I. Colonic Development

A. Embryonic midgut and hindgut contribute to development of colon, rectum, and anus
   1. Midgut components of colon
      a. Cecum to right 1/2 to 2/3 of transverse colon
         1) Blood supplied by superior mesenteric artery
   2. Hindgut components of colon
      a. Distal 1/3 to 1/2 of transverse colon, descending colon, sigmoid colon, rectum, and superior part of anal canal
         1) Blood supplied by inferior mesenteric artery
   3. Distal end of anorectal canal
      a. Blood supplied by iliac artery branches

II. Development of Colonic Midgut Components

A. Physiologic umbilical herniation of midgut out of abdominal cavity
   1. Starts at 6th week and ends 10th week
   2. Midgut rotates 90° counterclockwise around superior mesenteric artery axis, leaving caudal midgut to left
B. Physiologic umbilical herniation reduction occurs
   1. Large intestine returns after small intestine and does an additional 180°counterclockwise rotation
   2. Fixation of large intestine occurs
C. Ascending colon mesentery fuses with parietal peritoneum on posterior abdominal wall and disappears
   1. This leaves the ascending colon retroperitoneal
   2. The small intestine mesentery goes from median plane of posterior abdominal wall, and from duodenojejunal junction inferiorly to ileocecal junction
D. Cecum and appendix
   1. Cecal diverticulum develops into primordium of cecum and appendix, and appears around the 6th week
   2. Appendix initially at caudal midgut loop, then distal end of cecum at birth
      a. Unequal cecal growth leaves appendix medial of cecum
      b. High variability in appendix location: retrocecal (posterior to cecum—seen in 64% of people), retrocolic (posterior to colon), pelvic (over pelvic brim)

III. Development of Colonic Hindgut Components

A. Descending colon mesentery fuses with left posterior abdominal wall peritoneum and becomes retroperitoneal
B. Cloaca
   1. Terminal part of hindgut
   2. Lined with endoderm
   3. Divided by the urorectal septum into the urogenital sinus and rectum during the 6th week
   4. Cloacal membrane
      a. Composed of endoderm of cloaca and ectoderm of proctodeum (anal pit)
   5. By the 7th week, the urorectal septum fuses with the cloacal membrane, giving rise to anal membrane and urogenital membrane
   6. The perineal body in an adult is where the urorectal septum fuses with the cloacal membrane
7. The cloacal sphincter is divided by the urorectal septum to give anterior and posterior parts
   a. Posterior part = external anal sphincter
   b. Anterior part = superficial transverse perineal, bulbospongiosus, and ischiocavernosus muscles
8. At the end of the 8th week, anal membrane ruptures
   a. At this point, the anal canal communicates with amniotic cavity
C. Anal canal
   1. Superior 2/3 is derived from hindgut
   2. Inferior 1/3 is derived from proctodeum
D. Pectinate line is the junction of proctodeum ectoderm and hindgut endoderm
E. Anocutaneous line is ~2 cm superior to anus
   1. Anal columnar epithelium changes to stratified squamous
F. Superior 2/3 of the anal canal
   1. Supplied by superior rectal artery
   2. Drained by superior rectal vein
   3. Lymphatic drainage goes to inferior mesenteric lymph nodes
   4. Nerve supply
      a. Autonomic nervous system
   5. Tumors here generally are of columnar epithelium etiology, and are painless
G. Inferior 1/3 (from proctodeum, not from the hindgut)
   1. Supplied by inferior rectal arteries
   2. Drained by inferior rectal vein
   3. Lymphatic drainage goes to superficial inguinal lymph nodes
   4. Nerve supply
      a. Inferior rectal nerve
         1) Sensitive to pressure, pain, touch, and temperature
   5. Tumors here are generally from squamous epithelium, and are painful
H. Dentate line
   1. Divides hindgut (endoderm) from distal anal canal (ectoderm)

IV. Normal Anatomy of Colon
A. Large intestine
   1. Ileocecal valve to anus
      a. Divided into colon, rectum, anal canal
B. Colon
   1. Junction of terminal ileum and cecum until rectum (3–5 feet)
   2. 5 layers of colon and rectal wall:
      a. Mucosa, submucosa, inner circular muscle, outer longitudinal muscle, serosa
      b. Colonic outer longitudinal muscle is separated into three taenia coli that converge at the appendix and rectum
      c. Rectosigmoid junction: where three taenia coli coalesce, forming a longitudinal smooth muscle layer of rectum
      d. Distal rectum: inner smooth muscle layer forms internal anal sphincter
      e. Colon that is intraperitoneal and proximal 1/3 rectum is covered by serosa
   3. Cecum
      a. Widest and thinnest part of colon
   4. Ascending colon
      a. Fixed to retroperitoneum
   5. Transverse colon
      a. Starts at hepatic flexure until splenic flexure
      b. Intraperitoneal and mobile
      c. Attached to colonic mesentery and gastrocolic ligament
      d. Greater omentum is attached to the superior anterior edge
   6. Descending colon
      a. Starts at the splenic flexure
      b. Lineocolic ligament attaches the spleen with splenic flexure
      c. Fixed to retroperitoneum
7. Sigmoid colon
   a. Narrowest portion
   b. Very mobile

C. Vascular supply of colon
1. Highly variable
2. Ileocolic artery, as a branch of superior mesenteric artery, provides the blood supply
   a. Absent in 20%
   b. Supplies T1 and the proximal ascending colon
3. Right colic artery
   a. Supplies ascending colon
4. Middle colic artery
   a. Supplies transverse colon
5. Left colic arterial branch of inferior mesenteric artery
   a. Supplies descending colon
   b. Sigmoidal branches supply sigmoid
6. Superior rectal artery
   a. Supplies proximal rectum

D. Nerve supply to the colon
1. Sympathetic T6–T12 and L1–L3 (inhibitory)
2. Parasympathetic (stimulatory)
   a. Vagus nerve to right and transverse colon
   b. Sacral nerves S2–S4 to left colon

V. Normal Anatomy of Anorectum
A. Rectum
1. 12–15 cm long
2. Valves of Houston
   a. 3 submucosal folds in lumen
3. Dentate line
   a. Transition from columnar rectal mucosa to squamous anoderm
   b. 1–2 cm proximal
      1) Anal transition zone with columnar, cuboidal and squamous epithelium.
   c. Columns of Morgagni
      1) Longitudinal mucosal folds surrounding dentate line
4. Distal rectum
   a. Internal anal sphincter
      1) Thickened inner smooth muscle.
      2) Innervated by sympathetic and parasympathetic nerves
      3) Both inhibit contraction of sphincter

VI. Colonic Physiology
A. Functions
1. Absorption of water/electrolytes
2. Mucous secretion
3. Fecal material formation/propulsion/storage
4. Residence of microbes
B. Passage of food to the rectum
1. Initial ingested food reaches the cecum in ~4 hours (all by 8–9 hours)
2. Average transit time first 1/3 of the colon = 6 hours
3. Second 1/3 of the colon = 9 hours
4. Reaches the sigmoid in 12 hours
C. Digestion in the colon is generally a result of colonic microbes
1. Microbial fermentation of carbohydrates leads to release of short-chain fatty acids (FA) acetate, butyrate, propionate
   a. Short-chain FA are an important energy source for colonic cells and for maintenance of a healthy colonic epithelium
   b. Metabolism of short-chain FA by colonocytes provides energy for active Na+ transport
D. Water absorption
   1. Up to 5 L water/day absorbed in colon
      a. Removes 90% of fluid from the digested food bolus
         1) 1–2 L isotonic chyme that enters colon is converted to 200–250 mL
            semisolid feces

E. Electrolyte absorption
   1. Colon absorbs sodium against gradient via Na-K ATPase
      a. Can absorb up to 400 mEq of Na+/day
      b. With volume depletion, aldosterone increases sodium conductance in colon
   2. Potassium
      a. By active secretion into lumen and passive absorption
   3. Chloride
      a. By active transport through exchange with bicarbonate
   4. Ammonia
      a. Result of bacteria degrading protein and urea
      b. Absorbed (influenced by lumen pH) and then transported to liver

F. Secretion
   1. Mainly mucin, which lubricates lumen and forms barrier to microbes/pathogens

G. Bacteria
   1. 30% of the fecal dry weight
   2. $10^{11}–10^{12}$ bacteria/g feces
   3. Mainly consists of anaerobes, especially Bacteroides
   4. E coli is the most common aerobe
   5. Endogenous bacteria
      a. Important for metabolism of bilirubin, bile acids, estrogen, cholesterol, and
         breakdown of carbohydrates and proteins in the colon
      b. Produce vitamin K

H. Flatus production
   1. 400–1200 mL/day, depending on diet

I. Colonic motility (see colonic motility section for further description)
   1. Contractions
      a. No migrating motor complexes/cyclic activity like small bowel
      b. The colon is rarely inactively
      c. Segmental
         1) Predominate contraction, occurs throughout the day, isolated/bursts,
            rhythmic/arrhythmic
         2) Mainly mixes contents of colon, thus facilitating absorption
         3) Maximizes intestinal mucosa exposure to luminal contents to enhance
            absorption of water, electrolytes, bacterial products
      d. Rectal motor complex
         1) Rhythmic contractions in cycles of 3–6 per minute (independent
            of small bowel MMCs) that help maintain fecal continence
   2. Propagated
      a. High vs low amplitude contractions, but likely continuum
      b. To move feces and gas rapidly over long distances
   3. Cholinergic activity increases motility in colon
   4. Mass action contraction
      a. Unique to colon
      b. Simultaneous smooth muscle contraction over large areas, propelling feces
         along colonic segments or into rectum
   5. Gastrocolic reflex
      a. Colonic mass peristalsis after meal, and contraction of rectum in response to
         distension of stomach by food
   6. Gastroileal reflex
      a. Cecum relaxes and chyme goes through ileocecal valve when food leaves the
         stomach
VII. Anorectal Physiology

A. The anorectum maintains fecal continence and allows defecation
   1. Continence requires puborectalis muscle and anal sphincter contraction
   2. Defecation requires puborectalis relaxation by sacral parasympathetic nerves

B. Reflex sympathetic relaxation of internal (involuntary) and external sphincters occurs in response to rectal distension

C. Defecation pattern
   1. Involves coordination of internal and external anal sphincters, abdominal muscles, pelvic floor
      a. High-amplitude propagating contractions deliver stool to rectum
      b. Rectal distension reflexively relaxes internal anal sphincter due to excitation of sympathetic nerve supply (rectoanal inhibitory reflex)
      c. External sphincter and pelvic floor muscles contract
      d. Feces contact the anal canal, and the sensory epithelium distinguishes solid/liquid stool and gas, providing the urge to stool
      e. If stool is not released, the rectum relaxes and the urge subsides (accommodation response) and the stool is retained until a bowel movement occurs
         1) The bowel movement is a coordination of increased abdominal pressure by Valsalva, contractions of rectum, relaxation of puborectalis muscle, and opening of the anal canal (initiated voluntarily, and then spinal reflexes take control)

Recommended Reading


I. Normal Colon Histology
   A. The colon has four layers: mucosa, submucosa, muscularis externa, and serosa (Figure 1)

II. The mucosa of the colon
   A. Formed by epithelium, lamina propria, and muscularis mucosae (Figure 2)
   1. The mucosal thickness increases as it goes from the cecum to the rectum. It contains numerous straight tubular glands or crypts of Lieberkühn
   2. The surface epithelium
      a. No villi, thus it has a smooth surface epithelium which is lined with simple columnar epithelial cells
      b. A mixture of absorptive cells at the luminal surface and mucous-secreting goblet cells at the base of the glands
      c. The number of goblet cells are increased compared to small intestine cells, which increase in number distally
         1) Goblet cell depletion can be seen in chronic inflammation
      d. The absorptive cells have shorter and less abundant microvilli than found in the small intestine
         1) Like the brush border enzymes, they have no role in digestion
         2) The main function of these absorptive cells is to absorb electrolytes and water
      e. The crypts are longer and straighter than those in the small intestine
      f. Low concentration overall of enteroendocrine cells in the large intestine
         1) Need special immunohistologic stains for proper visualization
      g. Paneth cells are seen scattered only in cecum
   3. Muscularis mucosa
      a. Several thin layers of smooth fibers oriented in different directions
         1) Layers are penetrated by nerve twigs from the submucosa plexus, which extend vertically into the lamina propria
   4. Lamina propria is a highly cellular layer which contains lymphocytes, plasma cells, macrophages and scattered eosinophils. Lymphoid follicles are also present in colonic mucosa, and may extend through muscularis mucosae into submucosa (part of Gut Associated Lymphoid Tissues [GALT]). Neutrophils are seen occasionally in lamina propria, however, their presence in excess in the surface epithelium or crypts may indicate an active infection or inflammation

III. Submucosa
   A. Composed of a loose connective tissue, with collagen and elastic fibers that connects mucosa and muscularis externa layers closely together.
   1. Also composed of blood vessels, lymphatics, and nerves
      a. Contains specialized nerve ganglions (Meissner’s plexus), defined below
   2. No glands in the submucosa

IV. Muscularis externa
   A. Thin smooth muscle layer that has inner circular and outer longitudinal layers of smooth muscles
   1. The outer layer is primarily condensed into three muscular bands called taenia coli (seen throughout the colon except the rectum)
      a. Contraction of the taenia coli and circular muscle layer draws the colon into sacculations called haustra, which are characteristic for the colon
   2. Muscularis externa is responsible for the propulsive force of the large intestine
   3. Large intestine peristalsis is mediated by intrinsic (myenteric plexus) and extrinsic (autonomic innervation) neural control
      a. Meissner’s plexus resides at the base of submucosa
1) Consists of two neural networks
2) Auerbach’s plexus lies between the inner circular and the outer longitudinal muscle layers of the wall

V. Serosa
A. Outer layer of the colon
   1. Single layer of avascular, flat, nucleated cells, simple squamous epithelial cells
      a. Lubricates by producing serous fluid

VI. Appendix and rectum
A. Different in some aspects from the other parts of the colon
B. Appendix
   1. Thin, finger-like extension of the cecum. Characterized by long crypts without villi
   2. There is a large accumulation of lymphoid tissue in the lamina propria and submucosa. Inflammation in this area leads to hyperplasia of these lymphoid follicles, causing obstruction of its lumen, bacterial proliferation, and subsequent appendicitis
   3. Appendices epiploicae
      a. Adipose structures protruding from the serosal surface of the colon
         1) Lobulated masses of pericolic fat, usually 2–5 cm long
            a) Can undergo a spontaneous torsion, leading to infarction, which produces symptoms similar to appendicitis

C. Rectum
   1. The dilated terminal portion of the intestinal tract that does not have mesentery
   2. Divided into two segments; the upper part (rectum proper), and the lower part (anal canal), which extends from the anorectal junction to the anus
   3. Rectal mucosa is thicker compared to other parts of the colon, with more prominent veins
      a. The crypts are longer than those in the small intestine, and are lined predominantly by goblet cells
      b. At the level of the anal canal, the crypts gradually disappear
   4. The rectum is distinguished from the other parts of the colon by:
      a. The absence of taenia coli in its muscularis externa
      b. The presence of transverse rectal folds in its submucosa (columns of Morgagni), each ending in a small valve called anal valve
         1) Between columns of Morgagni are depressions called anal sinuses, which contain anal glands. The anal sinuses end at the lower part of the anal columns, called the dentate line or pectinate line (Figure 3)
            a) When the canal is distended with stool, the columns, sinuses, and valves flatten, and mucus is discharged from sinuses to lubricate the passage of the stool
            b) The valves and sinuses prevent leakages from the anus
   5. Beyond the dentate line
      a. The simple columnar epithelium of the rectum abruptly changes to a stratified, squamous, nonkeratinized epithelium (Figure 4)
      b. Becomes keratinized in the anus, which contains sebaceous glands and apocrine sweat glands
   6. The inner circular layer of the muscularis externa thickens to form the internal sphincter at the level of the anus
   7. The outer longitudinal layer becomes the fibroelastic septum
   8. The external anal sphincter is formed by skeletal muscle and lies inside the levator ani muscle
Figure 1. Colonic wall segment shows the different layers of the colon. Adapted from the University of Western’s Blue Histology Web page.

Figure 2. Mucosa layer of the colon. Adapted from the University of Western’s Blue Histology Web page.


Figure 4. Anorectal junction area shows the transition area and the different mucosa between them. Adapted from the University of Western’s Blue Histology Web page.

**Recommended Reading**


I. Normal Physiology

A. Nervous System of the Colon
   1. Intrinsic innervation = enteric nervous system
      a. Ontogeny of enteric nervous system
         1) Majority of bowel neurons are derived from vagal segment neural crest cells of the fetal CNS
         2) 20% of bowel neurons are from the sacral segment of the fetal CNS
         3) Myenteric plexus develops first
         4) Submucosal plexus is derived from myenteric nerve cells that migrate across the muscle layer
      b. Myenteric (Auerbach plexus)
         1) Regulates smooth muscle function
         2) Has a net inhibitory influence
      c. Submucosal (Meissner plexus)
         1) Regulates the mucosal ion transport and absorption

B. Extrinsic innervation = autonomic nervous system
   1. Parasympathetic
      a. Excitatory pathways lead to increased colonic contractions
         1) Proximal colon innervated by vagus nerve
         2) Distal colon innervated by S2–S4 of pelvic plexus
      b. Main excitatory neurotransmitters include:
         1) Acetylcholine
         2) Substance P
   2. Sympathetic
      a. Inhibitory pathways lead to increased sphincter muscle tone and relaxation of nonsphincter muscle
         1) Proximal colon innervated by splanchnic nerves
         2) Distal colon innervated by lumbar nerves
      b. Main inhibitory neurotransmitters
         1) \( \alpha_2 \) adrenergic

C. Colonic Contractions
   1. Segmental contractions
      a. Occur throughout the day
      b. Act to mix intraluminal contents and increase contact with mucosa, leading to maximized water and electrolyte absorption
      c. Rectal motor complexes are specialized segmental contractions that occur more frequently at night, and are thought to aid in nocturnal continence

D. Propagated contractions
   1. High-amplitude peristaltic contractions are responsible for movement through colon
      a. Occur several times a day
      b. Can be associated with defecatory stimulation
   2. Low-amplitude peristaltic contractions are not completely understood
   3. Increased high-amplitude peristaltic contractions are seen after a meal and upon awakening
   4. Rectal distention leads to decreased propagated contractions

E. Anorectal Motility
   1. Nervous system
      a. Internal anal sphincter
         1) Parasympathetic innervation
a) Activation leads to relaxation
b) Supplied by pelvic nerves
2) Sympathetic innervations
   a) Activation leads to constriction
   b) Supplied by hypogastric nerves
b. External anal sphincter
   1) Somatic innervation of striated muscle by the pudendal nerve
c. Rectoanal inhibitory reflex
   1) With distention of the rectum, there is relaxation of the internal anal sphincter and contraction of the external sphincter

F. Modalities to Measure Colonic and Anorectal Motility
1. Radiopaque marker studies
   a. Ingestion of radiopaque markers, with follow-up abdominal x-ray on Day 4
      1) Delayed transit is described as >20% retention of markers after 96 hours
2. Radionuclide scintigraphy
   a. Ingestion of radiolabeled indium, with follow-up gamma camera scans at 6, 24, 48, 72, and 96 hours
      1) No standardized values for pediatrics
      2) Not commonly used
3. Wireless capsule
   a. Location of the ingested pill is monitored as it passes from different areas of the GI tract, as identified by changes in pH
      1) No pediatric data available
4. Colonic manometry
   a. Manometry catheters can be placed endoscopically or radiographically
   b. Indications for manometry
      1) Medically refractory constipation
      2) Persistent symptoms after surgical repair of Hirschsprung's disease
      3) Evaluation for pseudoobstruction
      4) Evaluation of colonic function prior to intestinal transplant
      5) Determination of the utility of antegrade enemas
      6) Evaluate colonic function prior to reanastomosis of diverting ileostomy
   c. Typical observations demonstrating abnormal motility
      1) Decreased frequency of high-amplitude propagating sequences
      2) Decreased colonic response to ingestion of meals
      3) Decreased colonic response to awakening
      4) Abnormal colonic response to chemical stimulation or rectal distention
5. Anorectal manometry
   a. Placement of manometry catheter into rectum
      1) Measures internal and external anal sphincter contraction and relaxation upon stimulation with rectal distention from a balloon
      2) Determines volume of rectal distention necessary to elicit the rectoanal inhibitory reflex
      3) Can evaluate defecatory dynamics of straining

II. Diseases Causing Abnormal Colonic/Anorectal Motility, and the Finding on Motility Study
A. Constipation/encopresis
   1. Delayed colonic transit time
B. Chronic intestinal-pseudoobstruction
   1. Absent colonic response to a meal as measured by colonic manometry
C. Hirschsprung’s disease
   1. Absent relaxation of the internal sphincter with rectal dilation
D. Spinal cord injury
   1. Absent contraction of the external anal sphincter with no urge to defecate with rectal dilation
E. Anismus or paradoxic puborectalis contraction
   1. Contraction of the external anal sphincter and puborectalis with attempted defecation
**Recommended Readings**


Hirschsprung disease (HD) is a developmental disorder of the enteric nervous system, characterized by a congenital absence of ganglion cells in the myenteric (Auerbach) and submucosal (Meissner) plexus of the distal bowel extending proximally from the internal anal sphincter. The extent of the aganglionic segment is variable.

I. Overview/Epidemiology
   A. Affects about 1 in 5,000 live births
   B. Male to female ratio is 4:1 for short-segment disease
   C. Male to female incidence approaches 1:1 as the length of the affected segment increases
   D. Short segment or classic HD is limited to the rectum and sigmoid colon in 75%–80% of cases

II. Genetics
   A. More than 11 susceptibility genes have been implicated in the pathogenesis of HD
      1. Genetic factors that predispose to HD are heterogeneous, and there is no clear pattern of inheritance
      2. A familial incidence of 15%–21% has been reported. This incidence increases to about 50% in cases of total intestinal aganglionosis
      3. Risk of recurrence of HD in the sibling of a proband is 4% (relative risk of 200)
   B. RET (receptor tyrosine kinase) is the major susceptibility gene for HD. Approximately 50% of familial and 15%–20% sporadic cases of HD have been attributed to mutations of RET gene
   C. 70% of HD cases occur as an isolated malformation (nonsyndromic HD)
   D. 30% of cases have associated anomalies
      1. Malformations of other neural crest derivatives—such as cardiac conotruncal derivatives, melanocytes, craniofacial musculature, skeleton, and rarely, irides—may be present
   E. Chromosomal anomalies are associated in 12% cases with trisomy 21 occurring in 2%–10% of HD cases
   F. HD has been reported along with several syndromes, such as MEN2, Waardenburg syndrome, Smith-Lemli-Opitz syndrome, X-linked hydrocephalus, congenital hypoventilation syndrome, and neurofibromatosis

III. Pathogenesis
   A. Failure of normal migration of vagal neural crest cells between the 5th and 12th weeks of gestation
      1. The earlier the arrest of migration, the longer the aganglionic bowel segment
   B. Upon distension of the normal rectum, mechanoreceptors are stimulated and activate inhibitory neurons in the myenteric plexus, resulting in relaxation of the internal anal sphincter. Nitric oxide is the main inhibitory neurotransmitter in this reflex
      1. Abnormal innervations in HD result in absence of relaxation of affected bowel segments, impaired propagation of peristaltic waves, and lack of recto-anal inhibitory reflex (RAIR) on distension of the rectum

IV. Diagnosis
   A. Clinical Presentation
      1. 80%–90% of patients with HD are diagnosed in the neonatal period
      2. 95% of healthy infants pass meconium on Day 1 of life. 60%–90% of neonates with HD fail to pass meconium on the first day of life
      3. HD should be suspected in any patient with difficulty passing stools in the newborn period
      4. Presenting with:
         a. Constipation with abdominal distension (63%–91% cases)
         b. Bilious vomiting (19%–37% cases)
         c. Encopresis is not typically seen in patients with HD
d. Stools are of thin or normal caliber  
e. Patients can present with failure to thrive  
f. One-third of patients with HD can present with diarrhea without any other symptoms  

5. Rectal exam of a HD patient may reveal a tight anus, with an empty collapsed rectal vault  
6. In a patient with HD, foul-smelling, explosive diarrhea, with fever and abdominal distension, can indicate enterocolitis  
   a. Enterocolitis is associated with high morbidity and mortality  
   b. Can progress to potentially fatal toxic megacolon, which is associated with dehydration and shock  

B. Evaluation  
1. Tests available for assessment of patients suspected of having HD include:  
   a. Contrast enemas done in an unprepared bowel may show a caliber change between the small or normal-sized distal aganglionic segment and dilated proximal segment  
      1) Can assist in estimating the length of aganglionic segment  
      2) An abnormal mucosal pattern can be seen with contrast enema in some patients with enterocolitis  
   b. Rectal suction biopsy is used in infants with no anesthesia and minimal risk  
      1) Several posterior rectal biopsies are taken above 2 cms and <4 cms above the anal margin  
   c. Full thickness rectal biopsy  
      1) The gold standard for diagnosis is a full thickness rectal biopsy, although it is a more invasive test requiring general anesthesia  

2. Rectal biopsies demonstrating the absence of ganglion cells and presence of acetyl cholinesterase (AChE) with positive hypertrophic nerve fiber is confirmatory for HD  
3. In patients with HD, anorectal manometry is used, with rectal distention using a balloon, to demonstrate lack of RAIR  
4. Rectal suction biopsy (even without AChE staining) has been shown to be more sensitive and specific than contrast enema and anorectal manometry in diagnosing HD  

V. Differential Diagnosis  
   A. Hypo/hyperganglionosis  
   B. Intestinal neuronal dysplasia  
   C. Meconium plug syndrome  
   D. Meconium ileus (secondary to cystic fibrosis)  
   E. Anorectal malformation  
   F. Hypoplastic left colon syndrome  
   G. Intestinal atresia  
   H. Intestinal malrotation (volvulus)  
   I. Maternal infections  
   J. Maternal intoxications  
   K. Drugs  
   L. Congenital hypothyroidism  
   M. Sepsis  

VI. Treatment/Management  
   A. Basic principle of surgical treatment of HD is to reconnect the ganglionic bowel to the anus  
   B. Many surgical techniques have been described for HD  
      1. Swenson’s procedure: Rectosigmoidectomy  
      2. Duhamel’s procedure: Retrorectal-transanal approach  
      3. Soave: Endorectal procedure  
   C. Most commonly encountered postoperative problems include constipation, encopresis, and enuresis. Rarely, obstruction and fistulae formation may occur  
   D. Prompt recognition of enterocolitis and treatment with fluids, antibiotics, and rectal irrigations decrease associated risk of mortality. There is a risk of enterocolitis, even after surgery
Recommended Reading


Constipation is a common problem in childhood, accounting for 3% of general pediatrician visits and 25% of pediatric GI consults. While functional constipation is the most common, there are several other conditions that lead to constipation, including celiac disease, hypothyroidism, cystic fibrosis, and structural anomalies.

I. Background
A. Most common cause is functional (aka idiopathic constipation, functional fecal retention, fecal withholding)
B. Normal stool frequency varies (~4 stools/day as infant, 1.2 stools/day at 4 years old and older, with range of 3/day to 3/week)
   1. Healthy breastfeeding babies can have infrequent stools after 2 months of age due to almost complete absorption of breastmilk with little residue for stool formation
C. Normal defecation mechanics:
   1. Anatomy: Internal and external anal sphincters surrounding the anal canal form an angle with the puborectalis muscle (85°–105° at rest)
      a. Stool is propelled into the anorectum during defecation, where rectal distension results in reflex relaxation of the internal anal sphincter (IAS) with simultaneous external anal sphincter (EAS) contraction until defecation is socially appropriate
      b. At the time of defecation, increased intrarectal pressure moves feces toward the anal canal; the puborectalis muscle relaxes, straightening the anorectal angle, thus inhibiting the external anal sphincter and allowing fecal evacuation
      c. Voluntary contraction of the puborectalis muscle and external anal sphincter decreases the anorectal angle <85°–105°, which prevents defecation

II. Evaluation
A. History:
   1. Timing of first bowel movement after birth, parent’s definition of constipation, duration of symptoms, frequency of stools, presence of blood or pain with stools, toilet training history, abdominal pain, presence of withholding symptoms (see below), medical history, medications, previous treatments, allergies, surgeries, hypothyroid symptoms, urinary continence, neurologic deficits
   2. Developmental and nutritional history
   3. Family history: GI disease (especially Hirschsprung disease (HD), constipation, celiac disease), cystic fibrosis, and thyroid disease
   4. Psychosocial: family/household structure, interaction with peers, temperament, toilet habits at school
   5. Red flags concerning for organic disorder
      a. Fever, abdominal distension, anorexia, nausea, vomiting, weight loss or poor weight gain, bloody diarrhea (worrisome for enterocolitis seen with HD)
B. Physical Exam:
   1. General physical exam, including vitals and growth parameters
   2. Abdomen: distension, fecal masses, tenderness, bowel sounds
   3. Back: signs of spinal abnormalities such as sacral dimple, tuft of hair
   4. Neuro exam: Lower extremity tone and strength, cremasteric reflex, deep tendon reflexes
   5. Perineum, perianal, and digital rectal exams:
      a. Position of anus
      b. Fissures or fistulas
      c. Perianal sensation
      d. Anal sphincter tone
      e. Size of rectum, presence of polyps, hemorrhoids
      f. Presence of anal wink
      g. Size and consistency of stool and location within rectum
h. Presence of soiling
i. Test for occult blood if indicated
j. Findings concerning for HD
   1) Rectum devoid of stool (though not seen in short-segment HD)
   2) Explosive discharge of foul-smelling liquid stool when finger withdrawn

If there are no red flags in history and/or physical exam, patient most likely has functional constipation and does not require further evaluation.

C. Other tests to consider if constipation is refractory to medical management:
   1. Thyroid function tests
   2. Serum calcium level
   3. Serum lead level
   4. Sweat test if clinically indicated
   5. TTG IgA, serum IgA (or prometheus celiac panel if 2 years of age)
   6. MRI of lumbosacral spine: if clinically indicated to evaluate for tethered cord, tumors, sacral agenesis, and other intraspinal problems

D. Anorectal or colonic manometry: more advanced testing used in situations of constipation refractory to medical therapy. Evaluate for myopathy and neuropathy, including HD

E. Rectal biopsy: detect HD, neuronal intestinal dysplasia, other myenteric abnormalities

F. Barium enema: detect anatomic abnormality (should be unprepped if evaluating for possible HD)

G. Psychological evaluation

Management of organic causes of constipation will not be further discussed in this section.

III. Functional Constipation

A. Definition: Constipation without objective evidence of a pathologic condition

B. Most commonly caused by painful stools → voluntary withholding of feces → prolonged fecal stasis with resorption of fluids, increased size/consistency of stools → Rectal dilation → Larger amounts of stool needed to activate rectal stretch receptors → Urge to defecate disappears, stool withholding becomes automatic

   1. Causes of painful stools include:
      a. Difficult or stressful toilet training
      b. Changes in routine or diet
      c. Stressful events
      d. Illness causing dehydration
      e. Unavailability of toilets
      f. Withholding while busy or playing

   2. Withholding behaviors that may be observed by family:
      a. Tiptoeing
      b. Rocking back and forth, fidgeting
      c. Stiffening buttocks and legs, sitting on edge of seat
      d. Hiding in a corner, often with unusual postures

C. Patients can present with hard stools, painful stools, bright red blood in stools, abdominal pain, cramps, abdominal distension, decreased oral intake, irritability, encopresis

D. Encopresis:

   1. When large stool volumes stretch the rectum, the IAS relaxes and anal canal is shortened. The EAS is eventually unable to function adequately to prevent defecation and stool leakage occurs
   2. Rarely occurs in patients < 3 years old, usually resolves before late adolescence

E. Management:

   1. Determine whether fecal impaction is present
      a. Fecal impaction defined as:
         1) Hard mass in lower abdomen (abdominal exam)
         2) Dilated rectum filled with large amount of stool (rectal exam)
         3) Excessive stool in colon (KUB)
            a) KUB not needed to establish impaction if above findings seen on exam
b) Of note, a recent JPGN article (Pensabene 2010) reports that KUBs may have very limited value in assessing functional constipation due to low sensitivity and low interobserver reproducibility.

c) Having stool in the colon is not abnormal.

2. Treat the impaction if present
   
a. Oral and/or rectal approach may be used. Choice of treatment best determined after discussing options with family and child.

1) Oral route is noninvasive and empowers children with management of their problem.

a) Below approaches can be used in initial disimpaction alone or in combination:

   1. Mineral oil
   2. Magnesium hydroxide
   3. Magnesium citrate
   4. Lactulose
   5. Sorbitol
   6. Senna or bisacodyl
   7. Polyethylene glycol 3350 (e.g., Miralax) or polyethylene glycol with electrolytes (e.g., Golytely)

b) Rectal disimpaction is faster than oral approach, but is invasive, and can be more emotionally draining and difficult to administer. May be helpful to do rectal disimpaction prior to starting oral laxative.

   a) Saline enemas
   b) Mineral oil enemas
   c) Suppositories usually not as effective, but may be helpful adjunctively:
      1. Glycerin suppositories for infants
      2. Bisacodyl suppositories in older children

3. Maintenance therapy:

   a. Goal is to pass 1–2 soft stools daily and allow rectal vault to approach normal size (may take several months to years).

   b. Dietary interventions:

      1. Increase fluid intake
      2. May use small amounts of absorbable carbohydrates (e.g., sorbitol in prune, pear, and apple juice)
      3. Nonabsorbable carbohydrates (fiber)
         a) Titrate gradually towards goal
         b) Excessive intake may worsen constipation

   c. Behavioral modification:

      1. Unhurried time on toilet 30 minutes after meals, in order to work with peristaltic contractions
      2. Appropriate toileting hygiene: feet flat on the floor, no prolonged toilet time (rule of thumb is 1 minute for every year of age up to age 15)
      3. If behavioral/motivational problems interfere with treatment, consider referral to mental health care provider

   d. Oral medications:

      1. Stool softeners
         a) Mineral oil (lubricant): not recommended in children <1 years old or with other aspiration risk
         b) Docusate sodium
      2. Osmotic laxatives
         a) Magnesium hydroxide
         b) Lactulose
         c) Sorbitol
         d) Polyethylene glycol 3350 (Miralax)

   e. ± stimulant laxative for rescue therapy for short periods (<30 days)

      1. Senna
      2. Bisacodyl
f. Biofeedback therapy
   1) Sensory retraining, learning how to relax EAS during defecation
   2) More likely to be useful in patients with abnormal defecation dynamics on anorectal manometry

g. Surgical treatment (rare)
   1) Malone appendicocecostomy for antegrade colonic enemas (MACE): appendix used as conduit to cecum; appendix used as stoma through which colon can be irrigated in antegrade fashion
      a) Can also use cecostomy buttons in place of appendicocecostomy
   2) Proctocolectomy: in a small number of cases with debilitating symptoms, persistently abnormal colonic manometry, and nondilated colon

4. Educate patient and family
   a. Explain pathophysiology
   b. Remove negative attributions with soiling
   c. Promote consistent, positive supportive attitudes with treatment. Forceful adherence to treatments is NOT helpful
   d. Advise parents that treatment can be prolonged and difficult, with relapses common
   e. Patient should not stop treatment abruptly, as this may lead to relapse

5. Close follow-up
   a. If refractory to medical treatment:
      1) Consider laboratory work-up as above, and HD evaluation with at least unprepped barium enema and/or anorectal manometry
      2) Consider trial of cow’s milk-free diet
         a) There is a clear association between cow’s milk consumption and constipation in more than one-third of children, likely non-IgE–mediated
   b. Prognosis
      1) Long-term outcome is not well established
      2) Predictors of poor outcome include:
         a) Early onset of constipation
         b) Family history of constipation
         c) Long duration of symptoms prior to referral to a pediatric gastroenterologist

Recommended Reading


4F. Rectal Prolapse

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Rectal prolapse refers to either a mucosal or full-thickness protrusion of the rectum through the anus, and presents as concentric rings of mucosa on examination. Affects males more than females.

I. Etiology
   A. The most common underlying condition: chronic constipation
   B. The next most frequent etiology is acute diarrhea
   C. One must consider cystic fibrosis as a possible cause
   D. Other causes include increased intraabdominal pressure, parasitosis, juvenile polyps, malnutrition, and conditions predisposing to pelvic floor weakness
   E. Pathophysiology is not completely understood; some theorize this is due to sliding hernia or result of an intussusception

II. Clinical Presentation and Diagnosis
   A. Usually self-limited and intermittent during the period of toilet training
   B. History of constipation or other underlying condition, as mentioned above
      1. Often no underlying cause is identified
   C. If recurrent and pronounced, and no anatomic abnormality is identified, children should have a sweat chloride test and possibly a screen for intestinal parasites

III. Treatment
   A. Initial management: manual reduction and the treatment of the primary inciting factor
   B. If persistent: surgical intervention may be required, such as injection of a sclerosant submucosally or submuscularly above the dentate line, using D50W (1 cc/kg), phenol in oil, or hypertonic saline
   C. For prolapse that fails sclerotherapy and in children with pelvic anatomic distortion caused by previous surgery: more aggressive surgical efforts may be needed, but there is no consensus on the operation of choice. Regardless of the approach, the prognosis is generally good

Recommended Reading


I. History and Prevalence in the United States
   A. Hemorrhoidal venous cushions are normal structures of the anorectum
   B. Hemorrhoids are more common in adults, and rarely seen in children
   C. They are common causes of anal pathology due to their rich vascular supply, highly sensitive location, and tendency to engorge and prolapse
   D. Prevalence in the United States is 4%
   E. Peak incidence is between ages 45–65 years
   F. Equal between both genders
   G. Hemorrhoids generally cause symptoms when they become enlarged, inflamed, thrombosed, or prolapsed

II. Features of hemorrhoidal disease include:
   A. Bleeding
   B. Anal pruritus
   C. Prolapse
   D. Pain due to thrombosis

III. Risk factors:

IV. Anatomy
   A. Hemorrhoids arise from a plexus of dilated veins arising from the superior and inferior hemorrhoidal veins
   B. Located in the submucosal layer in the lower rectum
   C. There are three primary cushions (left lateral, right anterior, and right posterior) corresponding to the end branches of the middle and superior hemorrhoidal veins
   D. Internal and external hemorrhoids communicate and drain into the internal pudendal veins and, ultimately, the inferior vena cava
   E. Hemorrhoids have direct communication with the portal system. However, they are not more common in patients with portal hypertension

V. Anatomical Classification: Hemorrhoids are classified by their anatomic origin within the anal canal and by their position relative to the dentate line
   A. Internal hemorrhoids develop above the dentate line from embryonic endoderm. They are covered by the simple columnar epithelium of anal mucosa, and lack somatic sensory innervation and are therefore painless
   B. External hemorrhoids develop from ectoderm and arise distal to the dentate line. They are covered by stratified squamous epithelium, and receive somatic sensory innervation from the inferior rectal nerve, rendering them painful when irritated
   C. Both types of hemorrhoids often coexist
VI. Internal Hemorrhoids Staging: There is no classification for external hemorrhoids, whereas internal hemorrhoids are staged according to the degree to which they prolapse from the anal canal, as follows:
   A. Stage I: Internal hemorrhoids that bleed
   B. Stage II: Internal hemorrhoids that cause bleeding and prolapse with straining, but return to their resting point by themselves
   C. Stage III: Internal hemorrhoids that bleed and prolapse with straining, requiring manual effort for replacement into the anal canal
   D. Stage IV: Internal hemorrhoids that do not return into the anal canal

VII. Pathogenesis
   A. The cause of symptomatic internal hemorrhoids is not completely understood, but may be due to multiple factors:
      1. Low-fiber diets
      2. Decreased venous return
      3. Prolonged sitting on a toilet
      4. Aging causes weakening of the support structures, which facilitates prolapse and/or swelling of the hemorrhoidal cushions

VIII. Clinical Presentation
   A. Bleeding
      1. Usually painless bleeding with bowel movements
      2. Bright red blood typically coats the stool at the end of defecation
      3. Blood may also drip into the toilet or stain toilet paper
      4. Chronic blood loss can induce iron-deficiency anemia
   B. Pruritus
      1. Common symptom results from combination of:
         a. Prolapse of internal hemorrhoids may permit leakage of rectal contents
         b. Skin tags associated with external hemorrhoids may be difficult to clean, resulting in prolonged contact of fecal material with the perianal skin and leading to local irritation
         c. Patients with leakage may clean aggressively, irritating the perineum and also allowing contact of fecal material with denuded skin
   C. Pain
      1. Usually results from thrombosis
      2. Occurs in both internal and external hemorrhoids
      3. Thrombosis of external hemorrhoids may be associated with excruciating pain
      4. The thrombosed external hemorrhoid is an easily visible, purple mass extending from the anal to the perianal skin. It is extremely painful to palpation, and a thrombus may be appreciated
      5. Thrombosed internal hemorrhoids may cause pain, but to a lesser degree than external hemorrhoids; except when internal hemorrhoid strangulation leads to gangrene, which is life-threatening if not immediately treated surgically

IX. Diagnosis
   A. Detailed clinical history
   B. Careful examination of the rectum and anus
   C. Further diagnostic procedures such as anoscopy or proctosigmoidoscopy may be needed to confirm the diagnosis

X. Differential Diagnosis
   A. Many anorectal disorders may present like hemorrhoids:
      1. Anal fissures
      2. Condyloma
      3. Rectal prolapse
      4. Anal cancer
      5. Inflammatory bowel disease

XI. Treatment: Treat hemorrhoids only if they cause problems for the patient
XII. Conservative Management
   A. Treatment of all first- and second-degree internal hemorrhoids and non-thrombosed external hemorrhoids consists of:
      1. Sitz baths (BID/TID)
      2. High-fiber diet
      3. Adequate fluid intake
      4. Stool softeners
      5. Topical and systemic analgesics
      6. Proper anal hygiene
      7. Short course of topical steroid cream, as the prolonged use of topical steroids should be avoided

XIII. Nonoperative Treatments
   A. First-line treatment of all first- and second-degree internal hemorrhoids that do not respond to conservative therapy. Nonoperative methods include:
      1. Rubber band ligation—Most widely used procedure for Grade II and Grade III hemorrhoids and is the standard to which other methods are compared
         a. No anesthesia is required
         b. Successful in approximately 70%–80% of patients
         c. Complications are uncommon and usually benign
      2. Laser, infrared, or bipolar coagulation may be as effective as banding, with fewer and less severe complications
         a. Laser therapy is more costly, and provides no advantage over other methods
      3. Sclerotherapy is less effective than rubber band ligation
      4. Radiowave ablation followed by suture ligation could prove to be a safe, cost-effective, and convenient way to treat prolapsing hemorrhoids

XIV. Surgical Management
   A. Hemorrhoidectomy is the most effective treatment, and is indicated in the following situations:
      1. Nonsurgical treatment fails (persistent bleeding or chronic symptoms)
      2. Grade III and IV hemorrhoids with severe symptoms
      3. Presence of concomitant anorectal conditions (e.g., anal fissure or fistula) requiring surgery
      4. Patient preference
      5. 5%–10% of people with hemorrhoids eventually require surgical hemorrhoidectomy
      6. Postoperative pain remains the major complication, with most patients requiring 2–4 weeks before returning to normal activities

Recommended Reading


4H. Lower GI Bleeding

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I. Definition: Bleeding distal to the ligament of Treitz.

II. Presentation: Dark black or red blood in the stool, with or without pain (see Table 1).

### Table 1. Etiology by Age Group

<table>
<thead>
<tr>
<th>Neonatal</th>
<th>Infants</th>
<th>Younger Children</th>
<th>Adolescents</th>
</tr>
</thead>
<tbody>
<tr>
<td>Swallowed maternal blood</td>
<td>Anal fissure</td>
<td>Juvenile polyps</td>
<td>Infectious colitis</td>
</tr>
<tr>
<td>Anal fissure</td>
<td>Allergic colitis</td>
<td>Anal fissure</td>
<td>Polyps</td>
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<td>Allergic colitis</td>
<td>Infectious colitis</td>
<td>Infectious colitis</td>
<td>Inflammatory bowel disease</td>
</tr>
<tr>
<td>Infectious colitis</td>
<td>Intussusception</td>
<td>Hemorrhoids</td>
<td>Hemorrhoids</td>
</tr>
<tr>
<td>Necrotizing enterocolitis</td>
<td>Volvulus</td>
<td>Meckel diverticulum</td>
<td>Anal fissure</td>
</tr>
<tr>
<td>Coagulopathy</td>
<td>Meckel diverticulum</td>
<td>Lymphonodular hyperplasia</td>
<td>Meckel diverticulum</td>
</tr>
<tr>
<td>Meckel diverticulum</td>
<td>Juvenile polyps</td>
<td>Intussusception</td>
<td>Hemolytic uremic syndrome</td>
</tr>
<tr>
<td>Volvulus</td>
<td>Pseudo membranous colitis</td>
<td>Meckel diverticulum</td>
<td>Henoch-Schönlein purpura</td>
</tr>
<tr>
<td>Intussusception</td>
<td>Intestinal duplication</td>
<td>Inflammatory bowel disease</td>
<td>Pseudomembranous colitis</td>
</tr>
<tr>
<td>Hirschsprung disease</td>
<td>Pseudo membranous colitis</td>
<td>Hemolytic uremic syndrome</td>
<td>Ischemic colitis</td>
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<td>Intestinal duplication</td>
<td>Ischemic colitis</td>
<td>Henoch-Schönlein purpura</td>
<td>AV malformation</td>
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<tr>
<td></td>
<td>Vascular lesion</td>
<td>Hemolytic uremic syndrome</td>
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<td>Pseudomembranous colitis</td>
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<td></td>
<td></td>
<td>Vascular lesions</td>
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</tr>
</tbody>
</table>

III. Initial Evaluation

A. Test for blood in the stool
   1. Hemoccult
      a. The reagent contains peroxide, which interacts with peroxidases in hemoglobin to cause a color change
   2. False negatives can be caused by large amounts of ascorbic acid in the diet, or if intestinal bacteria degrade hemoglobin to porphyrin
   3. False positives can be caused by large amounts of rare red meat and certain vegetables, including broccoli, cauliflower, turnips, radishes, and cantaloupe

B. Foods and medicines that can make stool appear bloody
   1. Red licorice
   2. Red soda, Kool-Aid® and Jell-o®
   3. Beets
   4. Iron
   5. Pepto-Bismol
   6. Red Hot Cheetos

C. Upper vs lower intestinal tract bleeding
   1. If there is blood on the surface of the stool, this is usually of anal-rectal origin
   2. Bright red blood mixed in with stool is usually from below the ligament of Treitz, but could be from above if massive
   3. Melanotic stools are usually from above the ligament of Treitz

D. Evaluation of bleeding
   1. History
      a. Amount of blood and appearance of stool (bright red blood vs tarry stools)
      b. How long has there been bleeding?
c. Associated symptoms of fever, weight loss, diarrhea, vomiting, constipation, pain, change of appetite
d. Diet
e. Travel
f. Family history
g. Growth

2. Physical exam
a. Pallor
b. Rashes, petechiae, purpura, hemangiomas, jaundice, telangiectasias
c. Mouth lesions
d. Abdominal exam for masses, tenderness
e. Rectal exam
f. Vital signs
g. Jaundice (hepatic failure) or cutaneous bruising

IV. Initial Management
A. Assess the airway, breathing, and circulation (ABC’s)
B. Hemodynamic stabilization
   1. Isotonic crystalloid and PRBCs
   2. Tachycardia indicates >10% loss of intravascular blood volume
   3. Positive orthostatics indicates 20% loss
   4. Prolonged capillary refill indicates 25% loss
   5. Mental status changes indicates 30%–40% loss
C. Place NG and assess aspirate if melanotic stools are the concern
   1. Be cautious if there are signs of portal hypertension
D. Monitor HR, BP, and urine output
E. Correct coagulopathies and electrolyte abnormalities
   1. If active bleeding and PT is >1.5 x control value, infuse FFP
   2. If platelets <50,000, transfuse
F. Endoscopy once stabilized
G. Surgical emergencies: volvulus, nonreducible intussusception, Meckel diverticulum, vascular lesions and malformations
H. Capsule endoscopy: if unidentified bleed despite endoscopy, do UGI with SBFT prior
I. Consider CT angiography if capsule does not define etiology

V. Specifics on selected causes of lower intestinal bleeding
A. Intussusception
   1. Part of the intestine invaginates into another section of intestine
   2. Early symptoms can include nausea, vomiting, pulling legs to the chest area, and intermittent, moderate-to-severe, cramping abdominal pain. Later signs include rectal bleeding, often with red currant jelly stool
   3. Treatment
      a. Air or water soluble contrast enema
      b. If unable to reduce the intussusceptions, surgery is required
B. Meckel diverticulum (see Meckel Diverticulum chapter)
   1. The etiology of GI bleeding is ileal ulceration caused by acid secretion from the ectopic gastric mucosa
      a. Erosion into small arterioles leads to painless, brisk rectal bleeding
      b. The site of ulceration is generally at the base of the diverticulum, where the ectopic mucosa and the normal ileum join

Recommended Reading


I. **Presentation**

A. **Common presenting features of Crohn's disease (CD):**

1. **Abdominal pain (67%–75%):**
   a. RLQ (terminal ileum, cecum), periumbilical (colon, diffuse), epigastric (stomach, duodenum)
   b. Persistent, severe, awakes patient from sleep
   c. Odynophagia, dysphagia (esophagus)

2. **Diarrhea (30%–65%):**
   a. Severe, frequently nocturnal
   b. Gross blood: more frequent with colonic disease and severe small bowel ulceration

3. **Weight loss (55%–65%):**

4. **Growth failure (30%):** Decreased height and/or weight velocity, delayed puberty

   **Etiology:** Deficient nutritional intake, poor digestion and absorption, increased metabolic demand, corticosteroid use

5. **Nausea/vomiting (6%–25%):** With any bowel involvement, especially severe colitis

6. **Perirectal disease (25%):** Tag, fissure, abscess (painful), fistula

7. **Hematochezia (20%–43%):**

8. **Fever:** Low grade or waxing and waning

9. **Fatigue (13%–27%):**

10. **Anorexia**

B. **Extraintestinal manifestations (EIM) (anywhere between 25%–35%):**

1. **Arthralgia (17%–40%), arthritis (1%–10%):** axial or peripheral joints, colon > small bowel disease
   a. May precede GI symptoms, often improves as IBD is treated
   b. Type I: <5 joints, larger joints, brief, associated with Crohn's flares
   c. Type II: multiple small joints, independent of Crohn's activity

2. **Aphthous stomatitis (5%–20%):** tends to parallel IBD activity

3. **Skin**
   a. Perianal disease (common) - abscess, fistulae, tags, and fissures
   b. Erythema nodosum (1.5%-10%): active disease
   c. Pyoderma gangrenosum (<1%–2%): may be unrelated to disease activity
   d. Metastatic Crohn's disease: granulomatous lesions, independent of disease activity

4. **Hepatobiliary/pancreas:** often asymptomatic with liver disease
   a. Elevation of aminotransferases (10% at diagnosis)
   b. Primary sclerosing cholangitis (<1%–1%), autoimmune hepatitis (<1%), and overlap syndrome
   c. Pancreatitis (<1%)

5. **Ankylosing spondylitis (<1%):** seronegative vertebral arthropathy, associated with HLA-B27, sacroiliitis and progressive fusion of vertebral column

6. **Eye:** often with other EIM
   a. Uveitis (<1%–6%): slit lamp, often asymptomatic and independent of IBD activity
   b. Episcleritis: often parallels IBD activity
   c. Iritis

7. **Clubbing:** particularly with small bowel involvement

8. **Hypercoagulable state:** deep vein thrombosis, pulmonary emboli, neurovascular disease; higher risk with active disease
9. Renal: ureteral obstruction and hydronephrosis (due to phlegmon), enterovesicular fistula, perinephric abscess, nephrolithiasis (oxalate, urate, phosphate)

10. Bone:
   a. Osteopenia: malnutrition, inadequate calcium intake or absorption, vitamin D deficiency, proinflammatory cytokines, corticosteroids
   b. Bone loss: fractures, loss of height, severe pain and disability

11. Anemia: iron, vitamin B₁₂, and folic acid deficiency, autoimmune hemolysis, suppression of erythrocyte production by cytokines

12. Granulomatous inflammation at any body site

C. Distribution:
   1. Ileocolitis (40%–60%), gastroduodenal (up to 30%), small bowel alone (20%–30%)
   2. Under 5 years old: higher likelihood of isolated colonic involvement

D. Physical exam features of CD
   1. Short stature, low BMI; RLQ tenderness, fullness, and/or mass; clubbing; pallor (if anemic); oral aphthous ulcers; perianal disease (tag, fissure, ulceration, fistula, abscess); scleral injection; skin rashes; joint pain

II. Diagnosis
A. History of common presenting features and consistent physical exam
B. Lab testing
   1. Evaluate for infection: Salmonella, Shigella, Campylobacter, E coli O157:H7, Yersinia, Aeromonas, Clostridium difficile, Cryptosporidium, Giardia
   2. Elevated ESR and CRP (85%–100%), thrombocytosis (85%), anemia (16%–77%), leukocytosis, hypoalbuminemia (35%–64%), guaiac-positive stool (35%), elevated aminotransferases (10%)
   3. May have decreased iron, zinc, magnesium, calcium, phosphorus levels
   4. ASCA (specificity 88%–97%), pANCA, anti-OmpC, and anti-CBir may be positive, although these markers can vary significantly in pediatrics from year-to-year and thus may not be considered a reliable marker for this population
   5. Stool lactoferin and calprotectin (markers of neutrophil inflammation): elevated (>7.25 μg/dL and >100 μg/g respectively)
C. Radiologic evaluation
   1. Plain abdominal radiograph (abnormal in 2/3): mural thickening, dilatation, abnormal gas and stool
   2. Contrast studies: upper GI series with small bowel follow-through (differentiates UC from CD, strictures, fistulae) and barium enema
   3. Abdominal CT scan: bowel wall thickening, luminal narrowing and obstruction, mesenteric involvement, abscess, fistulae
   4. MRI: has the advantage of avoiding radiation, good soft tissue visualization, good abscess visualization
   5. Ultrasound: abscess, wall thickening, hyperemia, very operator dependent
D. Perianal fistula evaluation (diagnostic accuracy): examination under anesthesia (91%), MRI (87%), endoscopic ultrasound (91%), any two (100%)
E. Endoscopy:
   1. Early: focal aphthous ulcers
   2. Later: ulcers enlarge and become deep, linear transverse ulcers, with skip lesions.
   3. Severe: cobblestone appearance, strictures, stenosis
   4. Terminal ileum: most commonly involved (exudates, thickening, and stenosis)
   5. Upper intestinal endoscopy:
      a. Esophagus: erythema, small erosions to transmural disease and fistula, polypoid lesions, pseudomembranes, strictures
      b. Stomach and duodenum: ulcers (superficial, aphthous, linear, and serpigenous), nodularity, cobblestoning, rigidity
F. Histology: transmural inflammation, cryptitis, focal crypt abscesses, increased lamina propria cellularity, some mucous depletion, deep granulomas, fissures and sinuses, submucosal fibrosis, neuromatous hyperplasia
III. Management

A. Medical Therapy

1. 5-ASA (sulfasalazine, mesalamine)
   a. Use: induction of remission in mild-to-moderate disease, maintenance of remission. Lacking strong evidence in pediatrics
   b. Mechanism: likely through anti-inflammatory action: inhibits prostaglandin, leukotriene synthesis, other effects. Location of drug release dependent on formulation. Drug is minimally absorbed
   c. Side effects: headache, nausea, anorexia, diarrhea, joint pain, allergic reaction, folic acid deficiency (sulfasalazine), interstitial nephritis, proteinuria, pancreatitis, leukopenia, hepatitis
   d. Monitoring: CBC, liver chemistries, BUN, creatinine, and urinalysis

2. Antibiotics (ciprofloxacin, metronidazole)
   a. Use: induction of remission in mild-to-moderate disease, maintenance of remission, perianal disease. Lacking evidence in pediatrics
   b. Mechanism: reduction of luminal bacterial content, altering colon microflora, reduction of bacterial invasion, and limiting bacterial translocation
   c. Side effects: peripheral neuropathy (metronidazole), bone growth effects in animals (ciprofloxacin)
   d. Monitoring: none

3. Steroids (prednisone, methylprednisolone, budesonide)
   a. Use: induction of remission in mild-to-severe disease
   b. Mechanism: immune suppression via gene transcription: proinflammatory mediators (prostaglandins) suppressed, anti-inflammatory mediators (IL-10) increased. Nongenomic mechanisms also exist (NO production). Often leaves mucosal healing incomplete
   c. Side effects: growth delay, bone loss/disease, hypertension, hyperglycemia, acne, hirsutism, facial swelling (moon facies), weight gain, infection, mood disturbance, insomnia, and cataracts
   d. Monitoring: before starting therapy: PPD, chest x-ray if symptomatic, and Varicella titer (if possible, immunize before therapy if negative). During therapy: growth, eye exam

4. 6-MP/azathioprine
   a. Use: maintenance of remission, perianal disease
   b. Mechanism: antimetabolite actions leading to immunosuppression and lymphocytotoxicity
   c. Side effects: nausea, vomiting, diarrhea, allergic reaction, bone marrow suppression (dose related), hepatotoxicity (dose related), pancreatitis (idiosyncratic), infections (HSV, HPV), lymphoma including hepatosplenic T-cell lymphoma (HSTCL), nonmelanoma skin cancer (NMSC)
   d. Monitoring: TPMT phenotype or genotype before initiating therapy (adjust dose with low activity and do not use with absent activity), CBC and liver enzymes at 0, 2, 4, and 8 weeks, then every 3 months. Varicella titer (if possible, immunize before therapy if negative)

5. Methotrexate
   a. Use: induction and maintenance of remission in moderate-to-severe disease
   b. Mechanism: in lower doses (for IBD), mechanisms not fully known (possibilities: induction of apoptosis, alteration of adenosine concentration and subsequent adaptive immune response, direct effect on cytokines). In higher doses, blocks DNA synthesis, leading to antiproliferative effects
   c. Side effects: nausea and vomiting (may need antiemetics), stomatitis, anorexia, diarrhea, bone marrow suppression, hepatotoxicity, upper respiratory infections, pneumonitis, hypersensitivity skin reactions, teratogenicity, folate deficiency
   d. Monitoring: CBC and liver enzymes at 0, 2, 4, and 8 weeks, then every 3 months. Varicella titer (if possible, immunize before therapy if negative). Consider PFTs
6. Tacrolimus, cyclosporine
   a. Use: induction of remission in moderate-to-severe disease, perianal disease
   b. Mechanism: calcineurin inhibitors, leading to decreased production of IL-2 and IL-4, which impairs T-cell > B-cell function
   c. Side effects: hypertension, nausea, transaminitis, infection, nephrotoxicity, glucose intolerance, hypomagnesemia, seizures, infection (PCP, Aspergillus), cosmetic (cyclosporine)—gingival hyperplasia, hirsutism, coarsening facial features
   d. Monitoring: Ca, Mg, Phos, BUN/creatinine, CBC, transaminases, lipids, cholesterol, fasting glucose, drug trough levels, use PCP prophylaxis

7. Anti-TNF (infliximab, adalimumab-approved for use in children with JRA and adults with Crohn’s)
   a. Use: induction and maintenance of remission in moderate-to-severe disease, perianal disease
   b. Mechanism: monoclonal IgG1 antibody to TNFα (infliximab-chimeric, adalimumab-fully human), neutralizes TNF, blocks leukocyte migration, induces apoptosis of T-cells and monocytes, complement fixation, complement-dependent cytotoxicity, antibody-dependent cellular cytotoxicity
   c. Side effects: infusion reaction, nausea, fever/chills, hives, fatigue, lymphoma including HSTCL, NMSC, TB, cytopenia, transaminitis, psoriasis, demyelination syndromes, lupus-like reactions
   d. Monitoring before starting therapy: PPD, chest x-ray if symptomatic, and Varicella titer (if possible, immunize before therapy if negative). CBC, transaminases, skin exams

IV. Non-medical Therapy
   A. Surgery (70%–80% of patients during course of illness)
      1. Indications include those listed in the Complications section below
      2. NOD2/CARD15 variant alleles increase risk for surgery
      3. Limited small bowel resection, ileocecectomy, ileostomy, colectomy (segmental, subtotal, or proctocolectomy), stricturoplasty, fistulotomy, incision and drainage of abscess, transanal dilation
      4. May result in surgical remission of disease, but post-op recurrence is common
   B. Nutrition therapy:
      1. Use: induction and maintenance of remission in moderate-to-severe disease
      2. Mechanism unknown. Elemental and polymeric formulas with equivalent efficacy. Ideally 80%–100% caloric intake through formula
      3. Side effects: largely related to NG tube placement; may have diarrhea

V. Complications
   1. Intestinal obstruction
   2. Intestinal perforation
   3. Phlegmon
   4. Drug allergies
   5. Perianal disease
   6. Progression of disease
   7. Bleeding
   8. Fistula
   9. Abscess
   10. Drug resistance
   11. Urologic complications
   12. Growth failure

VI. Outcomes
   A. Dependent in part on disease phenotype (inflammatory, stricturing, penetrating) – may change over time to latter two
   B. Relapse of disease activity is common after induction of remission
   C. Though children often respond to steroids, dependence is common (31% at 1 year with immunomodulator use)
   D. Drug-free maintenance of remission may be possible in small subset of patients
   E. Young adults who develop CD often have short stature as adults (25% <5 percentile)
   F. Cancer: risk unknown in children; increased in adults (colon, small bowel, lymphoma)
Recommended Reading


Stephens M, Rosh JR. A case-based monograph focusing on IBD: optimizing therapeutic safety in children and young adults with IBD. NASPGHAN, CDHNF and TCL Institute, 2010.

Section 4 - Colon
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4I-2. Inflammatory Bowel Disease—Ulcerative Colitis

Steven Colson, MD
Edwin deZoeten, MD, PhD

I. Presentation

A. Common presenting features of ulcerative colitis (UC):
   1. 40%–50%: mild disease; 35%: moderate disease; 10%–15%: acute, fulminant disease
   2. Diarrhea (74%–98%)
      a. Most common in the morning when arising, after eating, at night
      b. Often tenesmus and urgency
   3. Hematochezia (83%–96%): streaks of blood, clots or large blood
   4. Abdominal pain (43%–88%): crampy, lower abdomen
   5. Anorexia (6%–50%)
   6. Nocturnal diarrhea (43%)
   7. Weight loss (31%–42%)
   8. Growth failure (5%–10%)
   9. Fever (13%)
   10. Vomiting (11%)
   11. Fatigue (2%–12%)

B. Extraintestinal manifestations (EIM) (any 24%)
   1. Arthralgia (15%–32%), arthritis (2%–20%)
      a. Arthritis can be peripheral migratory of large joints, or monoarticular (knees and ankles) and nondeforming
      b. Often mirrors bowel disease activity
   2. Hepatobiliary/pancreas: often asymptomatic with liver disease
      a. Elevation of aminotransferases
      b. Primary sclerosing cholangitis (PSC) (3%), autoimmune hepatitis (<1%) and overlap syndrome
         1) Appears before, during or after IBD diagnosis
         2) PSC increases risk for colorectal cancer; risk decreased in adults by using ursodeoxycholic acid
      c. Pancreatitis (1%)
   3. Aphthous stomatitis (3%)

C. Distribution:
   1. Pancolitis (41%), left-sided (34%), proctitis/proctosigmoiditis (26%)
   2. Can have esophageal disease (15%–50%) gastroduodenal inflammation (25%–69%) and backwash ileitis

D. Physical exam features of UC:
   1. Abdominal tenderness often in LLQ or mid-epigastric, without mass; pallor (if anemic); perianal inspection usually normal; scleral injection; skin rashes; joint pain
II. Diagnosis

A. History of common presenting features and consistent physical exam

B. Lab testing

1. Evaluate for infection: *Salmonella, Shigella, Campylobacter, E coli O157:H7, Yersinia, Aeromonas, Clostridium difficile, Cryptosporidium, Giardia*

2. Elevated ESR and CRP (23%–60%), thrombocytosis (70%), anemia (9%–67%), leukocytosis, hypoalbuminemia (15%), guaiac-positive stool (35%), elevated aminotransferases

3. pANCA (specificity 65%–95%), ASCA, anti-OmpC and anti-CBir may be positive, although these markers can vary significantly in pediatrics from year to year and thus may not be considered a reliable marker for this population

4. Stool lactoferin and calprotectin (markers of neutrophil inflammation): elevated (>7.25 μg/dL and >100 μg/g respectively)

C. Radiologic evaluation

1. Plain abdominal radiograph: nonspecific mucosal edema occasionally noted, marked colon dilation in toxic megacolon

2. Contrast studies:
   a. Upper GI series with small bowel follow-through: differentiate UC from CD
   b. Barium enema: rarely used, but can help evaluate extent/extent of disease and complications. Changes usually contiguous, circumferential and symmetric without skip lesions. Findings include fine granular pattern (early), flask-shaped or collar-button ulcers, inflammatory pseudopolyps and lead pipe colon (longstanding disease)

3. Abdominal CT scan (oral and/or rectal contrast), ultrasound (to monitor disease activity and assess response to treatment) and MRI (little value over CT in evaluating colonic IBD, though this assists in avoiding radiation) are also options

D. Endoscopy

1. Early: diffuse erythema and dull-appearing vasculature with friability

2. Later: small to larger ulcers on background of diffuse, continuous inflammation extending from rectum proximally

3. Longstanding: pseudopolyps

4. Terminal ileum: normal or backwash ileitis

5. Upper intestinal endoscopy: often normal, though may see mild gastritis

E. Histology: acute and/or chronic inflammation limited to mucosa and superficial submucosa, cryptitis, extensive crypt abscesses, increased lamina propria cellularity, mucous depletion, villous surface transformation, absence of deep granulomas

III. Management

A. Medical Therapy — For drug mechanisms, side effects and monitoring, see IBD, Crohn's Disease section.

1. 5-ASA (sulfasalazine, mesalamine)
   Use: induction of remission in mild to moderate disease, maintenance of remission

2. Antibiotics
   Use: few studies show efficacy in treating UC

3. Steroids (prednisone, methylprednisolone)
   Use: induction of remission in moderate to severe disease

4. 6-MP/azathioprine
   Use: maintenance of remission

5. Methotrexate
   Use: less effective in UC than CD

6. Tacrolimus, cyclosporine
   Use: induction of remission in severe disease

7. Anti-TNF (infliximab, adalimumab—neither approved in pediatrics)
   Use: induction and maintenance of remission in moderate to severe disease
B. Surgical Therapy — 30%–40% of patients will require surgical therapy at some point.
   1. Indications include those listed in Complications section below: urgent/emergent (1-6), elective (7-10)
   2. Types:
      a. Proctocolectomy with ileal pouch-anal anastamosis (IPAA): current standard of care, most often J-pouch, usually 2–3-stage procedure with temporary ileostomy
      b. Subtotal colectomy with closure of rectum (Hartmann procedure) and ileostomy: for urgent operations
      c. Proctocolectomy with end ileostomy: ileostomy is permanent
   3. Complications (up to 50% of IPAA)
      a. Postoperative period: wound infection, ileus, high ileostomy output, anastamosis dehiscence
      b. Adhesion and small bowel obstruction, parastomal hernia, pelvic abscess, cuffitis (with residual rectal tissue)
      c. Pouch: pouchitis (common, acute or chronic, metronidazole and/or ciprofloxacin), anastamotic stricture (10%–15%, require dilation), irritable pouch syndrome, mechanical pouch dysfunction
      d. Ileostomy: prolapse, stenosis, retraction
C. Complications
   1. Intractable bleeding
   2. Toxic megacolon (increased risk with steroid, opiate use)
   3. Persistent pain
   4. Repeated sepsis
   5. Colonic perforation
   6. Colonic stricture
   7. Refractory to medical management or complications
   8. Chronic malnutrition leading to poor growth, delayed puberty
   9. Steroid dependence
   10. Dysplasia
D. Outcomes
   1. Changing as diagnosis and therapy improves; data may differ in current biologic therapy era
   2. Recent data (1996): >80% resolution of symptoms by 6 months, 55% symptom-free at yearly follow-ups
   3. Corticosteroids used in 70% of moderate/severe disease by 1 year
   4. Colectomy: at 1–5 years: 1%–8% initial mild disease, 8%–26% moderate-severe disease
   5. Cancer: mucosal dysplasia, although rare, can be found in children and warrants colectomy. Colonoscopic surveillance should begin around 8 years postdiagnosis

Recommended Reading


Stephens M, Rosh JR. A case-based monograph focusing on IBD: optimizing therapeutic safety in children
and young adults with IBD. NASPGHAN, CDHNF and TCL Institute, 2010.
4I-3. Other Inflammatory Lesions of the Bowel

The differential diagnosis for bowel inflammation includes infection, inflammatory bowel disease, vasculitis, Henoch-Schönlein purpura, hemolytic uremic syndrome, protein-losing enteropathy and Behçet’s disease.

I. Henoch-Schönlein Purpura (HSP)
   A. Epidemiology
      1. 90% of HSP patients are under 10 years old, most commonly between 3–7 years old
      2. Typically occurs during autumn and winter
   B. Etiology
      1. Genetic predisposition (HLA-DRB1*01 and DRB1*11)
      2. Infection, most often viral or Streptococcus
      3. Mediated by IgA deposition in various sites
   C. Clinical manifestations
      1. Skin (first sign): painless palpable purpura on back, buttocks and legs, nonpitting edema
      2. GI (small bowel most affected): colicky periumbilical and epigastric abdominal pain worse after eating, nausea, vomiting, bleeding (occult > overt bleed, melena > hematochezia), ileoileal intussusception, perforation, mesenteric vasculitis (which may lead to bowel necrosis and massive GI bleed), protein-losing enteropathy (PLE), cholecystitis, pancreatitis
      3. Joints: symmetrical arthralgia or arthritis of large joints in legs
      4. Renal (onset about 1 month after appearance of purpura): microscopic hematuria with or without proteinuria, may develop rapidly progressive glomerulonephritis or ESRD
   D. Histology
      1. Leukocytoclastic vasculitis affecting capillaries, venules and arterioles
      2. IgA and C3 deposits
   E. Labs and imaging
      1. UA—hematuria with or without proteinuria
      2. Moderate leukocytosis
      3. Mild elevation of acute phase reactants
      4. Increased serum IgA
      5. Elevated ALT and GGT
      6. US—bowel wall thickening, intussusception, hepatomegaly, gallbladder wall thickening
      7. Barium studies—mucosal fold thickening, separation of loops due to intramural edema and bleeding, mucosal scalloping, thumb printing
      8. CT—bowel wall thickening, engorged mesenteric vessels, target sign
      9. Endoscopy—erythema, edema, petechiae, submucosal hemorrhage, purpura, erosions, ulcerations, gastritis, duodenitis
   F. Management
      1. Supportive care
      2. Maintain hydration, nutrition and electrolyte balance
      3. Analgesics for joint pain
      4. NSAIDs for severe arthritis (avoid in patients with GI and renal problems)
      5. Antihypertensive medications and dialysis as needed
      6. Steroids controversial and reserved for severe systemic manifestations and renal involvement
         a. In patients with glomerulonephritic disease, may treat with steroids with or without cytotoxic agents
         b. Abdominal pain will eventually resolve, but steroids will shorten its duration
         c. Steroids may be effective for massive GI bleed and ischemic bowel from widespread mesenteric vasculitis
         d. Steroids may be used in children with painful cutaneous edema
e. Surgery for intussusception (if it does not reduce spontaneously over 24 hours), infarction, perforation

G. Prognosis
1. Self-limited, usually lasts 1–4 weeks
2. Correlates with degree of renal pathology, defined as presence of crescents
3. 15%–40% have at least one recurrence within 4 months, which is usually milder and shorter than the first episode

II. Hemolytic Uremic Syndrome (HUS)

A. Etiology
1. Triggers of vascular injury (eg, Shiga toxin, virus, immune complexes, drugs) and predisposing conditions (such as disorders of complement system) lead to endothelial cell damage and thrombotic microangiopathy

B. Clinical manifestations: hemolytic anemia, thrombocytopenia, acute renal failure

C. Diarrheal associated form (>90% of HUS cases)
1. Most common between 6 months and 5 years old
2. Triggered by intestinal infection with enterohemorrhagic E coli (EHEC) that produce Shiga toxin (Stx)
3. Manifestations
   a. GI: diarrhea (nonbloody > bloody), abdominal pain, dehydration
   b. Neuro: seizures, coma, brain edema
   c. Heme: pallor
   d. Renal: hematuria (usually microscopic), edema, hypertension, renal insufficiency
4. Labs
   a. Anemia with schistocytes, thrombocytopenia
   b. High creatinine or low GFR
   c. Increased LDH, decreased haptoglobin
   d. Positive stool culture
   e. Elevated amylase, lipase, transaminase, alkaline phosphatase, GGT
5. Self-limited course (1–3 weeks) with relatively good short-term outcome, but some may develop renal sequelae

D. Nondiarrheal associated form (aka atypical HUS)
1. Not associated with diarrhea and Stx-producing E coli
2. Caused by various triggers (eg, infection, disorders of complement system, drugs, malignancy)
3. Small percentage caused by streptococcus pneumonia, which presents with more severe symptoms, higher risk of renal complications and higher mortality rate
4. Poorer prognosis
5. More likely to have severe HTN and chronic end-stage renal failure, and to recur

E. Management
1. Find cause of HUS
2. Maintain hydration, nutrition and electrolyte balance
3. Transfuse with PRBC and platelets prn (caution: platelets may lead to microthrombi)
4. Dialysis as needed
5. Antihypertensive and antiseizure medications prn
6. No antibiotics given for EHEC

III. Protein-losing Enteropathy (PLE) — (see section on protein-losing enteropathy)

IV. Behçet's disease

A. Chronic relapsing multisystemic vasculitis
1. Starts around 2nd to 4th decade of life
2. Etiology unknown, but possibly secondary to autoimmune reaction triggered by infection or antigen in a genetically predisposed person (HLA-B51)
3. Prevalent among Silk Route population from Eastern Asia to Mediterranean Basin
4. Diagnosis based on clinical criteria

B. Clinical manifestations
1. Mucocutaneous lesions (hallmark) often precede other manifestations
   a. Multiple recurrent painful oral and genital ulcers similar to aphthae in appearance
2. Eye: uveitis > retinal vasculitis
3. Vascular: systemic vasculitis (venous > arterial system) affecting vessels of all sizes
   a. Thrombophlebitis, Budd-Chiari, pulmonary arterial aneurysm contributes to mortality
4. Joints: nonerosive, nondeforming, monoarticular arthritis
5. GI: abdominal pain, GI bleed, fever, weight loss, diarrhea, constipation, perforation, fistulas, ischemia, infarction, aphthous-like ulcers in ileocecal area, pancreatitis, hepatobiliary complications, normal growth
6. Skin: erythema nodosum, pustules, acne-like lesions, positive pathergy test (pustule develops 24–48 hours after needle prick to skin)
7. Neuro (rare but poor prognosis)

C. Studies
1. Barium studies: ulcers, thickening of surrounding mucosal folds
2. CT or MRI: bowel wall thickening
3. Colonoscopy: ulcers in ileocecal area, discontinuous bowel involvement with relative sparing of rectum, no granulomas or cobblestoning
4. Capsule endoscopy: ulcers, pseudopolypoid lesions

D. Treatment
1. Topical treatment: corticosteroids, antimicrobial agents, sucralfate, silver nitrate, anti-inflammatory agents
2. Systemic corticosteroids, colchicine, dapsone, thalidomide, methotrexate, azathioprine, cyclophosphamide, cyclosporine A, mycophenolate mofetil, interferon-alpha, anti-TNF agents

Recommended Reading


**4I-4. Colitis Not Due to Inflammatory Bowel Disease**

Ghassan Wahbeh, MD

Infectious and noninfectious causes beyond chronic idiopathic inflammatory bowel disease.

I. Introduction
   A. The right colon is tasked with absorption of residual intestinal fluid and salt
   B. The left colon handles the storage and evacuation of stool
   C. Abundant bacteria and yeast colonize the colon
   D. The composition of the flora varies according to dietary factors and host-specific defenses and susceptibilities
   E. The term colitis is used to denote inflammation of the colon and/or symptoms thereof, namely pain, diarrhea, tenesmus, passage of mucus and blood
   F. At the microscopic level, colitis indicates a change in the number and makeup of immune cells within the colonic wall or its structural architecture

II. Infectious Colitis
   A. Symptoms of infectious colitis are generally acute
   B. Macroscopically, acute infectious colitis can look like ulcerative colitis
   C. Microscopically, there are no significant architectural changes and neutrophils are the predominant immune cell type present
   D. Most infections are self-limited in the immune-competent host
   E. The most common agents include:
      1. *Clostridium difficile* (Figure 1)
         a. Gram-negative, anaerobic, spore-forming, toxin-producing bacteria
         b. In nosocomial setting:
            1) Rising cause of morbidity and mortality due to increasing strain virulence, toxin novelty (binary toxin) and antibacterial resistance
         c. Part of the normal flora
         d. Very commonly colonizing the younger gut (immunity to toxins thought to be due to absence of epithelial toxin receptors)
         e. Alteration in the commensal flora is what drives *C diff* to turn from bystander to pathogen
         f. Risks factors
            1) Antibiotics, hospitalization, older age, immune suppression and IBD
            2) Association with acid suppression possible
         g. Symptoms are variable and can be severe, with fever, leukocytosis and toxic megacolon
         h. Worth noting that frank bleeding with *C diff* (a noninvasive pathogen) is uncommon and its presence should prompt suspicion for other underlying causes
         i. In the right clinical setting, demonstrating toxin presence (toxin assays, recently PCR) is diagnostic
         j. Gross appearance
            1) Pseudomembranes are quite typical in moderate/severe disease (Figure 1)
         k. Treatment options include metronidazole, vancomycin, supplemental probiotics, toxin binders and pooled immune globulin infusions
         l. *C diff* can be detectable for weeks after therapy
         m. Disease recurrence can be challenging to address
2. *Yersinia enterocolitica*
   a. Ileocecal inflammation in younger children and infants
   b. Causes pain and diarrhea with bleeding
   c. Can be confused with Crohn's disease
   d. Course can be self-limited without need for antibiotic treatment

3. *Campylobacter jejuni*
   a. The most common cause of colitis worldwide
   b. (see section on Enteric Infections)

4. *Salmonella typhi, Shigella and E coli O157:H7*
   a. Invasive pathogens that occur endemically or sporadically
   b. (see section on Enteric Infections)

5. Amoebiasis
   a. In endemic areas
   b. Left-sided colitis and systemic symptoms

6. Cytomegalovirus (CMV) (Figure 2)
   a. Causes colitis in immunocompromised host
   b. Manifests with ulceration and edema
   c. Can be a complicating infection in IBD, more so when steroids are used

II. Infectious Colitis
   In this category, chronic idiopathic IBD is relatively common and will be reviewed separately.
   Some less common causes are listed below.

A. Microscopic colitis
   1. Grossly normal-appearing colon
   2. Microscopic inflammation: lymphocyte predominant lymphocytic colitis and/or collagen deposit–related “collagenous colitis” (Figure 3)
   3. Presents with persistent watery diarrhea
   4. Cause remains unknown, some association with celiac disease and NSAID has been suggested
   5. The inflammation can improve spontaneously. Therapies have not been extensively evaluated, including bismuth salicylate, budesonide, cholestyramine and azathioprine

B. Behçet's disease
   1. Multiorgan disease that affects young adults
   2. (see section on Other Inflammatory Lesions of the Bowel)

C. Eosinophilic colitis
   1. Commonly a benign transient phenomenon
   2. In infants attributed to cow's milk protein (or other protein) allergy
   3. Also found in exclusively breastfed babies
   4. Beyond infancy, isolated eosinophilic colitis is rare (vs colitis as part of a systemic eosinophilic syndrome like Churg-Strauss syndrome)
   5. If at risk, parasitic infections should be ruled out as a cause
   6. Seen in postorgan transplantation patients with immune suppression (eg, tacrolimus) or other drug exposure
   7. Manifestations are variable, including diarrhea, rectal bleeding, abdominal pain, anemia and peripheral eosinophilia
   8. Gross exam may show a normal colon or prominent lymph nodules, with eosinophils on histologic exam
   9. If symptomatic, medication withdrawal or allergy trigger elimination (when identified) are indicated
   10. Rarely, steroids are needed

D. Graft-vs-Host disease (GVHD)
   1. One of the most common complications of hematopoietic stem cell transplantation
   2. (see section on Graft Vs Host Disease)

E. Neutropenic colitis (typhilitis)
   1. Presents with a triad of fever, abdominal pain and neutropenia
   2. The colon wall is thickened when imaged
   3. Conservative treatment is usually successful
   4. Colonoscopy and surgery are not commonly indicated in this setting.
F. Nonsteroidal anti-inflammatory drugs
1. Cause intestinal injury by inhibiting the cyclooxygenase system and perhaps other nonprostaglandin-related mechanisms
2. Similar to the upper gastrointestinal tract, NSAIDS can cause colonic ulceration, inflammation and bleeding
3. Most NSAID effects on the lower intestines are asymptomatic
4. Degree of injury varies with the NSAID type. For example, some pass through the enterohepatic circulation
5. The bacterial flora composition and concomitant antibiotic use may affect the degree of NSAID injury as well

G. Solitary rectal ulcer
1. Uncommon condition
2. Localized ulceration in the anterior rectal wall, edema and, occasionally, polypoid lesions are seen
3. It is attributed to straining and dysfunctional stooling dynamics that cause the anterior rectal wall to face direct mucosal pressure against a nonrelaxing pelvic floor
4. Treatment lies in improving defecation pattern, including stool softeners and, rarely, surgery

H. Radiation colitis
1. Acute or chronic
2. Appears months to years after radiotherapy
3. Symptoms are variable and can be severe
4. Last for months to years

I. Other causes of colitis occur less commonly
1. Ischemic colitis is rare in children
2. Diversion colitis is nonspecific in appearance macro- and microscopically, although usually mild. This stresses the importance of the fecal stream and flora in the stability of the colonic milieu

Figure 1. Clostridium difficile
Figure 2. CMV
Figure 3. Microscopic colitis
Figure 3B. Bechet’s
Recommended Reading


4J. Perianal Disease

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I. Rectal Fissure

A. Background
   1. Superficial tears of the anoderm, inferior to the dentate line
   2. Majority located at the posterior (90%)
   3. Typically due to constipation, although this history is only elicited in 25% of cases

B. Classification
   1. Primary fissures
      a. Not related to underlying pathology
      b. Sharply demarcated edges
      c. Pathogenesis related to local trauma, typically with passage of a large-caliber, hard stool in the context of:
         1) Anal sphincter hypertonicity and/or
         2) Poor anoderm perfusion in the posterior midline
         3) The above two entities result in poor wound healing
      d. Diarrhea is another possible etiology
   2. Secondary fissures
      a. Generally the consequence of systemic illness, such as Crohn’s disease

C. Presentation
   1. Severe, sharp perianal pain may occur during defecation
   2. Pain lasts minutes to hours after passage of stool
   3. Associated passage of blood is also common

D. Diagnosis
   1. Examination of the anal canal, which may require an anoscope
   2. Acute fissures are typically small
   3. Chronic fissures may be associated with anal papilla hypertrophy, fibrosis or a skin tag
   4. Child abuse should be considered when a large fissure is associated with perianal bruising

E. Management
   1. Acute fissures
      a. Three-fold:
         1) Decreasing anal trauma associated with stooling using stool softeners, lubricants or fiber supplementation
         2) Reducing anal sphincter tone with warm baths/sitz baths
         3) Increasing anal perfusion
      b. >80% heal with conservative management
      c. Failure to maintain good hygiene may prolong the healing process
      d. Refractory cases may respond to a trial of cow’s milk restriction
      e. Topical steroids/anesthetics have not been shown to be advantageous
   2. Chronic fissures
      a. Defined as a lesion persisting for at least 6 weeks after initial management
      b. Uncommon in children
      c. Despite underlying etiology, chronicity can lead to fibrotic edges or a sentinel tag
      d. Management includes:
         1) Decreasing the resting tone of the anus
            a) In infants, gentle, daily anal dilatation at home can diminish anal spasm and pain
         2) Other approaches include:
            a) Nitric oxide, administered as 0.2% glyceryl trinitrate topically 3 times daily
b) Injectable botulinum toxin, which shows a higher rate of healing, not adequately studied in children

e. Cases refractory to medical management may require anal dilatation and fissure excision under general anesthesia
f. In older children and adolescents, lateral internal sphincterotomy without fissure excision is the approach of choice

II. Anterior Ectopic Anus

A. Background
1. Part of the spectrum of anorectal developmental abnormalities, from high imperforate anus to anteriorly displaced anus
2. Ectopic anus should not solely explain constipation unless severely displaced

B. Diagnosis
1. Documenting an anal opening not located in the center of the perineal pigmented area
2. Anal Position Index (API) can be used as a guide, to support a suspicion of ectopic anus:
   a. Girls: Anus-fourchette/coccyx-fourchette
      mean ± SD for API is 0.45 ± 0.08
   b. Boys: Anus-scrotum/coccyx-scrotum
      mean ± SD for API is 0.54 ± 0.07

C. Management
1. API <2 SD from the mean (eg, <0.29 in girls and <0.40 in boys) is consistent with anteriorly displaced anus and identifies roughly 4% of infants with the most severe lesions
2. Surgical consult should be considered if severe constipation is associated with and API <2 SD from the mean

III. Acute Perianal Strep (Perianal Infectious Dermatitis)

A. Presentation
1. Typically between 6 months to 10 years of age
2. 70% of cases occur in boys
3. Cellulitis occurs in 90% and pruritis in 80% of cases
4. Majority of patients complain of rectal pain, often described as anal burning during defecation
5. 33% of patients have blood-streaked stools
6. Fecal retention may occur due to pain associated with defecation
7. No fever, headache or malaise should be present, and if present would suggest subcutaneous involvement
8. Familial spread is not uncommon, particularly between siblings who bathe together
9. Exam reveals a superficial, confluent, erythematous, well-demarcated rash without induration, extending radially from the anus
10. In the acute stages, affected skin is moist, bright red, tender and may have an associated white pseudomembrane
11. In chronic cases, painful fissures, dried mucoid discharge or psoriasiform plaques with yellow peripheral crust may develop
12. Vulvovaginitis or penile involvement may occur

B. Diagnosis
1. Moderate to heavy growth of group A streptococcus (GABHS) from perianal culture differentiates this from other possible etiologies:
   a. Differential diagnosis: S aureus dermatitis psoriasis, seborrheic dermatitis, candidiasis, pinworm infestation, sexual abuse, guttate psoriasis and IBD
2. Asymptomatic perianal colonization will show light GABHS growth on blood agar
3. Direct GABHS antigen is less sensitive than culture and false negatives are relatively common early in the course
4. ASLO or anti-DNase B are not helpful
5. Index cases should be cultured

C. Management
1. A 10-day course of oral penicillin treats the majority of cases
2. 40%–50% recurrence rate, hence close follow-up is recommended
3. Erythromycin ES or erythromycin estolate excellent choice for:
   a. Penicillin-allergic patients
   b. Persistent positive cultures after penicillin
   c. Patients infected with S aureus

4. Recurrent perianal dermatitis can be treated effectively with clindamycin or a macrolide, with or without concurrent mupirocin

IV. Perirectal Abscesses

A. Background
   1. Majority result from a crypt of Morgagni infection
   2. Resultant fistula is due to spontaneous drainage of the abscess, which results in a chronic inflammatory tract
   3. Fistula in ano occurs in 20%–80% of patients

B. Classification
   1. Determined by the anatomic location of the lesion relative to the levator ani and sphincteric muscles
   2. Lesions are located, in decreasing frequency, in the perianal, ischioanal, intersphincteric and suprarectal regions

C. Presentation
   1. More common in males
   2. 98% report persistent perirectal pain
   3. History of a diarrheal illness or anal fissure may be elicited
   4. Infectious process due to DM, Crohn's disease, tuberculosis or AIDS is less common
   5. Infants may present with crying or irritability especially with diaper change
   6. Tender, indurated area may be appreciated early in the disease process, which may become erythematous
   7. Fevers possible, not necessary
   8. Abscesses are identified in 95% of cases when an external perianal exam is combined with a digital rectal exam
   9. Fistulae typically traverse the lowest fibers of the interval sphincter and ultimately connect to the rectum near the crypts of Morgagni
      a. More common in the first 12 months of life

D. Management
   1. Depends upon age
      a. Infants
         1) Uncomplicated lesions successfully managed with careful hygiene and sitz baths, with or without concurrent antibiotics
         2) Fistulae typically follow a self-limited course in healthy infants and are safely managed with nonoperative approaches
         3) Abscesses or Fistulae-in-ano, refractory to conservative management, may require a surgical approach
      b. Older Children
         1) Often managed with surgical drainage and examination under general anesthesia since lesions extend to involve deeper tissues in this age group
         2) Chronic fistulae persisting beyond 3 months despite medical management with associated recurrent abscesses or persistent drainage are an indication for surgery
         3) Surgical options include fistulectomy, fistulotomy or the use of a seton loop, which results in division and fibrosis of existing fistulous tracts
         4) Patients with persistent or recurrent fistulae should be evaluated for neutropenia, leukemia, HIV, immunosuppression, diabetes mellitus and Crohn’s disease
Recommended Reading


Intestinal polyposis syndromes are rare. The polyps found in children can be classified by their histology into hamartomatous, adenomatous, inflammatory and other. It is important to identify these children due to the health risks associated with several polyposis syndromes.

I. **Classification**
   A. Hamartomatous polyps
      1. Solitary juvenile polyp
      2. Juvenile polyposis syndrome
      3. Peutz-Jeghers syndrome
      4. Phosphatase and tensin homologue gene mutation (PTEN) hamartoma syndrome
         a. Bannayan-Riley-Ruvalcaba syndrome
         b. Cowden syndrome
         c. Gorlin syndrome
   B. Adenomatous polyposis syndromes
      1. Familial adenomatous polyposis (FAP)
      2. Gardner syndrome
      3. Turcot syndrome
      4. MYH-associated polyposis
   C. Inflammatory polyps
   D. Mixed polyposis syndromes

II. **Solitary Juvenile Polyp**
   A. Presentation: painless rectal bleeding or polyp prolapse
   B. Typical age: 2–6 years. Rare before 1 year or after 10 years
   C. May be multiple: \( \leq 5 \) by definition
   D. No malignant potential
   E. Appears as a pedunculated 1–3 cm in size, with smooth red surface
      1. Microscopically: dilated cysts filled with mucin, abundant lamina propria with inflammatory infiltrate
      2. Present at any location in colon

III. **Juvenile Polyposis Syndrome**
   A. Multiple hamartomatous polyps and increased risk of GI malignancies
   B. By definition, \( >5 \) juvenile colonic polyps, extracolonic juvenile polyps or juvenile polyps with positive family history of cancer
   C. Three forms of the syndrome
      1. Juvenile polyposis of infancy
         a. Presents in infancy with anemia, rectal bleed, diarrhea, protein-losing enteropathy (PLE), intussusception
         b. Fulminant course, death often before 2 years of age despite colectomy due to uncontrolled PLE, bleeding
      2. Juvenile polyposis coli (JPC): multiple juvenile polyps only in the colon
      3. Generalized juvenile polyposis
         a. JPC and generalized juvenile polyposis with 50–200 polyps over a lifetime
         b. At least 5 polyps required to make diagnosis (some say 3)
         c. Present with chronic and acute GI bleed, anemia, prolapsed rectal polyps, abdominal pain, diarrhea
         d. Polyps found in stomach, small bowel, colon and rectum
         e. Associated findings: digital clubbing, macrocephaly, alopecia, cleft lip/palate, congenital heart disease, GU abnormalities, mental retardation
D. Complications
   1. Premalignant condition
      a. 15% incidence of colorectal carcinoma <35 years of age
      b. Neoplasias arise in polyps and in normal-appearing colonic mucosa
      c. Higher risk of cancer in generalized form compared to colorectal form

E. Genetics
   1. Fully penetrable, variable expression; 40% of mutations are sporadic
   2. Germline mutations of SMAD4 (20% of JPS patients), BMPR1A (20%)

F. Treatment/Follow-up
   1. After gene mutation identified in index patient, all at-risk family members should be tested
   2. If parent carries mutation, all children have a 50% chance of inheriting disease
   3. Affected children should undergo colonoscopy every 2 years, or more frequently if symptomatic
   4. If no gene mutation identified, siblings of patient should have screening colonoscopy starting at 12 years of age
   5. Annual colonoscopy until all polyps are resected and then every 2–3 years for patient
   6. Gastroscopy starting in mid-teens for patient
   7. Colectomy indicated if patient develops dysplasia, cancer or high number of polyps with uncontrollable symptoms
   8. Screen first-degree relatives starting at 10 years of age if asymptomatic

IV. Peutz-Jeghers Syndrome (PJS)
   A. Autosomal-dominant (1:50,000–200,000 live births)
   B. Mucocutaneous pigmentation and hamartomatous polyps throughout the GI tract
      1. Small bowel (jejenum) > stomach, and colon
      2. Bleeding/anemia, intussusception/obstruction
   C. Presumptive diagnosis made by positive family history and typical PJS freckling
   D. Rarely polyps occur in renal pelvis, bladder, lungs, and nares
   E. Pigmented macules
      1. Arise in infancy
      2. Located around mouth, buccal mucosa, nostrils, perianal area, fingers and toes, and dorsal and volar aspects of hands and feet
      3. May fade with puberty; however, buccal lesions tend to persist
   F. Genetics :
      1. STK11 (LKB1) gene on Chromosome 19p13.3
      2. Identified in up to 90% of patients
   G. Management and Complications
      1. Midgut complications best dealt with polypectomy rather than resection because of high reoperation rate
      2. Upper and lower endoscopy, video capsule endoscopy ± patency capsule (to ensure safety of passage of capsule) or magnetic resonance endoscopy to visualize small bowel starting at age 8 years; if symptoms start earlier, need to start screening earlier
   H. Malignancy risk:
      1. In order of greatest risk: colorectal, breast, stomach, small bowel, and pancreas
      2. Risk of malignancy at 20 years: 1%; risk at 40 years: 19%; risk at 70 years: 81%
      3. Tumors of the GI tract: colorectal (38%), stomach (29%), small bowel (13%), pancreas (11%–36%)
      4. Extraintestinal tumors:
         a. Females: breast (32%–54%), ovary (21%), cervical cancer (10%); benign ovarian tumors (sex-cord tumors) cause hyperestrogenism and sexual precocity
         b. Males: Sertoli cell testicular tumor (9%)

V. TEN – Hamartoma Tumor Syndrome
   A. Three syndromes affiliated with a mutation in PTEN gene at 10q23.3
      1. Bannaya-Riley-Ruvalcaba syndrome (BRRS)
      2. Cowden syndrome
      3. Gorlin syndrome
B. BRRS
1. Presents in childhood with polyps of the ileum and colon
2. Intussusception, rectal bleeding, hypoalbuminemia
3. Macrocephaly, developmental delay, lipomatosis, hemangiomatosis
4. Requires regular colonoscopy and small bowel surveillance
5. After age 18 surveillance for thyroid, renal and breast cancer is recommended

C. Cowden syndrome
1. Rarely presents in childhood
2. Macrocephaly, papillomatous papules, acral keratosis
3. 50% risk of breast cancer in women; 10% risk of epithelial thyroid cancer
4. 90% have polyps distal to hepatic flexure

D. Gorlin syndrome
1. Autosomal-dominant
2. Upper GI hamartomas and pink/brown macules on the face and hands
3. Frontal/parietal bossing, hypertelorism, skeletal abnormalities, intracranial calcification
4. Risk of medulloblastoma

VI. Familial Adenomatous Polyposis
A. Usually more than 100 colorectal adenomatous polyps
B. Appear in childhood/adolescence and multiply with age
C. Colorectal cancer by 5th decade unless colectomy is performed
D. Attenuated FAP: fewer adenomas, later presentation
   1. Risk of cancer almost 100% by 45 years of age
E. Gastric fundic polyps and small bowel adenomas can occur with dysplastic changes, but rarely progress to carcinoma
F. Adults at increased risk of cancer of duodenum, pancreas, thyroid and ampulla of Vater
G. Extracolonic manifestations of FAP in childhood/adolescence
   1. Bone: osteomas (mandibular, maxillary), exostoses, sclerosis
   2. Teeth: impacted/supernumerary teeth, unerupted teeth
   3. Connective tissue: desmoid tumors, fibroma, subcutaneous cysts
   4. Eyes: congenital hypertrophy of the retinal pigment epithelium (CHRPE)
   5. CNS: glioblastomas (Turcot syndrome)
   6. Adenomas: stomach, duodenum, small intestine, adrenal cortex, thyroid, ampulla of Vater
   7. Carcinomas: thyroid (papillary form reported in adolescence), adrenal
   8. Liver: hepatoblastoma (seen under 5 years of age)
H. Genetics
   1. Autosomal-dominant caused by mutation in APC gene
   2. 1:10,000 births
   3. 20%–30% due to spontaneous mutation with no family history
I. Surveillance and management of established FAP
   1. Genetic tests for at-risk family members of those with >100 adenomas
   2. Once colonic polyps are detected, one needs to do a full colonoscopy to determine extent
   3. Indications for colectomy: >1 cm adenomas, profuse polyposis or adenomas with villous histology and/or high-grade dysplasia
   4. Sparse or <5 mm adenomas: follow endoscopically yearly; schedule colectomy around school schedule (ie, after finishing high school)
   5. Even after colectomy, patients are still at risk for adenomas and adenocarcinomas
   6. After total colectomy, patients still need regular surveillance of ileal pouch
   7. Extracolonic tumors:
      a. Screening EGD with side viewing (for papillary adenomas) and forward viewing scopes when colonic polyps are diagnosed or at 20–25 years of age
      b. Endoscopic removal of duodenal adenomas or those of ampulla of Vater
      c. Biopsy of papilla if appears abnormal or has history of pancreatitis or biliary obstruction
      d. Gastric polyps:  
         1) Biopsy gastric fundic polyps to check for dysplasia
         2) Antral polyps typically adenomas – remove completely endoscopically
      e. Thyroid palpation yearly ± FNAC of nodules
J. Children in FAP families:
   1. If child has a negative gene test in a family with a known genotype for FAP, there is no need for colonoscopy
   2. If gene test is positive, do annual sigmoidoscopy starting at age 10–14 years of age until rectal adenomas are confirmed or negative until 35–40 years of age

K. Surveillance in Attenuated FAP (AFAP)
   1. Annual colonoscopy starting 20–25 years of age for gene carriers or those in at-risk family with inconclusive gene tests
   2. Patient with AFAP needs colonoscopy with yearly surveillance if all polyps can be removed endoscopically
   3. If there are too many polyps to remove endoscopically, consider prophylactic colectomy

L. Prognosis
   1. Currently, most deaths from FAP are due to extracolonic disease because of increased use of prophylactic colectomy

M. Desmoid disease
   1. Locally aggressive, non-metastasizing myofibroblastic lesions
   2. Majority located in the abdominal wall or intraabdominally
   3. Risk factors: APC gene mutation site, mutation of CTNNBI, germline mutations, abdominal surgery, family history of desmoids, estrogens
   4. Within peritoneal cavity most common, and may cause small bowel, ureteral or vascular obstruction
   5. Detected by CT and MRI
   6. May progress rapidly or resolve spontaneously
   7. Surgical resection associated with high morbidity and mortality and stimulates further growth
   8. Nonsurgical treatment: NSAIDS and/or antiestrogens, chemotherapy, radiotherapy

N. Chemoprevention with NSAIDs
   1. May reduce the number of polyps and slow the increase in number, but degree of prevention of development of colorectal carcinoma is unknown
   2. Sulindac:
      a. Causes incomplete regression of colorectal adenomas
   3. Celecoxib:
      a. Decreases number of colorectal polyps
      b. Decreases extent of duodenal polyposis
   4. Use of NSAIDs: to slow development of adenomas prior to colectomy and to delay new polyp formation in the rectum after subtotal colectomy

VII. Gardner Syndrome
   A. Variant of FAP
   B. Colonic adenomas, upper GI polyps
   C. Extraintestinal manifestations:
      1. Osteomas
      2. Epidermal inclusion cysts, other benign skin tumors
      3. Desmoid tumors of abdominal wall/abdomen
      4. Fibrosis of mesentery
      5. Dental abnormalities
      6. Carcinoma of periampullary duodenum
      7. Carcinoma of thyroid

VIII. Turcot Syndrome
   A. Primary brain tumor (often glioblastoma multiforme) and multiple colorectal adenomas
   B. Occurs in adolescence
   C. Management of polyps similar to FAP

IX. MYH-associated Polyposis
   A. Autosomal-recessive inheritance
   B. Colorectal polyposis resembles FAP or attenuated FAP

X. Mixed Polyposis Syndromes
   A. Dominant genetic syndrome
   B. Mutation at 15q13-14 (CRAC-1) or in BMPR1A gene
   C. Colorectal polyps of mixed histology (hyperplastic, serrated adenomas, atypical juvenile)
   D. Progresses to colorectal carcinoma
XI. Inflammatory Polyps (Pseudopolyps)
   A. Occur in areas of longstanding inflammatory colitis
   B. Colon predominantly, rarely in rectum
   C. No malignant potential

Recommended Reading

Burt RW. Gastric fundic polyps. *Gastroenterology* 2003; 125:43-49


Pseudo-obstruction is a severe disabling disease characterized by repetitive episodes or continuous symptoms and signs of intestinal obstruction, including radiographic documentation of dilated intestines and air-fluid levels, in the absence of fixed lesion which is occluding the lumen of the intestine. It can be congenital, acquired, primary, or secondary.

I. Presentation
A. Symptoms are variable and dependent on the length and location of involved bowel. Based on a pediatric patient cohort with chronic intestinal pseudo-obstruction, the most common symptoms included:
   1. Abdominal distention (98%)
   2. Nausea/vomiting/feeding intolerance (91%)
   3. Constipation (77%)
   4. Failure to thrive (62%)
   5. Abdominal pain (58%)
   6. Sepsis (34%)
   7. Diarrhea (31%)
B. Prenatal
   1. Ultrasound may show dilated bowel loops and/or bladder, with or without polyhydramnios
C. Neonatal
   1. Most common symptoms include delayed meconium passage, bilious vomiting, abdominal distention, and constipation
   2. Dilation and slow intestinal transit may lead to bacterial overgrowth and resulting malabsorption, diarrhea, and malnutrition
   3. 75% of congenital pseudo-obstruction patients present within the first year of life, and the majority (67%) present within the first month of life
D. Syndromic
   1. Including megacystis, microcolon, intestinal hypoperistalsis syndrome, mitochondrial disorders, or autoimmune disorders
E. 25% of patients have associated intestinal disorders (malrotation, gastroschisis, and atresias)
F. Urinary problems are commonly found in cases of myopathy

II. Diagnosis
A. Based on clinical symptoms
B. Motility testing can confirm the diagnosis
C. Radiography and laboratory studies are primarily used to rule out other potential causes
D. Abdominal radiographs may show dilated loops of small bowel and air-fluid levels
E. Upper GI contrast studies (with water-soluble contrast) show dilated loops of bowel and slow transit
F. Radiopaque markers may help in identifying an area of functional obstruction
G. Antroduodenal and colonic manometry can be used to distinguish myopathy from neuropathy or mixed patterns
   1. Myopathy: contraction amplitude is reduced by spatial and temporal relationship is normal
   2. Neuropathy: normal contraction amplitudes and abnormal spatial/temporal relationships
   3. May be difficult to interpret with dilated colon
H. Manometry can help to determine areas of preserved motility, which can also help in determining therapy
I. Pathology including light microscopy, electron microscopy, immunohistochemistry and enzyme histochemistry, but it is not consistently used, and not recommended in routine cases
III. Management
   A. Treatment is mostly supportive, and should focus on fluid and electrolyte balance, nutrition, and preventing complications
   B. Enteral nutrition is preferred
      1. Low-fat, liquid supplemental diets are tolerated best
      2. If enteral feeds are not tolerated, parenteral nutrition should be used
      3. Frequently, a combination of feeding methods is used
   C. Bacterial overgrowth is frequent, and should be treated aggressively, since it can worsen motility
   D. Avoid medications which slow intestinal motility
      1. Opioids and drugs with anticholinergic properties
   E. Surgery
      1. For IV access
      2. To provide enteral routes for feeding or for decompression
      3. Surgery should be avoided if possible, as adhesions can complicate future evaluations and management
   F. Prokinetics
      1. Cisapride, erythromycin, amoxicillin, metoclopramide, and octreotide have been effective
   G. Pain
      1. Should be managed with non-narcotic agents, including tricyclic antidepressants, gabapentin, SSRIs, and clonidine
      2. Pain can also be managed with behavioral and relaxation therapy
   H. Small intestinal transplantation
      1. Only indicated in TPN-dependent patients with life-threatening complications or no venous access
      2. Survival after transplant may be lower than for other conditions

IV. Complications
   A. High morbidity and mortality can occur
      1. Related to the severity of intestinal abnormalities, concurrent infections from bacterial translocation from the gut, parenteral nutrition-related side effects, line problems, and the need for frequent hospitalizations because of pseudo-obstructive crises

Recommended Reading


