

Common Gastrointestinal Infections

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KEYWORDS

• Gastrointestinal infections • Diarrhea • Food-borne illness • Traveler's diarrhea

KEY POINTS

- Viral infections, with norovirus being the most common, account for most cases of acute diarrhea in the United States.
- Nontyphoidal *Salmonella* species are the leading cause in the United States of hospitalization and death from gastrointestinal infections.
- The immunocompromised, children under the age of 5, and adults over 65 years of age are the most severely affected.
- For most patients in the United States presenting with diarrhea, no testing is necessary if the presentation is consistent with a viral cause and of mild to moderate severity.

INTRODUCTION

Gastrointestinal infections account for a large burden of acute and chronic disease worldwide. Diarrhea is defined as 3 or more stools in 24 hours and is the most common manifestation. It is defined as acute if lasting less than 7 days, prolonged if lasting 7 to 13 days, persistent if lasting 14 to 29 days, and chronic if lasting 30 days or longer.¹ Common bacterial, viral, and parasitic pathogens are spread via food, via contaminated water, or from person to person. According to the World Health Organization, diarrhea is the cause of 4% of deaths globally and kills approximately 2.2 million people each year.² Those in developing countries, and particularly children, are most affected. In the United States, not all cases are actively reported, but it is approximated that 179 million cases of acute diarrhea in adults occur each year, resulting in 500,000 hospitalizations and more than 5000 deaths.³ Nationally, children less than 5 years old account for the largest portion of infections, but those older than 65 years old account for greatest number of hospitalizations and deaths.⁴

Despite modern advances in food preparation and delivery, gastrointestinal infections in the United States are commonly caused by food-borne pathogens. In

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2011, it was found that norovirus (58%) caused the most food-borne infections followed by nontyphoidal *Salmonella* spp (11%), *Clostridium perfringens* (10%), and *Campylobacter* spp (9%). Nontyphoidal *Salmonella* spp (35%) was the leading cause of hospitalization followed by norovirus (26%), *Campylobacter* spp (15%), and *Toxoplasma gondii* (8%). Nontyphoidal *Salmonella* spp (28%) also caused the most deaths followed by *T gondii* (24%), *Listeria monocytogenes* (19%), and norovirus (11%).³

Diarrhea also accounts for the largest number of travel-related illness in the United States, with acute diarrhea accounting for 22% of travel-related diagnoses in US residents.⁵ Areas with the highest risk of acquiring traveler's diarrhea include Africa, South Asia, Latin America, and the Middle East. Risk is increased for those taking medications that lower gastric acid.⁶ Traveler's diarrhea (**Table 1**) is more likely bacterial in contrast to infectious diarrhea acquired in the United States, which is most commonly viral. Protozoa are less common causes of traveler's diarrhea but may result in longer duration or persistence of symptoms upon return to the United States.

CLINICAL MANIFESTATIONS

History

A comprehensive history is important to determine potential infectious causes of gastrointestinal diseases with a focus on sick contacts, food exposures, and travel history (**Table 2**). The onset, duration, severity, and frequency of diarrhea should be determined with attention to the stool volume and character. It is important to note if the stool has been watery or contains blood or mucus. Fever, tenesmus, and the presence of blood in stool may be more suggestive of invasive bacterial pathogens. Additional systemic symptoms, such as decreased urine output, weakness, dizziness, and confusion, may be signs of dehydration. Pathogens that primarily affect the small bowel are more likely to cause watery larger volume diarrhea with bloating, gas, and cramping. Those that affect the large bowel may cause more frequent, small volume, or painful bowel movements.

Environmental exposure or a history of immunocompromise may help identify specific pathogens. History of prior abdominal surgeries, radiation exposure, or recent antibiotic use should be obtained. A detailed sexual history may also be relevant because anal receptive sex, sharing of toys, or oral-anal contact may increase the risk of transmission of fecal pathogens, particularly *Shigella*, *Salmonella*, *Campylobacter*, *Escherichia coli*, *Entamoeba histolytica*, and *Giardia*.⁷

Physical Examination

A comprehensive physical examination in patients with suspected gastrointestinal infections should focus on a thorough abdominal examination with consideration

Table 1
Common causes of traveler's diarrhea

Bacterial	Viral	Parasitic
Shiga-toxin producing <i>E coli</i>	Rotavirus	<i>Giardia lamblia</i>
Other <i>E coli</i> types	Norovirus	<i>Cryptosporidium</i>
<i>Salmonella</i>		<i>Cyclospora</i>
<i>Campylobacter</i>		<i>E histolytica</i>
<i>Shigella</i>		
<i>Aeromonas</i>		
<i>Vibrio</i>		

Source	Pathogen
Camping, untreated river water	<i>Giardia</i>
Fried rice	<i>Bacillus cereus</i>
Raw milk	<i>Salmonella</i> , <i>Campylobacter</i> , <i>Listeria</i> , Shiga toxin-producing <i>E coli</i>
Seafood	<i>Vibrio cholerae</i> , <i>Vibrio parahaemolyticus</i>
Undercooked meat	<i>Bacillus cereus</i> , <i>Campylobacter</i> , <i>C perfringens</i> , <i>Listeria</i> , <i>Salmonella</i> , STEC, <i>Staphylococcus aureus</i> , <i>Yersinia</i>

of a rectal examination to identify blood or stool quality. The examiner should also look for signs of dehydration, such as orthostatic vital signs, dry mucous membranes, skin tenting, or delayed capillary refill. After the acute phase of diarrhea, examination may be helpful to identify postinfectious complications of enteric pathogens, as listed in [Table 3](#).

DIAGNOSIS/MANAGEMENT

Differential Diagnosis

A thorough history and physical examination may point to a clear infectious cause, whereas the differential may also include other noninfectious causes, such as medication adverse effects, other intrinsic gastrointestinal diseases, or endocrine disorders that affect the gastrointestinal system ([Table 4](#)).

General Diagnostic Approach

For most patients in the United States presenting with diarrhea, no testing is necessary if the presentation is consistent with a viral cause and of mild to moderate severity.¹ The Infectious Disease Society of America (IDSA), based on low quality of evidence, recommends that those with fever, bloody, or severe diarrhea should be evaluated for treatable enteropathogens, such as *Salmonella*, *Shigella*, and *Campylobacter*.¹ Recent travel to an endemic area or known exposure would be other reasons to consider specific testing. Stool testing is recommended for those with diarrhea and fever, bloody stools, mucoid stools, severe abdominal pain or cramping, diarrhea lasting longer than 14 days, or signs of sepsis.¹ Stool testing is most commonly obtained to specifically assess for *Salmonella*, *Shigella*, *Campylobacter*, *Yersinia*, *C difficile*, and

Postinfectious Complication	Commonly Associated Organisms
Hemolytic uremic syndrome	<i>Shigella dysenteriae</i> serotype 1, STEC
Reactive arthritis	<i>Campylobacter</i> , <i>Salmonella</i> , <i>Shigella</i>
Erythema nodosum	<i>Campylobacter</i> , <i>Salmonella</i> , <i>Shigella</i> , <i>Yersinia</i>
Guillain-Barre syndrome	<i>Campylobacter</i>
Hemolytic anemia	<i>Campylobacter</i> , <i>Yersinia</i>
Irritable bowel syndrome (IBS)	<i>Campylobacter</i> , <i>Salmonella</i> , <i>Shigella</i> , STEC, <i>Giardia</i>

Data from Shane AL, Mody RK, Crump JA, et al. 2017 Infectious Diseases Society of America clinical practice guidelines for the diagnosis and management of infectious diarrhea. Clin Infect Dis 2017;65(12):1963–73.

Cause	Examples
Medication adverse effects	Antibiotics Metformin Orlistat Acarbose Nonsteroidal anti-inflammatory drugs Metoclopramide Iron Fibrates Proton pump inhibitors Lithium Aminosalicilates (5-ASA) ACE inhibitors Laxatives Colchicine Calcitonin Chemotherapy Antacids Protease inhibitors Magnesium Weight loss supplements
Gastroenterologic diseases	Inflammatory bowel disease Irritable bowel syndrome Ischemic colitis Mesenteric ischemia Diverticulitis Malabsorption Colorectal cancer Celiac disease Lactose intolerance Short bowel syndrome Constipation with overflow
Endocrine diseases	Hyperthyroidism Adrenal insufficiency Carcinoid tumors

Data from Chassany O, Michaux A, Bergmann JF. Drug-induced diarrhoea. *Drug Saf* 2000;22(1):53–72; and Schiller LR, Pardi DS, Sellin JH. Chronic diarrhea: diagnosis and management. *Clin Gastroenterol Hepatol* 2017;15(2):182–93.e3.

Shiga toxin-producing *E coli* (STEC). Blood cultures should be collected for those with signs of sepsis, the immunosuppressed, infants <3 months of age, or those with a febrile illness of unclear cause. Stool nonmicrobiologic diagnostic tests have historically been considered in evaluating persons with suspected gastrointestinal infections, but the IDSA in their 2017 guideline recommends against testing for fecal leukocytes and lactoferrin, based on moderate evidence of lack of benefit.¹ Additional testing may be necessary to diagnose postinfectious complications of enteric pathogens (see [Table 3](#)).

Abdominal imaging with ultrasound, computed tomography (CT), or MRI may be considered in those with peritoneal signs or to evaluate for other noninfectious causes, such as those listed in [Table 4](#). More invasive endoscopic examination may be considered in those with persistent diarrhea of unclear cause, particularly in those with AIDS or a suspected noninfectious cause.

PATHOGEN-SPECIFIC DIAGNOSIS, MANAGEMENT, AND PREVENTION**Bacteria*****Campylobacter***

Campylobacter are gram-negative spiral, rod-shaped, or curved bacteria and are a common bacterial cause of gastrointestinal infections in the United States. *Campylobacter jejuni* causes most human infections and is transmitted via undercooked poultry and unpasteurized milk.⁸ Symptoms typically present 1 to 3 days after exposure and last a week. Most cases of infection are self-limited with fever, abdominal pain/cramping, and diarrhea, with blood in a third of cases. Stool culture remains the gold standard for diagnosis with increasing utilization of culture independent diagnostic testing (CIDT).⁹ Treatment is supportive. Azithromycin may be considered if symptoms are more severe, because treatment may reduce duration of diarrhea. A 2014 systemic review and meta-analysis showed postinfection rates of reactive arthritis (2.86%), irritable bowel syndrome (4.01%), and Guillain Barré syndrome (0.07%).¹⁰

Salmonella

Salmonella is a motile, gram-negative anaerobic rod, and nontyphoidal species are a common cause of traveler's diarrhea and gastroenteritis in the United States. Nontyphoidal *Salmonella* causes the most deaths worldwide and is more prevalent in the summer. Exposure commonly is due to food (eg, eggs, unpasteurized dairy, undercooked poultry) or animals (eg, turtles, iguanas, poultry). Symptoms are typically self-limited. Stool culture and/or CIDT should be considered in those with more severe symptoms and those at risk for transmission, such as food handlers or health care workers. Blood culture should also be considered in those with sepsis, the immunocompromised, the hospitalized, or those with prosthetic heart valves or joints. Antibiotics should be reserved for those at greater risk for complications (**Box 1**) because they may not reduce diarrhea nor fever duration and risk increasing fecal carriage. Postinfectious sequelae of nontyphoidal *Salmonella* may include reactive arthritis in 5.8% and irritable bowel syndrome in 3.3%.¹¹

Shigella

Shigella are gram-negative, anaerobic nonmotile rod-shaped bacteria closely related to *E coli* and is one of the leading causes of diarrhea worldwide, with milder disease severity in the United States (**Table 5**). *Shigella* and enteroinvasive *E coli* (EIEC) are the primary causative agents of bacillary dysentery (**Table 6**), characterized by bloody

Box 1**Criteria for consideration of antibiotics for treatment of nontyphoidal *Salmonella* infection**

- Patients less than 3 months old or greater than 50 year old
- Patients with valvular heart disease
- Patients with severe atherosclerosis
- Patients with malignancy
- Patients with prosthetic joints, heart valves, or vascular grafts
- Patient who are immunocompromised
- Patients with bacteremia

Data from Shane AL, Mody RK, Crump JA, et al. 2017 infectious diseases society of America clinical practice guidelines for the diagnosis and management of infectious diarrhea. Clin Infect Dis 2017;65(12):1963–73.

Subtype	Global Prevalence	Severity of Disease
<i>Shigella sonnei</i>	Most common subtype in the United States	Least severe
<i>Shigella dysenteriae</i>	Rare in the United States	Most severe
<i>Shigella flexneri</i>	Primary cause of endemic disease in developing countries	More severe
<i>Shigella boydii</i>	Most commonly found in Indian subcontinent. Rare in the United States	Mild

Data from Centers for Disease Control and Prevention. Questions & Answers | Shigella – Shigellosis | CDC. Available at: <https://www.cdc.gov/shigella/general-information.html>. Accessed April 9, 2018.

diarrhea. Toxin mediated symptoms occur 1 to 2 days after exposure and include diarrhea, fever, abdominal pains, and tenesmus, lasting an average of 5 to 7 days. Shigellosis has been found to be more common in men who have sex with men (MSM) (odds ratio [OR] 8.24), persons with HIV (OR 8.17), direct oral-anal contact (OR 7.5), and foreign travel (OR 20.0).¹² Diagnosis may be made via stool culture or stool polymerase chain reaction (PCR), although differentiating *Shigella* from EIEC and other *E coli* species may require specialized laboratories. Most cases do not require antibiotic treatment. A Cochrane review found that antibiotics reduce the duration of dysentery in patients with moderately severe illness, but there was insufficient evidence to recommend a specific antibiotic class as superior.¹³ *Shigella* species develop antibiotic resistance through both clonal spread and horizontal gene transfer, and increased fluoroquinolone and azithromycin resistance has been noted in the United States, particularly in MSM.¹⁴

Escherichia coli

E coli has 6 subtypes that cause gastrointestinal symptoms (Box 2), with Shiga toxin-producing *E. coli* (STEC) being the most common subtype in food-borne outbreaks. Specifically, *E coli* O157:H7 is the STEC type that is found in 36% of STEC infections and can cause more severe symptoms when compared with non-O157 types. Symptoms typically start 3 to 4 days after exposure and can cause diarrhea, abdominal pain,

	Organisms
Bacterial	<i>Shigella</i> Enteroinvasive <i>E. coli</i> (EIEC) Nontyphoidal <i>Salmonella</i> <i>Yersinia enterocolitis</i> <i>Campylobacter enterocolitis</i> Enterohemorrhagic <i>E coli</i> <i>C difficile</i> <i>Aeromonas</i> <i>Vibrio</i>
Parasitic	Amebiasis Schistosomiasis
Viral	Cytomegalovirus

Data from Pfeiffer ML, DuPont HL, Ochoa TJ. The patient presenting with acute dysentery—a systematic review. *J Infect* 2012;64(4):374–86.

and fever, lasting an average of 5 to 7 days' duration.¹⁵ Transmission is typically from unpasteurized milk, unpasteurized apple cider, soft cheeses, infected water, or contact with cattle. Antibiotics are not recommended and may increase the risk of hemolytic uremic syndrome,¹⁶ which occurs in 4% to 17% of cases of STEC¹⁷ and presents typically 7 days after onset of diarrhea with decreased urination, fatigue, and pallor.

Yersinia

Y enterocolitica is a facultative anaerobic gram-negative coccobacillus that is more common in the winter and commonly transmitted by eating raw or undercooked pork, unpasteurized milk, untreated water, or contact with animals. The incubation period is 4 to 6 days and diagnosis can be made by isolation from stool, blood, bile, wound, throat swab, mesenteric lymph nodes, cerebrospinal fluid, or peritoneal fluid.¹⁸ Antibiotic therapy can be considered for more severe cases but has no effect on postinfectious complications, such as reactive arthritis and erythema nodosum.¹⁸

Listeria

Listeria is more common in older adults, the immunocompromised, and particularly pregnant women. *L monocytogenes* is a gram-positive, anaerobic motile bacillus transmitted via contaminated food (see [Table 2](#)) and maternal-fetal transmission. Listeriosis can cause bacteremia, meningitis, miscarriage, fetal loss, and death with 15% of cases in the United States occurring in pregnant women, with Hispanic women being at greater risk.¹⁹ In pregnant women, *Listeria* presents with fever (65%), flu-like symptoms (32%), abdominal or back pain (21.5%), vomiting/diarrhea (7%), headache (10.5%), myalgia (4%), or sore throat (4%),²⁰ requiring a high index of suspicion during pregnancy. The American College of Obstetricians and Gynecologists does not recommend routine testing for asymptomatic women.²¹ Invasive listeriosis in nonpregnant individuals is more common in those older than 65 years of age, with 89% of cases resulting in hospitalization and 23% in death in 2014.¹⁹ Diagnosis can be made via culture of blood or cerebrospinal fluid. Empiric antibiotic treatment of pregnant women may be considered during outbreaks or in those that are symptomatic and with fever.²¹ Those that are immunocompromised or pregnant should be encouraged to avoid foods commonly associated with *Listeria* ([Box 3](#)).

Clostridium perfringens

C perfringens is a spore-forming gram-positive bacterium that is a common cause in the United States of food-borne illness, in raw meat and poultry. Its spores can survive high

Box 2

***Escherichia coli* diarrheal subtypes, as classified by the Centers for Disease Control and Prevention**

- Shiga toxin-producing *E coli* (STEC) also known as Verocytotoxin-producing *E coli* or enterohemorrhagic *E coli*
- Enterotoxigenic *E coli*
- Enteropathogenic *E coli*
- Enteroaggregative *E coli*
- Enteroinvasive *E. coli* (EIEC)
- Diffusely adherent *E coli*

Data from Questions and Answers | *E.coli* | CDC. Available at: <https://www.cdc.gov/ecoli/general/index.html>. Accessed April 9, 2018.

Box 3**Foods commonly associated with *Listeria monocytogenes***

- Mexican-style cheese, such as queso fresco, queso blanco
- Unpasteurized dairy products
- Raw meats, delicatessen meats, hot dogs, cold cuts, pâtés, and meat spreads
- Smoked or raw seafood
- Soft cheeses, such as feta and brie or blue-veined cheeses

Data from Centers for Disease Control and Prevention (CDC). Vital signs: listeria illnesses, deaths, and outbreaks—United States, 2009–2011. MMWR Morb Mortal Wkly Rep 2013;62(22):448–52. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/23739339>. Accessed January 1, 2018.

temperatures, germinating and reproducing in incorrectly stored or reheated foods. The toxin produced by *C perfringens* causes diarrhea and abdominal cramps within 6 to 24 hours of exposure and typically lasts 24 hours with spontaneous resolution. Fever and vomiting are uncommon with *C perfringens* infections, and the illness is not spread from person to person. Treatment is supportive with no role for antibiotic use.

Clostridium difficile

C difficile is a gram-positive, spore forming, anaerobic bacillus spread via fecal oral transmission that can survive on dry inanimate surfaces for up to 5 months,²² making infection control particularly important. *C difficile* infection (CDI) has become common in both community and health care environments, causing 12.1% of health care-associated infections.²³ Multiple recurrent CDI is associated with older age, female gender, use of antibiotics, proton pump inhibitors, corticosteroids within 90 days of diagnosis, chronic kidney disease, and nursing homes.²⁴ A 2014 systemic review found that mortality was associated with older age, comorbidities, hypoalbuminemia, leukocytosis, acute renal failure, and infection with ribotype 027.²⁵ Community-acquired CDI was found in a 2013 meta-analysis to be greatest with use of the following antibiotics: clindamycin (OR 20.43), fluoroquinolones (OR 5.65), cephalosporins (OR 4.47), penicillins (OR 3.25), macrolides (OR 2.55), and sulphonamides/trimethoprim (OR 1.84).²⁶

Fever, cramping, abdominal discomfort, passage of mucus or occult blood in the stool, and peripheral leukocytosis are common. It is important to distinguish CDI from colonization, because asymptomatic *C difficile* colonization prevalence can be as high as 15% in healthy adults and 18% to 90% among healthy newborns and infants.²⁷ Diagnosis of CDI is made in those that are symptomatic and over 2 years of age by the presence of stool toxin. Stool toxin in children under 2 years of age does not confirm diagnosis because of the high rate of colonization, requiring exclusion of other causes of diarrhea.²⁸ Less commonly, diagnosis is made by histopathology, endoscopy (eg, pseudomembranous colitis), or CT (eg, severe colitis, megacolon or ileus).

Medical management can be based on disease severity, as is outlined in **Table 7**. Complications of severe *C difficile* colitis include dehydration, electrolyte disturbances, hypoalbuminemia, toxic megacolon, bowel perforation, hypotension, renal failure, systemic inflammatory response syndrome, sepsis, and death. Surgical colectomy may be considered for severely ill patients. A 2017 study showed that despite increased infection rates, *C difficile*-associated fatality decreased from 3.6% in 2004 to 1.6%.²⁹ Newer treatment methods for recurrent or refractory cases include fidaxomicin therapy, monoclonal antibodies, and fecal microbiota transplantation. There is insufficient evidence to recommend probiotics for treatment of CDI,³⁰ but a Cochrane review showed moderate evidence of benefit for prevention.³¹

Disease Severity	Criteria	Treatment
Mild-moderate	WBC \leq 15,000 cells/ μ L Cr \leq 1.5 times baseline	Metronidazole 500 mg PO tid \times 10–14 d
Severe	WBC \geq 15,000 cells/ μ L Cr \geq 1.5 times baseline	Vancomycin 125 mg PO qid \times 10–14 d
Severe-complicated	Meets criteria for severe disease PLUS hypotension, shock, ileus, megacolon, or perforation	Vancomycin 500 orally or per nasogastric tube qid PLUS metronidazole 500 mg IV q8h (consider rectal vancomycin if complete ileus)

Abbreviations: Cr, creatinine; WBC, white blood cell count.

Adapted from Cohen SH, Gerding DN, Johnson S, et al. Clinical practice guidelines for *Clostridium difficile* infection in adults: 2010 update by the Society for Healthcare Epidemiology of America (SHEA) and the Infectious Diseases Society of America (IDSA). *Infect Control Hosp Epidemiol* 2010;31(5):447; with permission.

Viruses

Norovirus

Noroviruses are highly contagious and a significant cause of gastroenteritis worldwide.³² Prolonged viral shedding, persistence in the environment, and the small inoculum required to cause infection contribute to increased transmission.³³ Norovirus causes approximately 20 million cases of acute gastroenteritis and up to 800 deaths per year in the United States, with most cases presenting during the winter.³⁴ Outbreaks occur in health care facilities, schools, daycare centers, restaurants, and cruise ships. In countries where the rotavirus vaccine has been implemented, norovirus has surpassed rotavirus as the predominant cause of acute gastroenteritis in children.³⁵

The incubation period is between 24 to 48 hours, and treatment is mainly supportive, with correction of dehydration and electrolyte abnormalities as the primary focus.³³ Polymerase chain reaction (PCR) testing which is highly sensitive and specific and allows for viral typing, is considered to be the gold standard for diagnosis, with immunoassays having inferior sensitivity to PCR.³⁶ Early identification, reporting, and implementation of infection control measures such as contact precautions, hand washing with soap and water, environmental disinfection with bleach solutions, mask use for individuals who may be exposed to vomitus, visitor restrictions, and ward closures may help to reduce transmission.³⁷

Rotavirus

Rotavirus is the most common cause of severe diarrhea in infants and children under 5 years of age worldwide and has been responsible for up to 600,000 deaths annually.³⁸ Disease can occur year-round but typically peaks in the winter and spring. Most unvaccinated children have evidence of rotavirus infection by the age of 5.³⁸ Rotavirus has an incubation period of 48 hours, causing vomiting, fever, and watery diarrhea lasting 3 to 8 days.³⁹ Less commonly, development of seizures, necrotizing enterocolitis, intussusception, central nervous system involvement, and death can occur. Stool enzyme immunoassays are most commonly used for diagnosis, although PCR is more sensitive. Alternative diagnostic methods include culture, electron microscopy, and serology to detect antibodies to rotavirus. Treatment is primarily supportive. Although improvements in water quality and sanitation have led to decreased incidence of some enteric pathogens, the incidence of rotavirus infection has been

largely unaffected. Vaccination, on the other hand, which was introduced in the United States in 2006, is estimated to prevent more than 60,000 hospitalizations each year.⁴⁰

Parasites

Cryptosporidium

Cryptosporidium was more common during the AIDS epidemic and can be transmitted via water, animal exposure, as well as person-to-person contact. A small inoculum (10–100 oocysts) may transmit infection, with spores surviving for months in water or soil and resistant to water purification chemicals, resulting in outbreaks in lakes and swimming pools.⁴¹ Cryptosporidiosis typically causes self-limited watery diarrhea, nausea, vomiting, and abdominal pain, with more severe, protracted symptoms and extraintestinal disease in the immunocompromised or malnourished children, who may exhibit respiratory tract involvement or failure to thrive.⁴¹

Cryptosporidium is detected by microscopy, requiring special staining for visualization, PCR, or stool antigen assays, which are costlier. Both PCR and immunoassays offer improved sensitivity over microscopy.⁴² Nitazoxanide shortens the duration of diarrhea and parasite excretion in immunocompetent hosts.⁴³ In immunocompromised hosts, nitazoxanide may still be of some benefit, but at higher doses and longer duration. For patients with HIV and low CD4 counts (<50 cells/ μ L), antiretroviral therapy is the primary treatment because nitazoxanide has been of little benefit.⁴⁴

Giardia

Giardia intestinalis is among the most common causes of human parasitic infections in the United States, with approximately 20,000 cases reported annually.⁴⁵ *Giardia* can be transmitted via water, via food, or person to person. Most outbreaks occur in summer months, because of increased recreational exposure to contaminated water. Human infection occurs after ingestion of as few as 10 cysts, causing both acute and chronic infections. Common symptoms include diarrhea, nausea, vomiting, malaise, abdominal cramping, steatorrhea, and weight loss. In patients with chronic infection, significant weight loss can occur. First-line treatment options for *Giardia* include metronidazole 250 mg orally 3 times daily for 5 to 7 days, tinidazole 2 g orally once, or nitazoxanide 500 mg orally twice a day for 3 days. Albendazole, paromomycin, and furazolidone have been used as alternative therapies.

Entamoeba histolytica

Amebic dysentery is caused by the protozoan parasite, *E histolytica*, via fecal-oral transmission of cysts. Risk factors include communal living, oral and anal sex, immunosuppression, and travel to endemic areas.⁴⁶ *E histolytica* can cause mild diarrhea or fulminant dysentery. Severe disease can be fatal or cause colonic ulcers, toxic megacolon, perforation, chronic carriage or amebic liver abscesses. Of note, only 10% to 20% of infected patients develop symptoms.⁴⁷

Available methods for detecting *E histolytica* infection include antibody testing, stool microscopy, culture, and enzyme-linked immunosorbent assay (ELISA) or PCR-based stool assays. Antibody testing has limited utility in patients from endemic areas because it can be difficult to distinguish between active infection and prior exposure. Microscopy is poorly sensitive and *E histolytica* is difficult to distinguish from nonpathogenic *Entamoeba* species. Stool assays using PCR and ELISA-based antigen detection are highly sensitive and specific but may not be available in resource-limited settings.⁴⁸

Symptomatic infections are generally treated with 7 to 10 days of metronidazole 500 to 750 mg orally 3 times a day, followed by a luminal agent such as paromomycin, for the treatment of intraluminal cysts.^{49,50} Colonization can be treated with solely an

intraluminal agent, such as paromomycin 25 to 35 mg/kg/d orally divided 3 times a day for 7 days or diloxanide furoate 500 mg orally 3 times a day for 10 days.⁵⁰ Treatment is recommended even in the absence of symptoms due to the risk of developing invasive disease and spread to close contacts.⁴⁶

Special Populations

Persons with HIV are at increased risk of acute and chronic diarrhea because of a combination of immunosuppression, direct HIV viral effects, adverse medication effects and behaviors that may increase exposure. HIV enteropathy can result from direct effects of HIV on gastrointestinal tract cells and gut-associated lymphoid tissue.⁵¹ After the introduction of highly active antiretroviral therapy in 1996, there was a reduction in opportunistic infections as the cause of chronic diarrhea from 53% to 13% in patients with AIDS, whereas the overall incidence of chronic diarrhea did not decrease.⁵² Lymphoma and Kaposi sarcoma are other noninfectious causes of diarrhea. In those with HIV and bacterial diarrhea, *C difficile* was the most common cause in persons studied from 1992 to 2002.⁵³ An acid-fast smear or immunofluorescent stain should be requested to look for *Cryptosporidium*, *Isospora*, and *Cyclospora*. In patients with CD4 counts less than 100 cells/ μ L, the possibility of *Microsporidium* should also be investigated via trichrome staining of a stool specimen. Biopsy may be required to confirm infection with *Mycobacterium avium complex* or cytomegalovirus.^{54,55}

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