

While amebiasis affects the cecum and ascending colon, most often, the sigmoid colon, rectum, and appendix can also be involved. Dysentery develops when the amebae attach to the colonic epithelium, induce apoptosis, invade crypts, and burrow laterally into the lamina propria. This recruits neutrophils, causes tissue damage, and creates a flask-shaped ulcer with a narrow neck and broad base. Histologic diagnosis can be difficult, since amebae are similar to macrophages in size and general appearance (Fig. 17-31D). Parasites may penetrate splanchnic vessels and embolize to the liver to produce abscesses in about 40% of patients with amebic dysentery. Amebic liver abscesses, which can exceed 10 cm in diameter, have a scant inflammatory reaction at their margins and a shaggy fibrin lining. The abscesses persist after the acute intestinal illness has passed and may, rarely, reach the lung and the heart by direct extension. Amebae may also spread to the kidneys and brain via the bloodstream.

Individuals with amebiasis may present with abdominal pain, bloody diarrhea, or weight loss. Occasionally, acute necrotizing colitis and megacolon occur, and both are associated with significant mortality. The parasites lack mitochondria or Krebs cycle enzymes and are thus obligate fermenters of glucose. Metronidazole, which inhibits pyruvate oxidoreductase, an enzyme required for fermentation, is the most effective treatment for systemic disease.

Giardia lamblia. These organisms, also referred to as *G. duodenalis* or *G. intestinalis*, were initially described by van Leeuwenhoek, the inventor of the microscope, who discovered the pathogen in his own stool. *Giardia lamblia* are the most common parasitic pathogen in humans and are spread by fecally contaminated water or food. Infection may occur after ingestion of as few as 10 cysts. Because cysts are resistant to chlorine, *Giardia* are endemic in unfiltered public water supplies. They are commonly present in rural streams, explaining infection in campers who use these as a water source. Infection may also occur by the fecal-oral route and, because the cysts are stable, they may be accidentally swallowed while swimming in contaminated water.

Giardia are flagellated protozoans that cause decreased expression of brush-border enzymes, including lactase. In addition they cause microvillous damage and apoptosis of small intestinal epithelial cells. Secretory IgA and mucosal IL-6 responses are important for clearance of *Giardia* infections. Immunosuppressed, agammaglobulinemic, or malnourished individuals are often severely affected. *Giardia* can evade immune clearance through continuous modification of the major surface antigen, variant surface protein, and can persist for months or years while causing intermittent symptoms.

Giardia trophozoites can be identified in duodenal biopsies based on their characteristic pear shape and the presence of two equally sized nuclei. Despite large numbers of trophozoites, which are tightly bound to the brush border of villous enterocytes, there is no invasion and small intestinal morphology may be normal (Fig. 17-31E). However, villous blunting with increased numbers of intraepithelial lymphocytes and mixed lamina propria inflammatory infiltrates can develop in patients with heavy infections.

Giardiasis may be subclinical or accompanied by acute or chronic diarrhea, malabsorption, and weight loss.

Infection is usually documented by immunofluorescent detection of cysts in stool samples. Although oral antimicrobial therapy is effective, recurrence is common.

Cryptosporidium. Like *Giardia*, cryptosporidia are an important cause of diarrhea worldwide. Cryptosporidiosis was first discovered in the 1980s as an agent of chronic diarrhea in AIDS patients and is now recognized as a cause of acute, self-limited disease in immunologically normal hosts. Cryptosporidiosis also causes persistent diarrhea in residents of developing countries. The organisms are present worldwide, with the exception of Antarctica, perhaps because the oocysts are killed by freezing. The oocysts are resistant to chlorine and may, therefore, persist in treated, but unfiltered, water. Contaminated drinking water continues to be the most common means of transmission. The largest documented outbreak, a result of inadequate water purification, occurred in 1993 in Milwaukee, Wisconsin, and affected more than 400,000 people. Like giardiasis, cryptosporidiosis can be spread to water sport participants via contaminated water. Food-borne infection occurs less frequently.

Humans are infected by several different *Cryptosporidium* species, including *C. hominis* and *C. parvum*. All are able to go through an entire life cycle, with asexual and sexual reproductive phases, in a single host. The ingested encysted oocyte, of which 10 are sufficient to cause symptomatic infection, releases sporozoites following activation of proteases by gastric acid. The sporozoites are motile and have a specialized organelle that attaches to the brush border and causes changes in the enterocyte cytoskeleton. These changes induce the enterocyte to engulf the parasite, which takes up residence in an endocytic vacuole within the microvilli. The presence of the parasite leads to sodium malabsorption, chloride secretion, and increased tight junction permeability, which are responsible for the non-bloody, watery diarrhea that ensues.

Mucosal histology is often only minimally altered, but persistent cryptosporidiosis in children and heavy infection in immunosuppressed patients can result in villous atrophy, crypt hyperplasia, and inflammatory infiltrates. Although the sporozoite is intracellular, it appears, by light microscopy, to sit on top of the epithelial apical membrane (Fig. 17-31F). Organisms are typically most concentrated in the terminal ileum and proximal colon, but can be present throughout the gut, biliary tract, and even the respiratory tract of immunodeficient hosts. Diagnosis is based on finding oocysts in the stool.

KEY CONCEPTS

Infectious Enterocolitis

- *Vibrio cholerae* secrete a preformed toxin that causes massive chloride secretion. Water follows the resulting osmotic gradient, leading to secretory diarrhea.
- *Campylobacter jejuni* is the most common bacterial enteric pathogen in developed countries and also causes traveler's diarrhea. Most isolates are noninvasive.
- *Salmonella* and *Shigella* spp. are invasive and associated with and exudative bloody diarrhea (dysentery).
- *Salmonella* infection is a common cause of food poisoning.