Antibiotic therapy has not been shown to reduce morbidity and may increase the risk of HUS in children.

Clostridium difficile

C. difficile is the main cause of nosocomial diarrhea among adults in the United States. Virtually all antibiotics have been implicated in the development of *C. difficile* infection, but the most common agents are clindamycin, cephalosporins, fluoroquinolones, and penicillins. Spores occur in the environment and are resistant to alcohol-based handwashing solutions. The spores of toxigenic *C. difficile* are ingested, survive gastric acidity, geminate, and colonize the lower intestinal tract, where they elaborate two exotoxins, toxin A (an enterotoxin) and toxin B (a cytotoxin). The toxins disrupt cell and tight junctions, leading to fluid leakage. The cellular toxicity results in formation of a pseudomembrane.

The epidemic strain referred to as the North American pulsed-field gel electrophoresis type 1 (NAP1) strain is associated with a severe course, higher mortality, and increased risk of relapse. Three bacterial factors have been implicated in outbreaks of *C. difficile* infection caused by the NAP1 strain, including increased production of toxins A and B, fluoroquinolone resistance, and production of a binary toxin. Patients often have abdominal pain and watery diarrhea but may also have bloody stools. Markers of severe infection include pseudomembranous colitis, acute renal failure, marked leukocytosis, hypotension, and toxic megacolon. The indigenous intestinal microbiota is important for colonization resistance and for recovery from antibiotic-associated *C. difficile* colitis.

Yersinia enterocolitica

Y. enterocolitica is a zoonosis caused by ingestion of contaminated food or water or undercooked meats. Oral inoculation requires 10^9 organisms for infection, with an incubation period of 3 to 7 days. The illness may mimic acute appendicitis and may be complicated by ileal perforation, mesenteric adenitis, or terminal ileitis. Postinfectious reactive polyarthritis and Reiter's syndrome may occur.

Viral Causes of Diarrhea

Viruses tend to cause diarrhea by adhering to the intestinal mucosa and disrupting the absorptive and secretory processes without causing inflammation. They may invade intestinal villous epithelial cells and cause sloughing of villi. Rotavirus was the most common cause of severe diarrhea in children in the past, but the incidence has fallen dramatically with widespread use of the rotovirus vaccine. Norovirus is highly contagious and is a very common cause of foodborne gastroenteritis in adults and children in the United States. It has been the cause of epidemic diarrhea on cruise ships. There is neither a vaccine nor specific treatment. Other viruses that cause diarrhea are adenoviruses, sapoviruses, and astroviruses. The incubation period is usually longer than 14 hours, and vomiting may be a prominent feature of diarrheal disease caused by viral agents.

Protozoan Causes of Diarrhea

Important parasitic causes of diarrhea include *G. lamblia*, *Cryptosporidium parvum*, and *E. histolytica*. Contaminated water sources tend to be the cause of outbreaks. *G. lamblia* multiplies in the small intestine and attaches to or invades, but does not destroy, mucosa cells. Ingestion of a few organisms can lead to disease. *C. parvum*, *Isospora belli*, and *Cyclospora cayetanesis* occasionally cause self-limited diarrhea in immunocompetent individuals but may cause severe disease in patients with advanced acquired immunodeficiency syndrome (AIDS). *E. histolytica* causes a syndrome ranging from mild diarrhea to fulminant amebic colitis and extraintestinal amebic abscesses.

Traveler's Diarrhea

Traveler's diarrhea affects 10% to 40% of travelers from industrialized countries who visit tropical and semitropical developing countries. The causative agent is identified in about one half of cases, and 80% of those identified are bacterial pathogens, most often ETEC or enteroaggregative *E. coli*. Other bacterial causes include *Shigella*, *Salmonella*, *Campylobacter*, *Aeromonas*, noncholeraic *Vibrio*, and *Plesiomonas*. The viral etiologies include rotavirus and norovirus; parasitic causes are rare. Patients with traveler's diarrhea should be treated empirically with antibiotics without stool examination.

CLINICAL PRESENTATION

The epidemiologic and clinical characteristics are important to identify the potential etiologic agent and to guide management (see Table 96-1). The initial evaluation should consider the severity of illness, signs of dehydration, and intestinal inflammation indicated by the fever, abdominal pain, blood in stools (dysentery), or tenesmus. Important epidemiologic clues in the history include age, travel history, ingestion of undercooked or raw food and meat, antibiotic use, sexual activity, daycare attendance, and outbreaks involving others with similar exposure (see Table 96-1). Fever (temperature 38.5° C or 101.3° F or higher) is associated with invasive pathogens that cause intestinal inflammation. The examination should determine the severity of dehydration and need for rehydration as well as the likely cause. Signs of dehydration or hypovolemia include lax skin turgor and tenting, dry mucus membranes, decreased urination, tachycardia, and hypotension.

DIAGNOSIS AND DIFFERENTIAL DIAGNOSIS

The approach to diagnosis and management of infectious diarrhea is shown in Figure 96-1. Examination of stools for erythrocytes and white blood cells (leukocytes) using methylene blue staining or the lactoferrin test can help differentiate diarrhea caused by invasive pathogens from that caused by noninvasive pathogens. Most cases of diarrheal illnesses are self-limited, and almost half resolve within 1 day. Therefore, microbiologic investigation is usually not necessary for patients who are seen within 24 hours of the onset of illness unless certain conditions are present.

The indications for stool culture include severe diarrhea (six or more stools per day), diarrhea lasting longer than 1 week, fever, dysentery, hospitalization, inflammatory diarrhea, and multiple cases in a suspected outbreak. Routine stool culture will identify *Shigella*, *Salmonella*, *Campylobacter*, and *Aeromonas*. If the patient has bloody diarrhea or HUS, stool culture for *E. coli* O157 and tests for shiga-like toxin should be performed. Enzyme immunoassay for *C. difficile* toxins A and B or polymerase chain reaction