perez et al. in São Paulo, Brazil, evaluated postneoadjuvant chemoradiation staging as a predictor of lymphatic involvement and recurrence. Only patients with an incomplete clinical response were included for evaluation ($n=289$). All patients underwent radical resection.
- Eighty-eight patients had ypT_2 tumors. Lymph node metastases were identified in 19 % of this group. The presence of perineural invasion, vascular invasion, and decreased interval between chemoradiation and surgery (12 vs. 18 weeks) were associated with lymph node metastases and tumor recurrence. The presence of tumor in mesorectal lymph nodes was associated with decreased disease-free survival (30 % vs. 49 %) even after radical surgery.
- These authors recommended radial resection for all patients with ypT_2 tumors following chemoradiation. The important clinical implication of this data is any patient undergoing local excision following chemoradiation found to have ypT_2 disease is at high risk for recurrence and should be considered for subsequent radical surgery.

- While response to neoadjuvant treatment has been advocated as a predictor of lymph node involvement by some, others have advocated identifying histopathologic factors present in the primary tumor to predict the presence of metastatic lymph nodes in the mesorectum.
- Kikuchi et al. evaluated the depth of submucosal tumor spread (sm level) as a predictor of lymphatic metastases and adverse outcome following endoscopic polypectomy in 182 patients. They identified polyp configuration (pedunculated vs. sessile), polyp location (rectum vs. colon), and sm level as predictors of adverse outcome.
- Conversely, Park et al. analyzed 90 patients with early colorectal cancer and found lymph node metastases in 8.9 %. Lymph node metastases were associated with deep sm invasion, lymphovascular invasion, vessel configuration, absence of a residual adenomatous component, and unfavorable histologic grade.
- Similarly, Choi et al. evaluated 168 patients with early colorectal cancer who underwent curative bowel resection. They again identified sm 3 invasion and poor differentiation as predictive of lymph node metastases. They, however, also identified tumor cell dissociation (TCD), solid cancer cell clusters and groups of dissociated cancer cells at the tumor front, as predictive of lymph node metastases. (TCD appears to be similar to tumor budding.)
- In a slightly different approach, Masaki et al. evaluated tumor budding (single cells or clusters of cells at the invasive margin) grade, lymphovascular invasion, tumor dedifferentiation at the invasive margin, residual adenomatous tissue, and depth and width of submucosal invasion in 76 patients with T_1 colon and rectal cancer. Multivariate analysis found only tumor budding to be associated with nodal disease.
- In summarizing the data from the above series, it appears that several factors consistently put patients at risk for untreated regional lymph node disease following local excision for early rectal cancer.
- The presence of lymphovascular invasion, increasing sm levels of tumor invasion, tumor budding at the invasive tumor margin, and poor differentiation are relatively consistent predictors of adverse outcome.
- In the future, perhaps a predictive “histologic score” will be developed to accurately identify patients at significant risk for lymph node metastases. These individuals may benefit from radical resection or more aggressive adjuvant chemoradiation.

Conclusions

- Local excision will likely continue to play a significant role in the treatment of selected patients with early-stage rectal cancer.
- TEM is utilized much more commonly due to its ability to access the entire rectum, its superior visualization, and its precise surgical technique. Early results indicate lower local recurrence rates and higher overall survival when compared to traditional techniques of transanal excision.

- In order to improve cure rates and decrease local recurrence, local staging must improve. Considering the significance of very small metastatic lymph nodes, it is unlikely that ultrasound will continue as the primary staging tool. Perhaps a "functional study" which utilizes tumor metabolism will provide more accurate staging. In addition, a "scoring system" based on anatomic tumor factors (i.e., TNM) combined with histopathologic and genetic factors may be developed to help predict success and failure of local excision.
- The future of local therapy for rectal cancer may evolve similar to that of breast cancer treatment. Patients will be staged based on anatomic, histologic, and genetic data, then treated with neoadjuvant chemotherapy and radiation. Local excision, likely TEM, will follow neoadjuvant treatment and will act as a "staging biopsy." If response to neoadjuvant treatment is deemed adequate, no further therapy will be necessary. However, tumors with a lesser response to therapy will receive radical resection. In this way, major surgery and its associated morbidity and mortality will be reserved for patients who truly require it.
- The above algorithm is by no means the current standard of care, but many unanswered questions remain and treatment recommendations are in flux. No progress can be made unless we honestly evaluate past treatments, let go of traditional prejudices and embrace sound scientific research, and be willing to change based on new information.

44. Surgical Treatment of Rectal Cancer

Ronald Bleday and Nelya Melnitchouk

Introduction

- Approximately 42,000 patients each year are diagnosed with rectal cancer in the USA. Approximately 8,500 die of this disease.
- Despite remarkable recent advances in new oncologic agents, cure is almost never achieved without surgical resection.
- Management of rectal cancer is varied and complex because of the evolution in multimodality therapy and refinements in surgical techniques.

Evaluation of the Patient with Rectal Cancer

History

- The patient with rectal cancer usually presents to the surgeon with an endoscopic diagnosis. The patient's initial complaint may be rectal bleeding, a change in bowel habits, or a sense of rectal pressure. However, with the increase in utilization of colonoscopy, many patients are completely asymptomatic on presentation.
- Patient's fecal continence should be discussed prior to therapy.

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- 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 sigmoidoscopy are essential and should be performed on the initial patient visit unless the patient has a painful invasive lesion. On DRE, fixation of the lesion to the anal sphincter, its relationship to the anorectal ring, and possible fixation to both the rectal wall and the pelvic wall can be evaluated.
- Colonoscopic estimates of the location of the lesion are often misleading. DRE and sigmoidoscopy allow accurate determination of the distance from the lower portion of the lesion to a standard distal landmark. It is important to determine how much normal rectum lies distal to the lower border of the tumor and whether a patient is a candidate for sphincter sparing surgery. The likelihood of the need for a temporary diverting ostomy and posttreatment anorectal function can be estimated as well.

Colonoscopy

- A colonoscopy should be performed before surgical resection of a rectal cancer. As it 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.

Preoperative Staging

- Preoperative staging of a patient with a rectal cancer is essential and discussed in Chaps. 40 and 42.

Imaging for Rectal Cancer

- Pretreatment abdominal and pelvic imaging is necessary to identify depth of invasion into the rectal wall within a stage, size of lesion, and location of the tumor. Distal and mid rectal cancer treatment management will differ depending on the preoperative staging and imaging. Upper rectal tumors often will not. NCCN guidelines recommend CT scans of the chest, abdomen, and pelvis.

Preparation of the Rectal Cancer Patient for Surgery

- After the diagnosis and staging, the surgical approach is dependent on the location of the tumor, its depth of invasion, and the presence of metastases.

Bowel Preparation

- There have been multiple studies questioning the benefit of a bowel preparation in colorectal surgery. The rationale for a bowel preparation is that it improves visualization of luminal surfaces and reduces fecal flora, which possibly translates into reduction of anastomotic and infectious complications.
- Recent RCTs published in 2007 have shown no difference in anastomotic leaks (4.8 versus 5.4 %) or other complications. There is inadequate data to draw conclusions regarding safety of omitting bowel prep for rectal cancer surgery, as most studies have focused on colon surgery. Bowel preparation is still widely practiced by most surgeons.
- Currently, there are several methods used to mechanically cleanse the large intestine. These methods include a diet of clear liquids 1–3 days before surgery combined with one of the following: laxatives, enemas, polyethylene glycol (PEG) electrolyte lavage solutions, or PEG-based tablets.
- The choice of preparation should be individualized. For instance, large volume lavage solutions should not be used in patients with gastric emptying problems (gastroparesis caused by diabetes). Saline laxatives are often phosphate or magnesium based and should be avoided in renal failure patients.

Antibiotic Prophylaxis

- Antibiotic prophylaxis is used to decrease the incidence of postoperative septic complications. Traditional prophylaxis uses an oral regimen known as the Nichols/Condon preparation. This regimen consists of neomycin 1 g and erythromycin base 1 g by mouth at 1:00, 2:00, and 11:00 p.m. on the day before surgery (8 a.m. case). Many surgeons have substituted metronidazole 500 mg for the erythromycin base because it is bacteriocidal against a greater percentage of gut anaerobes.
- Many surgeons use perioperative systemic antibiotics in addition or instead of oral antibiotics for antibiotic prophylaxis. Regimens need to include coverage for both aerobic and anaerobic gut bacteria. With rare exceptions, SCIP (Surgical Care Improvement Project) approved antibiotics should be utilized. For long procedures, redosing should be considered depending on the serum half-life of the antibiotics used. Ertapenem may offer benefit in this regard. Some have argued that double prophylaxis with both oral and intravenous antibiotics is of benefit in immunocompromised patients or in patients in whom the dissection is below the peritoneal reflection.

Other Perioperative Issues

- All patients are prepared in the usual manner for major surgery. Blood loss is usually quite minimal for most elective colorectal surgery, and typically patients are not asked to donate autologous blood. Cardiac, pulmonary, and nutritional evaluations are performed when necessary.

- Perioperative systemic antibiotic coverage may be 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. Intravenous ampicillin 2 g and gentamicin 1.5 mg/kg are given 1/2–1 h before the procedure and for at least one postoperative dose. Oral anticoagulation is stopped and patients are placed on intravenous anticoagulation or on Lovenox® approximately 5 days before surgery. The heparin or Lovenox® is then stopped at the appropriate time before surgery (8 or 12 h, respectively). Depending on the individual risk of the patient and the extent of the operative dissection, anticoagulation is restarted as early as 8 h after surgery, but without a bolus. Careful monitoring of the patient's hematocrit and partial thromboplastin time is necessary if early reheparinization is instituted.

Anatomic and Biologic Issues

Surgical Anatomy

- The type of operation offered on the tumor's stage and location. 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 for a traditional low anterior resection.

Biologic Issues

- It is important to understand the "clinical" biology, which means the typical pattern of growth and natural history of the spread of the disease.
- The biology of lymph node metastases differs from that of other solid tumors such as breast cancer. Gabriel et al. reported in 1935 that colorectal cancers tend not to have "skip" metastases. Rectal cancers usually proceed in an orderly sequence 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.
- This predictable progression means that early intervention along with proper locoregional resection will cure most cancers. 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.

- Surgical therapy may need to be customized in patients with certain polyposis syndromes or in cancers associated with inflammatory bowel disease. With both of these conditions, a total proctocolectomy is performed. Sphincter preservation can be considered in certain patients; however, it should be recognized that any mucosa left intact is at an increased risk of developing cancer.

Surgical Procedures: Principles

- Resection of the bowel with primary anastomosis was not a common phenomenon until the late 1940s. Before that time, surgery of the colon and rectum usually meant a permanent stoma.
- Recent advances allowed primary resection and anastomosis without a colostomy or ileostomy to be the rule rather than the exception.
- Palliation is the goal when curative resection is not possible. If the patient is a reasonable operative risk and the extent of metastatic disease is minimal, then complete but palliative resection of the primary tumor leads to a better quality of life and prevents many of the distressing symptoms of an advanced primary lesion such as obstruction, bleeding, and pain. If the primary lesion is not resectable, then diversion of the fecal stream can significantly improve the patient's immediate status.
- Nonoperative therapy should be considered when there is significant metastatic disease and the primary tumor is relatively small and uncomplicated. In these cases, a colonic stent can be used to relieve a significant partial obstruction. Placement of a stent, however, is just a temporizing maneuver. If the patient responds to chemotherapy after a stent is placed, then a more definitive diversion or resection can be reconsidered in the otherwise healthy patient. One has to individualize the therapy to each situation. Improvements in chemotherapy will allow us to reevaluate this clinical scenario on an ongoing basis.

Variability in Outcome

- The cancer resection margin in the extraperitoneal rectum is limited by the bony confines of the pelvis, as well as by the proximity of adjacent anterior organs. In some cases, locoregional recurrence may be inevitable. However, locoregional failure may also result from incomplete resection.
- There is accumulating evidence of variability among surgeons in local recurrence rates for stage-matched rectal cancers. McArdle and Hole presented a review of 645 patients undergoing colorectal cancer resection at the Royal Infirmary in Glasgow. They observed significant variability in patients' postoperative morbidity, mortality, and ultimate survival, depending on the surgeon. The proportion of patients undergoing

a curative resection varied from 40 to 76 %, operative mortality from 8 to 30 %, local recurrence from 0 to 21 %, and anastomotic leak rates from 0 to 25 %.

Total Mesorectal Excision

- Total mesorectal excision in conjunction with an LAR or an APR 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.
- Improved local control is translatable into improved overall survival. Survival ranges from 68 to 78 % are observed among large published series when this technique is applied.
- 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 such that many centers routinely fashion a protective diverting stoma.
- Conventional rectal surgery is associated with a significant incidence of sexual and urinary dysfunction related to damage to the pelvic autonomic parasympathetic and sympathetic nerves by blunt dissection forces.
- Autonomic nerve preservation yields good results in terms of morbidity and functional outcome.
- 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.
- If one proceeds with a dissection beneath the presacral or pelvic fascia from the sacral promontory around to the lateral pelvic sidewall, then one can injure both parasympathetic and sympathetic nerves, which can result in impotence and bladder dysfunction.
- 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.

- Finally, a dissection anterior to both layers of Denonvilliers' fascia in a man can also put at risk the nerve and nerve plexus.
- There are no randomized control data clearly showing benefits in terms of disease-specific and overall survival in patients undergoing TME as opposed to more conventional resection.
- Adjuvant therapy has been shown to improve the results of TME surgery. In a two-arm, randomized study comparing TME with or without preoperative radiotherapy for resectable rectal cancer, patients receiving the combined therapy had a lower rate of local recurrence at 2 years. Subset analysis showed the most significant benefit in node-positive cancers.
- Figure 44.1 demonstrates schematically how the dissection should proceed. Figure 44.2 shows a cross section of the rectum, the mesorectal fat, and the associated fascia.

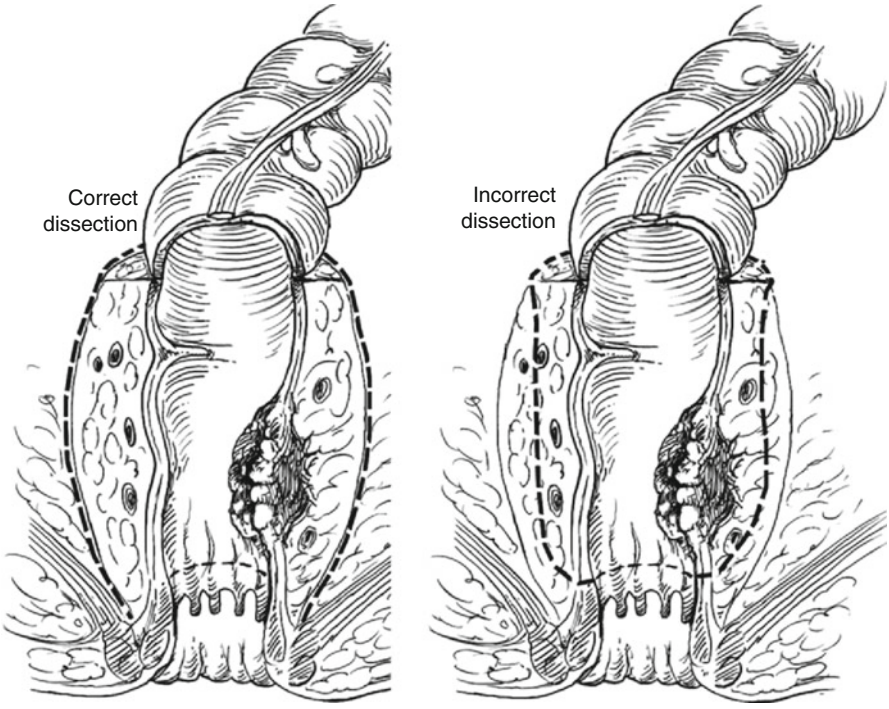

Fig. 44.1 Schematic representation of the correct TME dissection versus an incorrect dissection. The dissection should proceed between the mesorectal fascia and the pelvic wall fascia to ensure a "complete" TME

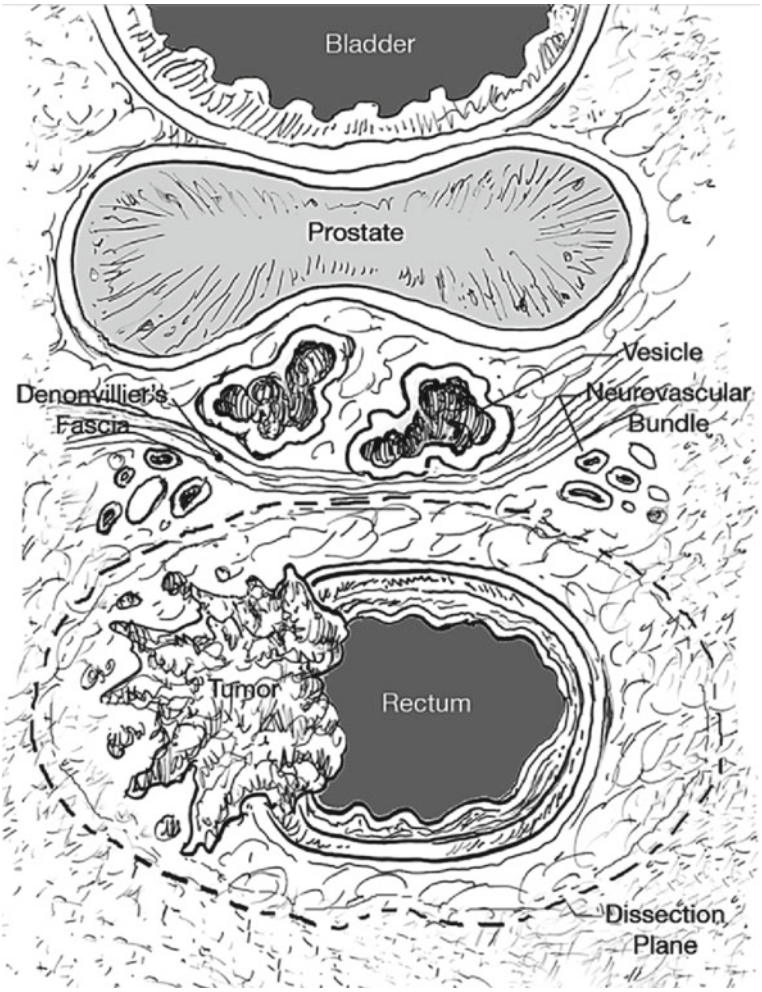

Fig. 44.2 Transverse diagram of the structures of the mid rectum. The proper dissection proceeds just outside the mesorectal fat and fascia but with sparing of the neurovascular bundle and hypogastric plexus that is located anterolaterally along the pelvic sidewall. One or both layers of Denonvilliers' fascia should be included in males and the equivalent fascial dissection along the back of the vagina in females

Distal Margins and Radial Margins

- The extent of resection margins in rectal cancer remains controversial. Although the first line of rectal cancer spread is upward along the lymphatic course, tumors below the peritoneal reflection may also spread distally by intramural or extramural lymphatic and vascular routes. When distal intramural spread occurs, it is usually within 2.0 cm of the tumor, unless the lesion is poorly differentiated or widely metastatic.

- Williams et al. in 1983 reported distal intramural spread in 12 of 50 resected rectal cancer surgical patients. It was observed that 10 of the 12 had Stage III lesions. Only 6 % had distal intramural spread greater than 2 cm. They concluded a "wet" margin of 2.5 cm was adequate in 94 % of the patients.
- They noted that only five patients (10 %) had tumors beyond a 1.5-cm margin, and all five of these patients had poorly differentiated, node-positive cancers. Also, the mortality in this group of patients was attributable to distant metastases, not local recurrence.
- Pollett and Nicholls observed no difference in local recurrence rates whether distal margins of <2 cm, 2–5 cm, or >5 cm were achieved.
- Finally, in two early studies from the British literature, surgical pathology of rectal and rectosigmoid cancer demonstrated the clinical biology of extramural lymphatic spread. In the series by Goligher et al. from 1951, only 6.5 % of patients had metastatic glands below the primary tumor, whereas 93.5 % had no retrograde spread. Approximately two-thirds of patients with retrograde spread had metastasis limited to within 6 mm of the distal tumor edge, and only 2 % had metastasis beyond 2 cm. Dukes published similar results in a study of more than 1,500 patients who had undergone APR.
- Further data from a randomized, prospective trial conducted by the National Surgical Adjuvant Breast and Bowel Project demonstrated no significant differences in survival or local recurrence when comparing distal rectal margins of <2 cm, 2–2.9 cm, and >3 cm. As a result, a 2-cm distal margin has become acceptable for resection of rectal carcinoma.
- Based upon these extensive data, a 2-cm distal margin is justifiable 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 frozen section analysis of the distal margin can be performed to confirm a cancer-free margin.
- The discussion concerning the distal margin should not be confused with the issues regarding a TME and the radial margin. It is now clear that the status of the radial margin is perhaps the most critical in local control and determining prognosis.
- Quirke et al. in 1986 demonstrated tumor spread to the radial margins of 14 of 52 rectal cancers on whole mount specimens (27 %). Twelve of these 14 patients subsequently developed local recurrence, suggesting that local recurrence is largely a result of radial spread.

Lateral Lymph Node Dissection

- A complete clearance of lateral lymph nodes or extended lateral lymph node dissection (ELD) for low-lying rectal cancers with suspected or high risk for lateral lymph node metastasis has been a routine practice in Japan.

The practice is based on the existence of lateral lymphatic drainage of the rectum, which TME does not encompass. Lateral lymphatic flow passes from the lower rectum and through lateral ligaments beyond mesorectum and ascends along internal iliac arteries and inside the obturator spaces. A study from Japan showed that the incidence of lateral lymph node involvement for low-lying rectal cancer is 16.4 %. A recent study from the Netherlands compared the treatment of rectal cancer between Japan and the Netherlands and showed 5-year local recurrence rates of 6.9 % for the Japanese ELD group, 5.8 % in the Dutch RT + TME group, and 12.1 % in the Dutch TME group.

- ELD is associated with a much higher rate of urinary and sexual dysfunctions as compared to standard TME.
- ELD is a controversial topic, and more studies need to be done on its effectiveness and the benefits versus increased morbidity before it can be recommended as a standard of care. However, in some patients where there are palpable nodes along the pelvic sidewall and along the iliacs, a patient may benefit from this extended dissection.

Selection of Appropriate Therapy for Rectal Cancer

- Three major curative options: local excision, sphincter-saving abdominal surgery, and APR.
- Clinical features may also have an impact on therapeutic decisions. 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. 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 is customized to their stage, gender, age, and body habitus (Fig. 44.3). With these issues in mind, the technical choices for a radical resection are discussed below. In all of these resections, a TME should be performed. Local treatments are discussed in detail in Chap. 43.

Techniques of Rectal Excision

Abdominoperineal Resection

- The APR was the first radical resection described by Miles in 1908 (reprinted in 1971). Miles set out several principles to be achieved with any radical resection. These principles included:
  - Removal of the whole pelvic mesocolon
  - Removal of the "zone of upward spread" in the rectal mesentery
  - Wide perineal dissection

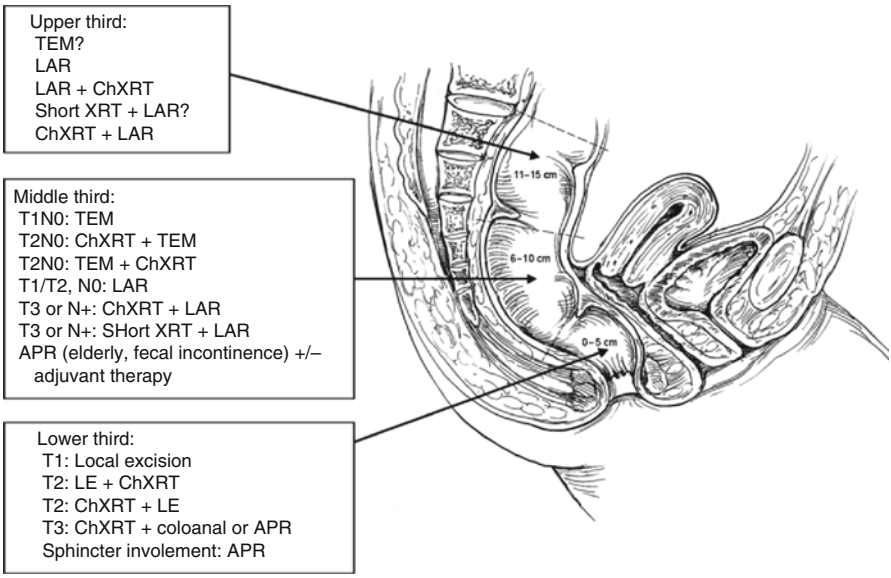

Fig. 44.3 Treatment options for rectal cancer depending on stage and location. Stage I (T1N0, T2N0 – the cancer is confined to the rectal wall, and no nodes are involved). Distal rectal cancers: T1 (invasion into the submucosa only): Local excision; Radical resection, often an APR; Adjuvant therapy is 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 (transanal endoscopic microsurgery); 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 before or after a TEM resection. Upper rectal cancers: T1 and T2: LAR; TEM? 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; 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

  - An abdominal anus
  - Removal of the lymph nodes along the iliacs.
- Four of five of these principles are the anchor of our technique even today (the dissection along the iliacs is not routinely done).
- Candidates for an APR include patients whose tumors are either 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.

- There are two approaches to APR with TME, excision of the sphincter and levators and creation of a permanent colostomy. Traditionally, the APR has been done in lithotomy position.
- Recently, there have been reports of oncologic superiority of cylindrical APR that is performed in prone position or robotically. The cylindrical approach closely resembles the original Miles APR. A recent paper by West et al. showed that cylindrical APR results in more cylindrical specimen (hence the name) and removes more tissue in the distal rectum and leads to lower radial margin involvement (14.8 versus 40.6 %) and intraoperative rectal perforations (3.7 versus 22.8 %).

Position

- For traditional APR, the patient is placed in the lithotomy position. We often elevate the mid and upper sacrum off the bed with a blanket or a towel so that the coccyx is away from the bed and therefore able to be more easily prepped into the field. For cylindrical APR, the patient is placed supine for TME portion of the operation and stoma creation and rotated to prone for perineal dissection. We usually have the second OR table ready with appropriate padding for all the pressure points so that the patient can be easily moved to prone position. With a robotic APR, the levators are excised from the abdominal approach obviating the need for prone positioning.

Incision and Exploration

- The abdomen is usually entered through a midline incision. In thin patients, the incision can often be kept below the umbilicus. The APR is also a good application of laparoscopic or robotic surgery as the abdominal portion of the procedure can be performed using laparoscopic techniques with extraction of the specimen through the perineum.
- The exploration of the abdomen and pelvis should be the first step after accessing the abdomen. The liver, aortic lymph nodes, superior hemorrhoidal lymph nodes, iliac lymph nodes, and the pelvis should all be examined. 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

- The sigmoid colon and left colon need to be mobilized to excise the whole pelvic mesocolon and “zone of upward spread.” The mobilization begins along the left pelvic brim. The gonadal vessels, ureter, and iliacs are reflected toward the retroperitoneum, and the colon and mesocolon are elevated toward the midline. The left colon is mobilized, but the splenic

flexure rarely needs to be fully taken down. The dissection then is started on the right pelvic brim. Typically, one can identify the sympathetic nerve trunks behind the superior hemorrhoidal artery (SHA) as one mobilizes the rectal mesocolon away from the sacral promontory.

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. 44.4). Because a high ligation of the SHA or of the IMA is planned, the blood supply to most of the sigmoid colon will be compromised.
- For most cases, a ligation of the SHA flush with the left colic artery should be performed. A higher ligation of the IMA should be performed if there

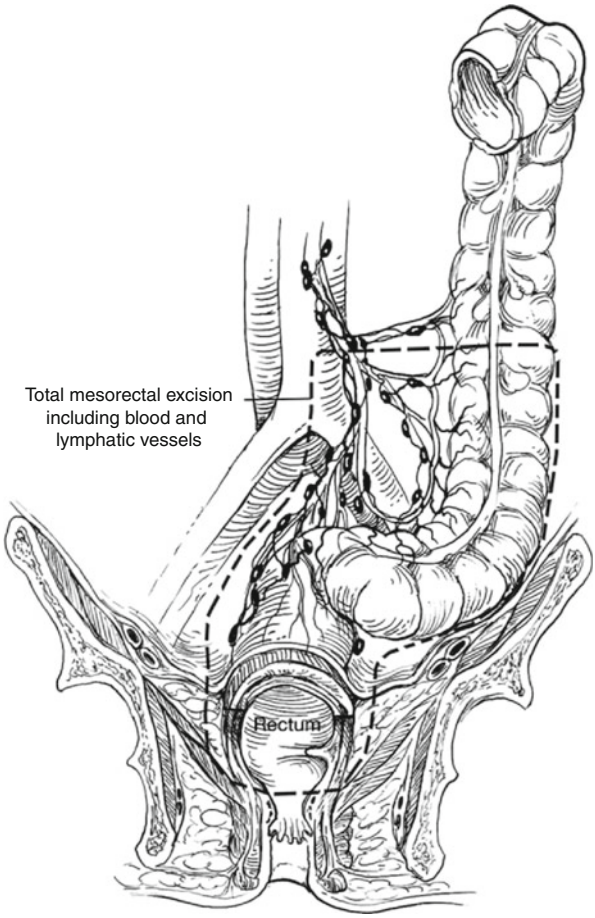

Fig. 44.4 The vascular supply of the sigmoid and rectum. A typical ligation is performed at the junction of the SHA and left colic artery. In patients with a clinical suspicion of positive nodes at the level of the IMA, or if vascular mobilization is needed for the left and transverse colon, a ligation of the IMA is performed at the aorta

is any question of lymph node involvement outside the pelvis (e.g., palpable nodes along the SHA up to or above the left colic artery).
- After dividing the bowel, the remaining mesentery is ligated and divided.

Total Mesorectal Excision

- A successful total mesorectal excision (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. Using the cautery or scissors, the nerves are reflected toward the pelvic sidewall, while the mesorectal fascia surrounding the mesorectal fat is kept as an intact unit. The dissection starts posteriorly and then at each level proceeds laterally and then anteriorly.
- In the mid rectal area along the lateral sidewalls, one can often see the parasympathetic nerves tracing anteriorly toward the hypogastric plexus. The plexus is usually on the anterolateral sidewall of the pelvis, just lateral to the seminal vesicles in the man and the cardinal ligaments in the woman.
- There is often a tough "ligament" (so called "lateral stalk") that traverses the mesorectum at this point. It theoretically contains the middle rectal artery. However, in a study by Jones et al., this artery is only present to any significance about 20 % of the time.
- The anterior dissection is often the most difficult. In men, one should try to include the two layers of Denonvilliers' fascia. This fascia is composed of peritoneum that has been entrapped between the seminal vesicles and prostate anterior and the rectum posterior (Fig. 44.5). In woman, the peritoneum at the base of the pouch of Douglas is incised, and the rectovaginal septum is then separated.
- If properly done, the mesorectum begins to appear as a bulky bilobed structure. As one progresses distally beyond the mid rectum, the mesorectal fat begins to attenuate. At the pelvic floor, there is often only a thin layer of mesorectal fat around the bowel.

Perineal Dissection

- In traditional APR, as the abdominal procedure proceeds distally, the perineal dissection can commence. Before the preparation and draping of the patient, the position of the perineum is ensured so as to allow a wide elliptical incision around the anus. The rectum is usually cleared of any stool or residual preparation, and the anus is sewn closed or clamped.
- 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. After incising the skin and subcutaneous ischiorectal membrane and fat, the levators are then encountered. A pair of long scissors or an electrocautery can be used to divide the ligaments in the posterior midline behind the rectum. Once a connection has been opened, the perineal surgeon places their finger above the levators and "hooks"

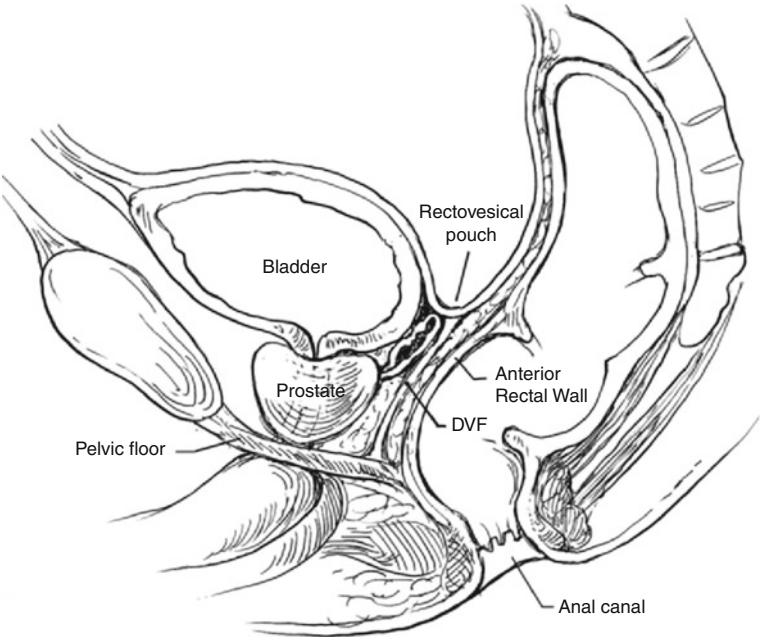

Fig. 44.5 Sagittal view of the rectum, bladder, Denonvilliers' fascia, and the prostate. The dissection should proceed anterior to one or both layers of Denonvilliers' fascia

them down toward the perineal field. The levators are then divided with the cautery. The dissection starts posteriorly and then proceeds laterally and anteriorly. Often, it is best to complete the anterior dissection after the proximal portion of the specimen has been everted out to the perineal surgeon. The remaining attachments in the anterior plane are then divided with the cautery.

- If a cylindrical open APR is planned, the patient needs to be changed to prone position after TME is complete and permanent colostomy is created. The pelvis is elevated on a pillow, and the buttocks are taped apart.
- The skin incision is marked in elliptical fashion to extend from coccyx to ischial tuberosities to perineal body. The incision is made with knife through the skin and extended down through subcutaneous tissues with electrocautery. At this point, two Gelpi retractors or a Lone Star retractor (Lone Star Medical Products Inc., Stafford, TX) facilitates the dissection. Similar to traditional approach, anococcygeal ligament is broken through with a pair of large scissors or an electrocautery and which are retracted wide open to create enough space for surgeon's finger to hook the levators, thus facilitating the lateral dissection of the rectum. Care is taken to dissect the levators off of the pelvic sidewall.
- After lateral attachments are taken down, the rectum is everted onto the field and by holding the rectum up anterior dissection is completed.

Ostomy

- Ideally, the patient has been preoperatively marked by a certified ostomy therapist. The end of the colon is carefully cleaned of any fat. The skin is divided in a circular shape at the ostomy site. The subcutaneous tissues are split and the fascia is divided in a vertical or cruciate manner. The muscle is split but not divided, and then the peritoneum is incised. The hole is made wide enough to accommodate the bowel and the accompanying mesentery. The bowel should then be brought up through the opening so that it is 1–3 cm higher than the skin and 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 the circular stapling device is largely responsible. An LAR involves dissection and anastomosis below the peritoneal reflection. An ultralow LAR indicates complete mobilization of the rectum down to the pelvic floor posterior mobilization through Waldeyer's fascia to the tip of the coccyx. Additionally, there is dissection of the plane between the anterior rectal wall and the vagina in a female patient and dissection of the plane between the rectum and the prostate in a male patient to a level distal to the inferior margin of the prostate gland.
- As long as the surgeon can obtain a distal margin of at least 1 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 ultralow 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 LAR is technically not possible.
- After an adequate distal margin is achieved, the rectum is transected at the level of the pelvic floor musculature. The remaining anal mucosa between the dentate line and the level of transection of the pelvic floor can then be "stripped," and an anastomosis between the colon and the anus is performed to restore continuity.
- Alternatively, the procedure can be started at the dentate line with a tubular mobilization of the distal rectum in the intersphincteric groove. This perineal resection can proceed up to the superior margin of the puborectalis muscle before dissecting into the pelvis and connecting with the pelvic and abdominal dissection.

- The procedure usually requires full mobilization of the splenic flexure, such that the vascular supply of the left colon now based on the middle colic vessels can reach the distal pelvis.
- The coloanal anastomosis can also be undertaken with a colonic J pouch. Because of the larger capacity of the J pouch construction, anorectal function is improved, especially early after the surgery. The J pouch is created by folding the distal end of the colon back on itself approximately 5–6 cm and then creating a common channel (Fig. 44.6). The actual anastomosis to the anus is then done from the apex of the J in side-to-end manner.
- 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 the following: baseline fecal incontinence from deteriorated anal sphincter muscles, tumor invasion of the anal sphincter musculature or rectovaginal septum, tenesmus, and technical factors such as body habitus, tumor location, and tumor size.

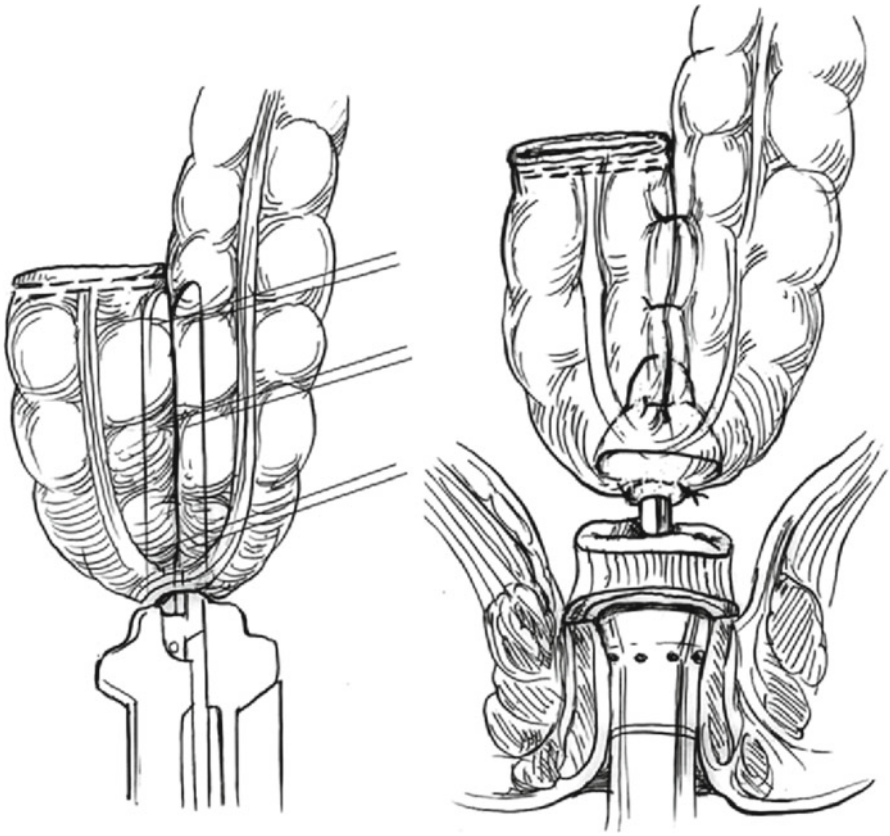

Fig. 44.6 Construction of a colonic J pouch after an ultra LAR. The distal colon pedicle is folded back on itself to make a "J." A common channel is then created using a stapling device that will staple and divide. A larger reservoir is then created. The J pouch is then anastomosed to the anus using a circular stapler or in a hand-sewn manner

- An end rectum to side colonic anastomosis is another option to the commonly used colonic J pouch.

Laparoscopically Assisted Resections for Rectal Cancer

- Exploration and mobilization of the colon and rectum can be done with the laparoscope and laparoscopic instruments. Ligation of the vascular pedicle is performed with laparoscopic clips, vascular stapling devices, or radiofrequency coagulation devices. The improved optics of laparoscopy can provide a much better view in the pelvis, thus facilitating rectal dissection.
- In recent years, there has been an increased use of laparoscopic resection for rectal cancer. Often, however, the actual resection of the bowel and an anastomosis are still more easily performed in an extracorporeal manner.
- The main questions about laparoscopic-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. It is of paramount importance that laparoscopic resection follows the same oncologic principle as open surgery including precise TME. Recent studies have indicated that there is no difference between laparoscopic and open surgery as far as 3- and 5-year survival, radial margin involvement, and local recurrence rate.
- The mean operative time for laparoscopic rectal surgery ranges from 180 to 260 min, although some studies report similar times to open surgery. The blood loss is usually less. Most of the studies report earlier return of bowel function, decreased hospital stay, and reduction in pain.
- The rate of anastomotic leak in sphincter-sparing rectal surgery is comparable between two approaches and is approximately 10 % and can be as high as 17 %.
- One of the indicators of feasibility of laparoscopic rectal surgery is the conversion rate, which is found to be between 6 and 15 %. It was also noted the conversion is associated with higher operative mortality, higher complication rate, and higher local recurrence rate.
- The ASCRS recommends that laparoscopic rectal cancer resection be practiced by expert, trained surgeons in an environment where the outcomes can be meaningfully evaluated. Ultimately, the question may be answered with the current American College of Surgeons Oncology Group (ACOSOG) trial comparing laparoscopic versus open resection of rectal cancers.

Robotic Assisted Resections for Rectal Cancer

- Similar to the laparoscopic approach, robotic assisted procedures have been gaining in popularity despite the lack of prospective evidence or

superiority, or even equivalence, the current ROLARR (Robotic versus Laparoscopic Resection for Rectal Cancer) trial should help reverse the role of this expensive technology

Local Excision Versus Radical Resection

- Although LAR and APR are the mainstays of therapy for many distal rectal cancers, radical resection is associated with significant morbidity and mortality. A review of the literature showed that mortality rates for APR range from 0 to 6.3 %, with studies showing up to 61 % incidence of postoperative complications.
- The majority of these complications are urinary dysfunction and perineal wound infections, with rates as high as 50 and 16 %, respectively.
- Radical surgery, especially APR, leads to a significant change in body image and social habits. In a patient survey performed in 1983 by Williams and Johnston, 66 % of patients complained of significant leaks from their stoma appliances, 67 % experienced sexual dysfunction, and only 40 % of patients who were working preoperatively returned to their jobs after their operation. Unfortunately, radical surgery does not guarantee a recurrence-free survival; the 5-year survival rate in the National Cancer Data Base for Stage I disease is 78 %.
- 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. This topic is discussed in Chap. 43.

Survival After Rectal Cancer Excision

- Overall 5-year survival rates after major surgery for rectal cancer is as follows:
  - Stage I, 85–100 %
  - Stage II, 60–80 %
  - Stage III, 30–50 %.

Extended Resection for Locally Advanced Rectal Cancer

- Carcinoma of the rectum will sometimes invade adjacent organs. Even when such invasion occurs, extended resection of the cancer along with the tissue or organ to which it has adhered can lead to a 5-year survival rate of >50 %, provided that the surgical margins are tumor-free.
- Patients with inflammatory adhesions to contiguous organs have a slightly higher survival rate than patients with malignant infiltration, but the

distinction between malignant and inflammatory contiguity often cannot be made until after en bloc resection. The organs that are usually involved with adhesions from rectal cancer include the uterus, prostate, urinary bladder, and vagina. 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. Although adjuvant treatment has beneficial effect on survival, surgery remains the mainstay in treatment of recurrent disease. Most often, the intent of surgery for recurrent disease is not curative but to improve survival or to palliate symptoms.
- There are three main patterns of recurrence after resection of a primary rectal cancer. The most common site of recurrence is the liver. However, isolated recurrences can also be seen locoregionally or in the lung.
- 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.
- Locoregional recurrence of rectal cancer has been decreasing over the past two decades. With the use of adjuvant therapy and the wider application of TME, local failure has been reported as low as 3 %. However, when a patient develops a local recurrence, it is often not just a suture line recurrence but a regional recurrence. The workup of these patients requires extensive imaging to identify features of the tumor that would make it unresectable.
- Wanebo et al. demonstrated a 25 % actuarial 5-year survival after abdominal sacral resection for recurrent colorectal cancer. They concluded that patients presenting after a long disease-free interval could benefit from such a large procedure.
- Noncurative surgery has only a small role in the treatment of symptomatic pelvic recurrence, particularly with sacral involvement. Newer approaches such as cryoablation of perineal recurrences may replace heroic procedures and may be useful in symptomatic relief of nonresectable pelvic recurrence.

ASCRS Guidelines

The American Society of Colon and Rectal Surgeons has published practice parameters for the management of rectal cancer.

45. Rectal Cancer: Locally Advanced and Recurrent

Robert R. Cima

Introduction

- Of patients with newly diagnosed colorectal cancer who will undergo surgery with curative intent as part of their treatment, approximately 5–12 % will have tumors that have spread beyond the anatomic landmarks of a standard resection and have invaded 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, resection (metastectomy) can be curative.
- The most important factor that influences tumor recurrence is the stage of disease at presentation.
- Other factors include obstruction or perforation at presentation, adjacent organ involvement, tumor aneuploidy, increased tumor grade, mucin production, or evidence of venous or perineural invasion.
- The preoperative evaluation, operative approach, and often the perioperative oncologic therapy are similar for primary locally advanced and recurrent rectal cancer.
- Locally advanced primary rectal cancers include tumors that are T4 N1-2 MX at the time of initial presentation. They are often associated with a higher rate of metastatic disease at the time of diagnosis and have a poorer overall prognosis than earlier stage disease.
- T4 rectal tumors are found to be fixed by physical examination or to be invading adjacent organs or structures by diagnostic imaging studies.

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- In cases where an extended en bloc resection cannot be performed to achieve complete resection, patient survival is dismal: after no treatment or after palliative surgery, mean survival time is less than 1 year.
- 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 survival for patients with locally advanced primary or recurrent colorectal cancers.
- To achieve these goals, appropriate surgery is combined with external-beam radiation (EBRT) and, under ideal circumstances, intraoperative radiation therapy (IORT) and adjuvant or neoadjuvant chemotherapy.
- Survival with an isolated, untreated, locoregional, rectal cancer recurrence is quite poor. Most of these patients 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.
- External-beam radiation alone or combined with systemic chemotherapy may result in temporary improvement of symptoms, but the 5-year survival rate is less than 5 %. 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 tumor outside of the rectum.

Preoperative Evaluation and Patient Selection

- Complete resection of a locally advanced primary or recurrent rectal cancer is a significant undertaking.
- Complete resection may be technically possible in some patients, but if their overall physical condition does not make them an appropriate candidate, surgical palliation combined with chemoradiation is the more prudent course of action.
- 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 classifications 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 spread.
- A thorough physical exam, with particular attention placed on the rectal and vaginal exam, needs to be performed, and any fixation of the tumor to rigid pelvic structures needs to be assessed.
- Imaging should be repeated before surgery is considered and compared to similar previous studies to give some reassurance that there has been no progression or spread of the disease that might change or preclude any surgical intervention.
- 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 worrisome lesion that is technically accessible should be biopsied percutaneously.
- Although the above tests are the standard evaluation for diagnosing recurrence and excluding extrapelvic spread of the tumor, other more tumor-specific tests have been proposed as adjuncts.
- Numerous nonrandomized studies have shown that FDG-PET imaging for recurrent colorectal cancer has a significantly higher sensitivity and specificity than CT scanning. When CT scanning was compared with FDG-PET imaging in postoperative patients with colorectal locoregional recurrences, the sensitivity of FDG-PET was significantly higher than CT plus colonoscopy (90 vs. 71 %, respectively), although the specificities were similar (92 vs. 85 %, respectively).
- FDG-PET imaging has been shown to maintain this high sensitivity and specificity, 84 and 88 %, respectively, even in the setting of the previously irradiated and postoperative pelvis.
- Thus, FDG-PET might be 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 of extremely high risk.
- Even the combination of physical examination and radiographic studies may not be able to prove that there is a pelvic recurrence of a rectal cancer, especially if the patient has undergone a previous pelvic operation or pelvic irradiation. We generally accept 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 histological evidence obtained from endoscopic, CT-, or ultrasound-guided biopsies of the suspicious tissue.

- Exploratory pelvic surgery should be strongly discouraged, as it poses an extreme risk to the patient and makes future evaluation of the pelvis even more difficult.

Determining Tumor 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 upon the anatomic location and what other structures are fixed to the lesion.
- Although there are other schemes for assessing resectability, we use the following one to classify our patients who are being considered for possible resection. The tumor is classified as F0 when it is not fixed to any pelvic organ or structure, FR when the tumor is fixed but resectable, and FNR when the tumor is fixed and not resectable.
- FR is further subdivided by noting the anatomical extent of the fixation (anterior, posterior, and lateral). The anatomic extent of the tumor determines 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 (Figs. 45.1, 45.2, and 45.3).
- Although we have found this classification scheme to be extremely useful, it does not reliably predict resectability before surgery because new findings may be discovered at operation.
- However, in our experience, some factors are clearly associated with an unresectable tumor (Table 45.1).
- 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.
- Finally, 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.
- Pain from nerve root involvement with tumor occasionally needs to be differentiated from sciatic nerve compression. Nerve compression symptoms may completely resolve after pelvic irradiation and chemotherapy. On the other hand, persistent buttock and perineal pain usually resulting from tumor expansion and ingrowth is a more ominous symptom.

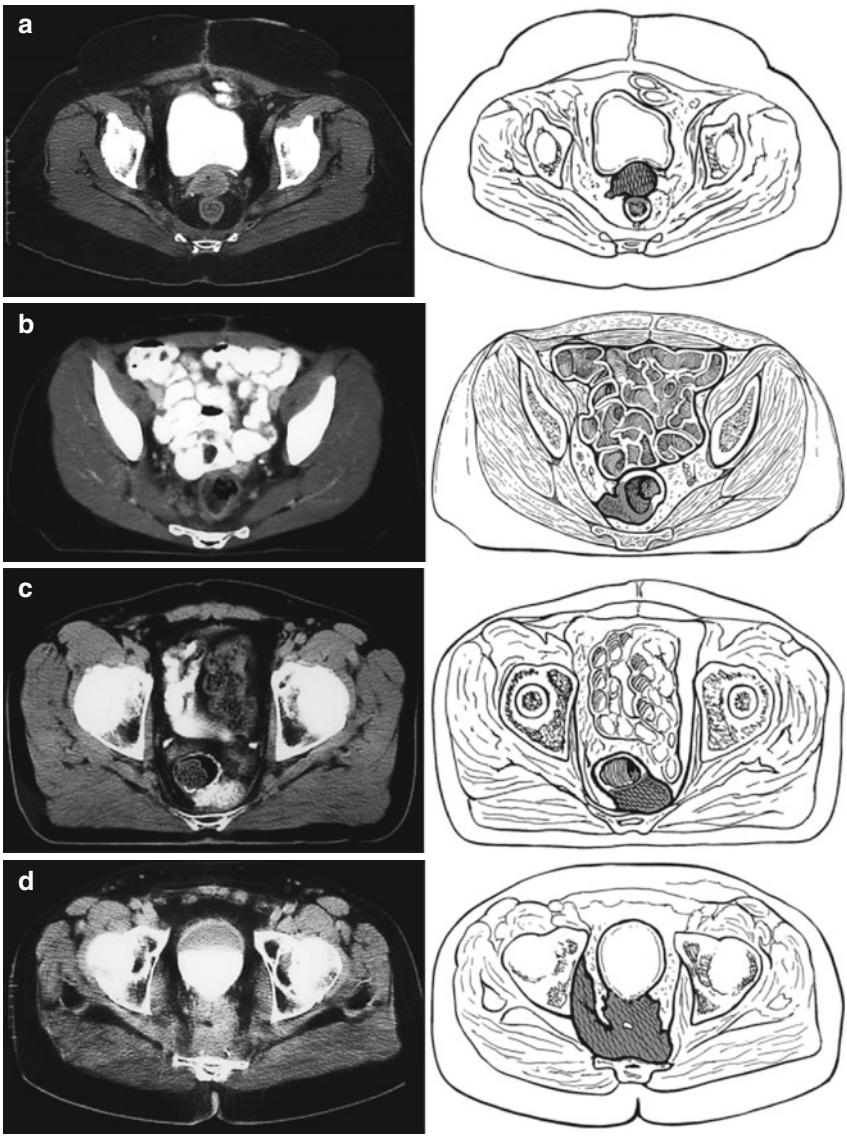

Fig. 45.1 (**a**) A primary T3N0M0 rectal cancer treated with a lower anterior resection without adjuvant therapy. The anterior recurrent tumor fixed at the base of the bladder was treated with preoperative chemoradiation and then resected with IORT. (**b**) After a primary low anterior resection for T2N0M0 rectal cancer without adjuvant therapy, this patient developed a lateral pelvic recurrence. After preoperative chemoradiation, the patient underwent an abdominal resection with negative margins. (**c**) A recurrence after a T3N0M0 lesion treated with postoperative chemoradiation therapy was found to invade the sacrum. After additional EBRT and chemotherapy, IORT combined with an en bloc resection of the tumor and distal sacrum was performed with negative margins. (**d**) A massive recurrent cancer found in the pelvis after an abdominal perineal resection and postoperative chemoradiation. The tumor was fixed to vital pelvic structures and was deemed unresectable (With permission from Nicholls RJ, Dozois RR, editors. Surgery of the colon and rectum. New York: Churchill Livingston; 1997)

Fig. 45.2 The IORT suite, showing the equipment, the position of the patient on the operating room table, and the linear accelerator

Fig. 45.3 (**a**) The assortment of the Lucite tubes used to direct the electron beam to a fixed site in the operating field to deliver the IOT. (**b**) Place of a large Lucite tube to deliver the IORT into the pelvis. The tube is fixed in place by securing it to an external support apparatus attached to the operating table

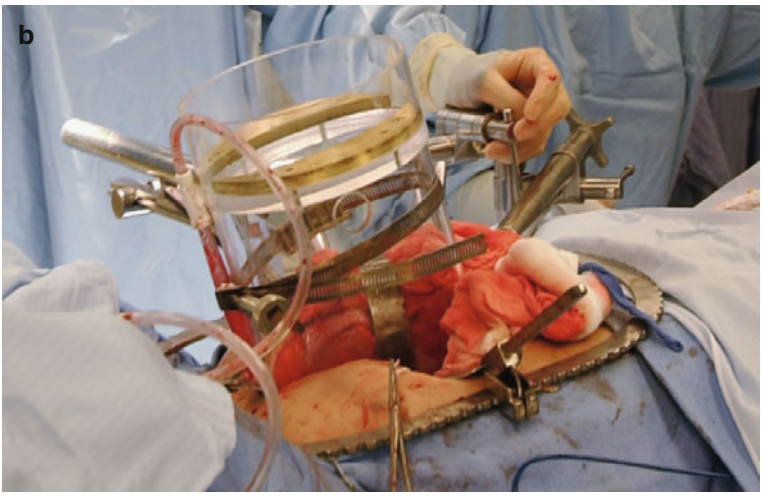

Fig. 45.3 (continued)

Table 45.1 Symptoms or findings suggestive of an unresectable tumor 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

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.
- To improve outcomes, surgery is combined with multimodality therapy, radiation, and chemotherapy. Radiotherapy is used to improve local control and systemic chemotherapy is used to treat possible disseminated disease.
- In the setting of a locally advanced or recurrent rectal cancer, centers have combined multimodality therapy with intraoperative radiotherapy – either as electron-beam radiation therapy, high-dose rate brachytherapy, or traditional perioperative brachytherapy to further improve patient outcomes.
- These forms of locally directed radiation reduce toxicity by limiting normal tissue exposure and deliver a high biologically equivalent dose to the localized area of the tumor.

- In general, patients who never received prior pelvic radiation therapy, a full course of external-beam radiation (5,040 cGy) is administered with concurrent 5-fluorouracil chemotherapy.
- Often, patients with recurrent rectal cancer have previously received a full course of pelvic external-beam radiation.
- Such patients can be treated with an additional course of 2,000 cGy of external-beam radiation combined with additional 5-fluorouracil chemotherapy before repeating pelvic surgery.
- A recent multicenter study has shown that hyperfractionated preoperative chemoradiation can be safely administered in recurrent rectal cancer patients who have previously received pelvic radiation. The overall tumor response rate was 44.1 %. Furthermore, there was no increase in postoperative complications as compared to patients who did not receive the hyperfractionated therapy.

Surgery

- Before surgery, the magnitude of the operation and the possible complications are discussed in depth with the patient and family members.
- In cases of large locally advanced primary rectal cancers, the sphincter mechanism is preserved. In recurrent cancers, there is little role for an attempt at sphincter preservation, as the risk of complications or poor functional outcomes is quite high.
- 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. All patients visit with and are marked for multiple ostomies by an enterostomal therapist.
- In the OR, the patient is placed in the lithotomy position with both arms tucked and the legs supported in Allen stirrups. Special care is taken to ensure that the arms are well padded and in a neutral position to avoid any nerve injury. The calves are positioned and padded to avoid any pressure from directly resting on the stirrups, since the lengthy operation may result in compartment syndrome and/or venous thrombosis.
- Bilateral ureteral stents are inserted cystoscopically preoperatively in all patients.
- A midline incision is usually made. Transverse abdominal incisions should be avoided, as 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.
- If the patient has had prior abdominal surgery, all adhesions need to be lysed.
- Once all adhesions have been lysed, the entire abdomen needs to be thoroughly explored for evidence of extrapelvic tumor deposits.

- The liver, omentum, retroperitoneum, peritoneal lining, and the area of any prior surgical incision should be carefully examined for metastatic disease.
- Any suspicious finding should be biopsied and analyzed by frozen section. The presence of extrapelvic disease would be a contraindication to radical resection.
- For rectal cancer recurrences that are not fixed to any pelvic structure (F0), a completion abdominoperineal resection (APR) is required. The scope of the resection is similar to a standard APR, but the pelvic fibrosis induced by any prior surgery would have distorted or eliminated the ideal, relatively bloodless plane between the mesorectum and sacral fascia.
- The distinction between fibrosis and tumor infiltration into adjacent tissue can be very difficult to discern at the time of the operation. If there is any question a frozen section should be analyzed. If tumor cells are seen, a complete resection with negative margins is not feasible. It is in this setting that the use of IORT improves clinical outcomes.
- When the tumor is fixed, either anteriorly or posteriorly, the scope of the operation is much larger than for the nonfixed lesion (F0).
- If the fixed tumor is considered resectable, we classify it as a FR (fixed, resectable) lesion. For anteriorly fixed tumors, there are different operations that need to be considered, whereas for a primary or recurrent posteriorly fixed tumor, our operation of choice is an en bloc distal sacrectomy.
- Postoperatively, these patients are managed quite conservatively as prolonged ileus and urinary retention is quite common. Given the high risk of venous thromboembolism, these patients are given unfractionated heparin three times a day, and use of mechanical compression devices and mandatory early ambulation are enforced.

Use of Intraoperative Radiation Therapy

- In cases of close margins, known microscopically positive margins, or minimal gross unresectable disease in the pelvis or after the sacrectomy, an option is to use intraoperative electron-beam radiation therapy (IORT).
- To give IORT, a Lucite cylinder is positioned in the pelvis to target the at-risk area. The patient is then positioned under the linear accelerator. One thousand to 2,000 cGy is delivered, depending on the extent of margin involvement.
- A dose of 1,000 cGy is recommended for minimal residual disease; 1,500 cGy is given for gross residual disease less than 2 cm, and 2,000 cGy is reserved for unresectable or gross residual disease more than 2 cm. The IORT dose that can be given should take into account the total of any prior external-beam radiation that has been administered.
- Other options exist of delivering intraoperative or prolonged local radiation therapy. One 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 or vinyl mesh. This is then sutured to the area of concern and other normal tissues are packed away and protected. The catheters are connected to a high-dose rate Ir source, either intraoperatively or postoperatively.

- These techniques do not require a dedicated OR with a linear accelerator to administer radiation regionally and may therefore expand where this type of surgery can be performed.
- One possible disadvantage with the use of more standard postoperative brachytherapy catheters is that it is difficult to protect normal tissue, particularly the small intestine, once the operation is complete. However, these alternative methods for delivering local radiation therapy, when combined with extended surgery and chemotherapy, seem to result in morbidity and survival outcomes that are comparable to the experience with intraoperative electron-beam radiation therapy.

Results of Multimodality Treatment for Advanced Primary or Locally Recurrent Rectal Cancer

- For patients with advanced primary rectal cancer, studies have shown the benefit of combined preoperative chemoradiation followed by radical surgery.
- In a retrospective review of 60 patients with primary locally advanced rectal cancers, 81 % were able to undergo curative resection. Their overall 2-year survival was 91 %, and their local regional recurrence rate was 7.5 %.
- In another study, preoperative chemoradiation with extensive surgery improved overall survival and control of pelvic disease compared to preoperative radiation therapy alone. In that study, the use of IORT improved local control in patients with microscopic residual disease or clinically fixed tumors. None of the patients treated with IORT developed local failure in the pelvis.
- In summary, a number of reports of patients with locally advanced primary rectal cancer who were treated with intraoperative radiation and surgery have shown an overall improvement in local control compared to historical controls.
- Surgery alone has been used to treat recurrent rectal cancers. Garcia-Aguilar and colleagues reported a series of 87 patients with recurrent rectal cancer:
  - Sixty-four patients underwent surgical exploration, and only 42 were able to undergo resection with curative intent. The estimated 5-year survival rate for patients who had curative-intent surgery was significantly better than that for patients who had only palliative or no surgery (35 vs. 7 %). 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. In general, patients treated with multimodality therapy including preoperative or intraoperative radiation therapy experience 3-year local control rates ranging from 25 to 78 %, and long-term survival has been reported to be between 25 and 40 %. The most consistent findings from all of these reports are that the most predictive factor associated with a better outcome, decreased local recurrence, cancer-specific, and overall survival is an R0 resection. The presence of microscopic positive or grossly positive margins markedly reduces survival.

- The institution with the largest reported experience using multimodality therapy including IORT for recurrent rectal cancer is the Mayo Clinic. Between 1981 and 1996, 394 patients were treated, 90 of whom had unresectable local or extrapelvic disease at the time of surgical exploration. Although 304 patients underwent resection of the recurrent tumor, only 138 (45 %) underwent a histologically confirmed curative resection:
  - The 166 remaining patients had a palliative operation because of either gross ($n=139$) or microscopic ($n=27$) residual cancer in the pelvis.
  - The 1-year, 3-year, and 5-year survival rates for the 304 patients were 84, 43, and 25 %. The median survival time was 31 months.
  - The 5-year survival rate was greater after curative surgery (i.e., negative histologic margins) than after palliative surgery (37 vs. 16 %, $P<0.001$). The presence of gross residual disease in patients who underwent nonpalliative resections resulted in decreased survival compared to those patients with microscopic residual disease.
  - However, survival for patients who had extended resections was not significantly different than that for patients who had a limited resection (28 vs. 21 %, $P=0.11$, respectively). Logistic regression analysis found several independent factors that contributed to the ability to perform a curative resection. On multivariate analysis, increasing number of tumor fixation sites was associated with a palliative resection. These factors also affected overall survival; patients with pain and more than one site of fixation had significantly lower survival rates.
  - The best 5-year survival rates were in patients who had nonfixed tumors (41 %) or asymptomatic recurrences (41 %).
- Other institutions that have used a multimodality approach that included some form of intraoperative radiation have reported similar improvements in local recurrence and survival.
- Perioperatively related mortality was very low in patients who undergo this multimodality treatment (0.3 %). Unfortunately, the treatment-related morbidity is relatively high.

- In one series of 304 patients who underwent surgery with curative intent, 96 (32 %) required prolonged hospitalizations, 78 (26 %) of whom required readmissions and/or additional surgical procedures.
- The most frequent complications included pelvic abscesses (6.6 %), bowel obstructions (5.3 %), enteric fistulas (4.3 %), and perineal wound complications (4.6 %).
- The complication rate was significantly higher in patients who underwent extended surgical resections and in patients who had recurrences fixed in more than two sites in the pelvis. These findings underscore the need for thorough preoperative patient selection to ensure that the patient is fit enough to tolerate the surgery and the potential complications and that there is no evidence of disease outside of the region of resection.

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. The local effect within the pelvis of an advanced or recurrent rectal cancer drives the need to address control of symptoms.
- These symptoms often include rectal bleeding, rectal obstruction, urinary obstruction due to local invasion, and severe pain related to invasion of the pelvic sidewall or direct invasion of pelvic nerves.
- Over the past decade, the choice of palliative options has expanded, and the choice of treatment requires careful consideration of the presenting symptoms, possible future symptoms, extent of local and distant spread of the disease, and the overall physical condition of the patient.
- Palliative interventions may be broadly classified as noninvasive, minimally invasive, and surgical.
- The primary noninvasive palliative option is radiotherapy. In patients who have never received pelvic radiation, a full course of external-beam irradiation may be a very effective treatment for bleeding, pelvic pain, and near obstruction. The use of external-beam radiotherapy may result in palliation of severe pelvic pain in 50–90 % of patients.
- However, virtually all patients will experience progression of the tumor and recurrent symptoms before they die.
- 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. In a review of the literature, palliation with SEMS was achieved in 90 % of patients.

- In the largest series to report on SEMS for malignant rectal obstructions, stents could be deployed successfully in 36/37 patients with rectal obstructions, and 28 had good long-term results with no need for subsequent intervention.
- Endoscopic lasers are an alternative to SEMS. The neodymium yttrium argon garnet (Nd:YAG) laser is the most commonly used. Endoscopic laser treatments remove the tissue from the lumen 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 appear to be a durable treatment. Effective palliation declines as patients survive longer; successful palliation at 1 year was only 42 %.
- There is no data on the use of palliative resections in patients with locally advanced or recurrent rectal cancer. However, a report from Memorial Sloan-Kettering has evaluated the role of palliative resection in 80 patients with stage IV rectal cancer. Twenty-four percent had clinical evidence of obstruction and 94 % had either T3 or T4 lesions. None had received prior surgery or radiation therapy. They underwent radical resection of the primary lesion and surgical treatment of solitary hepatic metastasis, if present.
- There was one death, a 15 % postoperative morbidity, and a 20 % colostomy rate. The overall local recurrence rate was 6 %, the actuarial local control at 2 years was 94 %, and the median survival was 25 months.
- This study shows that 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.

Summary

- For patients with advanced primary or recurrent rectal cancers, the only hope of cure requires a coordinated multidisciplinary approach to treatment. In general, EBRT, chemotherapy, extensive surgery, and the use of directed IORT appear to improve local control and survival.
- Surgery in these patients carries a higher morbidity rate than surgery for primary rectal cancer but one that is acceptable in appropriately selected patients. Before proceeding with multimodality therapy, patients should be thoroughly evaluated for the presence of disseminated extrapelvic or metastatic disease, which would, in most instances, preclude a curative operation.

46. Colorectal Cancer: Adjuvant Therapy

Kelli Bullard Dunn and Judith L. Trudel

Colon Cancer

- The stage of disease at presentation is the most important predictor of outcome for colon cancer patients. Stage I disease (T1-2N0M0) has a 5-year survival rate of 95 % after resection, and surgical treatment alone is considered sufficient.
- Stage II disease (T3-4N0M0) has a 5-year survival, averages 70–80 %, but a subset of high-risk patients have poorer prognosis and may benefit from adjuvant therapy.
- Stage III (TanyN1-2M0) disease has improved survival with adjuvant treatment, with 5-year survival of approximately 40–60 %.

Adjuvant Chemotherapy for Stages II and III Colon Cancer

- Nodal status is the single most important prognostic factor in colon cancer and recurrences are often systemic.
- 5-fluorouracil (5-FU)/leucovorin (LV)-based adjuvant chemotherapy is now considered to be the standard of care for stage III disease in the USA.
- Historically, single-agent chemotherapeutic agents such as thiotepa or fluoropyrimidines did not prove helpful. Combination trials of chemotherapy and immune modulators helped refine the recommendations made for adjuvant treatment.

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- The National Institutes of Health published a consensus statement in 1990 establishing 5-FU plus levamisole as the standard adjuvant therapy for stage III colon cancer.
- While the usefulness of 5-FU/levamisole in stage III disease was being confirmed, leucovorin emerged as a beneficial agent for the treatment of metastatic disease. Its applicability to stage II and stage III disease was confirmed by the IMPACT (International Multicenter Pooled Analyses of Colon Cancer Trials) study in 1995; 3-year disease-free survival increased from 62 to 71 % ($p=0.0001$), while overall survival increased from 78 to 83 % ($p=0.029$) in the 5-FU/leucovorin group.
- The relative merits of levamisole and leucovorin as modulators of 5-FU-based adjuvant chemotherapy and the optimal duration of treatment were documented in studies between 1998 and 2000.
- Based on these studies, treatment was changed to 6 months of adjuvant chemotherapy with 5-FU/leucovorin for stage III disease.
- While the efficacy and benefits of adjuvant chemotherapy for stage III node-positive disease are unequivocal, the role of adjuvant chemotherapy for stage II node-negative disease remains controversial.
- The likelihood of reaching a resolution on this subject is remote: in order to detect a significant survival benefit among stage II colon cancer patients (who have an estimated 5-year survival of 80 %), an adjuvant trial with a no-treatment control arm would require a sample size of 5,000–8,000 patients.
- Irinotecan and oxaliplatin are effective in treating stage IV (metastatic) colorectal cancer but no survival advantage was achieved by adding irinotecan to 5-FU (5-year survival was 74 % vs. 71 %) and toxicity (gastrointestinal and hematologic) was increased for stage III disease.
- The multicenter international randomized MOSAIC trial confirmed that the addition of oxaliplatin to 5-FU/leucovorin (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.
- This improvement in survival has proven durable in stage III disease and 6-year overall survival recently has been reported to be 73 % in the FOLFOX group compared to 69 % in the 5-FU group. Toxicity also proved to be acceptable, with fewer than 1.5 % of patients experiencing grade 3 peripheral sensory neuropathy.
- For stage II patients, the addition of oxaliplatin offered no survival advantage over 5-FU alone.
- As a result of these studies, FOLFOX is now recommended for adjuvant therapy in stage III colon cancer. In select stage II patients, especially those with high-risk features such as T4 tumors, vascular invasion, or poor differentiation, FOLFOX may have a role.

Targeted Biologic Therapy

- Monoclonal antibodies targeting specific tumor proteins have proven useful in treating selected patients with metastatic colorectal cancer. In the adjuvant setting, antibodies against epidermal growth factor receptor (cetuximab) and vascular endothelial growth factor (bevacizumab) failed to show benefit even when KRAS wild-type tumors were looked at separately

Radiotherapy

- Combined chemoradiotherapy has been shown to increase both local control and survival for patients with locally advanced and node-positive rectal cancer.
- Locoregional failure in colon cancer 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 salvageable surgically.
- The most important risk factors for local recurrence were (1) pathological 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 two- to threefold increase in local recurrence for any given pathological stage.
- At this time, the precise role of adjuvant radiotherapy in the treatment of colon cancer remains undefined. 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.

Rectal Cancer

- Local and distant staging orients the decision for adjuvant radiotherapy and/or chemoradiotherapy and for available surgical approaches, such as local excision or an abdominal procedure.

Adjuvant/Neoadjuvant Therapy for Stage I Rectal Cancer

- Like stage I colon cancer, 5-year survival after curative intent surgery (radical resection) for stage I rectal cancer exceeds 90 % and adjuvant or

neoadjuvant therapy is not recommended for patients who undergo radical resection of T1 or T2N0 tumors.

- The morbidity of radical surgery has led some surgeons to consider local (transanal) excision for these early lesions. Recurrence after local resection of T1 tumors ranges from 4 to 18 %; for T2 tumors, recurrence ranges from 27 to 67 %.
- For this reason, adjuvant radiation and/or chemoradiation therapy after local (transanal) excision have been suggested as an adjunct to surgery to improve local control and prolong survival. Uncontrolled studies suggest that the addition of adjuvant therapy improves outcome.
- ACOSOG Z6041 is evaluating patients with T2 N0 rectal cancers in an attempt to determine if preoperative chemoradiation followed by transanal excision will result in disease-free survival equivalent to that seen after radical surgery. Preliminary results have shown considerable morbidity for patients in whom medical comorbidities preclude an abdominal procedure; adjuvant or neoadjuvant chemoradiation therapy may be appropriate to improve local control.

Adjuvant/Neoadjuvant Therapy for Stages II and III Rectal Cancer

- Combined modality chemotherapy and radiation have long been used as adjuvant therapy for locally advanced (stages II and III) rectal cancer. Several studies demonstrated both improved local control and prolonged survival and resulted in the 1990 NIH consensus conference recommendation for postoperative chemoradiation therapy in these patients.
- There is little controversy regarding adjuvant or neoadjuvant therapy for stage III (TanyN1M0) disease. However, advances in surgical technique, such as total mesorectal excision (TME), for locally advanced node-negative cancers (T3-4, N0, M0; stage II) have improved local control with surgery alone, prompting some surgeons to abandon adjuvant therapy in these patients.
- Although the data from these studies are intriguing, other reports have shown that chemoradiation improves local control and survival even in patients who undergo TME. Adjuvant or neoadjuvant therapy is still recommended for all patients with stage III disease and the majority of patients with stage II disease. In well-selected patients with T3 tumors, favorable histology, and negative radial margins, chemoradiation may not be necessary, but larger prospective studies are required before this approach can be recommended.

Radiation Therapy

- Initial neoadjuvant radiation has long been considered an important adjunct in the treatment of rectal cancer. A short preoperative course, 20–30 Gy given over 1 week (most commonly used), is biologically equivalent to the traditional postoperative course of 45–55 Gy given over 5–6 weeks.

- In 1993, the randomized Swedish Rectal Cancer Trial (SRCT) demonstrated that a biologically equivalent short course (25 Gy) of preoperative radiotherapy with surgery within the next week significantly reduced local recurrence from 27 to 12 % and improved 5-year survival rates from 48 to 58 % when compared to surgery alone.
- The main objection to all trials showing improvement in local recurrence and survival rates with radiotherapy, including the SRCT, is that surgical technique was not optimal. The average local recurrence rate in the "surgery alone" arm in all trials discussed in the meta-analyses was 29–30 %.
- Although the undisputed major benefits of preoperative radiotherapy remain locoregional tumor control and decreased local recurrence, several reports have shown that lower local recurrence rates have been achieved in specialized centers using a more meticulous surgical technique.
- In the randomized multicenter study (Dutch trial) of 1,861 patients with rectal cancer, 2-year local recurrence rates were significantly improved from 8.2 to 2.4 % when preoperative radiation was given prior to TME. Five-year figures confirm a reduction in local recurrence rates from 11.4 % after TME alone vs. 5.6 % for preoperative radiotherapy followed by TME, but this does not translate into an improvement in 5-year survival rates.
- Neoadjuvant radiotherapy still has a place in the treatment of rectal cancer, even when surgical technique is optimized.
- A recent update of the EORTC 22921 trial confirmed that chemotherapy in addition to radiation therapy is beneficial for patients who respond well (ypT0-2) vs. those who respond poorly (ypT3-4).
- Because it is difficult, if not impossible, to predict tumor response to neoadjuvant therapy, most oncologists currently recommend combination chemoradiation therapy.

Adjuvant vs. Neoadjuvant Therapy

- Although combination chemotherapy and radiation have been shown to decrease local recurrence and improve survival for patients with stage III rectal cancer and many with stage II rectal cancer, the optimal timing of therapy has been controversial.
- According to three recently published meta-analyses, there is no doubt that neoadjuvant treatment is superior to adjuvant treatment with regard to reduction in local failure rates and cancer-specific survival.
- As such, preoperative chemoradiation is now recommended for all patients with clinical stage III disease and most with clinical stage II disease.

Chemotherapeutic Agents

- Like colon cancer, adjuvant and neoadjuvant therapy for rectal cancer have long utilized 5-FU-based regimens. Infusional 5-FU and, increasingly, oral 5-FU (capecitabine) have used as radiosensitizing agents.

- Because additional agents such as oxaliplatin have shown synergistic efficacy in the metastatic setting, the addition of this agent to neoadjuvant regimens has been suggested. Two recent phase II studies of oxaliplatin in combination with capecitabine and radiation demonstrated good complete pathologic responses (16 and 24 %) with acceptable toxicity (grade 3–4 toxicity in only 12 and 20 % of patients).
- Prospective randomized phase III trials (PETACC-6 and NSABP R-04) are currently underway to assess the efficacy of this approach.

Radiation Dose and Timing of Surgery After Completion of Treatment

- Controversy also exists as to the optimal radiation dose and timing of posttreatment surgery. Current regimens in the USA typically give a total of 45–54 Gy of radiation over 4–6 weeks. Surgery is then performed 6 weeks later.
- Many European centers, in contrast, favor a short course of radiation consisting of five fractions of 500 GY (total dose = 25 Gy) without chemotherapy followed by surgery within 1–2 weeks.
- Advocates of the short course of radiotherapy suggest that the lower dose of pelvic radiation will result in fewer complications while maintaining efficacy in tumor control. Earlier surgery theoretically may prevent tumor progression. Detractors counter that the lower dose may not be as efficacious and that immediate surgery does not allow enough time for maximal tumor shrinkage.
- The Swedish Rectal Cancer Trial has shown that short-course radiotherapy improves local control and long-term survival compared to surgery alone. Similarly, the Dutch Colorectal Cancer Group has shown that short-course preoperative radiotherapy decreases local recurrence and increases survival compared to total mesorectal excision alone.
- However, there are no studies to date that compare short-course vs. long-course chemoradiation and the majority of radiation oncologists in the USA continue to offer standard 45–54 Gy treatment.
- Delaying resection may improve the clinical response to chemoradiation and lead to a larger proportion of patients having a pathologic complete response (pCR). Several centers have begun to study the timing of surgery following neoadjuvant treatment.

Chemotherapy Alone

- In contrast to colon cancer, chemotherapy alone as adjuvant treatment in rectal cancer remains questionable. Early 1980s underpowered US radiotherapy trials concluded that chemotherapy improved survival compared to surgery alone. Two large randomized trials comprising more than 4,000 patients have studied the value of chemotherapy vs. surgery alone in

colorectal cancer. Rectal cancer patients were included in both studies. Combination 5-FU/levamisole and 5-FU/leucovorin were found to improve survival in colon cancer patients but showed no benefit in rectal cancer patients. These results underscore the difference in chemotherapy effectiveness for rectal cancer and colon cancer. The reasons for this are unclear: different tumor profiles or lack of proper surgical technique at the time of these trials may partly explain the results. At this time, adjuvant chemotherapy alone for stage III rectal cancer is not acceptable unless the patient cannot receive radiotherapy (history of previous pelvic radiation).

Neoadjuvant Therapy in Unresectable Rectal Cancer

- In this section, we define a nonresectable rectal cancer as a tumor which cannot be resected without a very high risk of local recurrence. These tumors are clinically tethered or fixed (due to cancer overgrowth or fibrosis). Such tumors probably involve the rectal fascia, and resection carries a high likelihood of involvement of the circumferential resection margin.
- Based on available data, patients with such large tumors benefit from long-course preoperative radiotherapy (45–55 Gy over 5–6 weeks) with the aim of downsizing the tumor.
- The role of additional chemotherapy has been unclear in this context.

Neoadjuvant Therapy and Sphincter Preservation

- 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.
- 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 to those with an anterior resection. This must be considered when selecting surgical options for individual patients.

Molecular Profiling and Chemoresistance

- Increasingly, tumor characteristics are found to influence response to chemotherapy and “personalized” treatment based upon molecular profiling shows increasing promise for increasing response to therapy while decreasing toxicity.
- Microsatellite instability (MSI) and rates of phenotypic expression of DNA synthesis-associated enzymes recently have been found to predict chemoresistance to 5-FU and irinotecan.

- For example, microsatellite instability not only appears to confer better prognosis but may also predict poor response to chemotherapy, suggesting that patients with MSI-high tumors may not benefit from adjuvant therapy.
- Similarly, polymorphisms in the enzymes that synthesize and metabolize folate may affect both efficacy and toxicity of 5-FU-based therapy.
- Finally, the observation that k-ras status predicts response to EGFR-targeted therapy in metastatic colorectal cancer has implications for adjuvant therapy. This is an area of research, which is evolving rapidly, and our increasing knowledge on the impact of molecular characteristics will certainly change the recommendations for adjuvant treatment in the future.

47. Colorectal Cancer: Metastatic (Palliation)

Elisabeth C. McLemore and Sonia Ramamoorthy

Introduction

- Approximately 20 % of colorectal cancer patients present with established distant metastases. A diagnosis of stage IV disease allows for appropriate operative and oncologic planning.
- Among these patients there is enormous heterogeneity with respect to sites of disease, extent of disease, symptoms, performance status, and comorbidities. 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, multiorgan metastases.
- While treatment algorithms may exist for some forms of metastatic disease such as a solitary liver lesion, others are still being defined.
- Despite considerable progress in the treatment of advanced colorectal cancer, the vast majority of stage IV patients are not curable by current treatment protocols. A recent analysis of data from the SEER population-based database estimates that the 5-year survival rate for stage IV patients diagnosed between 1991 and 2000 was 8 %.

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- Despite a low overall cure rate, treatment options are available to extend survival and enhance quality of life. 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 if indicated of the metastatic lesions can provide excellent palliation and in some cases can provide lasting cure.
- First-line therapy with either FOLFOX or FOLFIRI 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. Multiple effective drug combinations are available as well, and second-line chemotherapy has become more effective and more likely to impact survival.
- Over the past 10 years, the median survival for patients with metastatic disease who are treated with chemotherapy has improved from 12–14 to 21 months. Although cure from chemotherapy alone remains extremely rare, effective chemotherapy combined with aggressive surgery may be increasing the overall cure rate.

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.
- The biologic process of metastasis is poorly understood. The process relies on properties of the tumors cells, as well as the microenvironment of the primary and secondary sites. A series of major events must occur (Fig. 47.1).
- 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.

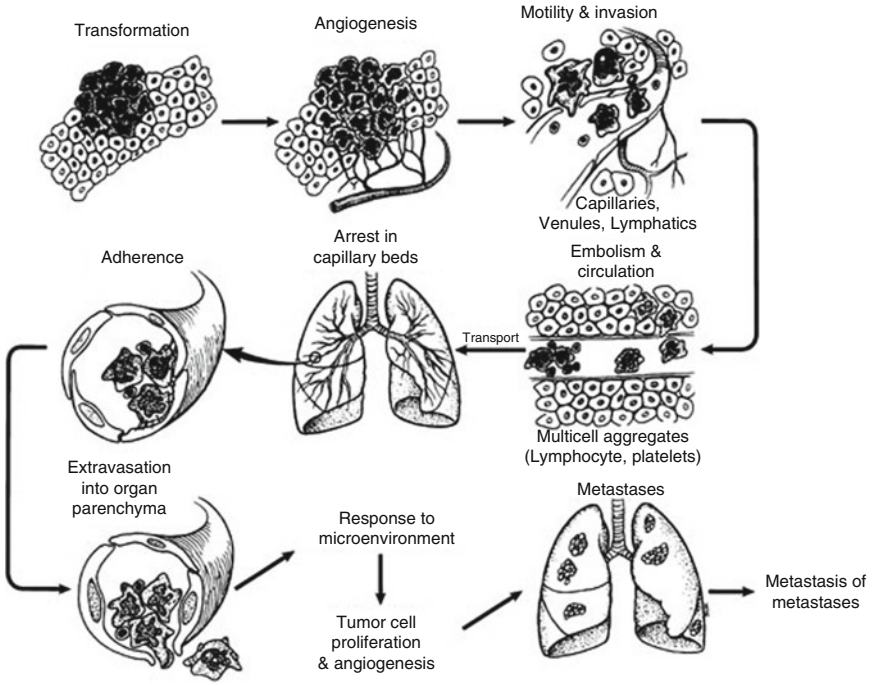

Fig. 47.1 Schematic illustrating the multistep process involved in the development of metastasis (With permission from DeVita VT Jr., Hellman S, Rosenberg SA. Cancer: Principles and Practice of Oncology, 6th ed., Lippincott Williams and Wilkins, copyright 2001)

- 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. Most researchers believe that there is a selection process resulting in the clonal expansion of certain cell subpopulations with growth advantages and invasive properties.
- Malignant invasion is characterized by downregulation 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.
- 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. 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.

- These metastatic cells can become dormant or proliferate; what determines this fate is not fully understood. Growth in the distant organ after deposition is a major limiting factor in the formation of metastasis.
- Recent studies have shown differences in the genetic fingerprints of matched primary tumors and their lymph node metastasis suggesting that tumors may undergo continual mutagenesis.
- This finding appears to confirm that there are genes specific to tumorigenesis, invasion, angiogenesis, and other steps.
- 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.

Diagnosis/Staging

- Spiral CT scanning of the chest/abdomen/pelvis is a highly accurate and efficient method of detecting metastases.
- 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.
- Increasingly, more patients are undergoing combination CT/PET scans to evaluate both the primary and metastatic lesions as this combined modality allows for better localization of tumor deposits and can assist with operative planning as well as radiation-based therapy.
- 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 comorbidities 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 are surgically resectable, and the patient can be treated with curative intent. If complete resection of all disease can be expected, then surgical intervention should be attempted.

Multidisciplinary Evaluation

- Management of patients with advanced disease is complex, and multidisciplinary evaluation can be helpful in determining initial therapy. The multidisciplinary team or "tumor board" ideally involves a surgeon, medical oncologist, radiation oncologist, pathologist, radiologist, and gastroenterologist.

Palliative Management of the Primary Cancer: Laser, Fulguration, and Stents

Incidence and Presentation

- 8–29 % of patients with colorectal cancer initially present with symptoms of partial or complete bowel obstruction.
- In a review of 713 obstructing carcinomas, 77 % were left-sided and 23 % were right-sided cases.
- The majority of patients with obstructing colorectal carcinomas have either stage III or stage IV disease.
- Acute malignant colon or rectal obstruction is an indication for emergent surgical intervention. However, these emergency operations are associated with a mortality rate of 15–34 % and a morbidity rate of 32–64 % despite advances in perioperative care.
- Therefore, alternative palliative endoluminal strategies aimed at relieving obstruction have gained increasing popularity.
- The initial symptoms of bowel obstruction include mild discomfort and a change in bowel habits. With disease progression and luminal narrowing, the symptoms may worsen ranging from crampy abdominal pain, abdominal distension, nausea, abdominal tenderness, and obstipation.
- Leukocytosis is a concerning finding and may indicate a near or complete obstruction. Without treatment, the process can progress to complete obstruction, ischemia, and perforation. The risk of cecal perforation is greatest in patients who have a competent ileocecal valve, which does not allow decompression of the large intestine into the proximal small intestine.
- In the setting of metastatic cancer, the clinician must first answer the following critical question, "is the colon or rectal obstruction a contraindication for systemic chemotherapy or radiotherapy?"
- The degree of obstructive symptoms, endoscopic, and radiographic findings are key elements to consider when answering this question. If the patient has minimal symptoms, the cancer can be traversed endoscopically, and there is no radiographic evidence of high-grade obstruction and many patients with partially obstructing colon and rectal cancers will tolerate aggressive chemotherapy.

- In those patients with partially obstructing rectal cancers, the addition of radiation therapy is also well tolerated and can be highly effective.
- Patients must be instructed to monitor their symptoms closely and to report any signs of worsening obstruction immediately.
- For patients with advanced obstruction, nonsurgical palliative options include laser therapy, fulguration, and colonic self-expanding metal stents. If less invasive endoluminal strategies are not successful in patients with nonresectable malignant obstruction of the colon and rectum, surgical creation of a palliative proximal diverting stoma or intestinal bypass should be performed.

Laser Therapy and Fulguration

- Laser therapy has been utilized for palliation of obstructing rectal cancers. The immediate success rate in treating obstructive symptoms is in the range of 80–90 %.
- 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 sessions are often required in order to achieve lasting relief of symptoms.
- Serious complications like bleeding, perforation, and severe pain have been reported in 5–15 % of patients, especially those undergoing multiple treatment sessions.

Self-Expanding Metal Stents

- Since their introduction in 1991, colonic stents have become an effective method of palliation for obstruction in colorectal cancer patients, especially those with unresectable metastatic disease.
- Stents can be placed in patients using minimal sedation and allow endoscopic assessment of the proximal colon. Moreover, these stents can be placed across relatively long lesions by overlapping stents in a "stent-within-stent" fashion.
- A systematic review from 1990 to 2000 included 29 case series and evaluated technical and clinical success, complications, and reobstruction.
- Stent insertion was attempted in 598 cases and was technically feasible in 551 (92 %) cases and clinically successful in relieving obstruction in 525 (88 %) cases.
- Palliation of obstruction was achieved in 302 (90 %) of 336 cases. Stent placement as a "bridge to surgery" was successful in 223 (88 %) of 262 insertions of which 95 % had a one-stage surgical procedure.
- There were three deaths (1 %). Perforation occurred in 22 cases (4 %). Stent migration was reported in 54 (1 %) of the 551 technically successful cases. Stent reobstruction occurred in 52 (10 %) of the 525 clinically

successful cases and trended toward a higher incidence of reobstruction in the palliative treatment group.

- There is limited data evaluating stent placement proximal to the splenic flexure. In a recent publication, colonic stenting was attempted in 97 patients with malignant large-bowel obstruction. Sixteen (17 %) patients had lesions proximal to the splenic flexure (eight ascending, eight transverse colon). Stenting was successful in relieving obstruction in 14 (88 %) of these patients.
- Complications reported in the literature for colonic and rectal stents include stent malpositioning, stent migration, tumor ingrowth (through the stent interstices), tumor overgrowth (beyond the ends of a stent), perforation, stool impaction, bleeding, tenesmus, and postprocedure pain. Stenting of cancers in the mid to low rectum may result in urgency, pain, and incontinence. While the complications associated with stents and other less invasive endoluminal strategies should not be taken lightly, one must keep in mind that emergency operations for malignant colon and rectal obstruction have a mortality rate of 15–34 % and a morbidity rate of 32–64 %.

Surgical Management of the Primary Cancer: To Resect or Not to Resect?

- The role of surgical resection of the primary colon or rectal cancer in patients with unresectable metastases is controversial, and no randomized controlled trials have demonstrated a survival benefit for bowel resection in stage IV patients.
- Randomized trials of 5FU-based chemotherapy vs. best supportive care, conducted in the 1990s, have shown that stage IV patients receiving systemic chemotherapy have increased length and quality of life.
- At this time, standard management for patients with unresectable metastatic colorectal cancer is systemic chemotherapy, at least initially.
- The proper use of elective colon and rectal resections in nonobstructed patients is a source of continuing debate. Loss of performance status, risk of surgical complications, and delay in chemotherapy are potential downsides to palliative surgical resection.
- On the other hand, elective operations have a far lower morbidity than emergency surgery. In addition, there are increased risks and potential complications associated with operations performed on patients who develop large-bowel obstruction while receiving chemotherapy or who present with more advanced disease after multiple cycles of ineffective chemotherapy.
- From the limited data in the literature, it is clear that initial colon resection is frequently practiced, particularly for patients with colon primaries and

with less extensive metastatic disease. However, it is difficult to assess the impact of colon and rectal resection on symptom control, tolerance to subsequent chemotherapy, quality of life, or survival from these studies.

- A recent meta-analysis evaluating patients with stage IV colorectal cancer treated with chemotherapy combined with and without surgical resection revealed prolonged survival in patients undergoing palliative surgical resection and chemotherapy when compared to chemotherapy alone. Chemotherapy regimens included 5-flourouracil, oxaliplatin, and irinotecan.
- Eight retrospective studies with a sum total of 1,062 patients met the inclusion criteria for this study. The median survival for palliative surgical resection combined with chemotherapy ranged from 14 to 22 months (data extracted from studies with 100 % patient participation in systemic chemotherapy). The median survival for chemotherapy alone was 6–15 months.
- The estimated standardized median difference in survival was 6.0 months in favor of palliative surgical resection (standardized difference 0.55; 95 % CI 0.29, 0.82; $p<0.001$). In addition, patients managed with chemotherapy alone were more likely to experience a complication related to the primary tumor (95 % CI 1.7, 34.4; $p=0.008$). There was no difference in the incidence of metastatic disease tumor burden becoming more favorable and amenable to curative resection after systemic chemotherapy in either group (0.85; 95 % CI 0.40, 1.8; $p=0.662$).
- There are obvious limitations of this meta-analysis given the retrospective nature of the studies available for review as well as the chemotherapy regimens utilized in these studies not being equivalent to current regimens.
- There is little published data evaluating the effectiveness of radiotherapy in palliative management of stage IV rectal cancer. Crane and colleagues reported 55 patients who received chemoradiotherapy and 25 patients who received chemoradiotherapy followed by surgery. The majority of both groups received systemic therapy (78 % of patients).
- Pelvic symptom control was high (81 %) in the chemoradiotherapy group but not as high as in the chemoradiotherapy combined with surgical resection group (91 %). There was limited data on the durability of symptom control over time.
- To summarize the treatment options for stage IV patients with unresectable metastases, treatment algorithms are shown for patients with stage IV colon cancer (Fig. 47.2) and stage IV rectal cancer (Fig. 47.3). The algorithms show multiple treatment options, reflecting the heterogeneity of disease presentation. The major variables to consider are location of the primary tumor, degree of colon and/or rectal obstruction, extent of metastatic disease, and fitness of the patient for surgery.

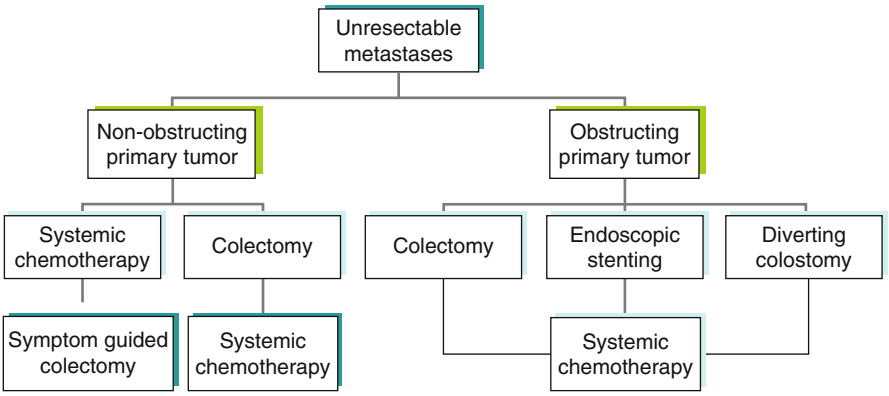

Fig. 47.2 Treatment algorithm for patients with stage IV colon cancer: use of palliative colon resection

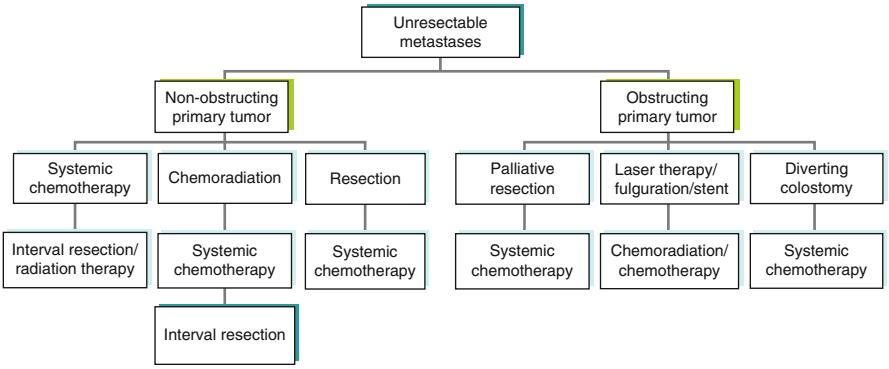

Fig. 47.3 Treatment algorithm for patients with stage IV rectal cancer: use of palliative rectal resection

Liver Metastasis

- Overall, it is been estimated that about 10 % of all patients with colorectal liver metastases are candidates for potentially curative hepatic surgery (with 5-year survival ranging from 28 to 45 %). The remaining majority of patients receive palliative therapy.
- This underscores the importance of patient selection in determining optimal treatment and highlights the fact that the majority of patients with liver metastases have unresectable disease.
- With improvements in chemotherapy, surgical technique, and ablative techniques, the number of patients eligible for hepatic surgery is on the rise.

Natural History of Untreated Liver Metastases

- To understand the impact of therapy, the natural history of untreated disease must be reviewed.
- Hepatic metastases left untreated result in median survivals of 5–10 months; long-term survival was rarely seen.
- Patients with limited metastases isolated to the liver, who would otherwise be potential candidates for surgery, had 3-year survival of 14–23 % and 5-year survival of 2–8 %.

Diagnosis

- After a diagnosis of hepatic metastases is made, careful evaluation accurately stages the patient. Complete cross-sectional imaging of the abdomen and pelvis with triple-phase CT and/or MRI is essential to rule out extrahepatic disease.
- The additional advantage of routine chest CT is low compared to that of a plain chest X-ray but should be considered. F-FDG positron emission tomography (PET) scanning is routinely performed because of prospective data documenting its utility (changes management decisions in patients with recurrent colorectal carcinoma 20–50 % of the time).
- The major strength of PET scanning appears to be the detection of occult extrahepatic disease. PET/CT provides more accurate tumor localization.
- Once the issue of extrahepatic disease has been addressed, high-quality imaging of the liver is essential in determining bulk of disease and resectability.
- 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.
- Routine CT scans can now evaluate the liver in combination with CT angiography or triphasic imaging of the parenchyma through various phases of intravenous contrast circulation.
- Ultrasound is excellent at distinguishing neoplastic tumors from benign lesions such as cysts, focal nodular hyperplasia, or hemangiomata; can evaluate the relationship of specific lesions to major vascular structures and the biliary tree; and is useful when performing intraoperative ablative procedures.
- MRI is an excellent method for characterizing liver multiple hepatic lesions; distinguishing malignant lesions from cysts, hemangiomata, and other benign lesions; and evaluating relationships of tumor to the biliary tree (via magnetic resonance cholangiopancreatography – MRCP) and to hepatic vasculature. High-quality MRI and triple-phase CT are probably equivalent for evaluating extent of liver disease and as aids in surgical planning.

Treatment Options

- In the patient who presents with liver metastases, the first consideration must be whether the liver disease is curable. The second consideration is whether the patient's disease if initially unresectable can be made amenable to surgery or ablative procedures with the addition of systemic chemotherapy.

Chemotherapy

- With the development of irinotecan, oxaliplatin, hepatic arterial infusional chemotherapy with FUDR, and newer molecular-based therapies, there are now more effective chemotherapeutic options for these patients.
- Irinotecan (CPT-11) in conjunction with 5FU/LV (FOLFIRI) is more effective than 5FU/LV alone for treatment of metastatic colorectal cancer response rates of 40 % and modestly improved survival (median 15–17 months vs. 12–14 months).
- Oxaliplatin/5FU/LV (FOLFOX) produced response rates in excess of 50 % (compared to 22 % for 5FU/LV). Early analyses of comparisons of irinotecan/5FU/LV to FOLFOX have so far shown FOLFOX to yield superior response rates.

Biomarker Targeted Therapy

- Epidermal growth factor receptor is a member of the tyrosine kinase family, and its activation stimulates many cancer-related processes such as proliferation, angiogenesis, invasion, and metastasis.
- Monoclonal antibodies that target epidermal growth factor receptor (EGFR) have increased the treatment options for patients with metastatic colorectal cancer.
- Several studies have found an association between a KRAS mutation and a lack of response to EGFR-directed therapy. The importance of defining the KRAS status of the primary tumor has provided oncologists with important information about response to treatment.
- The addition of cetuximab to FOLFIRI, in patients with metastatic colorectal cancer, improved overall survival (OS) by 3.5 months in KRAS wild-type patients. We are now seeing median survivals in excess of 20 months.

Hepatic Arterial Infusion

- Hepatic metastases derive their blood supply largely from the hepatic arterial branches. Thus hepatic artery infusional chemotherapy (HAI) has an advantage over systemically delivered chemotherapy as the drugs used in HAI have a higher therapeutic index due to high first-pass hepatic extraction and high systemic clearance and fewer systemic side effects.

- The most commonly used agent for HAI is fluorodeoxyuridine (FUDR), which has a 90 % hepatic extraction ratio, while this is beneficial for isolated hepatic disease, it limits treatment of occult extrahepatic disease. This can be addressed by giving additional systemic agents or by using 5FU via the hepatic artery with a higher "spillover" effect into the systemic circulation.
- Two meta-analyses of the first seven trials confirmed the increased response rates, and both showed a modest survival benefit.
- Finally, a meta-analysis of FUDR-HAI vs. systemic chemotherapy for unresectable liver metastases from colorectal cancer that included results from ten RCT has shown a greater tumor response rate with FUDR-HAI when compared with systemic therapy; however, this did not translate to a survival advantage over 5FU-based systemic therapy.
- One explanation for the lack of survival advantage is while control of hepatic disease was excellent with HAI, there was significant extrahepatic failure. FUDR while an effective agent for treating liver metastases can have liver-related complications including biliary sclerosis (18–29 %). Finally, the placement of the HAI catheter is an invasive procedure, and technical complications include primary catheter failure, catheter-related thrombosis, and infection.
- Many phase I and II trials are now evaluating combinations of HAI FUDR or oxaliplatin with systemically administrated 5FU/LV with irinotecan and/or oxaliplatin. Even in pretreated patients, impressive response rates in excess of 80 % are being seen.
- The combination of HAI and systemic 5FU/LV has further improved transformation rates of previously isolated unresectable colorectal liver metastasis into resectable lesions in as many as 26 % of cases.

Resection

- With effective systemic therapies, ablative techniques and treatment modalities aimed at "downstaging" the liver disease, more patients can be made amenable to resection.
- Mortality rates for hepatectomy for metastatic colorectal cancer are uniformly 5 % or less (Table 47.1).
- Morbidity has been reported between 20 and 50 %.
- Liver failure and significant hemorrhage are now distinctly uncommon. In a review of more than 1,800 liver resections (57 % of a lobe or greater) over the last decade, the median hospital stay was 8 days, morbidity was 45 %, and mortality was 3 %.
- Major institutional and multi-institutional reviews have now clearly documented the 5-year survival of patients undergoing hepatectomy for metastatic colorectal cancer ranges from 25 to 40 %, 10-year survival ranges from 20 to 26 %, and median survivals range from 24 to 46 months.

Table 47.1 Outcome of patients undergoing pulmonary metastasectomy for colorectal cancer

Study	*n*	Operative mortality (%)	5-yr survival (%)	Significant risk factors
Mori et al.	35	–	38	None found
McCormack et al.	144	0	44	Margin
McAfee et al.	139	1	31	Number of lesions, CEA
Yano et al.	27	–	41	Number of lesions
Saclarides et al.	23	–	16	Number of lesions
van Halteren et al.	38	–	43	DFI
Shirouzu et al.	22	–	37	Number of lesions, size
Girard et al.	86	1	24	CEA, margin
Okumura et al.	159	2	41	Number of lesions, LN status
Zanella et al.	22	0	62	None found
Zink	110	0	33	Size, CEA
Dahabre et al.	52	–	33	None found

Source: Adapted from Rizk et al.
n number of patients, *yr* year, *LN* lymph nodes, *DFI* disease-free interval

- These results obviously compare favorably to the results of no treatment (median survival 5–10 months) and to those of chemotherapy (median survival 10–14 months).
- True long-term cure from chemotherapy is extraordinarily rare, while at least half of the long-term survivors after liver resection are disease-free and presumably cured. For these reasons, no trial has ever compared hepatectomy to no treatment or chemotherapy alone. Liver resection for resectable hepatic colorectal metastases is the treatment of choice.

Patient Selection

- 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.
- A list of other poor prognostic factors exist; these include lymph nodes involved by the primary colorectal tumor, synchronous presentation (or shorter disease-free interval), larger number of tumors, bilobar involvement, CEA elevation greater than 200 ng/ml, and involved histologic margins.

- While it appears to be true that the stage of the primary tumor, the interval in which metastatic disease has developed, and the bulk of tumor in the liver (measured by size, number, and/or CEA level) can provide prognostic information on outcome after hepatectomy, none of these findings in and of themselves preclude the potential for long-term survival.

Margin Status

- The importance of obtaining negative margins with hepatectomy has been demonstrated in multiple studies showing improved disease-free and overall survival.
- Wide resection margins with >1 cm clearance is desirable; however, a consensus statement from the Society of Surgical Oncology concluded that while wide margins of >1 cm are desirable and should be sought, anticipation of a close margin should not preclude a resection.
- As a result, a more recent study examined the difference in outcomes between those patients with R0 resections vs. R1 resections. When coupled with SCT, the R1 resection group has similar 5-year overall survival rates to the R0 resection group (57 % vs. 60 %, $p=0.12$). Intrahepatic recurrence demonstrated a higher recurrence of 28 % for the R1 resection group vs. 17 % for the R0 resection ($p=0.004$) group.

Recurrence

- Recurrence following hepatectomy for colorectal metastases is common, occurring 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. Most of these recurrences are isolated to the liver. Other common sites are lung, bone, and various intra-abdominal sites.
- Currently, at least 14 series reporting on more than 700 patients have documented that repeat hepatectomy for metastatic colorectal cancer is safe and effective in well-selected patients. Mortality is less than 5 %, median survival from the time of the second liver resection ranges from 23 to 46 months, and 5-year survival ranges from 30 to 41 %.
- Because of the potential for further effective therapeutic interventions after primary liver resection, patients eligible for such treatment should be followed with serial CEA and imaging studies to detect recurrences at an early and potentially treatable phase.
- Since recurrence after hepatectomy for metastatic colorectal cancer is common, there is a sound rationale for use of adjuvant therapy.
- A 2008 EORTC trial showed significant benefit to perioperative FOLFOX therapy.
- Because the large majority of patients with hepatic colorectal metastases are technically unresectable, the development of more effective chemo-

therapy has inspired many oncologists to employ a "neoadjuvant" chemotherapy strategy in an attempt to render patients resectable.

- In a series from France, 701 patients with unresectable liver metastases received chronomodulated 5FU/LV and oxaliplatin. Ninety-five (14 %) of these patients became resectable, secondary to chemotherapeutic response, and underwent staged resection. The resections employed techniques such as portal vein embolization and intraoperative ablation to extirpate all tumors and achieved an actuarial 5-year survival rate of 35 %.

Ablative Procedures

- Other methods of tumor destruction utilizing thermal ablation techniques have also been developed to treat and palliate those tumors that are not amenable to resection.
- Cryotherapy has been used for decades and employs the use of probes to freeze tumors and surrounding normal hepatic parenchyma. Cryotherapy generally requires a laparotomy, and complications such as bleeding, liver cracking, and a cryoshock phenomena characterized by thrombocytopenia and disseminated intravascular coagulation can occur.
- Radiofrequency ablation (RFA) and microwave ablation (MWA) probes have been developed that can heat liver tumors and a surrounding margin of tissue to create coagulation necrosis. RFA and MWA can be employed 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.
- RFA can be used near blood vessels, but major bile ducts can be seriously injured, limiting the use of RFA in central tumors situated near major bile ducts.
- Local recurrence following RFA is a significant problem and appears to be strongly correlated with tumor size. Generally, recurrence is more common in tumors greater than 4 or 5 cm in diameter and in tumors abutting major blood vessels.
- Perhaps the greatest application of ablative techniques will be in their use as additions to resection in patients with multiple bilobar tumors.
- Yttrium-90 microspheres is a way of delivering a pure beta-emitting form of radiation to an unresectable liver lesion without suffering the locoregional side effects of external beam radiation. The microspheres are most often administered via an angiographic-guided catheter placement. The procedure first requires accessible feeding vessels that allow for treatment of the lesions, but it is imperative that healthy liver and lungs are excluded and therefore appropriate treatment dosing is critical.
- The first study to combine radioembolization (REB) with systemic chemotherapy (SCT) randomly assigned patients to either treatment with

SCT or with REB plus SCT. The overall median survival was 29.4 months in the study arm vs. 12.8 months in the SCT alone arm. This trial and others show promising results in patients with metastatic colorectal cancer.

Lung Metastasis

- Approximately 10 % of patients with colorectal cancer develop pulmonary metastasis. The vast majority of patients with metastatic colorectal cancer to the lung have advanced disease and are therefore treated with systemic chemotherapy or best supportive care.
- Approximately 11 % of these individuals will have isolated pulmonary metastases. Patients with isolated or limited pulmonary may be considered candidates for pulmonary metastasectomy.
- Modern series of lung resection for metastatic colorectal cancer report operative mortalities of less than 2 %. Five-year survival rates range from 16 to 64 % but generally cluster around 30–40 %.
- Most studies evaluate factors associated with outcome; however, given the limited number of cases, the statistical power of these studies to detect significant factors is limited.
- The most commonly cited significant factors associated with adverse outcomes include the number and size of pulmonary metastasis, short disease-free interval (DFI), elevated CEA, and incomplete resection.
- The use of video-assisted thoracoscopic surgery (VATS) has increased significantly and is often used in metastasectomy when a minimal parenchymal resection is necessary.
- Radiation therapy for colorectal cancer pulmonary metastasis has been of limited utility in the past due to radiation-induced pneumonitis, rib and spinal fractures, and skin toxicities.
- However, these toxicities can be minimized with the advent of robotic-assisted Gamma Knife radiotherapy or "CyberKnife." Initial reports appear to have minimal toxicity associated with single-session lung radiotherapy using robotic image-guided real-time respiratory and tumor tracking. This is an exciting field of research and may become an additional therapeutic modality in the future. However, the outcome and efficacy data is limited at this time, and the associated cost of robotic image-guided radiotherapy will be a limiting factor in widespread availability.

Peritoneal Metastasis

- Peritoneal carcinomatosis represents one of the most challenging presentations of metastatic colorectal cancer. The peritoneal surface is involved in approximately 10–15 % of colorectal cancer patients 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. It is characterized by intraperitoneal spread of metastatic nodules. Peritoneal metastasis occurs by direct implantation of cancer cells via one of the four mechanisms: (1) spontaneous intraperitoneal 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, and (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. Noninvasive imaging frequently misses small peritoneal lesions, even when these are widely disseminated. The sensitivity of CT scanning for lesions smaller than 5 mm is only 28 %, as compared to 70 % for lesions 2 cm or greater. Thus, indirect signs such as bulky primary tumor, ascites, or bowel obstruction are important clues.
- The utility of MRI in diagnosis of peritoneal carcinomatosis beyond that of CT is largely unknown, and PET scans are of limited value.
- Unfortunately, in the majority of cases, diagnosis is made at the time of primary resection.
- The extent of carcinomatosis is a major prognostic factor and is best assessed by either laparoscopic or open exploration. Two different peritoneal carcinomatosis staging systems (Gilly's classification and Peritoneal Cancer Index of Sugarbaker) can be used to assess the extent of carcinomatosis.
- Standard management of patients known to have peritoneal metastases at initial presentation is systemic chemotherapy. Colon resection plays an important role for patients with obstructing primary cancers and also for patients with occult metastases that are first detected in the operating room.
- Patient survival is highly variable, depending on the extent of metastatic disease and response to chemotherapy. Contemporary combination chemotherapy regimens have significantly greater efficacy and can produce long periods of disease control in certain patients.
- Despite the grim prognosis for patients with peritoneal carcinomatosis from colorectal cancer, a subset of patients once thought unsalvageable are now being considered for surgery with curative intent. Pioneered by Sugarbaker, the goal of cytoreductive surgery and intraperitoneal (IP) chemotherapy is to remove all macroscopic disease with peritonectomy procedures and visceral resections followed by perioperative IP chemotherapy to destroy residual microscopic disease. IP delivery offers a pharmacokinetic advantage over standard intravenous delivery by producing high regional concentrations of drug while simultaneously minimizing systemic toxicities.

- The most widely reported method of IP chemotherapy is intraoperative delivery of mitomycin in a hyperthermic (41C) circuit for 90 min (HIPEC – heated intraperitoneal chemotherapy).
- In carefully selected cases, there appears to be a survival benefit. Multiple phase II and one phase III study establish superiority over conventional palliative surgery or systemic chemotherapy. Several phase II studies show 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. Five-year survival rates reported for patients with completely resected disease range from 27 to 54 %.

Ovarian Metastasis

- Approximately 4–30 % of ovarian neoplasms are metastatic cancers, the most common being colorectal and breast cancer. Between 6 and 14 % of all women dying with colorectal cancer are found to have ovarian metastases at the time of autopsy.
- 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.
- The pathogenesis of colorectal cancer ovarian metastasis is variable. Metastatic spread occurs primarily through the peritoneum but can also occur via the blood stream, through lymphatic vessels, or by direct extension. Careful intraoperative assessment of the ovaries at the time of colon cancer surgery is essential.
- Synchronous metastases occur in 0–8.6 % of patients in various clinical studies, while metachronous metastases develop in 1.4–6.8 % of colorectal cancer cases, usually within 2 years after the primary resection.
- 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.
- Primary en bloc resection of CRC with direct extension to the ovary (T4) or resection of macroscopic metastatic disease to the ovary with prophylactic bilateral resection has been suggested to offer survival benefit and should be performed with curative intent in the absence of other significant metastatic disease.
- However, the removal of macroscopically normal ovaries, prophylactic oophorectomy, in women with colorectal cancer is the subject of much debate.

- Clinical studies attempting to document the benefit of ovarian metastasectomy in patients with colorectal cancer are small and retrospective. The majority of studies to date, however, fail to show any survival benefit for prophylactic oophorectomy, and most studies demonstrate that when ovarian metastasis is present, it is a poor prognostic sign.
- Based on the available data, it is reasonable to offer prophylactic oophorectomy to all postmenopausal patients, in particular to those women who have undergone pelvic radiation as part of their treatment for rectal cancer.
- 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.
- Reoperation for metachronous metastases should be considered in selected patients with good performance status and limited tumor burden elsewhere. The survival benefit of removing ovarian metastases has never been well documented, although complete metastasectomy is associated with significantly better outcome when compared to palliative debulking, especially in the setting of metastatic disease confined to the pelvis.
- The median postresection survival for women with isolated ovarian metastases is 18 months. Five-year survival after resection of established ovarian metastases is rare. In these cases, systemic chemotherapy should be strongly considered, particularly when residual disease is present. With the availability of stronger chemotherapeutic regimens containing oxaliplatin, irinotecan, and/or bevacizumab, better survival can be expected.

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.
- There are no curative modalities, but palliation of pain, fractures, or spinal cord involvement are important issues for these patients. Symptomatic relief from bony metastases can usually be accomplished with radiation and medical therapy.
- 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.

- 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.
- As with pulmonary metastasis, there is increasing interest and data in the literature regarding Gamma Knife and CyberKnife radiotherapy for bone and brain metastasis. The outcome and efficacy data is limited at this time, and the associated cost of robotic real-time image-guided radiotherapy may be a limiting factor in widespread applicability.

48. Colorectal Cancer: Surveillance

Nadav Dujovny and Jon S. Hourigan

Introduction

- The majority of patients with colon and rectal cancer undergo curative resection and become candidates for surveillance.
- The risk of colorectal cancer recurrence is largely dependent on the stage of disease at initial presentation, and the appropriate level of postoperative surveillance should reflect this degree of risk stratification.
- In theory, proper surveillance allows subsequent polyps to be removed before malignant transformation occurs and improves survival by early identification of treatable recurrent cancer. Furthermore, surveillance directs family members of patients with hereditary cancers to receive proper screening and genetic counseling.
- There is the lack of agreement on the most effective surveillance program.
- A survey of American Society of Colon and Rectal Surgeons (ASCRS) members indicates that only 50 % of practicing colorectal surgeons follow general surveillance guidelines.
- The importance of disease stage is noted, but the risk of recurrence is also influenced by a variety of other factors, including surgical technique (local vs. radical resection, total mesorectal excision, etc.), primary tumor location, disease clearance, and histologic grade. Patient age and comorbidities, in addition to patterns of recurrence, also influence the intensity of surveillance.

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- A recent population-based study by Guyot et al. demonstrated temporal improvements in resectability and management of recurrent disease. The authors of this study showed that the proportion of patients with recurrent disease resected for cure increased from 6.7 % (1976–1984) to 23.7 % (1994–2003; $p<0.001$) for distant metastases and from 15.9 to 58.1 % ($p<0.001$) for local recurrence.
- Improvements in outcome for metastatic colorectal cancer were also demonstrated by Kopetz et al. through the increased use of hepatic resection and advancements in medical therapy. In this study, 5-year survival improved from 9.1 to 19.2 %, and the median survival improved from 18 to 29.2 months in selected patients with Stage IV disease.

Risk and Timing of Recurrence

- In 2012, approximately 143,000 cases of colon and rectal cancer were diagnosed in the USA. Most patients presented with locoregional disease (Stages I–III) and underwent curative intent surgery. The 5-year survival rate in this collective group ranged from 64 to 90 % depending primarily on the stage at presentation.
- Overall, 30–38 % of patients who are treated with curative intent resection for locoregional disease develop recurrence.
- Patients with Stage IIb and Stage III disease are at the highest risk of recurrence.
- Approximately 20 % of patients presented with Stage IV, or metastatic, disease. Most patients with Stage IV colorectal cancer are not candidates for curative resection and undergo palliative treatment.
- Surveillance is not applicable for these patients unless their metastatic disease is limited and resected for cure.
- The majority of recurrences occur within 2 years of a curative resection, and more than 95 % of recurrences are evident within 5 years of surgery. Late recurrence, defined as recurrence after 5 years from initial resection, is unusual and typically represents less than 2 % of recurrent cancer diagnoses. The longer interval to recurrence in these patients often reflects the use of adjuvant therapy.

Hereditary Colorectal Cancer

- Hereditary factors play a role in 10–25 % of colorectal cancers, and identification of these patients often influences surgical management and surveillance intensity. Patients who are less than 50 years of age, have multiple polyps or synchronous cancers, or have a personal/family history of a malignancy should be recognized and considered for genetic counseling.

- The important noncolorectal malignancies to consider are those associated with hereditary nonpolyposis colorectal cancer (HNPCC), such as endometrial, ovarian, ureteral, gastric, and others.
- Obviously, family history plays a substantial role in identifying these patients and needs to be reviewed thoroughly at the initial consultation. Both HNPCC and familial adenomatous polyposis (FAP) are examples of genetic colorectal cancer syndromes that may affect patients and their families.

Surveillance Measures

Intensity of Follow-Up

- A study by Secco et al. showed statistically significant improved survival among patients in risk-adapted follow-up programs versus patients with minimal follow-up.

History and Physical Examination

- Various practice guidelines, including those of the ASCRS, American Society of Clinical Oncology (ASCO), and National Cancer Care Network (NCCN), recommend patient history and clinical examination be performed every 3–6 months for the first 2–3 years after curative resection. Subsequent follow-up then occurs for a total of 5 years of surveillance.
- Concerning symptoms include coughing, abdominal or pelvic pain, change in bowel habits, rectal bleeding, and fatigue. The physical exam should include wound examination, lymph node palpation, digital rectal exam, and a pelvic examination for female patients.
- Unfortunately, patients who present with symptomatic recurrences are less likely to be resected for cure. However, posttreatment surveillance also allows for the evaluation of psychosocial distress after colorectal cancer treatment and potential to offer help for other treatment-related sequelae, such as diarrhea, incontinence, and/or stoma care.
- It also helps to serve as a reminder for patients to check carcinoembryonic antigen (CEA) levels and schedule subsequent colonoscopies.

Laboratory Evaluation

- The only laboratory test recommended for colorectal cancer surveillance is the serum CEA level. CEA is an oncofetal protein, which is elevated in colorectal cancers along with other gastrointestinal malignancies.
- Failure of elevated preoperative CEA levels to return to normal after potentially curative resection is a poor prognostic indicator and may represent incomplete surgical resection or occult metastases.

- After colorectal cancer resection, postoperative CEA levels should be monitored in patients who are medically fit for further treatment if a recurrence were found. The recommended interval of testing varies between societies; however, most recommend checking CEA levels every 3 months for the first 2–3 years and then biannually up to 5 years after resection.
- Elevated CEA is often the first sign of recurrent disease. CEA often predates other testing modalities in terms of identifying recurrence with a median lead time of 4.5–8 months.
- Of note, sensitivity is much higher in detecting distant metastatic disease than locoregional disease (92 % vs. 62 %). CEA sensitivity also varies with the site of recurrence, being 78 % sensitive for hepatic metastasis, but only 42 and 45 % sensitive for pulmonary and local recurrences, respectively.
- Furthermore, an elevated CEA level should be rechecked prior to searching for recurrent disease because it may be falsely elevated. The false-positive rate for CEA levels ranges from 7 to 16 %.
- CEA levels should not be evaluated while the patient is receiving 5-fluorouracil-based chemotherapy because this may falsely elevate the CEA level.
- Serum hemoglobin, liver function tests, and fecal occult blood test should not be used as part of a surveillance regimen.

Chest Surveillance

- The incidence of isolated pulmonary metastases is approximately 5–10 %, and over 20 % of patients who develop recurrent disease after curative resection have pulmonary lesions in addition to other areas of metastases. This pattern of recurrence is variable depending on the initial stage and location of the primary malignancy.
- Even though pulmonary recurrence tends to occur more commonly with rectal cancer rather than colon cancer, both groups are followed collectively according to current surveillance recommendations.
- Plain chest radiograph (CXR) and chest CT scan are the two available options for chest surveillance, and their utilization is not mutually exclusive. As with other surveillance measures, the utilization of chest surveillance requires that a patient is medically fit for pulmonary metastasectomy to justify its use. The ability of surveillance CXR to first detect evidence of cancer recurrence is reportedly under 20 % and more realistically less than 10 %.
- Chest CT has shown an improved ability to primarily detect occult colorectal cancer recurrence within the chest in asymptomatic individuals and is more sensitive than CXR in identifying resectable pulmonary disease.

- Clear evidence indicating which option is superior is not available, and various surveillance programs preferentially use routine CXR or chest CT.
- Both ASCO and NCCN recommend annual chest CT for the first 3 years following curative resection.
- Regardless of which method of surveillance is chosen, initial and repeated pulmonary resection for isolated metastatic disease offers an excellent long-term survival advantage with 2- and 5-year survival rates greater than 60 and 40 %, respectively.
- Although the majority of patients has multiple pulmonary lesions and may not be candidates for metastasectomy, routine chest imaging for colorectal follow-up is warranted to identify the subset population of patients who benefit from pulmonary resection.

Abdomen/Pelvis Surveillance

- There has been continued improvement in both the identification and treatment of metastatic colorectal cancer, and patients now have more options for the treatment of recurrent and advanced stage disease. The detection of abdominal and pelvic recurrence has primarily focused on hepatic imaging because the liver is the most common site of recurrence.
- Over 30 % of patients ultimately develop hepatic metastasis after curative resection. This typically occurs within the first 3 years after surgery. Recommendations regarding the use of routine liver imaging are influenced by the ability of abdominal CT and/or liver ultrasound to identify liver metastasis before clinical symptoms develop or other modalities of surveillance are positive for recurrence.
- In general, the accuracy of abdominal CT is superior to liver ultrasound for hepatic metastasis. The sensitivity of liver ultrasound is under 60 % for the detection of colorectal metastasis, and the ability of ultrasound to identify liver lesions less than 1 cm is truly inadequate. Abdominal CT, on the other hand, is more accurate and able to detect liver metastasis with sensitivity greater than 75 %.
- The most recent Cochrane review suggested an overall survival benefit when routine liver imaging was included as part of intensive surveillance programs.
- Other topics of debate include the cost-effectiveness of liver imaging and its ability to complement routine surveillance when other measures are normal. Deveney and Way found similar specificity and sensitivity between a less expensive CEA and more costly abdominal CT for routine follow-up. The ability of hepatic imaging to act as the first indicator of recurrence is low and very rarely does it identify recurrence prior to CEA elevation.

- The most recent ASCRS published guidelines (2004) do not recommend the routine use of hepatic imaging. This is based on the lack of evidence that identification of hepatic recurrence leads to subsequent resection, the overlap of results between elevated CEA measurement and hepatic imaging, and the cost of routine CT imaging. In contrast, both ASCO and NCCN guidelines recommend annual abdominal CT for 3 years after curative resection in patients who are considered to be both high risk and candidates for subsequent resection if recurrence is found. The recommendations for annual imaging focus on a reduction in mortality when imaging strategies are compared to nonimaging strategies for surveillance. Earlier identification of asymptomatic recurrence allows for curative reoperation and improved survival.
- In conclusion, there is no clear consensus among published guidelines in regard to routine abdominal imaging after curative resection. There is strong evidence that early identification of hepatic recurrence by CT imaging, particularly in asymptomatic patients, improves survival through subsequent curative resection. Otherwise, liver recurrence left untreated carries a very poor prognosis. The survival benefit demonstrated in patients who undergo curative resection, therefore, should prompt serious consideration to imaging strategies in patients at high risk for recurrence. Clearly, the benefit of liver imaging is best realized when it is used as an adjunct to other modes of surveillance (in-office visit, CEA), and not as a single strategy.

Endoscopic Surveillance

- The options for endoscopic evaluation after curative resection include colonoscopy, flexible sigmoidoscopy, and rigid proctoscopy with or without endorectal ultrasound (ERUS).
- Synchronous colorectal polyps and cancers occur in 30 and 5 % of patients, respectively, and their identification at index colonoscopy may change the operative management of a patient. Preoperative colonoscopy, or postoperative colonoscopy within 6 months of surgery, is therefore fundamental in the management of patients with a newly diagnosed colorectal cancer.
- After curative resection, endoscopic surveillance is designed to detect metachronous colorectal neoplasms and early disease recurrence. The timing and frequency of this surveillance is variable among published consensus guidelines and a source of debate.

Metachronous Colon and Rectal Neoplasms

- A prior diagnosis of colorectal cancer is a significant risk factor for the subsequent development of polyps and/or cancer. Unlike colorectal cancer recurrence, which typically occurs within 2–3 years after treatment,

the risk of developing metachronous colorectal neoplasms is collective over the life of a patient.

- Metachronous polyps occur in up to 50 % of patients, and metachronous cancers develop in 2–9 % of individuals with a prior colorectal cancer diagnosis.
- A recent systematic review of post-cancer resection surveillance by the US Multi-Society Task Force on Colorectal Cancer described 137 metachronous colorectal cancers among 9,029 patients (approximately 1.5 %). Fifty-seven of the 137 malignancies reportedly occurred within 24 months of initial resection.
- Although some lesions likely may have been missed synchronous lesions, a high incidence of early metachronous cancers was identified. This prompted a joint update by the US Multi-Society Task Force and American Cancer Society to recommend intraluminal surveillance with post-resection colonoscopy 1 year after surgery.
- According to their most recent update for colon and rectal cancer surveillance in 2004, the ASCRS Standards Practice Task Force has not endorsed the utility of early (1-year) post-resection colonoscopy. ASCRS practice guidelines indicate that the initial posttreatment colonoscopy should occur 3 years after resection and at subsequent 3-year intervals.
- Obviously, clinical judgment recognizes that certain risk factors place some patients at greater risk for developing metachronous lesions. This influences the need for endoscopic evaluation with different timing and frequency. Patients who are at risk for hereditary colorectal cancer syndromes should undergo more frequent surveillance endoscopy. The absence of synchronous neoplasms at the initial diagnosis of colorectal cancer confers a lower risk of metachronous lesions.
- Overall, most authors recommend 1-year colonoscopy based on the reported higher risk and incidence of metachronous neoplasms within 2 years and the reality of missed synchronous lesions. In consideration of the risk associated with metachronous lesions, colonoscopy is the only option for continued endoscopic surveillance after curative resection. All other options are insufficient.

Locally Recurrent Colon Cancer

- In addition to the identification of metachronous lesions, endoscopic surveillance is also utilized to discover local and anastomotic recurrence of colorectal cancer.
- Recurrent colorectal cancer typically occurs within 2–3 years after initial treatment. There is a distinct difference, however, between local recurrence rates of colon cancer and rectal cancer, and their respective patterns of recurrence require different approaches to surveillance.

- Endoscopic surveillance for recurrent colon cancer has limited utility because local and anastomotic recurrence is unusual. Intraluminal recurrence of colon cancer typically occurs in only 2–4 % of patients after resection, and the time to recurrence is generally 13–16 months.
- Harris et al. defined factors predictive of local recurrence to include advanced stage of disease, poor differentiation, perforation, and fistula formation. Unfortunately, local anastomotic recurrence is frequently associated with unresectable widespread colon cancer recurrence.

Locally Recurrent Rectal Cancer

- Locally recurrent rectal cancer is more common than locally recurrent colon cancer; yet, endoscopic visualization remains limited because of the tendency for local rectal cancer recurrence to begin extraluminally.
- Total mesorectal excision (TME) and chemoradiation therapy have both contributed to improved tumor clearance and locoregional control of rectal cancer. Such improvements translate into patterns of recurrence that make endoscopic follow-up beneficial in only a small percentage of patients because primary anastomotic, or intraluminal, recurrence is low assuming proper surgical technique is employed.
- ASCO recommends 6-month endoscopic evaluation by flexible sigmoidoscopy or rigid proctoscopy for rectal cancer recurrence in patients who have not received pelvic radiation. Although the exact schedule for surveillance is not defined, periodic anastomotic evaluation is recommended by the most recent ASCRS guidelines.
- Local extraluminal recurrence, on the other hand, remains a problem for patients after rectal cancer resection and typically reflects advanced stage disease or incomplete tumor clearance.
- As a consequence of extraluminal recurrence, post-resection surveillance not only requires the ability to evaluate the anastomosis, but the ability to look outside the lumen, as well. Visualization of low anastomosis by flexible sigmoidoscopy or rigid proctoscopy is therefore enhanced with other modalities of surveillance, such as ERUS.

Positron Emission Tomography Surveillance

- Positron emission tomography (PET) technology uses radiotracers to detect and quantify cellular and biochemical processes noninvasively. $^{18F\text{-}2\text{-fluoro}}$-2-deoxy-D-glucose (FDG) is the most common radiotracer used in oncology. FDG concentrates in malignant tissue because of an increase in glycolysis compared to normal tissue.
- This modality is frequently combined with CT scans to improve anatomical and functional detail. NCCN guidelines do not recommend routine surveillance with PET scans in detecting recurrences without other evidence of recurrent or metastatic disease.

- FDG-PET scanning has developed a role in the evaluation of recurrent disease and in the setting of suspected recurrence. For those patients who are asymptomatic with an elevated CEA level, the diagnostic sensitivity and positive predictive value of PET for recurrence is 95.3 %. A meta-analysis by Huebner et al. found an overall sensitivity and specificity of 97 and 76 %, respectively, for FDG-PET detecting recurrent colorectal cancer.
- A randomized study by Sobhani et al. added PET scan to the surveillance of colorectal cancer patients with a high risk of recurrence. These patients had Stage III or IV disease who had undergone an R0 resection and completed adjuvant chemotherapy. PET scan was performed at 9 and 15 months compared to the conventional group which had a CT scan at those time points. The PET group had a significantly shorter time to recurrence (12.1 vs. 15.4 months, $p=0.01$), and recurrences were more frequently removed for curative intent (R0, $p<0.01$).

Abnormal Results

- Abnormal results from surveillance prompt further investigations to detect, confirm, or exclude recurrence. If the CEA level rises after resection, management should include physical exam, colonoscopy, and CT of the chest, abdomen, and pelvis. If the work-up is negative, consideration should be given to PET scanning as well. Repeat CT scans should be done every 3 months until recurrent disease is identified or the CEA stabilizes or declines.
- Abnormalities may require further evaluation, such as biopsies or serial imaging, to confirm lesion stability. If recurrence is identified, PET scan should be performed and consideration given to further resection if possible.

Quality of Life

- Surveillance after colorectal cancer resection can be stressful for patients and have a significant impact upon their quality of life. Patients undergo many tests that may lead to further investigations or treatments.
- Moreover, these tests have a false-positive rate and examinations such as colonoscopy have associated risks.

Cost-Effectiveness

- When considering an intensive surveillance regimen, expense needs to be considered. Since different societies have disparity among their follow-up

regimens, there is a variable cost to the insurers. Using 5-year Medicare allowed charges, the cost between follow-up regimens varied between $910 and $26,717 per patient.

- Another study performed in the UK found that the adjusted extra cost for each patient was $4,288 and for each life year gained was $5,885. Another study performed in France divided the cost-effectiveness of surveillance between Stage I and Stage II disease compared to Stage III. Only Stage III patients had a favorable cost-effective analysis of 1,058 Euro per quality-adjusted life-years.

Surveillance Effectiveness and Meta-analyses

- The effectiveness of surveillance after curative resection is based on its ability to detect recurrent and/or metachronous disease at a point in time when subsequent curative treatment is successful. Of equal importance is a willing patient who is healthy enough to undergo potential therapy.
- Most surgeons would agree that patients should receive some degree of follow-up after curative resection of colon and rectal cancer. Some studies have shown that intensive follow-up has demonstrated a small but significant survival advantage over minimal or no follow-up after curative resection.
- When compared with minimal follow-up, intense surveillance delivers a 5-year improvement in overall survival of 7–10 %. The process is most likely multifactorial and is thought to be secondary to earlier detection of both locoregional disease and curable liver metastasis.
- Surveillance strategies, however, are limited because the benefits from the independent components of a surveillance program are difficult to validate. Strategies are often classified as “less intensive” or “more” or “highly intensive,” and there is considerable variability among groups.
- Different meta-analyses of the available randomized-controlled trials show a significant survival benefit with intensive surveillance compared to nonintensive surveillance.
- Due to the disparities between the different meta-analyses, it is not possible to say specifically what frequency or combination of surveillance modalities yields the improved survival benefit.
- Table 48.1 summarizes the recommended surveillance protocols.

Table 48.1 Summary of recommended surveillance protocols

Test/procedure	ASCRS	ASCO	NCCN
History and physical	Minimum of three times per year for the first 2 years	Every 3–6 months for 3 years, then every 6 months during years 4 and 5, then per physician discretion	Every 3–6 months for 2 years, then every 6 months for 5 years
CEA	Minimum of three times per year for the first 2 years	Every 3 months for 3 years or longer, for patients with Stage II or III disease	Every 3–6 months for 2 years, then every 6 months for 5 years for T2 or greater
Flexible sigmoidoscopy or proctoscopy for rectal cancer patients	Periodic anastomotic evaluation is recommended for patients who have undergone resection/anastomosis or local excision of rectal cancer	Every 6 months for 5 years for patients who have not received pelvic irradiation	Consider proctoscopy every 6 months for 5 years
Colonoscopy	Every 3 years	At 3 years then every 5 years if normal	At 1 year, if advanced adenoma repeat in 1 year, if none repeat in 3 years, then every 5 years
Computed tomography of the chest–abdomen–pelvis	Not recommended	CT chest/abdomen every 1 year for 3 years, consider CT pelvis for rectal cancer patients especially if they have not received radiation therapy	Annually for 3 years, for patients at high risk for recurrence
Fecal occult blood test	Not recommended	Not addressed	Not addressed
Complete blood count	Not recommended	Not recommended	Not addressed
Liver function tests	Not recommended	Not recommended	Not addressed
Chest radiography	Not recommended	Not recommended	Not recommended
Abdominal ultrasound	Not recommended	Not addressed	Not addressed

These are the recommended surveillance protocols for those patients who are candidates for further intervention

Conclusions

- Colon and rectal cancer surveillance after curative resection is recommended for patients who can tolerate further surgery or therapy if needed.
- The optimal surveillance protocol has not been established; however, general agreement supports the use of routine office visits, serum tumor marker measurement, and endoscopic surveillance for post-resection follow-up.
- Although the timing and frequency of surveillance measures is variable, continued follow-up is recommended based on improved overall survival with intensive surveillance programs.

49. Miscellaneous Neoplasms

Robin P. Boushey and Husein Moloo

These tumors are based on their tissue of origin and include epithelial, mesenchymal, neural, vascular, or lymphoid tumors.

Carcinoid Tumors

- Carcinoid tumors are neuroendocrine in origin and originate from Kulchitsky cells in the crypts of Lieberkuhn, which represent a type of enterochromaffin cell.
- Kulchitsky cells use various amine precursors to synthesize several hormones, neuropeptides, and neurotransmitters such as serotonin, adrenocorticotrophic hormone, bradykinin, histamine, dopamine, substance P, neurotensin, kallikrein, and prostaglandins E and F.
- Carcinoid tumors can develop in the bronchopulmonary system (67 %) and gastrointestinal tract (25 %).
- There is a higher incidence in females (~2:1), with tumors for all patients occurring typically between the fifth and seventh decade of life.
- Within the intestinal tract, carcinoids occur mostly commonly in the midgut (62 %) followed by hindgut (30 %) and foregut (7 %).
- The most common site for a carcinoid tumor is within the appendix (35 %) and small intestine (23 %), usually within 2 ft of the ileocecal valve.
- Rectal carcinoid tumors account for approximately 20 % of all gastrointestinal carcinoids and account for 1 % of all rectal tumors.

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- Synchronous carcinoid tumors occur in approximately 25 % of patients with foregut and midgut carcinoids, but are rare with hindgut tumors.
- Carcinoid tumors are associated with an increased incidence (up to 50 %) of other malignant tumors that includes gastric, esophageal, colorectal, lung, prostate, and urinary tract tumors.

Pathology

- Increased cellular atypia, high mitotic activity, or necrosis are suggestive of more aggressive tumors and are termed atypical/anaplastic carcinoid tumors.
- Silver staining traditionally confirms carcinoid tumors as serotonin reduces silver salts to metallic silver (argentaffin positive). Tumors that uptake silver salts but cannot reduce silver unless an external reducing agent is added are termed argyrophilic.
- Midgut carcinoids are mostly argentaffin positive. Hindgut carcinoids are usually mixed with 60–70 % being argyrophil and 8–16 % being argentaffin positive.
- Immunohistochemistry uses antibodies that target various cytoplasmic proteins including chromogranin, synaptophysin, and neuron-specific enolase to diagnose carcinoids.

Clinical Presentation

- Carcinoid syndrome, occurring in only 10–18 % of all carcinoid patients and 50 % of individuals with advanced disease, is characterized by flushing, severe abdominal pain, diarrhea, hypotension, or hypertension, and can be precipitated by severe stress including surgery, anesthesia, and adrenergic agents.
- Less than 1 % will have the carcinoid syndrome as the initial clinical manifestation.
- Most patients will be symptomatic for a median duration of 2 years prior to diagnosis.
- Up to 90 % of symptomatic patients will have an advanced tumor often with metastasis.
- Approximately 50 % of all gastrointestinal carcinoid tumors will be diagnosed following appendectomy.
- Midgut carcinoid tumors present with abdominal pain in up to 40 % of individuals, while hindgut carcinoids are nonsecretory and are almost always asymptomatic and discovered incidentally by the pathologist following polypectomy.
- Occasionally, larger tumors will present with bleeding, obstructive symptoms, and tenesmus.

- Serotonin is responsible for abdominal cramping and intestinal hypermotility manifesting as diarrhea, and occurs in 80 % of patients with the carcinoid syndrome.
- Kallikrein secretion accounts for wheezing and flushing, the latter occurring in 85 % of affected patients.
- Intestinal obstruction leading to possible arterial insufficiency is due to mesenteric and retroperitoneal fibrosis.
- Right-sided heart failure, due to severe damage to the tricuspid and pulmonary valves, accounts for 50 % of the deaths from the carcinoid syndrome, and correlates with higher 5-hydroxyindolacetic acid (5-HIAA) levels.
- Midgut tumors are most commonly associated with the carcinoid syndrome as these tumors produce high levels of serotonin. Almost 90 % of individuals with the carcinoid syndrome will have a midgut carcinoid tumor.

Diagnostic Tests

Biochemical Tests

- 24-h urine 5-HIAA measurement is the most useful biochemical test for diagnosing carcinoid tumors in the symptomatic patient, with a sensitivity and specificity of 73 and 100 %, respectively.
- Chromogranin A is a sensitive serum marker but is nonspecific for carcinoid tumors.

Imaging Tests

- Computerized tomography (CT) scan of the thorax and abdomen/ pelvis should be performed in symptomatic patients to identify the primary tumor and extent of disease.
- Somatostatin receptor scintigraphy (SRS) scan can identify occult metastasis in patients being considered for curative resection and to determine if the patient is likely to respond to octreotide.
- Whole body positron emission tomography (PET) relies on differential metabolic uptake and is used increasingly for carcinoid tumors.
- Esophagogastroscopy and colonoscopy should be considered in patients with metastatic disease with an unknown primary.
- Electrocardiography and echocardiography should be performed in all patients to rule out right-sided valvular disease especially prior to elective surgical resection.

Treatment

- Carcinoid tumors greater than 2 cm diameter are usually malignant in most locations except in the ileum, where nearly all tumors will have metastasized.

Small Bowel Carcinoids

- Small bowel resection including a resection of the mesenteric lymph nodes is indicated even in patients with known metastatic disease to reduce the likelihood of developing small bowel obstruction or mesenteric fibrosis and ischemia.
- The entire small intestine should be carefully examined at the time of laparotomy to exclude the possibility of a synchronous tumor.

Appendiceal Carcinoids

- Appendiceal carcinoid tumors are the most common tumor of the appendix. These tumors are rarely multicentric and tumor size is the best prognostic indicator, with most tumors less than 2 cm rarely metastasizing to regional lymph nodes or distally.
- Patients with tumors under 1 cm are usually treated by simple appendectomy, as long as there is no evidence of local tumor spread.
- 30–60 % of lesions greater than 2 cm in diameter are associated with nodal or distant metastases and will require formal right hemicolectomy.
- Tumors 1–1.9 cm must be individualized based on the risk of recurrence vs. the risk of surgery. The presence of lymphovascular invasion, involvement of the mesoappendix (lymph node involvement or by direct extension), or a positive margin are poor prognostic indicators and usually warrant right hemicolectomy.

Colonic Carcinoids

- Approximately two-thirds of colonic tumors arise in the ascending colon (most in the cecum), and remain asymptomatic until they develop into large tumors with nodal spread or distant metastasis.
- Most patients with colonic carcinoids will require colonic resection and the extent is usually determined by the location of the disease.

Rectal Carcinoids

- Rectal carcinoids are usually asymptomatic and identified at the time of routine endoscopy in approximately 50 % of patients. Symptomatic patients usually have rectal bleeding, tenesmus, pain, constipation, and rarely the carcinoid syndrome.
- Tumor size correlates well with the likelihood of metastasis – tumors less than 1 cm in diameter metastasize in fewer than 5 % of patients. Most tumors greater than 2 cm will have metastasized at the time of diagnosis.
- The majority of rectal carcinoid tumors are smaller than 1 cm and can usually be treated with local endoscopic excision.

- The management of tumors 1–2 cm in diameter remains controversial. Some authors advocate for more extensive resection in the presence of muscular invasion, symptoms at diagnosis, or ulceration.
- Tumors with a diameter greater than 2 cm have traditionally been treated by proctectomy.

Metastatic Disease

- Treatment of liver metastasis is effective in providing long-term palliation of the hormone-related symptoms in patients who do not respond to or tolerate the somatostatin analogs.
- Tumor debulking can involve hepatic resection, cryotherapy, radiofrequency ablation, hepatic artery embolization, or chemoembolization.

Systemic Therapy

- The somatostatin analog octreotide is effective at controlling the hormonal manifestations of the carcinoid syndrome in up to 88 % of patients and may halt progression of some of the fibrosing effects, namely, cardiac and mesenteric fibrosis.
- Cytotoxic chemotherapy consisting of streptozocin and cyclophosphamide or streptozocin and 5-fluorouracil has been ineffective in the treatment of metastatic carcinoid tumors.
- The best responses to chemotherapy have been in patients with aggressive carcinoid tumors using cisplatin-based regimens.
- Interferon-alpha has been shown to provide symptom relief in one-third of patients refractory to octreotide treatment.
- External beam radiation therapy has not been used extensively in patients with carcinoid tumor, though may provide palliation of symptoms in patients with bony and central nervous system metastases.

Neuroendocrine Carcinoma

- The neuroendocrine (NE) system is comprised of endocrine cells found throughout the body including the pancreas, thyroid, lung, adrenal gland, and gastrointestinal system.
- NE tumors occur most commonly in the lung in the form of small cell carcinoma but have been reported less commonly in the colon and rectum.
- NE tumors of the colon and rectum tend to be poorly differentiated high-grade tumors, highly aggressive, and associated with a poor prognosis.
- As two-thirds of patients will have metastatic disease at the time of diagnosis, an extensive metastatic workup is critical to determine an appropriate treatment plan.
- Multimodality treatment is routine, involving surgical resection, when possible for curative intent, along with adjuvant chemotherapy and radiation treatment.

Melanoma

- Melanomas of the gastrointestinal tract can be divided into (1) metastatic melanoma usually from a cutaneous neoplasm or more rarely (2) a primary GI melanoma.

Metastatic Melanoma

- Less than 5 % of patients with melanoma are diagnosed with a GI metastasis.
- The majority of melanoma metastases to the GI tract are to the small intestine (up to 67 %), followed by the colon (up to 15 %) and stomach (5–7 %).
- Once a melanoma metastasizes, it carries a poor prognosis with usually less than 6 months survival.
- Gastrointestinal metastases most often present with bleeding, obstruction, or most commonly pain.
- Evaluation for a patient with suspected metastatic melanoma who presents with obstructive symptoms or anemia may include colonoscopy, upper endoscopy, and upper GI series with a small bowel follow-through.
- CT and PET scanning can also be used to help identify metastatic disease.
- For asymptomatic patients, a GI tract evaluation is likely not going to alter management and should not routinely be performed.
- Intervention in symptomatic patients (i.e., small bowel resection for obstruction) is likely beneficial even though it will be done for palliative purposes, with symptom improvement reported in 79–97 % of patients.

Primary Melanoma

- A primary melanoma of the gastrointestinal tract is rare (1–2 cases/million/year) but can occur in the esophagus, small intestine, rectum, and anus – with the anus being the most GI tract common location.
- A solitary melanoma in the gastrointestinal tract should be present without any metastatic disease to be confident in calling it a primary.
- In contrast to cutaneous melanomas, there does not appear to be a relationship to sun exposure; women may be at higher risk compared to males and individuals who are usually in their seventh decade.
- Anorectal melanoma presents with bleeding, pain, tenesmus, and change in bowel habit. Weight loss, decreased energy, and other systemic signs may suggest metastatic disease.
- Most of these lesions are pigmented; however, up to a third may be amelanotic, and morphologically, these lesions can be either ulcerated or polypoid.
- Biopsy should be done of any suspicious lesion or ulceration.
- The prognosis for these patients is poor with 5-year survival ~6 % and median survival after diagnosis is 12–18 months.

- Approximately half of these patients will present with metastatic disease and 20 % will have gross inguinal lymphadenopathy.

Treatment

- The only chance for cure in these patients is early diagnosis and excision.
- There does not seem to be a survival advantage with a radical approach.
- Tumors invading into the sphincters and causing intractable pain may benefit from an APR.
- In patients who are having only local symptoms, a local excision is a reasonable approach.
- Chemotherapy with dacarbazine, levamisole, interferon-alpha, and BCG has not yielded survival advantages.
- Molecular-based therapy targeting tyrosine kinase receptors is a promising therapy, but currently there is limited data to support its routine use.

Gastrointestinal Stromal Tumor (GIST)

Background and Pathogenesis

- GISTs represent the most common mesenchymal tumor of the GI tract.
- The cell of origin is thought to be the interstitial cell of Cajal.
- Mutations of c-kit (>90 %) and PDGFRA (up to 10 %) are thought to be two different pathways to the formation of GISTs.
- Microscopically, spindle cells are usually seen.
- CD117 (immunohistochemical marker for KIT) is a very sensitive and specific marker for GISTs. CD34 is seen in approximately 70 % of GISTs.

Epidemiology

- Middle aged and elderly (mean age of 60) with men affected more often.
- The stomach is the most common site followed by the small intestine. GISTs can also be seen in the rectum but rarely in the colon.
- When considering small intestinal GISTs, the jejunum is the most common location followed by the ileum. Duodenal lesions are usually in the second part.
- Tumors in the stomach have a lower rate of malignancy (20 %) compared to lesions in the small and large bowel (40 %). It is rare to find a GIST of the esophagus.
- Most GISTs occur sporadically but there are some hereditary entities to consider including Carney's triad ((1) synchronous or metachronous GISTs, (2) extra-adrenal paragangliomas, and (3) pulmonary chondromas) and neurofibromatosis type I.

Diagnosis

- Presenting symptoms are usually nonspecific and can include dyspepsia, bleeding, and pain. Advanced lesions can present as a palpable mass.
- As GISTs are usually submucosal, imaging is the most important tool in making the presumptive diagnosis with the final diagnosis made via pathology.
- Imaging modalities that can be used include CT, MRI, PET, and endoscopic ultrasound.
- GISTs usually involve the muscularis propria and an intramural mass that is well circumscribed. In tumors that are larger, there can be areas of central necrosis.
- Percutaneous biopsy with fine or core needle aspiration is not done due to risk of hemorrhage, tumor rupture, and spread.
- Metastases are most commonly seen in the liver and peritoneum. Lymphatic spread is not common and therefore lymphadenopathy is not usually seen. Lung and bone metastases have been seen in advanced cases.
- CT scan is usually best for staging and for determining if there is potential for surgical resection.
- PET is not normally required for diagnosis or determining resectability but can be used to see if there has been a response to treatment.
- Endoscopy as well as endoscopic ultrasound (+/− FNA) for lesions that are within reach of a scope can aid in visualizing the mass for operative planning as well as biopsy the tumor (when lymphoma is in question).

Treatment

- The treatment of GIST can be divided into (1) surgical resection and (2) imatinib and sunitinib.
- Surgical management involves en bloc resection of the tumor with any other associated contiguous involvement with microscopically negative margins.
- GISTs do not typically spread lymphatically, and therefore a wide excision of the mesentery is not necessary.
- A gross margin of at least 1 cm is suggested.
- Even after a complete resection, there is a high recurrence rate, and therefore adjuvant therapy with imatinib should be considered.
- If a complete resection is not possible due to the size, neoadjuvant use of imatinib can be used to decrease the size of the tumor to a point where surgical resection becomes feasible.
- Up to 15 % of GISTs will be resistant to imatinib.
- Treatment of recurrent or metastatic GISTs involves lifelong imatinib if the tumor responds.

- In patients who do not respond to imatinib, one option can be to increase the dose from 400 to 800 mg per day if the patient is only receiving the 400 mg dose. Sunitinib can be used as a second-line treatment.
- GISTs are considered to be resistant to radiation.

Prognosis

- Tumor size and mitotic rate are the most important prognostic parameters. A tumor with less than 5 mitoses per 50 high-powered fields is usually benign acting, although there are a small number that may metastasize. Lesions with a diameter of less than 2 cm are almost always benign.
- Median survival in patients with metastatic disease that respond to imatinib is 5 years. As imatinib does not offer a cure, surgery can be attempted.

Palliative Therapy

- Palliative treatment includes radiofrequency ablation or hepatic artery embolization for lesions in the liver, along with other chemotherapy regimens; vatalanib and dasatinib are other tyrosine kinase inhibitors that have not been as successful to date.

Rectal GISTs

- When rectal GISTs specifically are considered, the symptoms associated are bleeding, pain (abdominal or rectal), or mass found on DRE or with endoscopy.
- Complete excision is the best treatment including any pseudocapsule that is present.
- High local recurrence rates exist and are higher with wide local excision when compared to abdominoperineal resection or anterior resection.

Leukemia and Neutropenic Enterocolitis

Leukemia

- While leukemia can affect the entire gastrointestinal tract, the ileum, appendix, and colon are most commonly affected due to their higher concentrations of lymphatic tissue.
- Presenting signs include diarrhea, pain, obstruction, colitis, or watermelon colon.

- Appearance of the lesions ranges from ulcers to polypoid, which can cause obstruction from the mass itself and also from intussusception.
- Anorectal complications include plaques, fistulas, ulcers, fissures, and abscesses.
- Due to the higher risk of infectious complications in patients with leukemia and receiving chemotherapy, instrumentation of the rectum should be avoided if possible.

Neutropenic Enterocolitis

- Neutropenic enterocolitis affects the small bowel, appendix, or colon and is most frequently seen after the chemotherapy for leukemia, hematologic/solid malignancies, or aplastic anemia.
- Inciting organisms include Staphylococcus aureus, Acinetobacter, Enterobacter, Aspergillus, Pseudomonas, Candida, Klebsiella, and Morganella.
- The overall pathogenesis involves a combination of mucosal injury, neutropenia, and decreased defense against gastrointestinal bacteria.
- Fever and abdominal pain in the setting of neutropenia (absolute neutrophil count less than 1,500/mm^3) is the triad of findings associated with this diagnosis.
- Other findings can include nausea and vomiting, diarrhea, and distention. Abdominal pain and tenderness can be diffuse but is often localized to the right lower quadrant.
- CT scan may demonstrate bowel wall thickening, edema/hemorrhage, pneumatosis, free fluid, and free air.
- Characteristic patterns associated with neutropenic enterocolitis on ultrasound include "doughnut like hypoechoic, fluid-filled intestinal lumen separated from a thickened bowel wall by a thin mucosal layer."
- Patients that do not have peritonitis or perforation are typically managed medically initially. Conservative management consists of fluid hydration, bowel rest, a nasogastric tube if there is a significant ileus, TPN, and broad spectrum antibiotics. Granulocyte colony-stimulating factor may be a consideration.
- Surgical therapy usually consists of a bowel resection and an ostomy since complications have been reported if primary anastomosis is performed on leucopenic patients.

Lymphoma

- The gastrointestinal tract is the most common site of extranodal lymphoma, with primary colorectal lymphoma accounting for 15–20 % of GI lymphomas (stomach 50–60 %, small bowel 20–30 %).

- Diffuse large B-cell lymphoma is the most common histologic type seen in the colon with the second most common type being MALT-associated low-grade B-cell lymphoma.
- Colorectal lymphomas do not have the association with H. pylori and cannot be treated with H. pylori eradication therapy.
- Staging follows the modified Ann Arbor staging system.
- HIV, EBV, prolonged steroid therapy, and inflammatory bowel disease are all risk factors for the development of lymphoma.
- Average patient age is 50–70 years with a slight male predominance (1.5:1).
- Weight loss, gastrointestinal bleeding, and abdominal pain are the most common symptoms at presentation.
- Many patients present with a palpable mass as these tumors often progress without symptoms until reaching a large size; however, they rarely cause obstruction or perforation.
- Most colonic lesions are found in the cecum and ascending colon, with 70 % of colorectal lymphomas occurring proximal to the hepatic flexure likely because of the increased lymphoid tissue in this area of the bowel.
- Treatment involves both surgery and chemotherapy. Surgical excision remains the primary treatment for this disease as it provides staging information as well as the chance for cure (with or without chemotherapy).
- Chemotherapy as the initial treatment has not shown benefit compared to patients receiving surgical therapy or combined therapy.
- Radiation therapy is only used in selected cases.
- Five-year survival rates range between 27 and 55 %, with tumors larger than 5 cm or lymph node positivity having the worst prognosis.

50. Pediatric Colorectal Disorders

Marc A. Levitt and Alberto Peña

Hirschsprung's Disease

Background

- Hirschsprung's disease (congenital megacolon) occurs in approximately 1 in 5,000 births, and boys and Caucasians are more frequently affected.
- Hirschsprung's is secondary 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 translates into a lack of relaxation of the colon that results in partial colonic obstruction.
- The most common type (80 %) includes the rectum and most of the sigmoid colon.
- 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 %, where the absent ganglion cells sometimes extend to the distal terminal ileum.
- In the rather controversial condition of "ultrashort" aganglionosis, the ganglion cells supposedly are lacking for only a few centimeters above the pectinate line.

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Clinical Manifestations

- Clinical symptoms include partial colonic obstruction, a poorly characterized immunologic mucosal defect that can lead to enterocolitis (the main cause of death), and abnormal colonic flora.
- Symptoms occur in the first 24–48 h with delayed passage of meconium, abdominal distension (huge megacolon), and vomiting.
- A rectal examination may produce explosive passage of liquid bowel movements and gas.
- If the colon is not decompressed, the infant usually suffers from sepsis, hypovolemia, endotoxic shock, cecal perforation, and death (25–30 %).
- Hirschsprung's patients often suffer from malnutrition and a lack of normal development.

Diagnosis

- An abdominal film shows massive dilatation of small bowel and colon.
- A contrast enema is used to clarify the diagnosis, demonstrating a nondilated aganglionic segment of the rectosigmoid, followed by a transitional zone and then a proximal dilatation.
- In patients with total colonic aganglionosis, the entire colon is not distended; the dilatation affects the small bowel only.
- The definitive diagnosis is made by a full-thickness or suction rectal biopsy and is based on both, the histological absence of ganglion cells and the presence of hypertrophic nerves.
- Acetylcholinesterase staining is also used for diagnosis.

Medical Management

- Colonic decompression and irrigation with saline solution are the most valuable tools for the emergency management of newborns.
- Patients with Hirschsprung's disease are incapable of expelling this fluid, and therefore, enemas are contraindicated.
- A colonic irrigation, on the other hand, promotes the expelling of the rectocolonic contents through the lumen of a large rubber tube, which is cleared with small amounts of saline solution.

Surgical Treatment

- The surgical treatment consists of the resection of the aganglionic segment and pull-through of a normoganglionic segment to be anastomosed just above the anal canal, immediately above the pectinate line.
- A staged procedure consists of a two- or three-step approach involving a diverting colostomy, resection of the aganglionic segment and pull-through of the normoganglionic bowel, and colostomy closure.

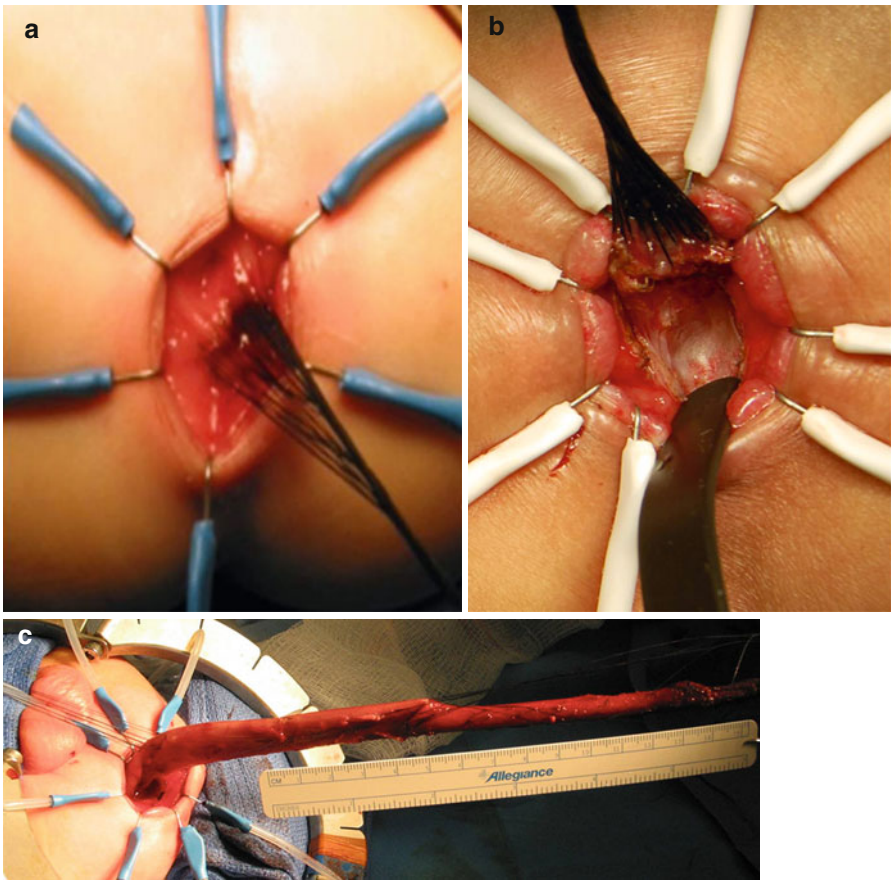

Fig. 50.1 Transanal procedure. (**a**) Exposure and placing traction sutures. (**b**) Start full thickness rectal dissection above pectinate line. (**c**) Pulling rectosigmoid down

- The treatment most commonly used currently consists of a neonatal primary procedure without a protective colostomy (Fig. 50.1).
- Full-thickness biopsies are taken to determine the place where the normoganglionic portion of the colon is reached.
- A primary procedure, without a protective colostomy, requires the presence of an experienced clinical pathologist, familiar with the interpretation of frozen sections, to identify the normoganglionic portion of the colon.
- In the absence of an experienced pathologist, the surgeon must create a colostomy proximal to the transition zone, in the right transverse colon or with an ileostomy.
- A Swenson operation consists of a resection of the aganglionic segment (transabdominal or transanal), including a part of the normoganglionic dilated colon, and pull-through of a normoganglionic bowel, with a coloanal anastomosis of the normoganglionic bowel to the rectum, above the pectinate line.

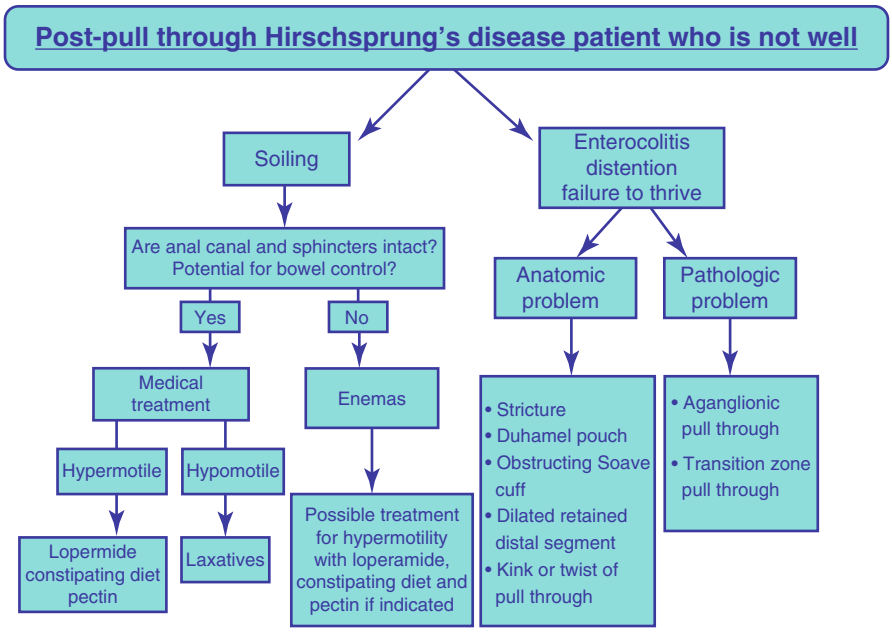

Fig. 50.2 Algorithm for post-pull-through Hirschsprung's disease patient who is not doing well

- A Duhamel operation preserves the aganglionic rectum, dividing the colon at the peritoneal reflection. The normoganglionic colon is then pulled through a presacral space, created by blunt dissection and anastomosed to the rectal wall above the pectinate line.
- A Soave procedure consists of an endorectal (submucosal) dissection of the aganglionic colon down to the pectinate line, leaving a seromuscular cuff. The normally innervated colon is passed through the muscular cuff and anastomosed to the rectum.
- A transanal approach can be performed provided the transition zone is in the sigmoid. If not, laparoscopy can be added for splenic flexure mobilization.

Complications

- An algorithm to the approach to post-pull-through Hirschsprung's patients with problems is shown in Fig. 50.2.
- To avoid incontinence, preservation of the dentate line and not overstretching the sphincters are crucial.
- Enterocolitis is a complication without a known etiology, unless there is an anatomic explanation, such as a stricture causing stasis, but is felt to be due to fecal stasis.
- Postoperative constipation can be avoided by resecting not only the aganglionic segment but also the dilated portion of the colon.

- Swenson operation may be associated with higher rates of nerve damage that may provoke urinary and sexual disturbances.
- The Duhamel procedure is commonly followed by severe problems of constipation and dilatation of the aganglionic piece of colon left in place.
- In the Soave operation, patients may suffer from fecal incontinence, as well as perianal fistulas and abscesses due to the presence of islets of mucosa left behind during the endorectal dissection.

Surgical Management of Total Colonic Aganglionosis

- An ileostomy is performed in a newborn and then at age 1–3 years resection of the entire aganglionic colon and pull-through of the normal ganglionic terminal ileum that is anastomosed just above the anal canal.
- They suffer from multiple stools and treatment is with loperamide, pectin, and a constipating diet.

Ultrashort-Segment Hirschsprung's

- Both the existence and treatment of the ultrashort-segment aganglionosis are controversial as normal individuals have variable length of aganglionosis above the pectinate line.
- Typically, Hirschsprung's in adults is of the short-segment variety.
- Many actually have idiopathic constipation that responds to laxative therapy.
- Some surgeons propose a myectomy, consisting of a resection of a strip of smooth muscle from the anal verge up to the area where ganglion cells are found.

Neuronal Intestinal Dysplasia (NID)

- Neuronal intestinal dysplasia refers to a histological condition that includes hypertrophy of ganglion cells, immature ganglia, hypoganglionosis, hyperplasia of the submucosal and myenteric plexus, and giant ganglion cells as well as hypoplasia or aplasia of the sympathetic innervations of the myenteric plexus.
- Most cases of NID are likely sampled areas of colon that are actually transition zone bowel in a Hirschsprung's patient.

Anorectal Malformations (Imperforate Anus)

- Anorectal malformations represent a spectrum of defects characterized by the absence of an external anal orifice, occurring in about 1 in every 5,000 newborns.

Table 50.1 Current classification of anorectal malformations

Male
Perineal fistula
Rectourethral fistula
Bulbar
Prostatic
Rectobladder neck fistula
Imperforate anus without fistula
Rectal atresia and stenosis
Female
Perineal fistula
Vestibular fistula
Imperforate anus without fistula
Rectal atresia and stenosis
Cloaca
Complex malformations

- The majority 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, the rectum, vagina, and urethra are fused together forming a common channel (cloacal malformation) and open into a single external orifice.
- In the male, the communication is with the urethra (rectourethral fistula) or the bladder (rectobladder neck fistula).
- The most common type of defects seen in boys is a rectourethral fistula and the most common type in girls is vestibular fistula (Table 50.1).

Associated Anomalies

- Urogenital abnormalities occur in about 50 % of all patients with anorectal malformations.
- Unilateral renal agenesis is the most common urologic anomaly, followed by vesicoureteral reflux.
- Other important abnormalities include cryptorchidism, hypospadias, renal ectopia, and hydronephrosis.
- Sacral and spinal abnormalities are also very common (agenesis, hypoplasia, hemivertebrae, scoliosis).
- A tethered cord occurs in 25 % of patients, where 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 particularly impacting bladder emptying.
- An anorectal malformation with hemisacrum and a presacral mass (dermoid, teratoma, lipoma, anterior meningocele) is known as the Currarino triad.

- Approximately 8 % have esophageal atresia.
- Approximately 30 % have an associated cardiovascular anomaly (PDA, ASD, VSD, tetralogy of Fallot).
- The higher the malformation, the worse the functional prognosis will be.
- The higher the anorectal defect, the higher the rate of fecal incontinence and the lower the rate of constipation.
- The lower the malformation, the higher the incidence of constipation, but the lower the incidence of fecal incontinence.

Specific Defects

Males

Perineal Fistula

- The rectum opens anterior to the center of the sphincter mechanism in the perineum.
- The end of the rectum often lies immediately below a very thin layer of epithelium with an external opening located at the base of the scrotum or sometimes at the base of the penis.
- The overwhelming majority of these patients have a normal sacrum; less than 10 % of them have associated defects.
- Treatment consists of moving the anal orifice back to the center of the sphincter, creating a normal-sized anus.

Rectourethral Fistula

- In this group of malformations, the rectum connects to the urethra, most commonly into the lower part of the posterior urethra known as the bulbar urethra, (rectourethral bulbar fistula; Fig. 50.3a). Most (~85 %) achieved bowel control after treatment and 30 % have associated defects.
- In the second subtype, the rectum opens into the upper part of the posterior urethra (rectoprostatic fistula; Fig. 50.3b). Only 60 % of these patients achieve bowel control later in life, and 60 % have significant associated defects.
- Most of these patients (rectourethral fistula) require a colostomy at birth, and subsequently (usually 1–2 months later) they receive the definitive repair of the malformation.
- The higher the malformation, the more likely the patient will have a flat bottom, meaning that the natural midline groove is absent and there is no distinguishable anal dimple. The lower the malformation, the more prominent the midline groove and the anal dimple.

Rectobladder Neck Fistula

- This is the highest of all defects in male patients (Fig. 50.3c), where the rectum is connected to the bladder neck.
- 90 % of these patients have significant associated defects.

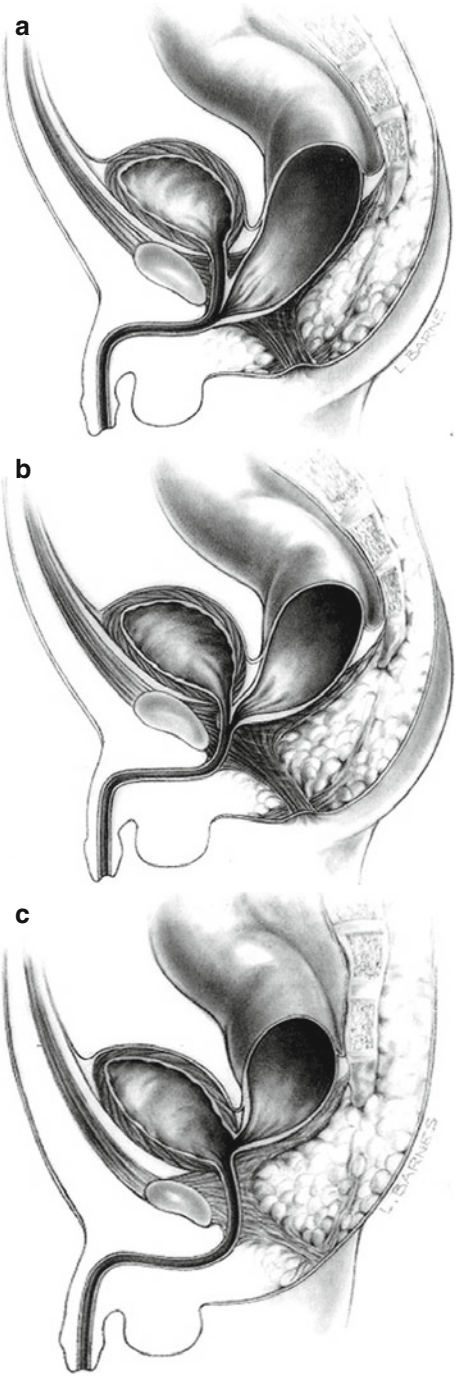

Fig. 50.3 (**a**) Bulbar fistula (**b**) Prostatic fistula (**c**) Bladder neck fistula (Reprinted from Pena, A (1989) Atlas of surgical management of anorectal malformations with permission from Springer)

- These patients are the only ones that require a laparotomy or laparoscopy in addition to the posterior sagittal approach to be repaired. Only 15 % of these patients achieve bowel control later in life.

Imperforate Anus Without a Fistula

- Occurs in ~5 % of all children with anorectal malformations, and half also suffer from Down syndrome.
- Patients usually have a good sphincter mechanism and a good sacrum, and 80–90 % will eventually achieve bowel control after an operation.

Rectal Atresia or Stenosis

- Occurs in only 1 % of all cases and consists of a complete or partial interruption of the rectal lumen located between the anal canal and the rectum.
- The external appearance of the perineum is normal, and the anal canal is normal or appears like a funnel with a long skin-lined canal.
- All of these patients (100 %) will have bowel control after a correctly performed operation.

Female Defects

Perineal Fistula

- 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, and prognosis is excellent.

Vestibular Fistula

- This is by far the most common defect seen in female patients (Fig. 50.4).
- The rectum opens in the vestibule of the female genitalia just outside the hymen, and the rectum and vagina share a very thin common wall.
- About 30 % of these babies have associated defects; 95 % of these babies will have bowel control when properly treated.
- Most cases are successfully operated on at birth without a colostomy. However, those undiverted patients can suffer from dehiscence and retraction; therefore, diversion is a safe approach.

Imperforate Anus Without Fistula

- Similar to males, except the distal rectum is adjacent to the posterior vagina rather than to the urethra.

Rectal Atresia or Stenosis

- Does not differ from the defect described in males, including the need to screen for a presacral mass.

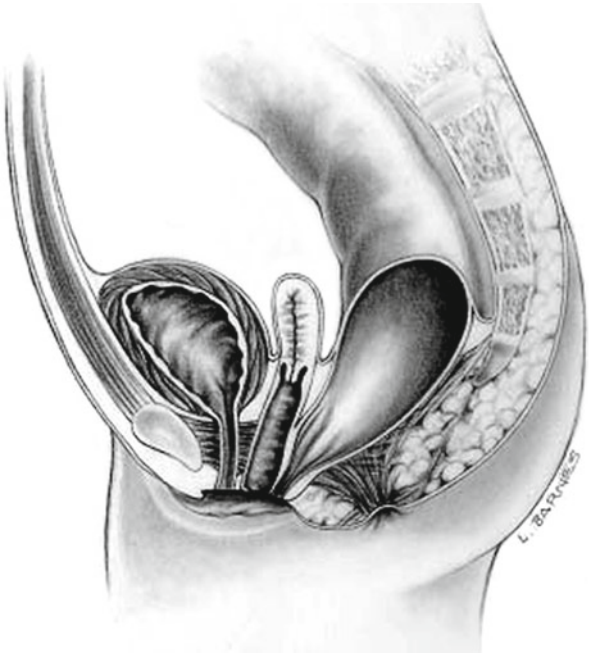

Fig. 50.4 Vestibular fistula (Reprinted from Pena, A (1989) Atlas of surgical management of anorectal malformations with permission from Springer)

Cloaca

- A cloaca is defined as a malformation in which the rectum, vagina, and urinary tract are fused together forming a common channel (Fig. 50.5).
- The length of the common channel varies from 1 to 7 or even 10 cm, and is directly related to the final functional prognosis for bowel and urinary control.
- Patients with a common channel shorter than 3 cm can be repaired posterior sagittally without opening the abdomen and the prognosis for bowel and urinary control is good.
- Common channels longer than 3 cm frequently require not only a posterior sagittal approach but also a laparotomy and a creative vaginoplasty or a vaginal replacement. The final functional prognosis is not very good, and associated defects occur in about 90 %.
- Approximately 40 % have different degrees of septation of the vagina and the uterus (Fig. 50.6) that may impact menses as well as obstetric potential.

Initial Management

Male Newborns

- Perineal inspection and urinalysis allow the clinician to determine the type of malformation that the baby has in about 90 % of cases.

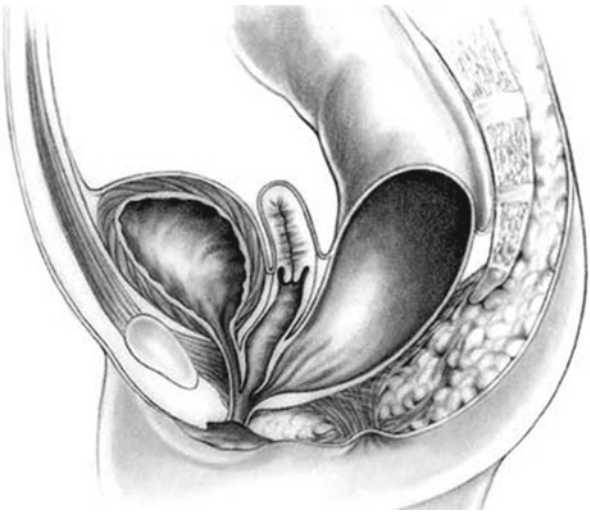

Fig. 50.5 Cloaca (Reprinted from Pena, A (1989) Atlas of surgical management of anorectal malformations with permission from Springer)

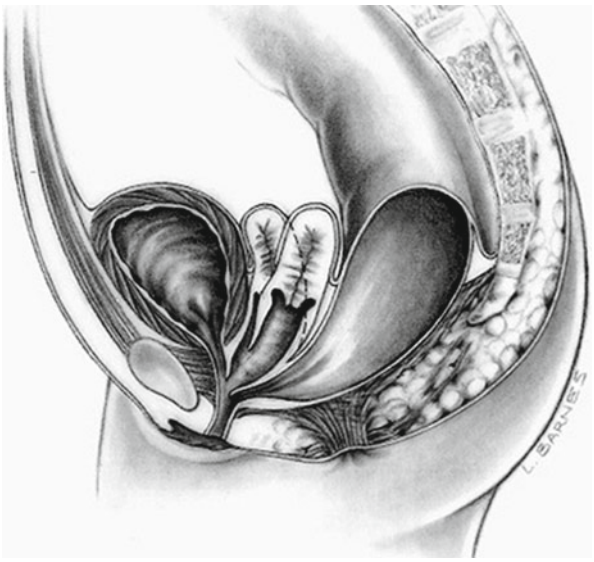

Fig. 50.6 Cloaca with double uterus and double vagina (Reprinted from Pena, A (1989) Atlas of surgical management of anorectal malformations with permission from Springer)

- If a patient has a good midline groove, an anal dimple, and meconium in the urine, that is consistent with a prostatic or rectourethral fistula.
- A flat bottom and bifid scrotum are signs of a very high malformation and high prostatic or bladder neck fistula.
- Diagnostic studies should be done after 24 h of life, but not later than 36 h to allow for rectal distension.

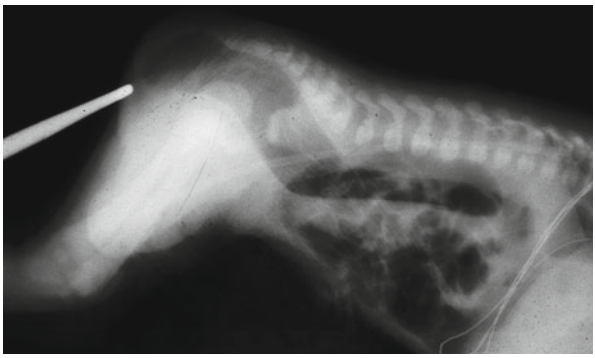

Fig. 50.7 Cross-table lateral X-ray (Reprinted from Levitt MA and Peña A (2010) Imperforate anus and cloacal malformations In Ashcraft's Pediatric Surgery, 5th edition with permission from Elsevier)

- 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 rule out the presence of hydronephrosis.
- An ultrasound of the spine is also useful to evaluate for the presence of a tethered cord.
- An X-ray film of the lumbar spine and the sacrum will assess for the presence of hemivertebrae and sacral abnormalities.
- A cross-table lateral film with the baby in prone position and the pelvis elevated should be performed (Fig. 50.7). If the rectum is visualized below the coccyx, a primary repair can be done. If the rectum is located higher than the coccyx, it is better to perform a diverting colostomy and to postpone the main repair for a later date.

Female Newborns

- Similar to males, inspection of the perineum will allow for a correct diagnosis during the neonatal period in most cases.
- The presence of a small opening in the perineum anterior to the sphincter mechanism makes the diagnosis of perineal fistula.
- The presence of a fistula in the vestibule establishes the diagnosis of a rectovestibular fistula (Fig. 50.4).
- The presence of a single perineal orifice makes the diagnosis of a cloaca (Fig. 50.5).
- 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 (Fig. 50.8).

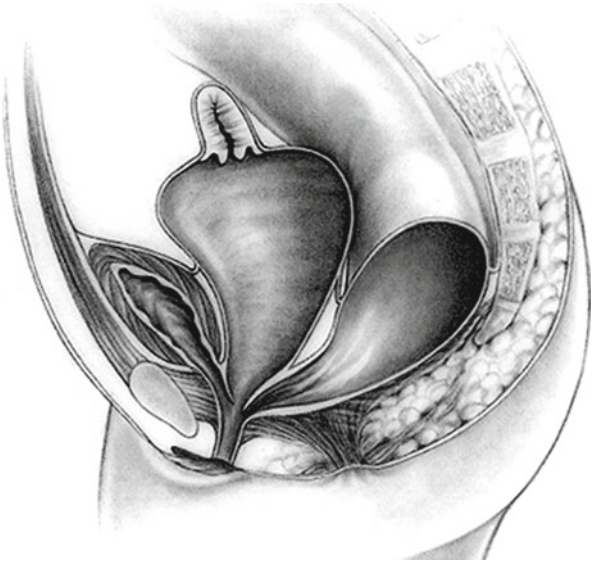

Fig. 50.8 Hydrocolpos in cloaca (Reprinted from Pena, A (1989) Atlas of surgical management of anorectal malformations with permission from Springer)

- Most babies with a cloaca need a diverting colostomy.
- The hydrocolpos must be drained at birth, usually with a tube at the time of colostomy opening, which will often also decompress the urinary system.

Colostomy

- Colostomies in babies with anorectal malformation should be totally diverting (Fig. 50.9).
- In cases of cloaca, the surgeon must also drain the hydrocolpos through a vaginostomy or a tube that is exteriorized through a separate hole in the abdominal wall.
- Two to four weeks after the colostomy, a high-pressure distal colostogram is performed to delineate the anatomy of the distal colon and to establish an accurate anatomic diagnosis (Fig. 50.10).

Main Repair

Male Defects

Perineal Fistula

- Perineal fistulas can be repaired performing a minimal posterior sagittal anoplasty.
- An alternative is to dilate the fistula with a plan for a future definitive repair.

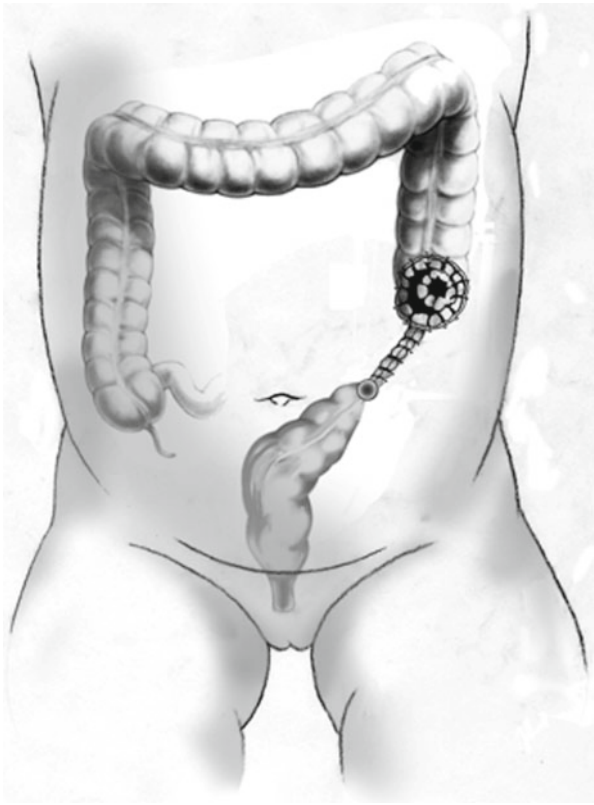

Fig. 50.9 Ideal colostomy (Reprinted from Pena, A (1989) Atlas of surgical management of anorectal malformations with permission from Springer)

- In cases of rectourethral fistulas, after their newborn colostomy, the patients undergo a posterior sagittal anorectoplasty (PSARP).
- The only difference in the surgical treatment between the rectourethral bulbar fistula and the rectoprostatic fistula is that the latter requires a more significant dissection to bring the rectum down.

Rectobladder Neck Fistula

- This is the only defect that requires a laparotomy or laparoscopic assistance in addition to the posterior sagittal operation because the rectum is located too high to be reached from below.

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.

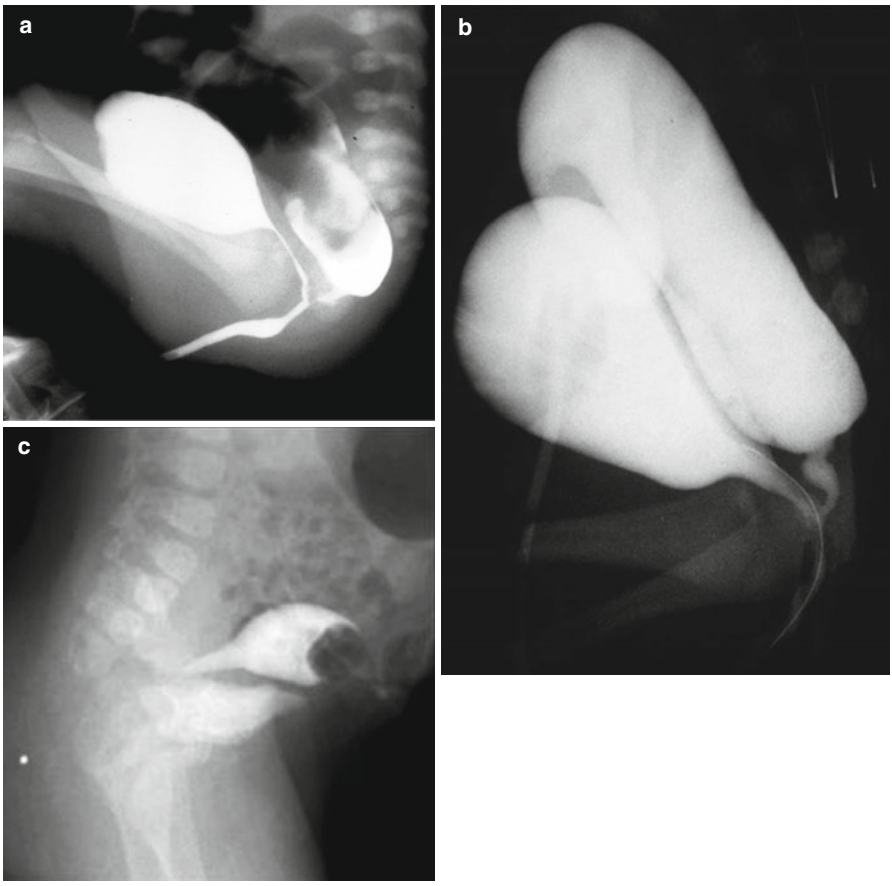

Fig. 50.10 (**a**) Colostogram showing bulbar fistula (Reprinted from Levitt MA and Peña A (2010) Imperforate anus and cloacal malformations In Ashcraft's Pediatric Surgery, 5th edition with permission from Elsevier). (**b**) Colostogram showing prostatic fistula. (**c**) Colostogram showing bladder neck fistula

Rectal Atresia or Stenosis

- These patients also require a posterior sagittal approach.

Female Defects

Perineal Fistulas

- The repair of this malformation is the same as that described for male patients, except that the rectum is usually separate from the vagina so there is minimal risk of vaginal injury.

Vestibular Fistulas

- The repair is performed through a posterior sagittal approach.
- The main technical challenge in this repair is the common wall that exists between the rectum and vagina, and one must make two walls out of one.

Rectovaginal Fistula

- A posterior sagittal approach is the same as vestibular fistula, except much more rectal mobilization is required to move it down and relocate it in the center of the sphincter.

Cloaca

Repair of Cloaca with a Common Channel Shorter Than 3 cm

- These patients are approached posterior sagittally.
- The entire sphincter mechanism and common channel are divided in the midline to expose the anatomy of the defect.
- The entire defect can be repaired through this incision without opening the abdomen.

Repair of Patients with Cloaca with a Common Channel Longer Than 3 cm

- It is recommended these patients 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 gynecology and urology.
- Patients with a common channel longer than 3 cm sometimes require a suprapubic cystostomy or vesicostomy at the end of the operation.
- The most common sequela from the urinary point of view in babies with cloaca is the incapacity to empty the bladder.

Results of Treatment of Anorectal Malformations

- About 75 % of all patients with anorectal malformations following a good operation have bowel control, though it may not be perfect.
- Twenty-five percent of all patients suffer from fecal incontinence and require some form of medical management.
- The clinical and functional results vary depending on the specific type of malformation.
- Patients with a cloaca with a common channel longer than 3 cm usually suffer from fecal incontinence and require intermittent catheterization to empty the bladder.

- Patients with a common channel shorter than 3 cm and a normal sacrum have bowel control 80 % of the time, and only 20 % of them require intermittent catheterization to empty the bladder and remain completely dry.
- 95 % of patients with rectovestibular fistulas have bowel control.
- Babies with perineal fistulas have bowel control 100 % of the time.
- Rectobladder neck fistula patients only have bowel control 15 % of the time, with rectoprostatic fistula patients at 60 %, and rectourethral bulbar fistula patients at 85 %.
- Patients with imperforate anus with no fistula will have bowel control between 80 and 90 % of the time depending on whether or not they suffer from Down syndrome.
- Constipation is a problem in most patients with anorectal malformations in whom the rectum was preserved during the main repair and may result in megacolon and overflow incontinence.

Management of Fecal Incontinence

- 25 % of anorectal malformation patients will suffer from fecal incontinence.
- Daily enemas to clean the colon will prevent the patient from passing stool for 24 or 48 h.
- Patients who lost the rectosigmoid during the main repair or suffer from intractable diarrhea or malabsorption are more challenging. They require daily enemas and constipating diet and/or medications.
- Daily X-ray films of the abdomen and adjusting the volume and concentration of the enema by trial and error help monitor progress.
- The Malone procedure (continent appendicostomy) creates a connection between the tip of the 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 leakage of stool. The patient will administrate the enema himself/herself will evacuate of the colon, and will remain clean the following 24 or 48 h.

Relevant Aspects for Adult Colorectal Surgeons

- A large number of adolescent and adult patients may still suffer from fecal incontinence despite successful repair in infancy.
- Workup includes a detailed history and physical examination, 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, and an MRI with a rectal coil to assess the location of the rectum are essential to classify patients into 1 of 4 groups.

- Patients with a poor sacrum, flat perineum, poor muscles, no sensation, and poor bowel movement pattern who are usually incontinent for both urine and stool. These patients are good candidates for a bowel management program.
- Patients with clinical and MRI evidence of a mislocated rectum with a good sacrum and well-developed muscles. These patients may benefit from a secondary pull-through procedure.
- Patients who suffer from severe constipation and have a contrast enema which shows a severely dilated mega rectosigmoid. These patients need aggressive laxative therapy and possibly a sigmoid resection.
- Patients with a well-located rectum, good sacrum, and good muscles but are still incontinent. They may benefit from biofeedback or bowel regimen programs.

Other Pediatric Colorectal Disorders

Idiopathic Constipation

- Constipation of unknown origin accounts for 6 % of pediatric consultations.
- Constipation is a result of a colonic hypomotility disorder with different degrees of severity, affecting mainly the rectosigmoid and sometimes the entire colon.
- The underlying incapacity to empty the colon results in the colon storing a large amount of stool and becomes very dilated (megacolon).
- The final result is chronic fecal impaction, which provokes overflow pseudoincontinence (encopresis).
- Treatment consists of using laxatives to produce 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, resection of the most dilated portion of the colon (usually the rectosigmoid) may be performed.

Rectal Prolapse

- Rectal prolapse occurs in children due to conditions such as myelomeningocele, spina bifida, malnutrition, cystic fibrosis, and severe constipation. It may also occur in some patients with inflammatory bowel disease or intestinal parasites.
- Most are treated with a bowel regimen and removal of any irritating conditions of the colon, such as milk allergy.
- Several surgical options are used as a last resort, and include abdominal (rectopexy) and perineal approaches (modified Altemeier procedure).

Perianal Fistula

- During the first year of life, many babies suffer from perianal abscesses that may be associated with a perianal fistula.
- This is typically a benign condition that does not require any treatment. If the babies have a perianal abscess, they do not require antibiotics. Very soon, the abscess drains by itself and if not, with a minimal incision and drainage. Following that, for a period of months, it drains intermittently without any discomfort to the patient. The vast majority of fistulas disappear after 1 year of age.
- School-age children with perineal fistula should be evaluated for inflammatory bowel disease.
- These abscesses and fistula may be treated similar to adults.

Juvenile Polyps

- Around the age of 4 years, children may suffer from polyps in the rectum and in the colon (mostly located in the posterior rectal wall).
- These polyps are benign inflammatory polyps. They grow and eventually amputate and disappear.
- Symptoms include the presence of blood surrounding the fecal matter, or occasionally prolapse through the anus. They do not cause pain.
- The polyps can be easily resected under general anesthesia.

Anal Fissure

- Anal fissures in pediatric patients are usually a consequence and not a cause of constipation.
- The patient suffers from painful bowel movements and that contributes to the constipation, and the patient becomes a stool retainer.
- The main treatment is laxatives to provide soft stool passing through the rectum for several weeks until the fissure heals.
- No surgical treatment is necessary, and lateral internal sphincterotomy should not be performed.
- Recently, 0.2 % NTG ointment has been used for intractable cases.

51. Health-Care Economics

David Margolin and Lester Rosen

Background

- Health-care expenditures have increased by double digits for the past decade, physician reimbursement have decreased over the past 10 years, and hospitals have closed and health-care systems have filed for bankruptcy.
- From 2009 to 2019, the average annual health-care spending growth is projected to grow at a rate of 6.0 %, well outpacing the expected average annual growth in the overall economy (4.4 %).
- By 2019, national health spending is expected to reach $4.5 trillion and comprise 19.3 % of GDP (Fig. 51.1).
- With the advent of the resource-based relative value scale (RBRVS), physicians have shifted from price setters to price takers.
- Technology costs, while providing an improvement in patient care, have skyrocketed.
- The current professional liability crisis has resulted in increased malpractice rates and driving specialists from specific locations.

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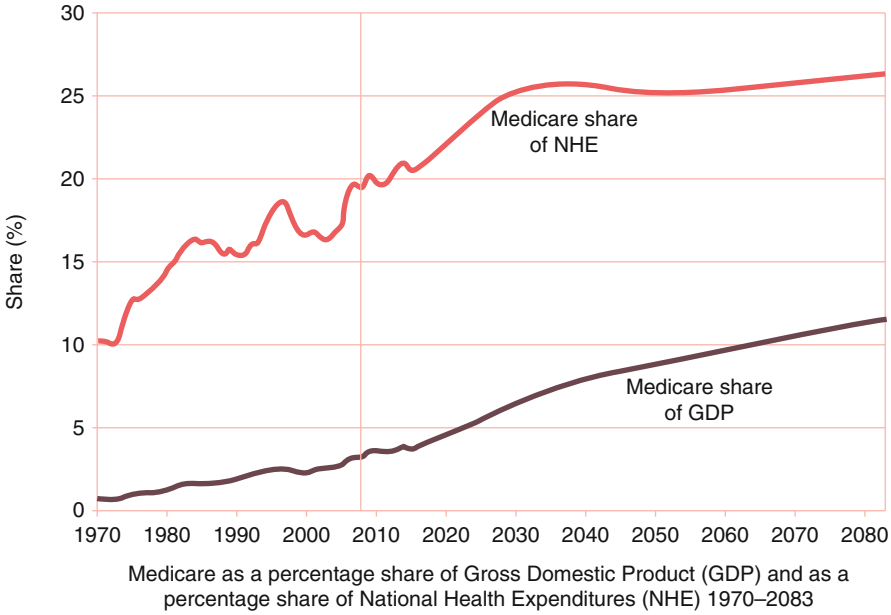

Fig. 51.1 By 2019, national health spending is expected to reach $4.5 trillion and comprise 19.3 % of gross domestic product (GDP)

The Reimbursement Process

Medicare

- Although private payers vary in their reimbursement rates and policies, most are tied in some form to the Medicare system.
- Medicare was created in 1965 by the Federal government as a social insurance program designed to provide all adults over the age of 65 with comprehensive health-care coverage at an affordable cost.
- Medicare is administrated by the Centers for Medicare and Medicaid Services (CMS).
- In 2004, Medicare had over 41 million enrollees and is forecasted to include almost 80 million people by 2030 (Fig. 51.2).
- Medicare is divided into two parts:
  - Medicare Part A, also known as Hospital Insurance, helps pay for inpatient hospitalizations, skilled nursing facility (SNF) care, and home health 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 over 24 months are also eligible for Part A.

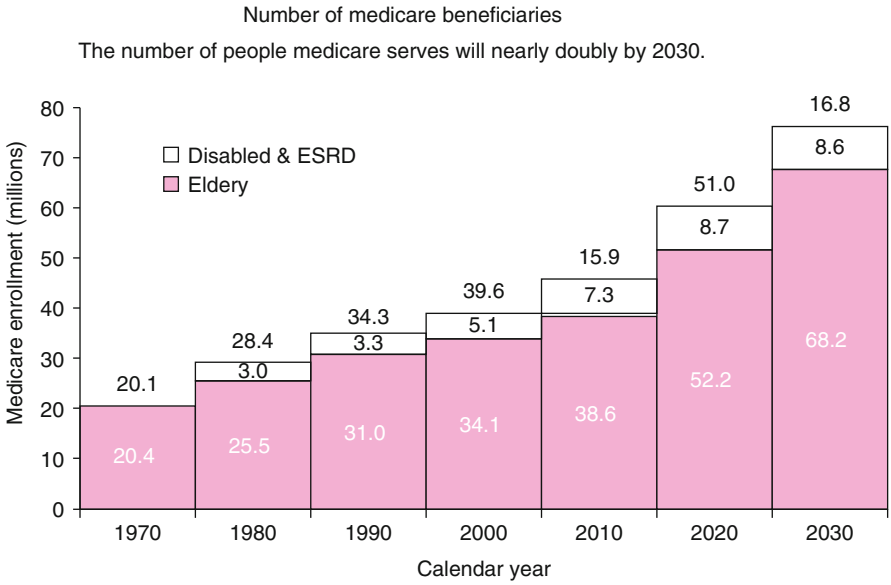

Fig. 51.2 In 2004, Medicare had over 41 million enrollees and is forecasted to include almost 80 million people by 2030

    - 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.
    - 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.
    - Unlike Part A, Medicare Part B has monthly premiums.
    - Patients can opt out of Part B.
    - Similar to Part A, Part B enrollees are responsible for copayments and deductibles.
- Medicare Part C or Medicare Advantage is the government's plan to shift the cost and risks of Medicare patients to the private sector.
  - In Medicare Advantage, private payers receive a monthly payment per covered individual (capitated amount) to provide all of Part A and B services.
  - Since 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 that provides for prescription drugs with an initial deductible of $250 and a monthly premium of $35.
- Individuals with incomes $160,000 and above will be subjected to higher Part B and Part D premiums.

Medicare Resources

- The Medicare budget is determined by legislation and is formula based, involving the Medicare Economic Index (MEI), a weighted index, and the sustainable growth rate (SGR).
- The SGR compares the cumulative actual spending for physicians' services since 1997 to a cumulative target amount of spending over the same time period.
  - The SGR says essentially that the amount Medicare pays doctors for an average Medicare patient cannot grow faster than the economy as a whole.

Hospital (Part A) Reimbursement

- In response to sharply rising hospital costs, the Federal government instituted a prospective payment system.
- This system categorized patients based on diagnostic-related groups (DRG), consisting of primary and secondary diagnosis, primary and secondary procedures, age, and length of stay.
- Each DRG sets 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).
- Hospitals have tried to increase their efficiency and shifted procedures from the inpatient setting to outpatient/ambulatory center.
  - Medicare has developed a prospective payment system called the ambulatory payment classifications (APC) that are specific reimbursement groupings that Medicare pays to facilities.
  - Specific medical devices and drugs called "pass throughs" are exempt from this and are reimbursed in addition to the APC fee.
  - Other devices that do not receive pass through are often charged to the patient.

Physician Reimbursement

- Currently, physician reimbursement from Medicare is a three-step process:
  1. Appropriate coding of the service provided by utilizing current procedural terminology (CPT®)
  2. The appropriate coding of the diagnosis using ICD-9 code
  3. CMS determination of the appropriate fee based on the resource-based relative value scale (RBRVS)

- To receive consideration for a new CPT code, a procedure must meet certain requirements:
  - Performed by a reasonable number of the specialty that presents the code
  - Performed at reasonable frequency
  - Performed throughout the country
  - 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).
- The Medicare fee schedule 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).
  - 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).
  - Intraservice work includes all "skin-to-skin" work that is a necessary part of the procedure.
  - Post-service work varies depending on the magnitude of the procedure.
    - There are currently three post-procedural global periods: 0, 10, and 90 days.
    - Routine post-procedure care includes physician work following skin closure that is done on the day of the procedure, including non-"skin-to-skin" work in the OR.
- 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.
- While the work RVUs (wRVUs) make 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 2009 was $36.0666 per RVU.

Private Payers

- Traditionally, there were two types of nongovernmental insurance, individual insurance and group insurance.
- Individual insurance allows a person to buy health insurance for themselves and their family.
  - Individual insurance is becoming prohibitively expensive.
- 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.
- 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.
    - No preapproval is required.
  - Managed care organizations utilize a variety of tools to manage preauthorization functions, control health-care costs, and share the risks associated with group coverage.
    - Health maintenance organizations (HMOs) restrict 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.
    - HMOs use gatekeeper requirements for specialist referral.
  - Preferred provider organizations (PPO) enter into contracts with health-care providers and hospitals to provide member care.
    - Often more choices 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 PPO's beneficiaries and be listed in the "network," physicians often agree to reduce their normal fees.

- "Point of Service" plans are a mixture of traditional HMO and PPO plans.
  - If a patient first sees their primary care physician to receive a referral, much like an HMO, the co-pay, if present, is negligible.
  - Patients are also able to see "network" physicians with minimal financial responsibility.

The Future

- Despite managed care, costs initially slowed and then they continued to rise at a rate higher than the consumer price index and personal income.
- Experts now tout a "consumer-centric" or "consumer-driven" health-care model as the future of health-care delivery.
- Individuals are given the opportunity to choose from specific benefit packages that will fit their particular need.
- With the rising number of consumers in need of health-care resources, experts see the Internet as a way of rapid dissemination of health-care information.
- Potential problems include:
  - This model assumes that consumers are sophisticated enough to make sound health-care choices, not just those based on cost.
  - 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.
- Further development of consumer-driven health care is the creation of "health reimbursement arrangements" (HRAs) in which the IRS gives a tax advantage to employers who contribute defined contributions to employee-controlled accounts for health-care spending.
  - Any monies not spent during the year are rolled over to help fund the following year's plan.
- Proponents of universal coverage envision a system that provides access to quality care when needed and effective preventative care in a cost-effective manner that is delivered and paid for in an equitable way.

52. Ethical and Legal Considerations

Ira J. Kodner, Mark Siegler, Daniel M. Freeman, and William T. Choctow

Considerations for Surgeons

General Concepts

- Defining the Problem. *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.
- *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* and does not always prohibit behavior deemed unethical; however, it usually sets a minimal standard for conduct.
  - To help patients make informed choices, we must communicate completely and compassionately the requisite information about the disease, treatment options, and long-range plans. We must learn and

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apply the ethical principle of *truth telling* and the doctrine of *informed consent* for the effective care.

- Bioethics and the legal underpinnings of bioethical decision-making are evolving all the time.

What Makes the Surgeon Special?

- Undergoing major surgery is an extreme experience that changes people's lives.
- There are special ethical considerations for surgeons that include rescue, proximity, ordeal, aftermath, and presence.
  - *Rescue* is the first pillar of surgical ethics and deals with the fact that surgery conveys power and that power is socially endorsed and may be reinforced by the surgeon's individual charisma.
  - *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. Patients yield autonomy, acknowledge dependence, place trust, face risk, confront embodiment and mortality, lose control over time and space, experience alienation, pain, fear, discomfort, suffering, and boredom.
  - *Aftermath* deals with the reality that surgery leaves physical and psychological scars that may persist for life. When death approaches our patients, we must remember, not deny, our own mortality.
  - *Presence,* as a virtue and a duty, is what the patient desires of the surgeon during all phases of the surgical encounter.
    - Most surgeons have the stamina and cognitive ability to be present for their patients, but not all of us process the personal attributes of charisma, confidence, energy, and empathy, which are necessary to engender *trust* from our patients and our staff.

Unique Problems of Surgery

- For the surgeon, the initial contact may just be the beginning of a longer-term relationship.
- This intense relationship is often established very quickly and under frequently adverse circumstances.
- Other issues include *informed consent, refusal of treatment, determination of decision-making capacity, treating patients despite their refusal, maintaining confidentiality* while respecting the duty to warn others,

limiting treatment over issues of "futility," *treating pain* at the end of life, and acting as a *Good Samaritan.*

- Surgeons often don't have a "second chance."
- For specific dilemmas, time permitting, surgeons should obtain an opinion from the hospital ethics consultation service and/or from hospital counsel.
- Similarly, doctors have a duty to themselves to avoid situations that violate their own personal beliefs, whether religious or medical.
  - If the anticipated actions may violate a doctor's own personal tenants, he or she should refer the patient to another physician.

Principles of Bioethics

General Concepts

Philosophical Principles

- Two major fundamental theoretical philosophical concepts exist for constructing a theory of ethics: *deontologic* and *consequentialist*.
  - A *deontologic theory* relies on *rules*, while a *consequentialist* theory relies on *outcomes*.
- From these theories are derived *principles of ethics:*
  - Respect for autonomy *(patient self-determination)*
  - Beneficence (*doing good*)
  - Nonmaleficence (*do no harm*)
  - Justice (*fairness*)

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.*
- It simply means that you as a physician cannot *touch* a person without first getting permission and without telling the individual of the possible ramifications of that "touching."
- 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 doctrine of the *reasonable man* is used in deciding what is acceptable in many areas of delivering emergency surgical care.
- The concepts of *living wills* and *durable powers of attorney* both facilitate and complicate the consent process because *consent* must be obtained, if time permits, through these documents or via surrogate decision-making.
- There are exceptions to this rule:
  - When a patient demands a certain kind of treatment that the doctor knows will not be efficacious.

Beneficence

- 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.*
  - This is the crux of the major debate that is ongoing over *physician-assisted suicide,* if not actual *euthanasia.*
  - *Abortion* and *embryonic stem cells* present other situations that, depending on personal beliefs, might fall into that same category.

Justice

- Justice is *fairness* and is required to ensure that medical decisions are made with reason and honesty.
- *Distributive justice* includes the surgeon's obligation not only to an *individual patient* but also to fairness in the allocation of resources for the good of the *broader society.*
  - It implies that all individuals and groups should share in society's benefits and burdens.

Religion and Medical Ethics

- In many societies, religion has been looked upon as the determinant of ethical norms.
- Clinical bioethics, in fact, uses many decision-making methods, arguments, and ideals that originated from religion.
- The individual clinician should understand his or her own personal spirituality to relate better to patients and families.
- Most religions are based on some form of the Golden Rule, which holds "do unto others as you would have them do unto you."
- Religion is one of the most common ways by which patients cope with medical illness and a strong influence on medical decisions.
- The purpose for taking a spiritual or religious history is to learn how patients cope with their illnesses, the kinds of support systems available to them in the community, and to learn of any strongly held beliefs that might influence the delivery of medical care.
- Physicians must be extremely cautious about prescribing religion to non-religious patients, forcing a spiritual history on patients who are not religious.

Legal Principles

General Concepts

Types of Law

- The fundamental document that creates and delineates these powers is the US Constitution.
- *Civil law*, including malpractice, is usually enforced by *monetary judgments*.
- *Criminal law*, including physician-assisted suicide, is usually enforced by *fines* and/or *imprisonment*.
- There are three kinds of law which affect the practice of surgery:
  - *Statutes.*
  - *Regulations* are written to comply with legislative directives.
  - *Case 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.

Statutory Law

- Statutory law is made by legislatures.
- This includes such issues as *the statute of limitations* and, in some states, statutes on *informed consent.*
- The EMTALA states patients without the means to pay for medical care cannot be turned away from the emergency room or "dumped."

Regulatory Law

- These administrative laws are created by regulatory agencies including State Medical Boards.
- One example is the Health Insurance Portability and Accountability Act of 1996 (HIPAA).

Malpractice

- Many successful legal actions against surgeons have been based on inadequate information about risks, complications, or adverse outcomes.
- It is clearly possible to accept *responsibility* without admitting *negligence.*
- Judges, not the legislature, establish the standards that constitute medical malpractice.
- The familiar elements of medical malpractice include *duty, breach, causation,* and *damages.*

- Decisions are based on the standard of care.
- Because the law has come to champion individual rights and hold physicians liable for malpractice, it has served to condemn medical *paternalism* as it has elevated *patients' rights.*

A Familiar Case-Management System

Physician-Based Ethics

The Clinical Ethics System

- In this system, every clinical case, especially those raising an ethical dilemma, should be analyzed by means of the following four topics (Table 52.1):

  1. Medical indications
  2. Patient preferences
  3. Quality of life
  4. Contextual features, *defined as the social, economic, legal, and administrative context in which the case occurs*

- Most ethical conflicts can be resolved by falling back on the *medical indications* that represent the medical facts of the case. This information, plus the second category of *patient preferences*, almost always will lead the clinical surgeon to a resolution of the ethical problem. If the ethical dilemma results from conflicts among the patient, the family, the healthcare team, or institutional policy, then adequate resolution may become dependent on applying analysis of the additional categories*, quality of life*, and *the array of contextual feature*.

Specific Dilemmas of Colon and Rectal Surgery

Special Considerations for Colon and Rectal Surgeons

- Colorectal surgeons frequently are confronted with ethical dilemmas. These may include issues such as:

  – Screening, preventive measures, understanding genetic predisposition to disease, and even the need for what has come to be called *preemptive surgery*
  – Challenges of respecting *confidentiality* and requesting *genetic counseling* to deal with the long-term aspects involving not only the patient but also the family members
  – *Quality-of-life* issues as body image and impairment of sexual function
  – Differentiating acceptable surgical *innovation* from truly *investigative* ventures that require research protocols and institutional approval

Table 52.1 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, or 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?
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 are 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 continued life might be judged undesirable?	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?
	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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Categories of Patient Encounters

- Severe Emergency: Life in Immediate Jeopardy
  - An example would be a critically ill person brought in from a severe motor vehicle accident.

- Urgent: Serious Problem Needing Surgery
  - An example would be a patient brought in with peritonitis.
  - When 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 a patient with known extensive intra-abdominal cancer who presents with a significant, unresolving intestinal obstruction.
  - Determination of *decisional capacity,* the existence of *advance directives,* or the presence of a reliable surrogate is very important.

Autonomy/Decision-Making Capacity/Competency

General Concepts

Autonomy Versus Paternalism: Trust Is the Bridge

- Individual freedom (autonomy) is one of the basic tenets of modern bioethics and implies that a person should be free to make his or her own decisions.
- Paternalism involves the physician acting on what he or she thought was good for the patient, whether or not the patient agreed.
- Patients often significantly rely on physicians for guidance through complicated choices, often where life itself is on the line.
- The key to accomplishing this is based on the principle of trust.

Refusal of Treatment

- *Ethical dilemmas usually occur when there is disagreement among the patient, the family, and the health-care team.*
- 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
  - The maintenance of the integrity of the medical profession
- Each competent patient has a right to refuse treatment, even if the results of such refusal will be their death.

- There are situations where parents or guardians are involved in refusal to accept and allow treatment on behalf of miners.
  - These are the most common instances where court intervention is sought, and to resolve the problem, the courts must balance the best interests of the child against the desires of the parents.

Telling the Truth/Disclosing Errors

General Concepts

- There may be circumstances where telling the *whole truth* to a patient will have a negative impact on his or her overall well-being.
- *Truth telling* also would apply in situations involving *medical mistakes,* even those mistakes that are minor and arguably have no detrimental effect on the patient.

Prognosis: Balance Between Giving False Hope and Removing All Hope

- Even what is anticipated to be a fairly straightforward operation may have unexpected, adverse results.
- Discussing prognosis with our patients and their families is one of the situations, which forces us most carefully to choose our words precisely.
- 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 to any possible hope.

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.
- Depending on the severity of their disease, they may well be able to participate in much of the decision-making process.

Suicidal Patients

- When treating a suicidal patient, the surgeon is faced with a conflict between the ethical principle of *beneficence* and *respect for autonomy.*
- 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.
- 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.

Advance Directives

General Principles: Talking About Death

- Often, the issues that are most difficult to address when patients are near the end of life are those that have not been attended to earlier in the patient's course of treatment.
- *Advance directives* express in written form what the patient's choices would have been if he or she had decision-making capacity.
  - There should be advanced informed consent for a myriad of courses of treatment, whether it be related to pain medication, "do not resuscitate orders," or management, should the individual enter some level of persistent vegetative state.
- Advance directives include living wills, durable powers of attorneys, and other written documents.
- The Patient Self-Determination Act (PSDA) required that health-care institutions advise and educate patients regarding advance directives, yet only ~20 % of seriously ill patients have advance directives.

Living Will

- The signatory indicates what his or her choices would be for medical treatment in the situation where *death is imminent* and the individual's wishes are unable to be communicated to the treating physician.
- This usually amounts to a "do not resuscitate" order but can also indicate the patient's wishes concerning the level of pain medication, hydration, and nutrition, which the patient would desire if he or she lapses into a nondecisional condition.
- A second physician's opinion is typically required corroborating a determination of *imminent demise.*

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 reason it is called "durable" is to ensure that the signatory knows that it can be revoked and/or changed at any time.

- Thus, the patient designates a *surrogate decision-maker* who should participate in all significant treatment decisions and be kept up to date regarding the patient's health care.
- If there is no durable power of attorney, there is usually a defined hierarchy regarding surrogate decision-makers: spouses, adult children, siblings, etc.

Problems

- The surrogate has the legal authority to make a decision but is not aware of what the patient would want.
  - Using the *substitute judgment* standard, the surrogate bases a decision on a prior expressed statement of the patient's preferences or on an in-depth knowledge of the personality of the patient and a willingness to do what the surrogate believes the *patient,* not the surrogate, would want in that specific situation.
  - The second standard is that of the *best interest* of the patient where the surrogate is supposed to do what he believes is in the best interest of the patient.
- A further problem is the application of such directives in situations for which they were not intended.
- *Verbal communication takes precedence over any written advance directive.*
- *If there is any confusion, advance directives limiting treatment should be ignored in favor of prudent medical care.*
  - In such situations, the hospital *ethics consultation service* can often prove very helpful.

Informed Consent

General Concepts

- A patient's *informed consent* to a medical or surgical procedure or test is *essential.*
- The physician must give the patient sufficient information to make an intelligent decision before any action is performed.
  - The nature of the procedure, risks, benefits, and alternatives, including no treatment at all
- Permission must be given *voluntarily.*
  - *Without coercion* from the physician or anyone else involved in rendering health care) or
- Those participating in the implementation of a *research* project

- The current interpretation of the law requires several elements to constitute *informed consent:*
  - The treatment that the doctor wishes to pursue, including a full explanation of the procedure and what it involves, including the necessity for anesthesia.
  - 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.
  - The risks of the recommended treatment, including a 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.
  - The benefits the patient will receive from the proposed treatment.
  - The chances that the proposed treatment will remedy the problem, including the *past experience and outcomes* of the surgeon in performing this specific procedure.
  - The alternative treatment options exist for the given problem.
  - 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.
- 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.
- *Exceptions* to the requirement for informed consent include:
  - When there is an emergency situation that could result in the death of the patient, when time is of the essence, and when there is no surrogate decision-maker present.
  - When the situation is not an emergency, but the patient is not able to give consent due to unconsciousness, coma, mental disability, or other cause of inadequate decision-making capacity, and when there is no advance directive or surrogate.
  - A *therapeutic exception* occurs when the physician believes that revelation of the normally required information would have a negative effect on the patient's health (e.g., a psychiatric patient).
  - When a competent patient *refuses* to receive information upon which to base a decision.
  - When the *government* requires certain medical tests or treatment in the face of possible medical or national security emergencies.
  - The *emergency 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.

- The action proposed would be that to which a *reasonable person* would consent.
- It does not apply if the patient has decision-making capacity and is able to communicate a decision about medical care.

Patient–Surgeon Relationship

- The three central ethical aspects of modern surgical practice are:
  1. Clinical competence
  2. Respect for patients and their health-care decisions
  3. Maintaining the primacy of the patient's needs in the face of external pressures in a changing social, economic, and political climate
- The relationship between patients and physicians has been evolving from one *paternalis*m 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.
- The surgeon must learn to take into account the cultural components of the relationship and find ways to respond to them in an ethically and medically responsible manner.

Communication and the Internet

- Communication over the Internet is usually not secure, and the information delivered can become a permanent part of the patient's record.
- A patient's employer and family can usually acquire easy access to the electronic message, potentially to the detriment of the patient and potentially leaving this sending physician legally liable.
- Currently, there are no guidelines available for the ethical transfer of confidential medical information via the Internet.
- All doctors are probably well advised to record in the patient's permanent record that discussions were held and permission was given to communicate *specific* information electronically.
- The other massive impact of the Internet is the availability of unlimited access to potentially confusing and harmful information to our patients.
  - Surgeons should guide our patients to appropriate and helpful Web sites.

Using Newly Deceased Patients for Teaching Purposes

- The issue is do we have the right to perform procedures on this newly deceased person without obtaining permission (informed consent) from the surviving family.

- The dilemma is complicated by the fact that no better teaching opportunity exists for our trainees who can then go forward, when adequately trained, to save lives and relieve suffering in the future.
- Although the law in this situation is very forgiving, compassionate and ethical considerations should supervene.
- It is probably prudent to approach the next of kin for permission before performing procedures on the newly deceased.

Special Concerns for Participation in Research/Innovation

General Concepts

- Surgeons may find themselves in situations where it is unclear whether they are doing an evolutionary variation on a standard procedure, a unique departure from accepted standards, or the first stage of what should become recognized as a formal surgical research project.
- Subjects and patients must be allowed to make an informed choice to participate, or not, without fear that their treatment might be compromised if they decline the request of the investigator.
- Special issues for informed consent arise when the surgical patient is asked to participate in a *research project.*
- To be ethical, studies must be well designed and worth the risk to patient and society.
- The Nuremberg Code obligates researchers to prepare descriptions of the probability and magnitude of all physical, psychological, social, and economic risks and to minimize unnecessary pain and suffering.
- In an emergency, the surgeon may be forced to act in the patient's best interests and to presume consent on the basis of necessity.

Placebo Surgery

- Using *placebo surgery* in clinical trials appears to violate the fundamental ethical principles of *beneficence* and *nonmaleficence.*
- Absolute prohibition of *placebo surgery* is not appropriate, but the standard of justification for its use must be extremely high and rigorously enforced.

Conflict of Interest: Industry and Drug Money

- Industry support for biomedical research now exceeds the financial support from all federal funding sources.
- Industry strives to complete clinical trials expeditiously and to publish positive results.
- Conversely, the primary goal of the surgical investigator is to advance and disseminate knowledge by the unimpeded exchange of ideas, despite secondary professional, financial, institutional, and sociopolitical objectives.

- This potential conflict of interest can only be resolved by scrupulously implementing the principles of integrity, honesty, respect, and equity.
- Investigators who receive industry-funded materials, discretionary funds, research equipment, and trips to meetings must be aware that subsequent restrictions and expectations can create conflicts of interest.
- Acceptance of individual gifts that do not benefit patients, such as trips and subsidies for medical educational conferences in which physicians are not speakers, is strongly discouraged.

Confidentiality

General Principles

- Patients or families might be reluctant to give such information to the treating physician if the situation is not conducive to confidential communication, something that is due to them.
- 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.

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 the results obtained.
- Although supposed to be protected by law, many individuals fear that determination of a genetic abnormality will have adverse effect on their insurability and employability.
- Most of these unpleasant situations can be avoided by appropriate genetic counseling *before* any genetic information is obtained.
  - Genetics counselors should be involved, since most surgeons have not been adequately trained in the skills required to obtain and verify such familial and generational information.

Abuse of Elderly Patients

- Approximately two million elderly Americans are mistreated each year, with a significant number falling into the definition of *abandonment.*
- Even in the face of injuries, such as fractures at uncommon sites, the elderly patient may continue to conceal the possibility of abuse for fear of embarrassment or abandonment by the abuser.
- The first priority of the physician is to ensure this victim's safety.

Futility/Withholding Treatment

General Concepts

- Withholding care has become more of an issue as the potential for resuscitating critically ill patients has become a progressive reality.
- Employing full, almost ritualistic, resuscitation has become the default position of those delivering critical care in cases where no advance directive exists.
- No physician has ever been successfully prosecuted for withholding or withdrawing of medical care from any dying patient in the legal history of the USA.
- The dilemma could be alleviated by early meaningful discussion with patients, families, and surrogates with regard to care *options at the end of life* and honest estimates of *prognosis.*
- Some clinicians and ethicists feel that the *withholding* of medical treatment is more problematic than later *withdrawal* of unwanted or useless interventions.
- This distinction between acts and omissions is now thought to be more of a difference in psychological preference than an ethical norm.
- 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.
- *Futility* is "any effort to achieve a result as *possible,* but that reasoning or experience suggests is *highly improbable* and cannot be systematically produced."
  - If the request goes beyond well-established criteria of reasonableness, the surgeon ought not feel obliged to provide it.
- Appropriate *allocation of resources* is another important consideration when one is making decisions regarding invasive, costly, or lengthy procedures.
- Withholding care requires the difficult objective determination of *ineffectiveness,* rather than any subjective decision based on the worth of the intervention or on the *value* of the patient's continued life.
- Physicians are under no obligation to render treatments that they ascertain to be of little or no benefit to the patient.

DNR and the Need for Surgery

- There is no universal agreement as to how this situation is to be handled, so 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.

Withdrawal of Treatment

General Principles

- 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.
- We should also understand the established criteria for the *determination of death* and should be prepared to assist families in decisions regarding the donation of the patient's organs for transplantation.

Euthanasia/Physician-Assisted Suicide/Terminal Sedation

- *Euthanasia,* which literally means "good death," 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.
  - This implies "mercy killing" of an individual, by a physician, to relieve pain and suffering.
  - *Passive euthanasia* is the result of withdrawing or withholding life support in situations judged to be medically futile. In the USA, this is both ethically and legally acceptable.
  - On the contrary, *active euthanasia* occurs when the physician *intentionally* administers an agent to cause a patient's death. This act is considered *unethical* and *illegal* everywhere in the world except in the Netherlands where it is practiced openly.
- *Physician-assisted suicide* 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.*
  - The decision and the act of ending life remain in the patient's control.
  - Currently, this is legal only in the states of Oregon, Washington, and Montana.
- *Terminal sedation* is the practice of sedating a patient to unconsciousness 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.
  - *No lethal doses of opiates or muscle relaxants are administered.*
  - As in *euthanasia, terminal sedation* directly intends the death of the patient, but the sedating medication is not the agent of death.

Applying the Principles

- In order to comply with the principle of *autonomy,* when a competent patient requests, or demands, the withdrawal of further treatment, the surgeon should ensure that the patient is given all the information necessary and then withdraw the specified treatment.
- The same principle should be invoked if the patient is not able to understand but has provided an advance directive discussing 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.
- 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.

Palliative Care/Hospice

General Principles

- A brief definition of *palliative care* is as follows: the act of *total* care of patients whose disease is not responsive to *curative* treatment.
- These deficiencies include the management of pain and other symptoms, including nausea and vomiting, dyspnea, depression, and anxiety.
- 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.*
- As the age of our surgical patients increases, performing operations whose desired outcomes are not met will increase.

Pain Relief and the Doctrine of "Double Effect"

Confusing Principles

- Pain control at the end of life balances providing enough pain medication for adequacy with prescribing too much 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* hastens 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.
- Adjustment of dosage can be aided by using one of the known *pain scales* or by observing patients' objective signs of distress, especially useful in the noncommunicative patient.
- The *rule of double effect* involves the dichotomy of treatment versus side effects, where death is the *unintended* side effect of adequate symptom control.

Hastening Death: The "Code"

- *Withdrawing life support* is just as acceptable as *withholding life support* initially.
- Deceitful practices include the "slow code," a charade consisting of a halfhearted resuscitation that seems to allow the surgeon to take the moral middle ground by giving the family a false impression of respecting patient autonomy, while knowing full well that the act will not be effective.
- 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.

Determination of Death

- The attending physician has the discretion and the responsibility to determine death.
- Some states use the "irreversible cessation of cardiopulmonary function" criteria, as do some religions.
  - The complete cessation of respiration and circulation constitutes "death" under this definition.
- In most states where this is the statutory definition, the courts have now ruled that "brain death" suffices.
  - Higher brain function includes the cognitive functions or the capacity for consciousness.
- 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.

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.*
- *Informed consent* of the *donor* is required.
  - Donor options are on driver's licenses or donor cards
  - Donors can request limits on the organs they wish to donate (i.e., kidney, lung, eyes, body)
- In circumstances where the family emphatically wishes to override the clearly stated intention of the donor, the body of the donor, after death, belongs to the family.
  - Leave the resolution of this situation up to the transplant coordinator.
- The duty of the physician in this case is to obtain the consent of the family *before* doing anything to preserve the functioning of the organs for potential transplantation.
- In cases with no directives at all, the best course of action, unfortunately, is to do nothing postmortem.

Ethics/Legal Consultation

- Most institutions provide a mechanism for obtaining help in sorting out challenging ethical dilemmas in the form of consultation from the hospital *ethics committee* or from in-house *legal consultation.*
- Hospital ethics committees are specifically charged to advise physicians, patients, and families who face ethical dilemmas.
- The hospital ethics committee should be charged with what is the right thing to do for the patient.
- Once *legal counsel* or *risk management* is brought in to deal with a complicated situation, it must be remembered that *they work for the institution.*
  - Their job is to protect the institution.

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.
- The Good Samaritan Ethic is one that is generally endorsed by our culture, which strongly supports assisting an individual who is in danger or in need of help.

- 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.
- However, a physician's *ethical obligation* inspires him to help in such an emergency.
- All states in the USA have enacted the 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.
- Generally, Good Samaritan acts include the following principles:

1. There is no legal obligation of doctors to answer or treat emergencies.
2. If the doctor chooses to intervene, the expected standard of care is modified by circumstances of the situation.
3. If aid is given, it needs to be stabilization only and not definitive treatment.
4. Implied consent exists to treat the victim if he or she lacks the capacity to consent.
5. These criteria apply whether or not the physician is paid for his or her services rendered.

Professionalism and Interpersonal Relations: Working as a Team

General Considerations

- The components of our health-care team frequently include nurses, enterostomal therapists, primary care physicians, consulting physicians, surgical and medical trainees, and the vast array of ancillary services required within our institutions.

Teaching Residents and Fellows

- At some point in our training, a more senior person turns over to each of us the responsibility to perform the major part of an operative procedure.
- The ethical challenge arises when the patient asks "who is going to do my surgery?"
  - The honest answer becomes blurred, especially working in a program with trainees who are senior residents or fellows.
  - What is true *informed consent* in such situations is a difficult concept.

Previous Suboptimal Care

General Concepts

- Surgeons can find themselves in the position of correcting or undoing the poor results of the action of another surgeon.

- Generally, 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."
- A surgeon who discovers a major error made by another physician has several options:
  - Waiting for the other doctor to disclose the mistake
  - Advising the other physician to disclose the error
  - Arranging a joint meeting to discuss the mistake
  - Telling the patient directly
- Ethicists suggest that surgeons fulfill their obligation to their patient by advising the doctor who erred to inform the patient; but if that fails, it is the surgeon's duty to tell the patient what happened.
- Physicians should be able to learn vicariously from mistakes made by others and thus avoid making the same mistake themselves.

"Blowing the Whistle" and Going to Court

- The next echelon of concern and potential activity, of course, involves serving as an "expert witness" in medical malpractice litigation.
- The American College of Surgeons and the American Society of Colon and Rectal Surgeons have issued guidelines in an attempt to insure that surgical specialists not abuse the system by offering false testimony or by presenting as "experts" in areas beyond their expertise.
- Credibility in the medical–legal system should be based on true expertise and on telling the truth, be it for the plaintiff or the defense.

Managed Care

- Managed care routinely involves someone other than the treating physician delivering care to our patients, usually without sharing in the responsibility of rendering the care and the untoward outcome that may be engendered by that care.
- It seems an impossible, and perhaps unethical, task to make a decision, which favors the economic advantage of a managed care organization over what we know, medically, is required by an individual patient in need.

Rationing Care/Cutting Corners

- We know, as well as others, that medicine, as a system, is in trouble, but the problem is rarely to be solved by rationing or withholding what we know is surgically best for our individual patients.
- Surgeons should become the strongest of all patient advocates and to fully participate in achieving needed improvements in the overall system.

Personal Challenges: Competition of Interests

Professionalism

- The profession of medicine and surgery requires extensive knowledge and skill and a high level of discretion and trustworthiness.
- The social contract between the profession and the public holds professionals to very high standards of competence and moral responsibility.
- In surgery, professionalism means that when confronted with a choice of what is good for us or what is good for our patient, we choose the latter.
- This occurs and is expected sometimes to the detriment of our own good and that of our families.

Family

- The challenge is to appropriately prioritize and balance the demands of patient care, family, education, teaching, and research.
- Among the many considerations of *family* is the issue of caring for and perhaps even operating on our own family members.
- The AMA has issued a statement on "Self-Treatment or Treatment of Immediate Family Members," speaking against treating family except in emergent situations and for short periods of time.

Competence/Impairment/Insight

- A patient's trust is based on the surgeon's diligent pursuit of competence in both judgment and technical skill.
- Surgical training programs have diligently attempted to guarantee the competency of individuals completing the process.
- The board certification process attempts to ensure that the interests of society are represented in these professional processes.
- The problem arises in maintaining a level of competence and assuring that established surgeons who take on new procedures both acquire and maintain competence in these new skills.
- *Impairment* remains a major concern with physicians.
  - Drug and alcohol abuse are the leading cause of sanction against physicians by professional oversight bodies in the USA.
- Unfortunately, most surgeons do not possess or exercise the *insight* required to know when we are impaired or when it is time to retire.
- If surgeons observe *impairment* or *incompetence* in our colleagues (who at times may also be close friends), they should never hesitate to request intervention.

53. Medical Legal Considerations

Michael J. Meehan

Introduction

- The increasing frequency and crushing severity of malpractice claims and lawsuits, data bank reporting, Web-based consumer claims data, privacy requirements, increasing clinical demands, greater government regulation and enforcement activity, and increasing malpractice premiums have caused many physicians to leave private practice, retire early, or move to more lawsuit-friendly jurisdictions.

Medical Malpractice

Elements of Malpractice

- The requisite elements that must be proved by a plaintiff in a medical malpractice case are determined by the laws of the various states.
- Generally speaking, medical malpractice is established when:
  - It is shown by a preponderance of the evidence that a patient's injury was caused by the act of a physician or surgeon that would not have been committed by a physician or surgeon of ordinary skill, care, and diligence under like or similar conditions or circumstances.
  - Or by the omission of an act that a physician or surgeon of ordinary skill, care, and diligence would have performed.
  - And that the patient's injury was the direct and proximate result of such act (or omission).

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- Standard of care is what a "physician or surgeon of ordinary skill, care, and diligence would or would not have done under like or similar conditions or circumstances."
- For there to be a plaintiffs' verdict the jury must believe that:
  1. There was a departure from the standard of care, and
  2. The departure from the standard of care was the direct and proximate cause of the patient's injury.
- For the defense to prevail, the jury must believe that either (1) or (2) above was not proved by a preponderance of the evidence or that neither was proved.

Recurring Malpractice Themes

- For colon and rectal surgery, the nature and frequency of allegations were as follows in recent years:
  - 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 the extent of procedures or endoscopy
- More recently, patients who present with fully developed cancers within 4 years of colonoscopies that apparently cleared the colon of neoplasia have emerged.
- Risk management suggestions relevant to colon cancer screening include:
  - Use of 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
  - Documenting cecal intubation and careful withdrawal techniques

Lawsuit Stress

- Many if not most physicians who are sued experience stress and other normal emotions when their professional care and judgments are criticized in a public lawsuit.
- The simple reality is that the profession which you have chosen frequently lends itself to the frustrations and anxiety of litigation.
- 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 fashion.
- Conversations with psychotherapists should normally be privileged and not admissible in the courtroom as evidence in the case.

Informed Consent

- 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.
- Nearly every malpractice lawsuit, however, contains a supplementary count that informed consent was not obtained.
- Properly obtaining and documenting informed consent can be critical to the defense of the entire lawsuit.

Obtaining of Informed Consent

- Obtaining informed consent is primarily a physician obligation.
- Informed consent is a communication process in which the physician should disclose and 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

- The following elements must normally be proved 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 the 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 prior to the therapy.

Documentation of Informed Consent

- Informed consent is usually documented with formal consent forms that patients sign.
- Forms can be challenged and criticized in the courtroom, and a form with errors or that is incomplete can distract a jury from the real issues involving informed consent.
- Claims of lack of informed consent are best 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 or patient information sheets or pamphlets are effective communication devices and serve well in the litigation defense.
- Charting the presence of any family members who are present for the informed consent discussion.
- Regardless of a minor's emancipation or maturity, it is wise to always obtain parental consent for elective procedures performed on minors.

Documentation

- The medical record can be your best friend when you are sitting on the witness stand, or it can be your worst enemy.

Defensive Charting

- "If it's not documented, it didn't happen," serves as a good rule of thumb for all caregivers.
- A good defensive chart notation is written with an eye toward deflecting practical and obvious criticisms that would be made of the health-care team or the writer of the notation. Examples include:
  - Descriptions of bedside visits, especially when multiple pages have been made by Nursing.
  - When you were there and what you did, including date, time, and signature.
  - Your thought process and differential diagnosis.
  - Presence of family members.
  - "Spoke with husband at bedside."
  - "Patient states that she understands a change in bowel habits should be reported."
  - "Patient refuses to comply with treatment recommendations because …"
  - "Patient not able to perform fecal occult blood test because …"

Etiology Speculation

- The charting of not only the facts but also speculative opinions can be as damaging as too little charting.
- Everything that is written in the medical chart is critical, and key phrasing is often highlighted or enlarged for juries to see on poster boards.
- Do not use a (legal) word if you are not absolutely certain of its meaning.
- Physicians need not always be correct in treating patients; rather, they must comply with the standard of care.

Plaintiff's Pre-claim Review

- Plaintiffs' attorneys often conduct a review of a new client's medical records before agreeing to take the case.
- Attorneys representing patients look for flaws in medical record documentation that juries can understand.
- While professional differences of opinion are expected, professional conflicts are best resolved verbally.
- Disagreement with colleagues that appear in the medical records should be kept to a minimum, unless necessary or appropriate to properly document the patient's course of care.
- Other items which attorneys and their reviewing physicians look for are missing lab reports, radiology interpretations, or the results of any tests or procedures that were ordered but not present in the chart.
- Multiple page attempts by the nursing staff that go unanswered are also fertile ground for review and focus.

Record Tampering and Deception

- Improper altering of the medical record or tampering with the medical record may be grounds for punitive damages and even loss of licensure and should be avoided at all costs.
- Post-event recording in a medical record should be done with proper disclosure of the timing and reason for the entry and with the advice of risk management or legal counsel if appropriate.
- A surgical error known to the physician but kept from the patient could flame juror anger if it later becomes known to the patient.

Electronic Medical Records

- Nearly all patient records, whether paper or electronic, are discoverable and admissible in medical malpractice lawsuits.
- HIPAA privacy regulations require nearly all providers to provide to a patient, upon request, an electronic copy of the patient's electronic health records in the form or format requested. If the information is not readily producible in the form or format requested, access should be provided in readable hard copy form or otherwise as agreed upon with the patient.

- Beware of drop-down menus and checklists, prefabricated medical descriptors, prefabricated informed consent notations, and easy click-on techniques.
- Physicians should use "free text" whenever appropriate as it is much easier to defend "your own words."

Communication

Adverse Events, Bad News, and Apologies

- After a critical incidents, first and foremost, the patient's medical needs must be promptly addressed.
- Without assigning blame or criticism of other practitioners, the patient and family should be informed that the event occurred, the current and future consequences to the patient, and what steps have been taken to address the patient's medical condition.
- Care should be taken not to speculate about the underlying causes for the complication, if unknown.
- Questions should be answered honestly and factually.
- It is usually advisable to contact the risk manager or legal counsel if applicable.
- Depending on institutional policy, risk managers or quality management personnel frequently assist in the interactions with patients and family.
- The administrative staff may also wish to convene a risk management and/or quality management review that would be protected from discovery in a lawsuit under applicable state privilege statutes.
- Physicians and institutions should be willing to express sympathy and perhaps even apologize.
- At family meetings, the family members should have an opportunity to ask all of their questions, and they should be given the name and contact information of someone to reach if additional questions arise later.
- Questions about malpractice can be deferred with the explanation that institutional legal counsel or an insurance representative will contact the family if desired.
- A senior member of the medical team, perhaps with the assistance of risk management or legal counsel, should be consulted in reviewing the chart and recording the events involving the critical incident.

Emails

- Special care should be taken when using email that contains patient-identifiable information.
- HIPAA provides that health-care providers have in place appropriate administrative, technical, and physical safeguards to protect the privacy of PHI.

- You may wish to inform your patients that email transmission involves privacy and security concerns.
- Sending emails containing Protected Health Information to patients and colleagues is permitted if reasonable safeguards are employed, e.g., double-checking email addresses.
- It is advisable for physicians to keep either paper or electronic copies of emails to and from patients that are relevant to patient treatment.
- Physicians may wish to include a Confidentiality Notice that is preprinted at the bottom of email transmissions.

HIPAA

- The Federal Privacy Law (HIPAA) provides national privacy protection for patients.
- The Federal Law establishes minimum privacy standards for health-care providers, health plans, and health-care clearinghouses (referred to in HIPAA as "covered entities") to follow when using and disclosing Protected Health Information (PHI) that they create or maintain.
- 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 health-care providers must make a good faith effort to give each patient a Notice of Privacy Practices that describes the privacy practices of the health-care provider.
  - Patients must be asked to acknowledge in writing that they have received this notice.
- The health-care provider may use and disclose PHI for reasons related to the treatment of the patient, payment for the patient's health care, and the health-care operations of the provider (TPO).
- To use or disclose PHI for reasons other than TPO or as otherwise permitted by law, a physician must obtain an additional written permission from the patient called an "authorization."
- Clinical research, for example, is not considered "treatment" and usually must be separately approved by research subjects by signing an authorization.
- 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 health-care payments.
  - Prior to 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.
- HIPAA requires that providers notify their patients and the federal government when there has been a "breach" of their PHI within 60 calender days.

- A "breach" is defined as the impermissible use, acquisition, access, or disclosure of PHI.
  - The definition excludes unintentional or inadvertent actions as long as the act was in good faith, within the scope of authority and the PHI is not further used or disclosed in an impermissible manner.

Research and Innovative Surgery

Research Versus Innovative Practice

- Research is usually described in a formal protocol, and departures from standard practice are not necessarily "research."
- The Belmont Report states:
  - It is the responsibility of medical practice committees to insist that a major innovation be incorporated into a formal research project.
- When medical practice crosses the line into "research" involving "human subjects" or investigational drugs, devices, or other test articles, the activity becomes subject to the regulation of the federal Office for Human Research Protection (OHRP) for the US Food and Drug Administration.
- "Research," as regulated, is a systematic investigation, including research development, testing, and evaluation, designed to develop or contribute to generalizable knowledge.
- "Human subjects" are living individuals about whom an investigator conducting research obtains data through intervention or interaction with the individual or identifiable private information.

Database Registries

- OHRP states that systematic collections of data performed off-chart carry an implicit prospective intent to conduct research 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.
- Physicians, especially surgeons experimenting with minor surgical modifications to accepted techniques, should use care when authoring articles about clinical experiences that did not involve "research" as defined above.
- When in doubt, physicians are encouraged to consult with their local institutional review boards for guidance.

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 or clearance.

Insider Trading

- If you are involved in clinical trials for pharmaceutical companies or medical device companies whose securities are publicly traded, you may have certain obligations to protect the confidentiality of sensitive information you acquire.
- Insider trading is illegal when a person trades a security while in possession of material, nonpublic information, including information from medical research trials, in violation of a duty to withhold the information or refrain from trading in that security.
- "Tipping" other traders of such information who then trade a security affected by the tip is also illegal as is acting on an illegal tip.

54. Surgical Education

David J. Schoetz Jr.

Background

- Surgical education is undergoing exciting and challenging major transformational change within the broader context of healthcare reform, physician shortages, and financial uncertainty.
- The traditional "see one, do one, teach one" paradigm of bygone years is no longer feasible; patients do not expect a partially trained and sleep-deprived resident to practice on them without supervision.
- Traditional "modern" surgical residencies are generally attributed to Halsted, who initiated the competitive pyramidal system.
- Objections to the Halsted model revolved around the master/apprentice relationship and thus the total reliance on the master without regard for validation of the qualities of the teacher.
- Churchill abolished the pyramid of Halsted and replaced it with a "rectangular" plan; those who wished to pursue academic careers would need to pursue extra experience outside the residency period.

Cognitive Learning

- The need to develop and teach a standardized basic body of knowledge was stimulated in part by the Accreditation Council for Graduate Medical Education (ACGME), the various Residency Review Committees (RRC) and certifying boards.

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- Curriculum may be "syllabus based," meaning a list of topics that forms the basis of what is being studied.
  - This is convenient but treats the learner as a passive recipient.
- "Objectives-based" curricula are predicated on the faculty identifying behavioral objectives and creating learning-based activities and evaluation tools based on these objectives.
- More complex is "curriculum as process," requiring continuous interaction between teacher and learner.
  - Its main advantage is the active participation of the learner in the process.
  - It is much more challenging for the faculty.
- In the lecture format, where the learner is a passive participant, is grossly inefficient.
- The learner should be an active participant who learns best when actively involved in an individualized interactive learning program.
- In 1999, the ACGME endorsed six competencies:
  - Patient care
  - Medical knowledge
  - Professionalism
  - System-based practice
  - Practice-based learning and improvement
  - Interpersonal and communication skills
- Within this construct, conferences such as M&M must be redesigned to reflect these competencies.
- Evaluation of the quality of the program and of the educational commitment of the institution is also defined by the competencies.
- Program goals and objectives are centered on the competencies, as well as the means of evaluating each individual resident.

Technical Skills

- Surgeons also have the need to provide technical training resulting in sufficient competence to practice independently at the completion of the training period.
- Validated teaching techniques for procedures are perhaps the most challenging aspect of present-day educational programs.
- Traditional teaching of technical skills centered on a brief period of observational learning (observing, assisting, then performing), perhaps with some training in "dog labs."
- Assessment was subjective and relied on the opinions of the faculty as well as excessively on pure numbers of cases performed without a formalized system of technical training with constructive feedback.

- Early teaching of technical skills should take place away from the operating room, allowing practice until there is a basic fluidity in the mechanical performance of the task.
- Expertise is developed by repetitive deliberate practice, from which master technicians are formed.
- The Objective Structured Clinical Examination (OSCE) is a proven accepted method of assessing clinical competence of medical students.
- Out of this, the Objective Structured Assessment of Technical Skill (OSATS) for surgical residents was formed, in which residents were observed performing various structured operative tasks.
- The Fundamentals of Laparoscopic Surgery (FLS) program, using box trainers and trained observers, teaches and evaluates five psychomotor skills of basic laparoscopy.
- Higher fidelity computer-based systems, although more costly, may provide more advanced procedural skills for residents and practicing surgeons.
- The major shortcoming of these devices, which are image based, is the lack of haptic feedback; this also limits their application in open surgery.
- Secrets to the success of these educational activities are the ability of the participants to suspend reality and a detailed debriefing among those involved after completion of the exercise.
- Acquisition of endoscopic skills is facilitated by the use of endoscopy simulators, which can teach basic manipulation of the shaft and dials as well as steering maneuvers.

Challenges

- The currently required duty hours regulations for trainees include the following:
  - Duty hours must be limited to 80 h/week.
  - One day in seven free from all educational and clinical responsibilities.
  - 10-h time period provided between all daily duty periods and after in-house call.
  - In-house call must occur no more frequently than every third night.
  - Continuous on-site duty, including in-house call, must not exceed 24 consecutive hours. Residents may remain on duty for up to six additional hours to participate in didactic activities, transfer care of patients, conduct outpatient clinics, and maintain continuity of medical and surgical care.
  - At-home call (or pager call).

    - The frequency of at-home call is not subject to the every-third-night or 24+6 limitation. However, at-home call must not be so frequent as to preclude rest and reasonable personal time for each resident.
    - Residents taking at-home call must be provided with 1 day in seven completely free from all educational and clinical responsibilities, averaged over a 4-week period.
    - When residents are called into the hospital from home, the hours that residents spend in-house are counted toward the 80-h limit.
- Night float rotations, non-physician providers, and staggered shifts were creative ways devised to control hours of resident work.
- These efforts were met with objections that continuity of care would suffer as a result of adoption of a "shift" mentality.
- There has been a shift in operative experience:
    - Junior residents spend less time in the operating room.
    - Interns spend most of their time in the hospital outside of the operating room environment.
    - Performance of complex cases is delayed until later in the residency, often resulting in residents who complete 5 years of training not having the skills or confidence to practice independently.
    - A greater percentage of graduates seek additional fellowship training.
    - Attendings must do extra work and hire physician extenders to perform tasks previously done by residents.
- A report from the University of Vermont demonstrated a significant reduction in morbidity and mortality after adoption of the hour regulations.
- The ACGME has responded to the IOM by creating a task force with the following recommendations:
    - The safety of patients is of utmost importance; the responsibility for safety resides with the resident, the attending, and the systems of care.
    - Graded authority and responsibility on the part of residents are substantially diminished, with concerns for inadequate training.
    - There is a need for some flexibility in standards between specialties.
    - There are effects (in some instances unintended consequences) of alterations in training schemes on other specialties.
    - Residents are more rested and do have more satisfaction with their life.
    - Absolute rules and "substantial compliance" are very different in practice; rigid adherence to absolute rules often challenges professionalism and patient care.
- Financing of graduate medical education from the Medicare budget is also an enormous long-term challenge to the training of physicians.

Colon and Rectal Surgery

- The duration of training in colon and rectal surgery is 1 year beyond general surgery; in the past, this had been sufficient to essentially double the volume of cases done by a 5-year surgery trainee in the one additional year.
- Proposed restructured training would provide for a basic core curriculum followed by advanced specialty and subspecialty training, divorced from practical considerations of funding of residency positions.
- The SCORE (Surgical Council on Resident Education) project is in the process of developing specific learning objectives for each of the topics within 28 organ system-based categories. Operations and procedures are classified as essential-common, essential-uncommon, and complex.
  - For colorectal procedures, total proctocolectomy, including ileoanal reservoir, is considered complex.
  - For anorectal procedures, complex procedures include:
    - Stapled hemorrhoidectomy
    - Repair of complex anorectal fistulae
    - Operation for incontinence/constipation
    - Abdominal operations for rectal prolapse, both open and laparoscopic
    - Perineal operations for rectal prolapse
    - Operations for rectal cancer, including transanal resection and abdominoperineal resection
- An important factor to consider when evaluating a change in residency design/construct is that a significant percentage of practicing colon and rectal surgeons continue to perform some general surgery as part of their practice.
- The Program Directors in Colon and Rectal Surgery have developed an essential curriculum, which has been ratified by the ABCRS, and forms the basis for didactic teaching and testing in colon and rectal surgery.
- Technical requirements for satisfactory completion of a colon and rectal residency are in flux.
- It has become increasingly clear that numbers of cases are a poor surrogate for technical competence.
- Considerable energy must be directed at the development of formative and summative evaluation instruments for assessment of procedural training.
- If the primary aim of residency training is to prepare safe practitioners and protect the public, then all efforts must be directed at improving our ability to do so and to continue that capability for a professional lifetime.

55. Continuing Medical Education

Martin A. Luchtefeld

Background

- The challenge for the surgeon is to stay abreast of relevant new information and learning new techniques in their field of practice.
- The American Board of Medical Specialists and Accreditation Council for Graduate Medical Education (ACGME) have attempted to define the competent physician by outlining six core competencies (Table 55.1).
- Several of these competencies speak directly to this issue of maintaining one's ability to practice medicine competently after residency: practice-based learning and improvement, medical knowledge, and patient care.
- The concept of a "learning curve" emerged to establish estimates of baseline proficiency for certain procedures.
  - ASCRS issued a position paper in 1994 that colorectal cancer should best be treated laparoscopically only if the surgeon was participating in a trial or a prospective registry that would allow the evaluation of results at a later date.
  - It was subsequently recommended that only surgeons who had performed at least 20 laparoscopic colon surgeries should attempt a laparoscopic colectomy for cancer with curative intent.
- There is still a lack of a cohesive system to provide ongoing education for the practicing physician as well as lack of a defined curriculum and/or standards of accreditation.

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Table 55.1 Six core competencies of the competent physician

1. Patient care
2. Medical knowledge
3. Practice-based learning and improvement
4. Interpersonal and communication skills
5. Professionalism
6. Systems-based practice

- CME, as defined by the Accreditation Council for Continuing Medical Education (ACCME), "constitutes educational activities that serve to maintain, develop, or increase the knowledge, skills, performance, and the relationships a physician uses to provide services for patients, the public, or the profession."
- There is little evidence to support the effectiveness of CME as it is currently structured to improve patient care or outcomes.

History of Ongoing Education

- The first requirements for CME began in 1934.
- CME remains the primary way that practicing physicians' document and continue their education outside of the university setting.
- State and territorial licensing boards require certain levels of completion of CME for recertification of their medical licenses.

CME Effectiveness on Practice Performance

- While the majority of studies report positive outcomes regarding the impact of CME on prescribing, screening, guideline adherence, and others, slightly less than 30 % did not.
- It is unknown which media was most effective for CME.
- Multiple techniques are more useful than single techniques in achieving a positive impact on practice behavior, including:
  - Academic detailing, audience response systems, case-based learning, clinical experiences, demonstrations, discussion groups, feedback, lectures, mentoring or preceptor programs, point-of-care techniques, problem-based learning, team-based learning, programed learning, readings, role play, simulations with standardized patients, and writing
- Almost two-thirds of studies that used multiple exposures to CME met their objectives.

Table 55.2 The ten conditions to facilitate learning

1. Feedback is provided during learning experiences
2. Learners engage in repetitive practice
3. Simulation is integrated into an overall curriculum
4. Learners practice tasks with increasing levels of difficulty
5. Simulation is adaptable to multiple learning strategies
6. Clinical variation is built into simulation experiences
7. Simulation events occur in a controlled environment
8. Individualized learning is an option
9. Outcomes or benchmarks are clearly defined or measured
10. The simulation is a valid representation of clinical practice

Adapted from Issenberg SB, McGaghie WC, Petrusa ER et al. Features and uses of high-fidelity medical simulations that lead to effective learning: a BEME systematic review. Med Teach 2005;27:10–28

CME Effectiveness for Knowledge Application and Psychomotor Skills

- Studies demonstrated effectiveness in improving knowledge application in the short term. Multiple exposures and longer duration led to better results.
- Weak evidence suggests the methods studied all improved psychomotor skills.

CME: Simulation Research

- Medical simulation is defined as "a person, device, or set of conditions which attempts to present [education and] evaluation problems authentically."
- Simulation can be done in many ways: computer models, anatomical models, and solitary or team performances.
- The evidence for the effectiveness of simulation in the literature is relatively weak.
- The conditions that facilitated learning are seen in Table 55.2.

CME: Best Educational Practices

- Ideally CME best practices would have the following three elements: mastery learning, deliberate practice, and recognition of cultural barriers in the medical profession that inhibit best educational practices.

Table 55.3 Elements of mastery learning

1. Baseline or diagnostic testing
2. Clear learning objectives, sequenced as units in increasing difficulty
3. Engagement in educational activities (e.g., skills practice, data interpretation, reading, focused on reaching the objectives)
4. A set minimum passing standard (e.g., test score) for each educational unit
5. Formative testing to gauge unit completion at a preset minimum passing standard for mastery
6. Advancement to the next educational unit given measured achievement at or above the mastery standard
7. Continued practice or study on an educational unit until the mastery standard is reached

Adapted from McGaghie WC, Siddall VJ, Mazmanian PE, Myers J. Lessons for continuing medical education from simulation research in undergraduate and graduate medical education: effectiveness of continuing medical education: American College Of Chest Physicians evidence-based educational guidelines. Chest 2009;135:62S–8

Table 55.4 Deliberate practice requirements

1. Highly motivated learners with good concentration
2. Engagement with a well-defined learning objective or task
3. Appropriate level of difficulty
4. Focused, repetitive practice
5. Rigorous, precise measurements
6. Informative feedback from educational sources (e.g., simulators or teachers)
7. Monitoring, correction of errors, and more deliberate practice
8. Evaluation to reach a mastery standard
9. Advancement to another task or unit.

Adapted from McGaghie WC, Siddall VJ, Mazmanian PE, Myers J. Lessons for continuing medical education from simulation research in undergraduate and graduate medical education: effectiveness of continuing medical education: American College Of Chest Physicians evidence-based educational guidelines. Chest 2009;135:62S–8

Mastery Learning

- Mastery learning has a number of key elements (Table 55.3).
- The objective in mastery learning is to assure that the final educational objectives are met by all learners with little or no variation in outcome.

Deliberate Practice

- Deliberate practice has at least nine requirements (Table 55.4).
- Deliberate practice should enable constant improvement of a skill or knowledge rather than simply maintaining a certain level of competence

Cultural Barriers

- There are a number of barriers to the implementation of best educational practices.

CME and Maintenance of Certification

- Board certification was originally considered lifelong but the issue of recertification was raised as early as 1936.
- Eventually, the rapid advance of medical knowledge leads to the recognition of the need for recertification.
- This process of Maintenance of Certification (MOC), developed and introduced by the ABMS in 2000, relies on the premises of *maintaining* competence and skills on a continuous basis rather than simply *recertifying* every 5–10 years.
- MOC has four elements (which are a distillation of the six elements of the competent physician):
  - Part I: Professional standing
  - Part II: Lifelong learning and self-assessment
  - Part III: Cognitive expertise
  - Part IV: Practice performance assessment
- In order to maintain certification, diplomats of the 24 member Boards (of which the American Board of Colon and Rectal Surgery is one) of the ABMS must satisfy all four parts of the MOC process.

The Future of CME

- To obtain certification, a variety of methods including bench models, simulation, simulators, and virtual reality must be used to ensure that participants reach predetermined levels of skill by the completion of the course.
- The concept of mini-fellowships has also arisen as a way to fill the void for the practicing surgeon who desires to learn new skills or techniques.
- CME in the future may include the three following elements: assessment of learner needs, program design to meet those needs, and outcome assessment.
- For colon and rectal surgery, there are several learner needs:
  - To learn technical skills related to new technology and new procedures
  - To have learning opportunities based on their own practice performance
- Technology has an evolving role in CME.

56. Quality

Formosa Chen, Hiroko Kunitake, Elise Lawson, Joan Ryoo, and Clifford Y. Ko

Background

- The spotlight has been on health-care quality since the publication of the Institute of Medicine (IOM) reports *To Err is Human*: *Building a Safer Health System* in 1999 and *Crossing the Quality Chasm*: *A New Health System for the 21st Century* in 2001.
- In-hospital deaths due to preventable medical errors represented the eighth leading cause of death in the USA in these reports.

Defining "Quality" in Health Care

- Currently, the most commonly cited definition of quality of care comes from the IOM:

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- Quality of care is the degree to which health services for individuals and populations increase the likelihood of desired health outcomes and are consistent with current professional knowledge.
- The IOM has proposed six key dimensions of quality as areas for emphasis and additional research for a health system: safe, timely, efficient, effective equitable, and patient-centered (STEEEP).

The History of Quality in Surgery

- Quality of care in surgery arose nearly a century ago with Dr. Ernest Codman who proposed the "end result system" in which doctors would follow up their patients to determine the results and complications of treatment and make these findings public.
- In 1935, the Philadelphia County Medical Society established the Anesthesia Mortality Committee, the antecedent to the now familiar Morbidity and Mortality Conference.
- Morbidity and mortality conferences are now a required educational activity mandated by the Accreditation Council for Graduate Medical Education (ACGME) for all residency programs.

A Conceptual Model of Quality of Care: The Donabedian Model of Quality of Care

- One of the most commonly used models for thinking about health-care quality is the Donabedian model of quality of care.
- The model was later refined into a causal chain of the three interrelated components of (1) structure, (2) process, and (3) outcome (Fig. 56.1).

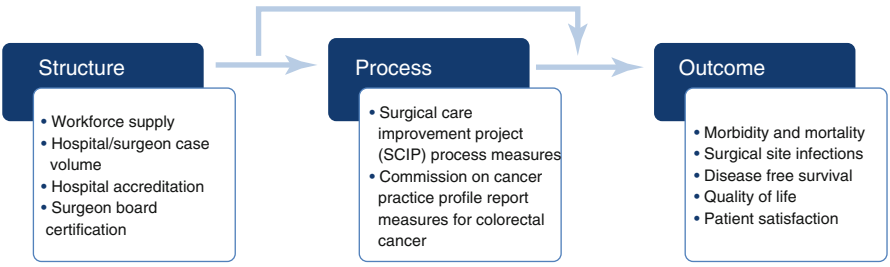

Fig. 56.1 The Donabedian model of quality of care: interrelated components of structure, process, and outcome

The Donabedian Model (Part 1): Structure

- "Structure" in the Donabedian model refers to the characteristics of the setting and providers in and through which health care takes place.

Structural Measure at the Health System Level

- An example of a structural measure that assesses quality at the level of the overall health-care system is the adequacy of the health-care workforce to meet the needs and demands of the population that it serves.
- The growing elderly population will increase the demand for surgical services.
- In the Donabedian model, the projected shortage of surgeons represents a potential structural flaw that will affect downstream processes and outcomes.

Structural Measure at the Institution Level

- Examples of structural measures at the institution level include hospital accreditation status, nurse-to-patient ratios, availability of specialty services (e.g., interventional radiology, transplant services), teaching status or affiliation with academic institutions, and hospital volume.
- From an institutional standpoint, accreditation activities are often integral to performance and quality improvement efforts.
- There are inconsistent findings regarding accreditation status and quality indicators.
- In colorectal surgery, supporters of accreditation have proposed that accrediting programs for rectal cancer or inflammatory bowel disease may be beneficial in promoting higher quality and more standardized care for these patient populations.
- The volume-outcome relationship is the observed association between provider case volume and patient outcomes, usually with increasing provider volume (hospital or surgeon) associated with improved patient outcomes.
- Proponents of the volume-outcome relationship argue that regionalizing high-risk procedures to select high-volume providers can save patient lives.
- Critics argue that it is unclear whether increased volume leads to improved quality or whether high-quality care attracts more volume, and volume measures penalize low volume but high-quality providers.
- Health-care payers have incorporated structural measures into their criteria for "Centers of Excellence" to incentivize patients to utilize qualifying facilities or providers.

Structural Measure at the Practitioner Level

- Examples of structural measures at the practitioner level include board certification and subspecialty training.
- Overall, studies have generally shown improved outcomes for surgeons with specialty training.
- However, it was unclear if the additional training or having a specialized practice was responsible for the difference in outcomes.

The Limitations of Structural Measures of Quality

- The most significant downside to structural measures is their relative immutability, especially from the perspective of an individual surgeon.
- While structural measures may have an important role in policy discussions and population-based planning, there may be little that the surgeon can change in the structure of their practice to ultimately impact patient outcomes.

The Donabedian Model (Part 2): Process

- Process refers to what providers do to the patient or do for the patient; essentially, everything that occurs in the continuum of patient care constitutes a process of care.
- The literature contains numerous clinical practice guidelines that describe treatment processes and algorithms that comply with the standard of care or represent best practices (e.g., NCCN, ASCRS Practice Parameters).
- The difference between practice guidelines and process measures is that guidelines are often qualitative recommendations that often include gray areas of variable appropriateness, allowing for a physician's clinical judgment and patient preferences.
- In contrast, process measures (e.g., SCIP) are quantitative measurements, have simplistic measurement algorithms, and can be used to set standards of care.
- A good process measure has the following characteristics: (1) it is explicit in its inclusion and exclusion criteria (denominator); (2) it is rigid in its requirements for satisfying the process (numerator); and (3) it is linked to outcomes.
- These quality indicators establish the standard of care that patients should receive; they are explicit, quantitative, and evidence-based; and there is a growing trend by regulatory bodies and payers to use such quality indicators to set standards for appropriate care (e.g., perioperative antibiotics, normothermia, DVT prophylaxis).

- Following baseline measurement of an organization's adherence to a set of quality indicators, tailored interventions can then be designed and implemented to target areas of poor performance.
- One of the best ways to identify processes of care is through randomized controlled trials (RCTs).

Limitations of Process Measures

- One of the limitations of process measures is that it is often difficult to prove that performance of a process measure directly results in improved patient outcomes.
- A second limitation is that there are no validated quality indicators for many areas in surgery where quality improvement may be warranted.
- A third limitation is that data collection to measure adherence to process measures or quality indicators is often labor- and cost-intensive.
- There also may be limited benchmarks against which an organization's performance can be compared.

The Donabedian Model (Part 3): Outcomes

- Outcomes are the end result of receiving health care.
- Traditionally, surgeons have examined their outcomes through morbidity and mortality conferences.
- The objectives of outcome measurement are to evaluate and compare providers as a means to inform providers and patients, adjust financial compensation, and facilitate quality assurance and improvement.
- In order to make valid comparisons between providers, appropriate patient risk adjustment must be performed.
  - Patient factors + Effectiveness of care + Random variation = Outcome.
- "Patient factors" represent the patient's variables, such as their diagnosis, age, gender, socioeconomic status, comorbidities, and illness severity.
- "Effectiveness of care" relates to the nature of the intervention being studied.
- "Random variation" is perhaps best described by the saying: "You can do everything wrong and have a good outcome, and you can do everything right and have a bad outcome."
- In addition to objective or "hard" patient outcomes such as mortality or complications, there are also subjective patient-reported outcomes such as patient satisfaction, functional status, and quality of life.
- There are many validated instruments available to evaluate physical function, clinical symptoms, and quality of life, and there are increasing numbers of instruments being developed for colorectal patients (Table 56.1).

Table 56.1 Patient-reported outcomes survey instruments

Area	Survey instrument	Description	Specific for cancer patients?
Clinical symptoms	Fatigue Symptom Inventory	Measurement of fatigue intensity, duration, and interference with daily functioning	Yes
Clinical symptoms	Brief Pain Inventory	Assessment of pain severity, location, and impact on function	Yes
Clinical symptoms	Neurotoxicity Scale (NTX-12)	Evaluate sensory and motor symptoms, auditory problems	Yes
Physical function	Instrumental Activities of Daily Living (IADL)	Assessment of independent living skills (e.g., using the telephone, shopping, paying bills)	No
Quality of life	Impact of Cancer	Measurement of positive and negative impacts of cancer	Yes
Quality of life	Life Orientation Test	Measurement of optimism and pessimism	No
Quality of life	Functional Assessment of Cancer Therapy-Colorectal (FACT-C)	Assessment of physical, mental, social well-being	Colorectal cancer specific
Quality of life Clinical symptoms Physical function	SF-36/SF-12	Summary physical health and summary mental health scores	No
Quality of life Physical function	European Organization for Research and Treatment of Cancer (EORTC) CR-38	Evaluate quality of life and function of colorectal cancer patients Y	Colorectal cancer specific

Limitations to Outcome Measures

- Outcome measures alone do not identify a specific structure or process that can be changed to alter the result of care.
- Overemphasis on adverse outcomes may encourage providers to "cherry pick" their patients.
- There is, unfortunately, no single perfect quality metric that serves as an adequate proxy for overall quality.

Quality of the Data

- As all providers rely on data to define quality and to guide them in delivering better care, it is paramount that the data are of high quality.
- Ideally, a database would capture comprehensive detailed information about the patient, their disease, the procedure and treatments they received, the provider, all outcomes from wound infection to disease recurrence and reoperation, patient's quality of life and function, mortality, and cost.

- Creating such a database would be prohibitively expensive both in terms of manpower and cost.
- Currently available *sources* of data may be divided into two main types: administrative databases and clinical databases.
  - Administrative databases (e.g., Medicare claims database) record admissions, diagnoses, and procedures from administrative/billing claims.
  - Clinical databases (e.g., SEER, NSQIP) use chart abstractors and hospital registrars to record patient-level clinical data such as comorbidities and search for evidence of wound infections, urinary tract infections, cancer recurrence, and other clinical outcomes.
- There are also research-focused databases (e.g., CanCORS) which combine medical record abstraction, patient surveys, and provider surveys in an attempt to provide a more complete assessment of the experience and outcomes of the colorectal surgery patient.
- Advantages of administrative databases include access to large amounts of demographic and procedural data on large population-based samples that is easily compiled. However, administrative databases are limited by the lack of clinically meaningful data.
- Clinical databases provide clinical findings such as wound infections and patient outcomes. However, intensive resource expenditures are usually necessary to collect this data by chart abstraction and individual patient assessment.

Appropriateness and Appropriateness Criteria

- An appropriate procedure has been defined as one in which "the expected health benefit (e.g., increased life expectancy, relief of pain) exceeds the expected negative consequences (e.g., mortality, morbidity) by a sufficiently wide margin that the procedure is worth doing, exclusive of cost."
- Appropriateness criteria are a method of explicitly delineating and weighing these benefits and harms, based on evidence in the literature and the clinical judgment of a multidisciplinary panel of physicians.
- They can also be used as clinical decision aids to guide shared decision making between the surgeon and patient.

Development of Appropriateness Criteria

- The gold standard for decision making in health care is the randomized controlled trial.
- Appropriateness criteria compensate for gaps in the literature by combining available scientific evidence with expert clinical judgment (e.g., RAND/UCLA Appropriateness Method (RAM)).

Use of Appropriateness Criteria

- Apart from research and setting standards, appropriateness criteria are also developed for use as clinical decision aids.
- One example is to determine the appropriate utilization of ancillary tests.

Limitations of Appropriateness Criteria

- A frequent criticism of appropriateness criteria is the reliance on expert opinion, which is inherently subjective.
- The utility and validity of appropriateness criteria are dependent upon the quality of the criteria, which in turn is dependent on both the available evidence base for the procedure as well as the judgment of the panel.
- Finally, concern is often raised regarding the clinical validity of appropriateness criteria.
- Appropriateness criteria should thus be thought of as an aid in clinical decision making and should not replace a clinician's judgment.

Comparative Effectiveness and Cost-Effectiveness

Comparative Effectiveness

- The focus of comparative effectiveness research (CER) is the *practical* comparison of different treatments or procedures to determine what works best for whom.
- CER is geared toward delineating effectiveness – the relative benefits of treatment options in *routine* clinical practice.
- The IOM has described six defining characteristics of CER:
  1. It directly informs clinical decisions from the patient perspective or policy decisions from the population perspective.
  2. It compares at least two treatment options, both of which could be considered "best practice".
  3. It describes results at the population and subgroup levels to inform more individualized decisions.
  4. The outcomes measured are important to patients.
  5. A variety of methods and data may be used, from observational studies and RCTs to meta-analyses or systematic literature reviews.
  6. The setting of CER should be similar to routine practice environments.
- Although cost cutting is not the main focus of CER, a consequent benefit according to its proponents is cost reduction by the elimination of less effective, ineffective, or even harmful services.
- Extreme opponents have viewed CER as a means to limit treatment options and effect health-care rationing.

Cost-Effectiveness

- Cost-effectiveness is a specific subset of comparative effectiveness research that provides explicit comparisons of "the relative value of different interventions in creating better health and/or longer life."
- What distinguishes cost-effectiveness from other types of comparative effectiveness studies is the explicit comparison of cost or values.
- Reluctance to place a monetary value on health outcomes has lead to the widespread use of the cost-effectiveness ratio, "incremental cost per quality-adjusted life year (QALY) gained."
  - QALY is a measure of disease burden that takes into account both the quantity and quality of life lived.
  - QALY values range from zero to one, with zero being death and one being 1 year of life lived in perfect health.
  - Researchers have often accepted a range of $50,000–$100,000 per QALY gained as cost-effective.
- In theory, cost-effectiveness methodology provides the advantage of combining the best scientific evidence, available clinical outcomes, and cost data.
- Cost-effectiveness studies are limited by their reliance on the use of appropriate assumptions in creating a model of care and accurate value and cost estimates.
- Direct costs involve near-term spending related to delivery of care, including that incurred secondary to complications of receiving that care.
- Indirect cost generally refer to economic and societal cost due to loss of productivity from health-care receipt, often estimated by measuring time to return to work following a surgical procedure.

Comparative Effectiveness and Cost-Effectiveness in Colorectal Surgery

- Examples include laparoscopic vs. open colectomy and "fast-track pathways" compared to traditional postoperative care in colorectal procedures.
- Available literature suggests that short-term and long-term outcomes may be similar between laparoscopic and open colectomy.
- A Cochrane Database systematic review of 12 eligible randomized controlled trials involving nonmetastatic colorectal cancer patients found no differences in cancer-related mortality, port-site or wound recurrences, or recurrence rate at the site of the primary tumor, suggesting that laparoscopic and open resections of colon carcinoma are equivalent with regard to these long-term outcomes.
- Studies on the economic impact of laparoscopic vs. open colectomy have generally been few in number and plagued by the complexity of accurately determining cost.

- Recent systematic reviews have suggested that enhanced recovery programs are safe and effective following colorectal surgery when compared with conventional postoperative care.
- The opportunity for further research in the realm of comparative effectiveness and cost-effectiveness of colorectal surgical disease management is immense.

Attribution of Quality

- The evaluation of quality of surgical care may be measured at different levels.
  - As an example, the rate of anastomotic leak or the rate of giving prophylactic antibiotics may be measured at the surgeon level, the facility level, the system level, or some other level altogether.
- Attribution asks who should be responsible for the performance/quality metric, an individual, a facility, or some sort of "team or service"?
- It is likely different for different metrics, and as the unit of measurement becomes smaller and smaller, the appropriateness of the measure becomes increasingly debatable.
  - For example, the number of nodes retrieved in a node negative colectomy relies on both the surgeon and pathologist.
- There are many metrics that are similar in nature, where it remains difficult to attribute a quality process or outcome to an individual provider.

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