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3

Gastrointestinal Diseases

Ramnik J Xavier, Harry J Thomas

Key features

More common in the tropics

- Duodenal ulcer
- Gastrointestinal infections
- Tuberculosis of the abdomen and intestine
- Malabsorption due to
 - giardiasis, capillariasis, strongyloidiasis
 - tropical sprue
 - chronic calcific pancreatitis
 - malnutrition
 - alpha chain disease
 - hypolactasia
- Intestinal obstruction due to ascariasis
- Intestinal volvulus
- Intussusception

Less common in the tropics

- Gastric ulcer
- Celiac disease
- Mesenteric ischemia
- Diverticulosis
- Inflammatory bowel disease
- Ischemic colitis

PRESENTATIONS

Gastrointestinal diseases are among the most common problems encountered in the tropics. The principal syndromes are diarrhea, abdominal pain, abdominal distension, intestinal obstruction and gastrointestinal bleeding.

DIARRHEA

Diarrheal diseases are a major cause of morbidity and mortality in the tropics and subtropics [1]. Children are most often and most seriously affected, with 1.8 million children under the age of five dying each year due to diarrhea. Dehydration is the main cause of death, whereas malnutrition is the main cause of morbidity.

Etiology and Distribution

Rotavirus is the most common cause of severe diarrhea in infants and young children worldwide. The second most common cause of viral gastroenteritis is norovirus. Among the bacterial agents, enterotoxigenic *Escherichia coli* (ETEC) is the most common pathogen affecting both native residents of and visitors to developing countries. *Salmonella* is a common cause of food poisoning in developed countries;

varying incidences have been reported from countries in the tropics. *Campylobacter* and *Shigella* spp. have a worldwide distribution and are relatively common causes of infectious diarrheal disease in all age groups. *E. coli* O157 causes a dysenteric illness very similar to shigellosis. Cholera remains endemic in many parts of Africa, Asia, and Central and South America.

Transmission and Epidemiology

Infection occurs by the ingestion of organisms in food and water contaminated by feces from a human or animal excreting the organism. This contamination is associated with inadequate public sanitation and low standards of personal hygiene. Defecation near pools and streams that are sources of water for domestic use is common, and simple sewage disposal systems often empty feces into the domestic water supply of the community. Person-to-person spread of infection also occurs. Seafoods such as shellfish, mussels and crabs transmit viruses causing gastroenteritis, *Vibrio cholerae* and *V. parahaemolyticus*. Flies carry bacteria from feces to food, on their mouthparts and legs. Low standards of kitchen hygiene in homes and public eating places also encourage transmission of intestinal infection. Pre-cooked food kept warm for long periods may transmit a number of gut pathogens and contain enterotoxin formed by staphylococci growing in warmed food. Poultry and eggs are important sources of nontyphoidal salmonellae and campylobacter. An important and avoidable source of intestinal infection in infants results from bottle-feeding with powdered milk solution instead of breastfeeding. Unsterile bottles and nipples and contaminated water all contribute to the considerable risk of gut infection.

Pathogenesis

Diarrhea can be defined as an increase in the water content of stools. Physiologically, the cause may be that: (1) the small intestine secretes more fluid than it reabsorbs; (2) solute absorption in the small intestine is impaired so that the osmotic load retains fluid in the gut lumen; (3) the volume of fluid entering the colon exceeds its capacity for water absorption; (4) the water- and electrolyte-reabsorbing capacity of the colon is reduced as a result of enterotoxigenic infection such as cholera; or (5) the water-reabsorbing capacity and motility of the colon are altered by localized or generalized colonic inflammation and ulceration. Infectious agents produce diarrhea by causing one or more of these effects. Enterotoxin-producing bacteria include *V. cholerae*, enterotoxigenic *E. coli*, *Staphylococcus aureus*, and *Shigella* and *Salmonella* spp. Enteroinvasive bacteria include *Shigella*, *Salmonella* and *Campylobacter* spp.

Clinical Manifestations

The onset of symptoms can vary from a few hours after ingesting food containing preformed toxins, to several days after ingesting bacterial pathogens, to two or more weeks in parasitic infections. Acute infectious diarrhea can be classified into watery diarrhea and bloody diarrhea (dysentery) (Box 3.1). Noninfectious causes of acute diarrhea are less significant in the tropics, but causes that should be considered include toxin-induced (e.g. organophosphate poisoning), medication-related and ischemic colitis. The most important physical signs to be

BOX 3.1 Causes of Acute Infectious Diarrhea

- Intoxication
 - *Staphylococcus aureus*
 - *Clostridium perfringens*
 - *Bacillus cereus*
 - Botulism (uncommon)
- Infection
 - Viruses
 - Rotaviruses
 - Noroviruses
 - Enteric adenoviruses
 - Coronaviruses
 - Bacteria
 - *Escherichia coli* (enterotoxigenic, enteropathogenic, enteroadherent, enterohemorrhagic, enteroinvasive)
 - *Campylobacter* spp.
 - *Salmonella* spp.
 - *Shigella* spp.
 - *Vibrio cholerae*, *V. parahaemolyticus*
 - *Yersinia enterocolitica*, *Y. pseudotuberculosis*
 - *Clostridium difficile*
 - *Aeromonas* spp.
 - *Plesiomonas* spp.
 - Protozoa
 - *Cryptosporidium hominis/parvum*
 - *Giardia lamblia*
 - *Entamoeba histolytica*
 - *Cyclospora cayetanensis*

BOX 3.2 Dehydration Assessment

Mild dehydration

- Decreased urine output

Moderate dehydration (≥5% volume loss)

- Irritability
- Delayed capillary refill time
- Tachycardia
- Orthostatic hypotension
- Deep respirations
- Decreased skin turgor
- Dry mucous membranes
- Sunken eyes
- Sunken fontanelle (infants)

Severe dehydration (≥10% volume loss)

- Decreased consciousness
- Hypotension
- Deep respirations with an increase in respiratory rate
- Cool extremities
- Peripheral cyanosis

elicited concern the assessment of hydration (Box 3.2); the patient should be weighed at first presentation, as weight gain or loss can be a valuable guide to the effectiveness of rehydration.

The rapid onset of nausea, vomiting and diarrhea after food consumption is most often due to the ingestion of a preformed toxin produced by *Staphylococcus aureus*, *Bacillus cereus* or *Clostridium perfringens*.

Large-volume watery diarrhea indicates a small bowel etiology, e.g. due to *V. cholerae*, enterotoxigenic *E. coli* and rotavirus infections. Toxin-induced secretory diarrhea continues independent of food intake. Malabsorption of carbohydrate in the small intestine leads to fermentation of unabsorbed substrates by colonic bacteria; this may cause bloating, the passage of much rectal gas and frothy stools, which are all characteristic of giardiasis. Cryptosporidiosis can involve both small and large bowel, causing short-lived and self-limiting diarrhea; however, the infection can be prolonged in patients with impaired immune responses. *Cyclospora cayetanensis* can also cause acute and more chronic diarrhea with abnormalities of intestinal absorption.

Frequent bowel movements with small volumes of stool and the passage of blood and mucus suggest colonic infection. Causes of bloody diarrhea (dysentery) include invasive bacteria such as *Campylobacter* spp., enterohemorrhagic *E. coli*, and *Salmonella*, *Shigella* and *Yersinia* spp.; nonbacterial causes include *Entamoeba histolytica* (amebic dysentery) and *Balantidium coli*, which is spread by close contact with pigs. Colicky abdominal pain is common in many gut infections and is especially severe in campylobacteriosis and yersiniosis, mimicking acute appendicitis. Fever, chills and generalized myalgia are usually associated with infection by invasive organisms; these patients appear ill and have generalized abdominal tenderness.

Antibiotic-Associated Colitis

Antibiotics may cause diarrhea through a number of mechanisms, a common cause being pseudomembranous colitis due to infection with cytotoxigenic *Clostridium difficile*. Originally described in patients who had received clindamycin, *C. difficile* infection has since been found to complicate treatment with a number of antibiotic classes, especially fluoroquinolones. The burden of *C. difficile* infection in North America and Europe has greatly increased since the emergence of a hypervirulent strain in 2003; the incidence in other parts of the world is not yet fully known, but appears to be increasing. Patients develop fever, diarrhea and marked leukocytosis. Sigmoidoscopy reveals an inflamed mucosa with pseudomembranous plaques adhering to the mucosa. Management consists of discontinuing unnecessary antibiotics, treating with metronidazole or oral vancomycin, and, for life-threatening cases, colectomy.

Antibiotic-associated hemorrhagic colitis, a form of antibiotic-associated colitis in which *C. difficile* is absent, is associated with penicillin treatment and has been found to be caused by *Klebsiella oxytoca* [2].

Chronic Diarrhea

Most acute infections of the gut have resolved or are resolving within 2 weeks. The most common causes of chronic diarrhea are repeated infection and persistent infection. Persistent infection is commonly due to parasitic infections, including those caused by protozoa (*Giardia lamblia*, *Entamoeba histolytica*, *Isospora belli*, *Cyclospora cayetanensis*, *Cryptosporidium hominis/parvum*, microsporidia) and helminths (*Strongyloides stercoralis*, *Capillaria philippinensis*) (Box 3.3) [3]. Patients have frequent, pale, offensive stools, which are characteristic of malabsorption [4]. Noninfectious causes of mucosal malabsorption include celiac disease, tropical sprue, Crohn's disease, and neoplasms of the small bowel. Malabsorption may also be caused by intraluminal maldigestion, which occurs in pancreatic exocrine insufficiency and bacterial overgrowth of the small intestine. Other causes of chronic diarrhea include medication effects, endocrinopathies (particularly hyperthyroidism and diabetes mellitus) and hormone-producing neoplasms.

Complications

The leading cause of death in patients with acute diarrhea is dehydration, which requires prompt fluid and electrolyte replacement. The nutritional state of children often deteriorates because of anorexia, nutrient malabsorption, and the practice of not feeding children who have diarrhea. Hypolactasia is a sequela of many gut infections and may cause persistent diarrhea. Dysentery can be associated with severe local complications such as hemorrhage, toxic megacolon and bowel

BOX 3.3 Causes of Persistent/Chronic Diarrhea

- Infection
 - Parasitic
 - *Giardia lamblia*
 - *Entamoeba histolytica*
 - *Isospora belli*
 - *Cyclospora cayetanensis*
 - *Cryptosporidium hominis/parvum* (immunodeficient)
 - Microsporidia
 - *Strongyloides stercoralis*
 - *Capillaria philippinensis*
 - Mycobacterial
 - *Mycobacterium avium-intracellulare*
 - *Mycobacterium tuberculosis*
- Malabsorption
- AIDS enteropathy
- Inflammatory bowel disease

perforation. In addition, invasive organisms can result in systemic manifestations including hemolytic uremic syndrome (which can complicate *Shigella dysenteriae* and *E. coli* O157 infections), reactive arthritis (following shigellosis, salmonellosis, campylobacteriosis, yersiniosis, and *Clostridium difficile* infection) and Guillain-Barré syndrome (campylobacteriosis).

Diagnosis

The range of laboratory tests and expertise needed to make a specific microbiologic diagnosis in most patients with diarrhea requires facilities not often available in the tropics. Some simple tests can be useful in most circumstances. It is important to examine the stool sample for blood. A smear of fluid stools should always be examined by direct microscopy for trophozoites of *Entamoeba histolytica* and trophozoites and cysts of *Giardia lamblia*. The presence of any cellular exudate in the smear should also be noted: the presence of polymorphonuclear leukocytes suggests infection with enteroinvasive bacteria, whereas a predominance of red cells may suggest amebic dysentery. Culture of stool samples or rectal swabs gives the bacteriologic diagnosis. A proctosigmoidoscopy should be considered in patients with persistent dysentery: diffuse inflammation, ulceration and bleeding of the rectal mucosa are the usual appearances; ulcerated or bleeding areas of mucosa should be scraped and the material examined immediately for amebic trophozoites.

Treatment and Prognosis

The mortality from dehydrating diarrheal diseases will decline if measures to correct and maintain hydration are started as early as possible.

Treatment of Dehydration

After assessing the severity of dehydration, the first goal of therapy is to replace water and electrolyte deficits. If dehydration is severe, patients should receive an intravenous bolus of isotonic fluid (either saline or lactated Ringers) in order to prevent progression to hypovolemic shock. Oral rehydration therapy has markedly reduced mortality from dehydrating diarrheal diseases and is the treatment of choice in children with mild to moderate dehydration. Community health providers can distribute oral rehydration salts (ORS) and teach others how to make and give the solution. The formulation recommended by the World Health Organization (WHO) contains the following: a sugar such as glucose, which facilitates the absorption of sodium and water in the small intestine; sodium and potassium, to replace gastrointestinal losses of these electrolytes; and citrate or bicarbonate,

which helps correct the acidosis that develops as a result of diarrhea. ORS solution is absorbed in the small bowel even in the presence of severe diarrhea. Use of a new reduced osmolality formulation (containing 75 mEq/L of glucose and 75 mEq/L of sodium) is currently recommended.

Antimicrobial Agents

Antimicrobials usually have a limited or secondary role in the treatment of patients with secretory acute watery diarrhea. Empiric treatment, taking into account WHO protocols and local antimicrobial resistance patterns, should be given to patients who have symptoms and signs of infection with enteroinvasive organisms – fever, abdominal pain, toxicity, tenesmus, and frequent stools containing mucus and blood. Fluoroquinolones are effective against the enteroinvasive bacteria, including *Salmonella* and *Shigella* spp., though increasing resistance has been observed. Macrolides are the drug of choice for *Campylobacter* spp. infection. Giardiasis and amebiasis will require specific treatment with metronidazole or tinidazole.

Additional Therapy

Zinc supplementation reduces the duration and severity of diarrhea and mortality in children with intestinal infection [5]; a similar effect of vitamin A has not been shown. The adverse effects of diarrhea on nutrition can be lessened by continuing feeding and increasing breast-feeding in infants. Patients should be fed as soon as they want to eat, with energy-rich, low-osmolality foods given in frequent, small-volume meals, and there should be increased feeding after the diarrheal episode. Intestinal sedatives should be avoided, as the reduced frequency of bowel movements causes fluid stagnation in the gut lumen, encouraging proliferation of organisms and keeping organisms and their toxins in contact with the mucosa.

Prevention and Control

Providing clean drinking water and proper sewage disposal reduces the incidence of gut infections. Tube wells are one means of providing clean water. The construction of acceptable latrines will help to break the cycle of fecal–oral transmission of gut pathogens. Health education regarding the importance of good sanitary practices and breast-feeding should be given by trained members of the community. Although such measures will be effective in the long term, a short-term decrease in the incidence of diarrheal diseases requires more immediate measures such as vaccination. Rotavirus vaccination has been shown to be effective in children in both developed and developing countries. An oral cholera vaccine was effective in preventing cases during an outbreak in Mozambique in 2004 [6]. However, it has not been widely implemented, owing in part to its short duration of protection and issues of availability.

Control of epidemics of gastrointestinal infection includes finding the source(s) of infection, detection of cases, and treatment, as necessary, to prevent transmission of the disease. Handwashing prevents transmission of enteric infection, as does fly control.

Traveler's Diarrhea

People from developed countries who visit the tropics are at risk for developing traveler's diarrhea [7]. The risk appears to be increased in younger individuals, those taking proton pump inhibitors, and people who fail to adhere to personal hygiene precautions. The most common pathogens are enterotoxigenic *E. coli* and enteroaggregative *E. coli*; other identified bacteria include *Campylobacter*, *Shigella*, *Salmonella*, *Aeromonas*, *Plesiomonas* and *Vibrio* spp. [8,9]. Noroviruses and rotaviruses are the most common viral agents of traveler's diarrhea, and *Giardia lamblia*, *Entamoeba histolytica* and *Cryptosporidium hominis/parvum* the most common protozoan pathogens.

Typhoid and hepatitis A vaccines should be offered to people traveling to endemic areas. The risk of traveler's diarrhea may be lessened by the administration of bismuth subsalicylate or probiotics. Antibiotic prophylaxis has been shown to be effective in the prevention of traveler's diarrhea, but is not advised for the general population due to the

potential adverse effects of antibiotics and the risk of antibiotic resistance.

In people who develop traveler's diarrhea, antibiotic therapy reduces the duration of symptoms, even in those in whom a pathogen cannot be identified. As the prevalence of fluoroquinolone-resistant *Campylobacter* spp. is increasing, azithromycin is emerging as an effective alternative in the treatment of traveler's diarrhea. Rifaximin is another option, though it is not recommended in patients with invasive disease. In addition to a short course of antibiotic therapy, patients should be advised regarding hydration and diet, and those without evidence of invasive disease may benefit from an antimotility agent.

ABDOMINAL PAIN

Upper abdominal pain is commonly due to peptic ulcer disease, and worsening of the symptoms may herald a complication such as perforation or penetration. The differential diagnosis of upper abdominal symptoms with ulceration in the stomach or duodenum includes infections (e.g. tuberculosis, *Mycobacterium avium intracellulare*, cytomegalovirus, herpes simplex virus), neoplasms (either primary tumor or metastatic disease) and infiltrative diseases. Acute pancreatitis is another cause of acute upper abdominal pain; gallstones and alcohol are the most common causes worldwide, though infectious etiologies are important in the immunocompromised. Chronic pancreatitis is characterized by abdominal pain, steatorrhea and diabetes mellitus. Alcohol abuse accounts for the majority of cases worldwide; however, in several parts of the tropics, the most common cause of chronic pancreatitis is tropical calcific pancreatitis, a condition of unknown etiology that commonly affects children. Pancreatic calcifications may be seen on plain film of the abdomen, and ductal dilatation may be evident on ultrasonography or computed tomography.

Right upper quadrant pain may be seen in biliary colic, acute cholecystitis, acute cholangitis, acute hepatitis, and liver abscess (see hepatobiliary chapter). Left upper quadrant pain may be caused by disorders of the spleen such as splenomegaly or splenic abscess or infarction. In evaluating the patient with upper abdominal pain, it is important to consider supradiaphragmatic causes such as pneumonia and myocardial infarction.

A number of parasitic worms may cause nonspecific gastrointestinal symptoms including epigastric pain. In addition, parasitic infections of the biliary tract may lead to acute pancreatitis, as exemplified by adult *Ascaris lumbricoides* worms, which can migrate from the jejunum and invade the papilla, obstructing the pancreatic and bile ducts.

Right lower quadrant pain is commonly due to acute appendicitis; not uncommonly, however, infection with *Yersinia* or *Campylobacter* can cause severe pain that is misdiagnosed as appendicitis. In females with acute lower abdominal pain, it is important to consider ectopic pregnancy, pelvic inflammatory disease, and adnexal pathologies.

Colicky abdominal pain is one of the cardinal features of bowel obstruction. It may also be seen in intussusception in children. Generalized abdominal pain and tenderness may be caused by peritonitis, which can occur as a result of perforated peptic ulcer, ileal perforation in typhoid fever, colonic perforation in amebic colitis, or rupture of a hydatid cyst. Severe abdominal pain with minimal or no tenderness is seen in acute mesenteric ischemia. In addition to considering such surgical emergencies, it is important to consider "medical" causes of abdominal pain. Patients with sickle cell disease may have acute painful episodes due to vaso-occlusion that is difficult to distinguish from other causes of an acute abdomen. Abdominal pain is a common symptom in several infectious diseases, most notably malaria.

ABDOMINAL DISTENSION

Patients with ascites may complain of abdominal pain, early satiety or dyspnea due to splinting of the diaphragm. Analysis of ascitic fluid is helpful in determining the cause of ascites: (1) to determine whether the fluid is infected (spontaneous bacterial peritonitis is defined as a polymorphonuclear leukocyte count over 250 cells/mL with a positive bacterial culture); and (2) to determine whether there

is underlying portal hypertension (indicated by a serum-ascites albumin gradient of 1.1 g/dL or greater). Cirrhosis and tuberculous peritonitis are among the most common causes. Chronic hepatic schistosomiasis is a common cause of ascites in endemic areas. Malignancy can cause ascites through a number of mechanisms; while ascitic fluid cytology may be positive in peritoneal carcinomatosis, it will be negative if the ascites is due to portal hypertension from massive liver metastases. In chylous ascites, the ascitic fluid appears cloudy due to the high levels of triglycerides; the most common causes in developing countries are infections leading to lymphatic obstruction, such as tuberculosis and filariasis. Cardiac ascites may result from tricuspid regurgitation, constrictive pericarditis, or any cause of right-sided heart failure. Spontaneous bacterial peritonitis may complicate ascites due to cirrhosis; however, it is very rare in non-cirrhotic ascites, as these patients have a higher concentration of ascitic fluid opsonins. The classic presentation is with fever and abdominal pain and tenderness, but it may be asymptomatic or present with encephalopathy or renal failure.

A massive ovarian cyst can present with abdominal distension, but the central location of the swelling, presence of a fluid thrill, and absence of shifting dullness help to distinguish this from ascites.

Abdominal distension may be due to gas, either within or outside the bowel lumen. Extraluminal gas is seen in bowel perforation, which is a surgical emergency. Gaseous distension of the bowel may be due to mechanical obstruction or motility disorder. Bloating is a common symptom in lactose malabsorption, which is commonplace among Africans and Asians after childhood, and in irritable bowel syndrome.

INTESTINAL OBSTRUCTION

The cardinal features are colicky abdominal pain, vomiting, constipation and abdominal distension. A bolus of worms can cause intraluminal obstruction in children with heavy *Ascaris lumbricoides* infestation; it may also serve as a lead point for intussusception and volvulus. Colorectal carcinoma is increasingly recognized in the tropics, but may not be evident until presentation with obstruction of the large bowel. The differential diagnosis includes inflammatory masses that can lead to intramural obstruction, such as: ileocecal tuberculosis, histoplasmosis, actinomycosis, amebiasis, schistosomiasis and angiostrongyliasis. Extramural obstruction is most commonly due to incarcerated hernia. Umbilical hernias are more common in African children, but usually the defects close spontaneously. Symptoms and signs of small bowel obstruction may also be seen in paralytic ileus, in which there is bowel dilatation without mechanical obstruction. This is a common complication of abdominal surgery, but may also occur in peritonitis or after trauma. Plain film or computed tomography of the abdomen in paralytic ileus shows gas in the colon and rectum, helping to differentiate it from small bowel obstruction in which the colon is decompressed. Treatment is supportive, consisting of fluid resuscitation, correction of electrolyte abnormalities (especially hypokalemia) and discontinuation of anti-kinetic drugs. Another motility disorder that may be misdiagnosed as mechanical obstruction is chronic intestinal pseudo-obstruction, which may occur in Chagas disease [10]. Here, gross dilation of the colon (megacolon), most commonly involving the sigmoid colon, causes constipation; it may be complicated by toxic megacolon or volvulus.

GASTROINTESTINAL BLEEDING

Upper gastrointestinal bleeding, defined as bleeding emanating from a source proximal to the ligament of Treitz, presents with hematemesis and/or melena. It is most commonly due to bleeding peptic ulcer. In areas with a high prevalence of cirrhosis, bleeding from esophageal and gastric varices is common. Mallory-Weiss tears are mucosal lacerations at the gastroesophageal junction that are most commonly associated with repeated retching. Gastric and duodenal neoplasms can present with overt gastrointestinal bleeding, though occult blood loss is more common. Unusual causes of upper gastrointestinal bleeding include vascular abnormalities.

Hematochezia is most often due to colorectal sources but may be the first sign of a brisk upper gastrointestinal hemorrhage. Patients with infectious colitis present with bleeding in association with diarrhea, abdominal pain and systemic upset. Gastrointestinal bleeding is a common complication of typhoid fever. Many causes of lower gastrointestinal bleeding that are common in the West – colonic diverticular bleeding, ischemic colitis, colorectal cancer and hemorrhoids – are unusual in the tropics due to epidemiologic differences. Lymphoma and Kaposi sarcoma may affect any part of the gastrointestinal tract and are common causes of gastrointestinal bleeding in patients with AIDS.

The initial management of patients with acute gastrointestinal bleeding consists of fluid resuscitation and, if coagulopathy or thrombocytopenia is present, transfusion of blood products. Once patients are stabilized, endoscopy should be performed in order to diagnose and treat the source of bleeding. Cirrhotic patients with upper gastrointestinal bleeding are at risk for bacterial infections including spontaneous bacterial peritonitis; broad-spectrum antibiotics may reduce this risk.

ANATOMIC DIFFERENTIALS

MOUTH

Dental Caries

Dental caries is a chronic disease in which the composition of the oral flora is altered as a result of chronic consumption of high-sugar substances. This leads to demineralization of the enamel, eventually causing a dental cavity. Dental caries is a major oral health problem worldwide, and the incidence is increasing in developing countries as people engage in Western dietary practices [11]. Three factors are important in the prevention of caries: dietary counseling, oral hygiene, and fluoride supplementation.

Oral Cancer

Oral cancer should be suspected in any patient with a nonhealing ulcer or mass in the mouth. As with all squamous cell carcinomas of the head and neck, the major risk factors are tobacco and alcohol use. Additional risk factors include viral infection (Epstein-Barr virus, which is strongly associated with nasopharyngeal carcinoma, human papillomavirus and HIV) and betel-nut chewing, which is widespread in South and Southeast Asia.

Candidiasis

Oral infection with *Candida* (“thrush”) is usually characterized by white plaques on the oral mucosa, though there is also an atrophic form that presents as erythema without plaques. It is a common finding in patients with HIV infection; other risk factors include treatment with antibiotics or steroids (both oral and inhaled). Treatment consists of a topical antifungal agent or, in patients with more severe disease, systemic therapy.

Herpes Simplex Virus Infection

Primary infection of the oral cavity with herpes simplex virus causes gingivostomatitis and pharyngitis. The lesions can be vesicular or ulcerative and may be associated with fever and cervical lymphadenopathy. Reactivation of the virus leads to vesicular lesions of the oral mucosa (“cold sores”). Treatment should be directed toward providing symptomatic relief; antiviral therapy may be helpful if primary infection is detected early or for patients with recurrent infection who can identify a characteristic precipitating factor or prodrome.

Cancrum Oris (Noma)

This is a gangrenous, polymicrobial infection affecting the orofacial tissues [12]. It starts as a gingival ulceration, which, if left untreated, spreads rapidly through the soft and hard tissues of the mouth and face, breaching normal anatomic barriers and resulting in gross

deformity. It is thought to occur after fecal–oral transmission in young children who are at risk due to a complex interplay between infection, malnutrition and immunocompromise – a combination that is common in impoverished areas of Africa, Asia and Latin America. The acute stage may present with unilateral facial pain and swelling, halitosis, oral discharge and systemic upset; management consists of broad-spectrum antibiotics and local wound care together with treatment of associated diseases and nutritional deficiencies. However, most patients are not brought to medical attention until the infection is well established – characterized by a necrotic center with a well-demarcated perimeter – at which time reconstructive surgery is required.

ESOPHAGUS

Esophagitis

The main presenting features are odynophagia, dysphagia and retrosternal chest pain. While noninfectious conditions such as gastroesophageal reflux disease and pill esophagitis are the most common causes in immunocompetent hosts, infections of the esophagus are common in the immunocompromised. In patients with HIV infection, the most common cause is esophageal candidiasis. While the presence of oropharyngeal candidiasis can be a clue to esophageal infection, its absence does not rule it out. Diagnosis can be made by endoscopy, which reveals white plaques on the esophageal mucosa; biopsy reveals the presence of budding yeasts. An alternative strategy is to undertake a therapeutic trial of a systemic antifungal agent; if the symptoms do not resolve within days, then further investigation is warranted. Cytomegalovirus esophagitis causes similar symptoms, but endoscopy reveals ulcerative lesions. Ulcers are also seen in herpes simplex virus esophagitis, but they tend to have heaped-up borders as opposed to the more shallow lesions of cytomegalovirus; there may or may not be associated oropharyngeal lesions. It is important to note that a number of patients with HIV infection presenting with esophagitis may have simultaneous infection with more than one agent, whereas others will have no infection identified. The latter condition, named idiopathic esophageal ulcer, may respond to steroids.

Caustic Esophageal Injury

Caustic injuries to the esophagus may result from ingestion of acid or alkali. The main complaint is pain, and there may be signs of complications such as perforation, mediastinitis or peritonitis. Attempts at inducing emesis or neutralizing the ingested substance must be avoided, lest the injury be aggravated. Endoscopy may be helpful for risk stratification and guiding further management. Late complications include esophageal strictures, which cause dysphagia and necessitate dilation, and squamous cell carcinoma.

Esophageal Varices

Esophageal varices are relatively common in the tropics. The causes of portal hypertension can be classified as pre-hepatic, hepatic and post-hepatic. Pre-hepatic causes include the tropical splenomegaly syndrome and portal or splenic vein thrombosis. Hepatic causes may be classified as pre-sinusoidal, sinusoidal and post-sinusoidal, exemplified by schistosomiasis, cirrhosis and veno-occlusive disease, respectively. Budd–Chiari syndrome and cardiac causes (restrictive cardiomyopathy, congestive heart failure) are post-hepatic causes. Variceal bleeding carries a high mortality rate worldwide. Initial management consists of restoration of the circulating volume, with caution to avoid over-transfusion, the use of agents to reduce portal pressure (e.g. terlipressin or octreotide), and antibiotic prophylaxis. After stabilization, endoscopic variceal ligation is the ideal approach. For patients with refractory bleeding, balloon tamponade can be a temporizing measure while awaiting portosystemic shunting.

Megaesophagus

Marked dilation of the esophagus is the most common gastrointestinal manifestation of chronic Chagas disease and occurs due to a loss of neurons in the enteric nervous system. Dysphagia is the most

prominent symptom, but patients may also complain of odynophagia and regurgitation; aspiration is a common complication. The condition cannot be reversed by antitrypanosomal agents, but symptomatic relief can be achieved through balloon dilations of the lower esophageal sphincter or through surgery.

Esophageal Cancer

Squamous cell carcinoma usually arises in the mid portion of the esophagus in patients with a history of tobacco and alcohol use or preexisting esophageal diseases. In contrast, adenocarcinoma affects the lower third of the esophagus in patients with Barrett's esophagus. Both types of cancer have a similar clinical presentation, with dysphagia and weight loss being the most common symptoms. Diagnosis is made at endoscopy with biopsy. Over half of patients present with incurable disease.

STOMACH

A variety of gastroduodenal pathologies are related to infection with *Helicobacter pylori*. This Gram-negative, spiral-shaped bacterium adheres to the gastric epithelium and is able to survive in the acidic environment of the stomach due to a urease that converts urea into ammonia, which increases the pH of the immediate vicinity. It is spread by person-to-person (likely fecal-oral) transmission and is usually acquired at an earlier age in developing countries than in developed countries. It is found worldwide, though the prevalence is decreasing with improved sanitation and hygiene. Infection causes acute gastritis, which leads to chronic gastritis. Peptic ulcer disease is a common complication, while a small minority of patients with *H. pylori* infection go on to develop gastric adenocarcinoma or MALT (mucosa-associated lymphoid tissue) lymphoma.

Gastritis

Both inflammation of the stomach (gastritis) and damage to the gastric epithelium with minimal or no inflammation (gastropathy) may cause epigastric pain and nausea and vomiting, but they may be asymptomatic. The most common infectious cause of gastritis is *H. pylori* infection. A number of agents cause gastropathy, the most common being nonsteroidal anti-inflammatory drugs (NSAIDs), alcohol, and bile reflux.

Peptic Ulcer Disease

Population-based endoscopy studies have shown that the prevalence of peptic ulcer disease is almost 10% in the East, twice as high as in Western countries [13]. Historically, duodenal ulcers were more common than gastric ulcers in the tropics – due to the higher prevalence of *H. pylori* and lower usage of NSAIDs – but this ratio is changing with time. While patients with peptic ulcer may be asymptomatic, the usual symptom is epigastric discomfort or pain, which may radiate to the back. The four major complications are hemorrhage, penetration, perforation, and gastric outlet obstruction. Bleeding peptic ulcer is a common cause of acute upper gastrointestinal hemorrhage; management consists of hemodynamic resuscitation, endoscopic therapy, and, for refractory cases, surgery. Treatment with a proton pump inhibitor reduces the risk of rebleeding after endoscopic hemostasis. Penetration of the ulcer through the bowel wall causes intense pain; further erosion results in bowel perforation, causing peritonitis and necessitating emergency laparotomy. Gastric outlet obstruction is usually a complication of a longstanding ulcer, due to chronic inflammation and fibrosis. A test for *H. pylori* should be performed in all patients with peptic ulceration; this may be performed either at endoscopy or noninvasively. If positive, eradication of *H. pylori* should be undertaken; this should consist of a proton pump inhibitor and two antibiotics, taking into account local resistance patterns. Unlike duodenal ulcers, which are very rarely neoplastic, gastric ulcers may be malignant in etiology, so follow-up endoscopy is necessary to ensure resolution.

Gastric Neoplasms

Gastric cancer is the second most common cause of death from cancer worldwide. Uncommon in developed countries, the incidence is highest in East Asia and parts of South America. Part of the geographic variation may be due to dietary factors and prevalence of *H. pylori*. The most common presenting symptoms are weight loss and abdominal pain; other features include dysphagia, early satiety, and iron deficiency anemia due to chronic blood loss. The majority of patients have metastatic disease at the time of presentation, precluding curative resection.

Over 90% of gastric cancers are adenocarcinomas; gastric MALT lymphomas make up a minority, but are important, as early lesions are curable with *H. pylori* eradication therapy alone. Nonresponsive or recurrent disease requires chemotherapy.

SMALL BOWEL

A wide variety of disease processes give rise to similar histologic abnormalities in the mucosa of the small intestine, resulting in predictable clinical manifestations. The first event is infiltration of lymphocytes into the epithelium, resulting in an intraepithelial lymphocytosis. Next, there is increased crypt cell proliferation, resulting in crypt hyperplasia. Then, loss of villous cells leads to increasing degrees of villous atrophy, eventually leading to a flat mucosa. As a consequence of mucosal malabsorption, patients present with diarrhea, steatorrhea and weight loss. Laboratory studies may be helpful in defining the extent of the malabsorption syndrome. Anemia may result from deficiencies of iron, folate and/or vitamin B12 – the latter implying that the mucosal damage extends to involve the terminal ileum. Prolongation of the prothrombin time may be due to a deficiency of vitamin K (one of the fat-soluble vitamins, along with A, D and E), which occurs in fat malabsorption. Hypophosphatemia, hypocalcemia and an elevated alkaline phosphatase are seen in vitamin D deficiency, which may cause osteomalacia or osteoporosis. Conditions that cause these histologic abnormalities and present with these clinical and laboratory features include parasitic infections, celiac disease, tropical sprue, bacterial overgrowth and Crohn's disease (Box 3.4). Similar clinical manifestations may be seen in other disorders with specific pathologic findings, such as intestinal lymphoma and amyloidosis. The general principles of treating disorders of the small intestinal mucosa include treating the underlying disease and correcting any nutrient deficiencies that may be present. In addition, a lactose-free, low-fat diet may be beneficial.

Tropical Sprue

Abnormalities of the small intestinal mucosa, resulting in increased intestinal permeability and decreased absorption, have been described in both residents of and visitors to certain tropical and subtropical

BOX 3.4 Causes of Malabsorption

- Infections
- Celiac disease
- Tropical sprue
- Bacterial overgrowth
- Crohn's disease
- Malignancies
 - Immunoproliferative small intestinal disease
 - Intestinal lymphoma
- Hypolactasia
- Pancreatitis
 - Alcoholic pancreatitis
 - Chronic calcific pancreatitis

countries. Various referred to as tropical sprue or tropical enteropathy, the disorder is characterized by a chronic malabsorption syndrome, either following an episode of acute infectious diarrhea or developing more insidiously; it has even been reported to develop years after leaving an endemic area. Its incidence appears to be decreasing, mainly as a result of the increasing recognition of nontropical sprue, or celiac disease, and perhaps also due to the increasing use of antibiotics for patients with acute diarrheal diseases. It occurs in the Indian subcontinent, Southeast Asia and some parts of the Caribbean; however, it is not endemic in all tropical areas, being notably rare or absent in Africa and other parts of the Caribbean such as Jamaica. There is considerable heterogeneity in disease presentation among these areas, suggesting that tropical sprue may represent a spectrum of related disorders. The etiology is unknown, but infectious etiologies are considered likely given the epidemiology of the disease and its response to antibiotics; although a number of infectious agents have been implicated, there has been little consistency between studies. In addition, folate deficiency has been implicated in the etiology of tropical sprue, given the prevalence of folate deficiency in these patients and the histologic improvement observed upon folic acid repletion; this and other theories – for example, implicating malnutrition or excess T-cell activity – are flawed due to the inability to separate cause from effect. The clinical, laboratory and endoscopic features of tropical sprue are largely similar to those of celiac disease. While the mucosal lesion can be patchy in both conditions, the villous atrophy in tropical sprue tends to be less severe – with a flat mucosa being uncommon – but more diffuse throughout the small intestine. The key factors distinguishing tropical sprue from celiac disease are the absence of celiac disease-specific autoantibodies and the absence of clinical and histologic improvement on a gluten-free diet. Thus, tropical sprue is a diagnosis of exclusion, suggested by villous atrophy in a patient with malabsorption who is living or has lived in an endemic area. The disease can be cured with antibiotics, usually tetracycline for up to 6 months, in combination with folic acid.

Celiac Disease

Various referred to as nontropical sprue or gluten-sensitive enteropathy, celiac disease is a chronic inflammatory disorder of the small bowel in which genetically susceptible individuals show an inappropriate immune response to wheat gluten and related proteins in barley and rye. Previously thought to be uncommon in the tropics, the discovery of specific and sensitive serologic tests has led to increased recognition of the condition, including among South Asians and Arabs of North Africa and the Middle East [14]. People from these areas with malabsorption and small intestinal villous atrophy, with no evidence of parasitic infection or bacterial overgrowth, were almost certainly misdiagnosed in the past as having tropical sprue. The prevalence of celiac disease in what was considered a low-risk group is evidenced by a study of 259 Indian children attending a pediatric gastroenterology clinic in New Delhi, in which over 40% were diagnosed with celiac disease. The condition classically presents after the introduction of gluten into the diet of infants, but adult-onset celiac disease is well recognized, and it can also present in the elderly; the prevalence is higher in females than males. Together with the increased recognition of celiac disease, there has been a greater appreciation of its protean manifestations: while classic disease presents with chronic diarrhea, abdominal distension, and failure to thrive or weight loss, a substantial proportion of patients present with atypical disease in which extraintestinal manifestations – for example, delayed menarche in girls, neuropsychiatric symptoms or osteomalacia – are more prominent; still others have silent or subclinical disease, with positive results on serologic testing and biopsy but no symptoms. Serologic tests are helpful in the diagnosis of celiac disease: the sensitivity and specificity of both of the currently used tests, IgA endomysial antibodies and IgA tissue transglutaminase antibodies, exceed 85% and 95%, respectively. However, small bowel biopsy remains the gold standard for the following reasons: in patients with positive serologic tests, biopsy helps to confirm the diagnosis and exclude complications such as lymphoma; and in patients with suggestive clinical features but negative serologic tests,

it is important to continue the investigation, as approximately 10% of IgA-competent celiac disease patients are seronegative. Although the diagnosis was previously restricted to those individuals with villous atrophy on biopsy, it is now recognized that patients with lesser degrees of mucosal damage – that is, crypt hyperplasia or intraepithelial lymphocytosis alone – have a mortality rate that is at least as high as those with frank villous atrophy [15]. Thus, current diagnosis of celiac disease is based on a positive small bowel biopsy (defined as intraepithelial lymphocytosis with or without crypt hyperplasia and villous atrophy) with clinical and/or histologic improvement upon removal of gluten from the diet. Serologic tests, though not necessary for the diagnosis, are also helpful in the management of celiac disease – as a positive test will turn negative once the patient is on a strict gluten-free diet. Nonresponsive celiac disease is usually due to intentional or inadvertent ingestion of gluten; if these are ruled out, it may be due to coexistent diseases such as microscopic colitis (which is associated with celiac disease), refractory celiac disease, or enteropathy-associated T-cell lymphoma. Epidemiologic studies have shown that patients with celiac disease have an increased risk of both gastrointestinal and non-gastrointestinal malignancies.

Protein-Losing Enteropathy

Loss of protein into the gastrointestinal tract may occur as a result of: (1) erosive mucosal disease, in which protein leaks across damaged membranes; (2) non-erosive mucosal disease, in which protein loss is due to altered epithelial permeability; and/or (3) lymphatic disease, in which lymph leaks into the lumen. The most common cause of non-erosive mucosal disease is intestinal infection. Lymphatic dysfunction may be due to obstruction, as in mesenteric tuberculosis, or impaired drainage, as occurs in portal hypertension or right-sided heart failure. The diagnosis is suggested by the presence of hypoalbuminemia without protein malnutrition, proteinuria or liver disease. In addition to correcting the underlying disorder, treatment consists of providing medium-chain triglycerides for nutritional support.

Immunoproliferative Small Intestinal Disease

Also known as alpha heavy chain disease or Mediterranean lymphoma, immunoproliferative small intestinal disease (IPSID) is a form of MALT lymphoma, characterized by secretion of truncated immunoglobulin alpha heavy chains without an associated light chain by plasma cells infiltrating the bowel wall [16]. Owing to its unique epidemiology – only being found in the Mediterranean, the Middle East and Africa – the association with poor sanitation, and response to antibiotic therapy, it is thought that environmental factors, including one or more infectious agents, are critical in the etiology of IPSID. Given the association between *H. pylori* and gastric MALT lymphomas, investigators have sought to associate this pathogen with IPSID. Although one case report has been published of an association, a subsequent case series has failed to replicate this finding. Following the detection of *Campylobacter jejuni* in an index patient with IPSID, investigators examined six additional patients and found evidence of *C. jejuni* in four of them, suggesting that this bacterium might be responsible, at least in part, for driving the antigenic response in IPSID [17].

Pathology

The second, third and fourth parts of the duodenum and the proximal jejunum are areas of maximal involvement, although ileal or total small bowel involvement has been reported. Gastric and colonic involvement is even more rare. The mucosa is grossly thickened with infiltrations producing a cobblestone appearance, localized nodules or polypoid tumors. The normal villous pattern of the gut is totally effaced by the massive infiltration of plasma cells. Villi are shortened but crypts remain small and are rather buried in the infiltrate.

Clinical Manifestations and Diagnosis

The disease is characterized clinically by a severe malabsorption syndrome with diarrhea, abdominal pain and weight loss. An abdominal mass may be palpable, while hepatosplenomegaly is a sign of

advanced disease. Laboratory findings are notable for hypoalbuminemia and hypogammaglobulinemia (from protein-losing enteropathy). The finding of alpha heavy chains in the serum is diagnostic, but this may be absent in a minority of patients; in the remainder, immunohistochemical staining of biopsy specimens is positive.

Treatment and Prognosis

Early-stage IPSID can be cured with antibiotic therapy, which historically has involved tetracycline with or without metronidazole (for associated parasitic infections) although newer agents may also be effective. In advanced disease, chemotherapy may be required. In unresponsive cases, surgery may be required for bulky abdominal disease causing obstruction.

Enteritis Necroticans (Pigbel)

This is a necrotizing infection affecting either the small or large intestine that occurs after ingestion of food containing the beta toxin of *Clostridium perfringens* type C. It classically affects chronically malnourished people who ingest a high-protein meal; it was first recognized in children and adults in Papua New Guinea after eating a pork feast, but has since been described in people from other parts of Asia and Africa. A cofactor for the infection is decreased trypsin activity, which is seen in protein malnutrition and in people ingesting foods with antitrypsin properties, such as sweet potatoes. The toxin causes tissue necrosis, usually affecting the small intestine but occasionally extending to involve the colon. Histologic examination reveals extensive inflammation and necrosis of the mucosa together with large numbers of bacteria on the affected surface. Patients present with abdominal pain and distension, bloody diarrhea, and shock. Surgical resection of the affected section of bowel may be curative, but the disease is often fatal.

Intussusception

Intussusception is defined as the telescoping of one part of the bowel into another. Ninety-five percent of cases occur in children, in whom the classic features are sudden onset of colicky abdominal pain and vomiting, a right-sided abdominal mass (as the ileocecal junction is the most common site), and currant-jelly stool (due to the mixture of blood and mucus). Most cases can be treated non-operatively using air, saline, or barium enemas. The majority of cases are idiopathic; in the remainder, a variety of lesions in the intestine can act as a lead point for intussusception – for example, Meckel's diverticulum, polyp or vascular malformation. The opposite is true in adults with intussusception, in whom an underlying disorder is almost always found; in addition to benign and malignant neoplasms, amebomas and schistosomal granulomas have been found to act as the lead point. Owing to the risk of underlying malignancies in adults with intussusception, surgical resection is favored over non-operative reduction.

COLON

Appendicitis

Acute appendicitis is one of the most common causes of the acute abdomen, occurring at all ages. Inflammation of the appendiceal wall leads to ischemia, necrosis, and eventually perforation, which may result in a localized abscess or generalized peritonitis. The inciting event is obstruction of the appendix, which is commonly due to fecaliths or calculi. However, the cause of the appendiceal obstruction varies by age, with lymphoid hyperplasia being common in children and tumors occasionally found in adults. In areas where schistosomiasis is endemic, schistosome ova have been found in the appendiceal wall in patients undergoing appendectomy, suggesting a potential causative role for certain parasitic infestations in the pathogenesis of acute appendicitis. Regardless of the etiology, the clinical features of acute appendicitis are similar: the classic symptoms include pain that migrates from the periumbilical area to the right iliac fossa, fever, anorexia and vomiting, though the diagnosis may be more challenging in children and the elderly who present with less specific

features. Laboratory findings are nonspecific, though a leukocytosis is usually present. In areas with access to radiographic studies, ultrasonography or computed tomography may establish the diagnosis, though imaging should not delay surgical exploration in cases where the diagnosis of acute appendicitis is very likely based on the clinical assessment. For patients presenting soon after the onset of symptoms, the treatment of choice is immediate appendectomy, with the addition of broad-spectrum antibiotics in those with frank perforation; patients with a longer duration of symptoms may be managed non-operatively with antibiotics. The differential diagnosis of acute appendicitis includes acute gastroenteritis, in which diarrhea is usually a prominent symptom and abdominal pain is more diffuse. In contrast, gastroenteritis due to *Yersinia* infection may present with little diarrhea and right lower quadrant abdominal pain, causing it to be misdiagnosed as appendicitis.

Intestinal Tuberculosis

This can affect any part of the gastrointestinal tract, but the ileocecal region is an area of predilection. In addition to the classic constitutional symptoms of fever, night sweats and weight loss, abdominal involvement may be manifested by distension due to ascites, diarrhea due to malabsorption, obstruction due to stenosing disease, or the presence of an abdominal mass. Less than half of patients with intestinal tuberculosis have open pulmonary disease. Laboratory tests usually reveal anemia and raised inflammatory markers, though these are nonspecific. Tuberculin tests are usually strongly positive in patients who are adequately nourished but are frequently negative in those with malnutrition or HIV infection. Sputum and gastric washings should be examined for tubercle bacilli. Radiographic contrast studies of the gut show a range of changes, including mucosal ulceration, stricture formation, segmental narrowing, and fistula formation. Colonoscopy may establish the diagnosis when acid-fast bacilli or caseating granulomas are found on biopsy; however, these findings are not always present, and other endoscopic findings can be difficult to distinguish from other diseases of the colon, most notably Crohn's disease. Laparoscopy or laparotomy with microscopic examination and culture of biopsies may be the only means of establishing the diagnosis in some patients. If facilities for investigation are inadequate, it may be necessary to treat the patient with antituberculous drugs on the basis of a clinical diagnosis.

Inflammatory Bowel Disease

The inflammatory bowel diseases, Crohn's disease and ulcerative colitis, are chronic inflammatory disorders of the bowel that are thought to occur as a result of the interplay between genetic factors, environmental factors and the host immune response. Classically considered diseases of the West, it is now appreciated that the incidence is increasing in many developing countries. Although the hygiene hypothesis is almost certainly an oversimplification of the etiology of these diseases, the altered Th1/Th2 balance as a result of decreased exposure to helminths in childhood may be partly responsible for the increasing incidence in tropical countries that are undergoing demographic transition [18]. In addition, it is likely that a substantial proportion of true cases were misdiagnosed in the past as infectious colitis.

Crohn's disease can involve any part of the gastrointestinal tract, but has a predilection for the terminal ileum and cecum. Inflammatory lesions cause right lower quadrant abdominal pain, diarrhea and weight loss. The differential diagnosis of ileocecal inflammatory lesions includes: bacterial infections such as yersiniosis or actinomycosis; tuberculosis; histoplasmosis; parasitic infections such as amebiasis; and helminthic infections such as strongyloidiasis. Microscopic examination of biopsy specimens is notable for transmural inflammation, lymphoid aggregates, and noncaseating granulomas. It can be challenging to differentiate Crohn's disease from intestinal tuberculosis on the basis of clinical, endoscopic and histologic features; in areas where tuberculosis is endemic, an empiric trial of antituberculous drugs is undertaken [19]. Management of Crohn's disease involves both medical and surgical approaches: medical therapies

include broad-spectrum antibiotics and immunosuppressive agents; surgical management is necessary if the disease is complicated by strictures, fistulizing disease or abscesses.

In ulcerative colitis, the inflammation starts at the rectum and spreads proximally; the mucosa appears red and raw on proctosigmoidoscopy. Histologic examination reveals that the inflammation is limited to the submucosa. In addition, there is an inflammatory cell infiltrate in the lamina propria, neutrophil accumulation in crypt abscesses, and depletion of goblet cells from the epithelium; granulomas are absent. Unlike Crohn's disease, in which lesions may occur throughout the bowel, ulcerative colitis is limited to the colon and rectum; thus, if the disease is not responsive to medical therapy, total colectomy is curative.

Megacolon

Patients with large bowel dilatation may be ill-appearing with abdominal pain, distension and tenderness. Toxic megacolon can complicate any of the infectious colitides, e.g. it is a relatively common complication of *C. difficile* infection; it is also seen in fulminant colitis from the inflammatory bowel diseases; rarely, it is due to drug-induced intestinal hypomotility. Abdominal examination is remarkable for a distended abdomen with absence of bowel sounds. Plain film of the abdomen shows a markedly distended colon. Stool should be sent for bacterial culture, *C. difficile* toxin, and examination for ova and parasites. However, regardless of the etiology, the treatment is colectomy; without surgical treatment, the risk of bowel perforation and peritonitis is unacceptably high.

In contrast, some patients may have large bowel dilatation without systemic toxicity. This results in constipation due to chronic intestinal pseudo-obstruction. It may be due to acquired absence of the ganglions in the enteric nervous plexus, as in Chagas disease.

Stenosing Lesions of the Colon and Rectum

Stenosing lesions of the bowel can be caused by amebiasis, schistosomiasis, tuberculosis and lymphogranuloma venereum, which involves the rectum. Strictures can also be inflammatory, occurring in Crohn's disease or after an episode of diverticulitis, or neoplastic.

The cecum is the most common site for ameboma formation, but any part of the colon may be affected. Occasionally, multiple amebomas occur in the same patient. Persisting diarrhea with blood in the stools and localized abdominal pain are the usual features, and one or more tender masses may be palpable in the abdomen. The lesion itself consists of granulation tissue with areas of necrosis and fibroblast proliferation. Amebas are often difficult to find, but serologic tests are positive in over 90% of cases. Rapid resolution follows specific treatment, and surgical excision is not required.

Granulomatous lesions of the colon due to schistosomiasis can cause narrowing of the bowel. Early lesions are reversible with antischistosomal treatment. The rare fibrotic strictures that form may require surgical removal.

RECTUM AND ANUS

Proctitis

Inflammation of the rectum causes rectal pain, tenesmus and a mucopurulent rectal discharge. While any of the infectious causes of colitis may involve the rectum, isolated proctitis is more commonly a sexually transmitted infection (STI), usually seen in men who have sex with men who engage in unprotected anal intercourse [20]. Common causes are gonorrhea, herpes simplex, lymphogranuloma venereum secondary to chlamydia (which is endemic in Africa, South and Southeast Asia, and Central and South America), and syphilis. Noninfectious causes of proctitis include the inflammatory bowel diseases, radiation, ischemia and neoplasia. Infectious workup should include rectal swab cultures for gonorrhea, lymphogranuloma venereum and herpes simplex virus, and blood for syphilis serologic

testing. STI testing should be performed prior to rectal examination, as some lubricants are bacteriostatic. Anoscopy may not be possible due to pain; if performed, the mucosa is seen to be edematous, erythematous and friable with exudates or ulceration. If the proctitis is likely due to an STI but the causative agent is unknown, empiric antimicrobial therapy should be started; the combination of ceftriaxone, doxycycline and valacyclovir is effective against the four main causes. Sexual partners should be identified and treated; counseling regarding barrier protection is important, as proctitis increases the risk of HIV transmission.

Rectal Prolapse

Either the mucosa or all layers of the rectal wall may prolapse through the anus. This is almost always secondary to an underlying disorder. Common causes in children in the tropics are diarrheal diseases, especially shigellosis, parasitic infestations (e.g. with *Trichuris trichiura*), and malnutrition. Among adults, rectal prolapse is more common in elderly women due to pelvic floor weakness as a result of vaginal delivery. Treatment is focused on correcting the underlying disorder and, if repeated manual reductions are necessary, surgical repair.

Anal Lesions

Common benign lesions that occur around the anus include ulcers and warts. Both may cause pruritus, bleeding and pain. Ulcers are usually caused by herpes simplex virus, syphilis or chancroid; in addition, patients with HIV are susceptible to ulcers caused by cytomegalovirus, tuberculosis and fungal infection. A proportion of patients with HIV have ulcers without evidence of any of these infectious agents, so-called idiopathic anal ulcers. Condylomata acuminata (anal warts) are caused by human papillomavirus infection, which is related to sexual activity. These exophytic, flesh-colored lesions should be distinguished from the flat lesions of condyloma lata, seen in secondary syphilis.

Anal Cancer

Cancer of the anal canal, usually squamous cell carcinoma, makes up only a small proportion of gastrointestinal malignancies. However, the incidence is increasing worldwide, likely due to the widespread prevalence of human papillomavirus infection. The risk may be increased further in patients co-infected with HIV. Patients present with rectal bleeding or a mass at the anal verge. The treatment options are chemoradiotherapy or surgery.

GASTROINTESTINAL DISEASES IN PATIENTS WITH HIV/AIDS

Acute HIV-1 infection presents with a mononucleosis-like illness in which gastrointestinal symptoms are not usually prominent but may include nausea and vomiting and diarrhea. Rarely, patients may have pancreatitis or hepatitis. In contrast, advanced HIV infection commonly involves the gastrointestinal tract, with the main syndromes being esophageal disease and chronic diarrhea (Box 3.5). The causes of organ-specific disease in HIV-infected patients can usually be attributed to one of three causes: due to HIV infection itself; due to opportunistic infection; or due to the medications used to treat HIV or prevent its complications [21]. The etiologies vary depending on the degree of immunosuppression.

Chronic diarrhea is a common problem in patients with AIDS, causing significant morbidity and mortality. While the CD4 cell count is preserved, the causes are similar to those in patients without HIV. As the infection becomes more advanced, parasitic, fungal and viral infections become more prevalent. Many of these pathogens can also be identified in AIDS patients without diarrhea, showing that asymptomatic infection is common. Workup should include stool specimens for bacterial culture and ova and parasite examinations. If these

BOX 3.5 Gastrointestinal Involvement in AIDS

- Dysphagia
 - Candida esophagitis
 - CMV esophagitis
 - HSV esophagitis
 - Idiopathic esophageal ulcer
- Diarrhea
 - Opportunistic infections
 - CMV
 - Salmonellosis, campylobacteriosis
 - Tuberculosis, *Mycobacterium avium-intracellulare* infection
 - *Cryptosporidium hominis/parvum*, *Cyclospora cayentanensis*, *Isospora belli*, *Entamoeba histolytica*, *Giardia lamblia*, *Strongyloides stercoralis*
 - Microsporidiosis, cryptococcosis, coccidioidomycosis, histoplasmosis
 - AIDS enteropathy
 - Medications
 - Lymphoma
- Malignancy – any location, due to
 - Kaposi sarcoma
 - Non-Hodgkin lymphoma

are unrevealing, flexible sigmoidoscopy with biopsy may be helpful in the diagnosis, especially in the identification of cytomegalovirus infection. Treatment should be directed at the specific enteric pathogen identified and antiretroviral therapy, which is the only treatment for some infections such as cryptosporidiosis and microsporidiosis, should be initiated.

In a substantial proportion of AIDS patients with diarrhea, no enteric pathogens are isolated. Small intestinal biopsy specimens from these patients are notable for villous atrophy and lymphocytic infiltration into the lamina propria. This idiopathic condition is named AIDS enteropathy, and may represent the mucosal response to atypical pathogens, including HIV.

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