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Acute Gastroenteritis

Nancy S. Graves, MD

KEYWORDS

• Gastroenteritis • Infectious • Vomiting • Diarrhea • Abdominal pain

KEY POINTS

- Acute gastroenteritis is a common infectious disease syndrome, causing a combination of nausea, vomiting, diarrhea, and abdominal pain. The Centers for Disease Control and Prevention (CDC) estimate there are more than 350 million cases of acute gastroenteritis in the United States annually, and 48 million of these cases are caused by foodborne bacteria.
- Traveler's diarrhea affects more than half of people traveling from developed countries to developing countries. Prevention can be summarized by the caution, "boil it, cook it, peel it, or forget it."
- Except in cases of fever, bloody diarrhea, immunocompromised patients, or patients with significant comorbidities, identifying a specific pathogen is rarely indicated in acute bacterial gastroenteritis because illness is usually self-limited.
- In both adult and pediatric patients, the prevalence of *Clostridium difficile* is increasing in the United States. Contact precautions, public health education, and prudent use of antibiotics are still necessary goals. Complicating these efforts are that there is increasing antibiotic resistance to *C difficile* and a new strain, NAP1/027/III, has been emerging since the early 2000s. This new strain has a high association with community onset and has been linked to increasing frequency and severity of illness. There is research into the possibility that the community onset may be related to animals and to retail meat, where the new strain has been detected.
- Preventing dehydration or providing appropriate rehydration is the primary supportive treatment of acute gastroenteritis.

INTRODUCTION

Definition

Gastroenteritis is inflammation of the stomach, small intestine, or large intestine, leading to a combination of abdominal pain, cramping, nausea, vomiting, and diarrhea. Acute gastroenteritis usually lasts fewer than 14 days. This is in contrast to persistent gastroenteritis, which lasts between 14 and 30 days, and chronic gastroenteritis, which lasts more than 30 days.[1]

Department of Family and Community Medicine, Milton S. Hershey Medical Center, Penn State Hershey, 500 University Drive, Hershey, PA 17033, USA
E-mail address: ngraves@hmc.psu.edu

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Epidemiology

In the United States, acute gastroenteritis is often viewed as a nuisance rather than the life-threatening illness it can be in developing countries. Although significant morbidity and mortality have been attributed to acute diarrheal illnesses in the United States, epidemiologic studies in this country have not been as comprehensive as those conducted in developing nations. The CDC, however, estimate that there are more than 350 million cases of acute diarrheal illnesses in the United States annually. Acute gastroenteritis compares with upper respiratory illnesses as the most common infectious disease syndrome.[2,3]

Using data from the National Center for Health Statistics, the CDC recently reported that deaths from all-cause gastroenteritis increased from approximately 7000 to more than 17,000 per year from 1999 to 2007. Adults over 65 years old made up 83% of these deaths and *C difficile* accounted for two-thirds of these deaths, reflecting that the most significant morbidity and mortality are experienced by the extremes of age.[4]

Etiology

Etiology of acute gastroenteritis

Acute gastroenteritis is caused by many infectious agents as listed in **Table 1**.

Assessing the precise incidence and cause of acute infectious gastroenteritis is made difficult because not everyone reports their symptoms or seeks medical care. In addition, stool cultures, which are used to identify bacterial causes of gastroenteritis, are only positive in 1.5% to 5.6% of cases.[5]

Viral causes of acute gastroenteritis are dominated by rotavirus and norovirus. In the United States, it is estimated that 15 to 25 million episodes of viral gastroenteritis occur each year, leading to 3 to 5 million office visits and 200,000 hospitalizations.[6,7]

Rotavirus causes a particularly severe dehydrating gastroenteritis that affects young children. The severity of the infection is made worse by malnourishment, making rotavirus a significant cause of mortality in children worldwide, responsible for approximately 500,000 deaths annually.[8,9] The introduction of the rotavirus vaccine in the United States and Europe has been effective at reducing rotavirus gastroenteritis. There has been a 67% decrease in positive laboratory diagnosis attributed to vaccination.[10]

Norovirus, however, causes the most outbreaks of nonbacterial acute gastroenteritis in all age groups. It often occurs in epidemic outbreaks in schools, nursing homes, cruise ships, prisons, and other group settings. Symptoms of severe vomiting are usually self-limited, lasting 12 to 60 hours. Transmission of this stable virus is through the fecal-oral route, with viral shredding lasting on average 10 to 14 days after onset of symptoms.[11]

Table 1
Infectious causes of acute gastroenteritis

Viral: 50%–70%	Bacterial: 15%–20%	Parasitic: 10%–15%
Norovirus	Shigella	Giardia
Rotavirus	Salmonella	Amebiasis
Enteric adenovirus types 40 and 41	Campylobacter	Cryptosporidium
Astrovirus	*E coli*	Isospora
Coronavirus	Vibrio	Cyclospora
Some picornaviruses	Yersinia	Microsporidium
	C difficile	

Rotavirus and enteric adenovirus can be detected by rapid assays for the viral antigen in stool. Norovirus is best detected by reverse transcriptase–polymerase chain reaction.

Medications and toxic ingestions that cause acute diarrhea or gastroenteritis include those listed in **Table 2**.

Etiology of chronic gastroenteritis

Causes of persistent or chronic gastroenteritis include parasitic infections, medications, inflammatory bowel disease (ulcerative colitis, Crohn disease, collagenous colitis, and microscopic colitis), irritable bowel syndrome, eosinophilic gastroenteritis, celiac disease, lactose intolerance, colorectal cancer, bowel obstruction, malabsorption, and ischemic bowel.

Immunocompromised hosts are most vulnerable to chronic gastroenteritis infections. *Crytosporidium* has been a cause of chronic diarrhea in persons with AIDS. It is also responsible for large outbreaks in day care centers and public swimming pools and has contaminated public water supplies. One of the reasons for these outbreaks is that the oocytes are resistant to bleach or other disinfectants, making them easily transmittable by contact with contaminated surfaces or by person-to-person contact. *Giardia* is another common cause of chronic gastroenteritis. It is found in contaminated streams but is also common in day care centers and swimming pools. *Giardia* causes bloating, flatulence, and explosive, pale, foul-smelling diarrhea.

TYPES OF ACUTE GASTROENTERITIS

The remainder of this article focuses on acute bacterial gastroenteritis, reviewing the common pathogens that cause traveler's gastroenteritis, foodborne gastroenteritis, and antibiotic-associated gastroenteritis. Each section addresses transmission, pathophysiology, the incubation period, symptoms, symptom duration, management, and prevention.

Traveler's Diarrhea

Travelers to developing countries often present to their primary care providers with concerns about traveler's diarrhea and how to avoid or treat this problem should it occur; 40% to 60% of travelers to developing countries acquire this problem. It should also be considered if diarrhea develops within 10 days of their return home.

For epidemiologic reasons, traveler's diarrhea is divided into classic, moderate, and mild forms.

Table 2
Medications and toxic ingestions that cause acute diarrhea or gastroenteritis

Medications	Toxic Ingestions
Antibiotics	Organophosphates
Laxative abuse	Poisonous mushrooms
Sorbitol	Arsenic
Colchicine	Ciguatera or scombroid
Cardiac antidysrhythmics	
Nonsteroidal anti-inflammatory drugs[12]	
Chemotherapeutics	
Antacids	

- Classic: 3 of more unformed bowel movements per 24 hours plus 1 of the following: nausea, vomiting, fever, abdominal pain, and blood in the stool
- Moderate: 1 to 2 unformed bowel movements per 24 hours plus 1 of the above symptoms OR more than 2 unformed bowel movements
- Mild: 1 to 2 unformed bowel movements

Transmission

Traveler's diarrhea is usually transmitted by contaminated food or water. It can be caused by bacteria, viruses, or parasites. Bacteria cause the majority of cases of traveler's diarrhea. The most common are enterotoxigenic *E coli* (ETEC), followed by *Salmonella*, *Campylobacter jejuni*, and *Shigella*. In 1 study of 322 patients, ETEC caused 12% of bacterial traveler's diarrhea, *Salmonella* 8%, *Campylobacter jejuni* 6%, and *Shigella* less than 1%. In another study of 636 travelers, ETEC caused 30% and enteroaggregative *E coli* caused 26% of cases.[13,14]

Coinfection with an additional pathogen was found in 20% of travelers.[14]

Areas of the world with the highest risk are countries in Asia, outside of Singapore, on the African continent, outside of South Africa, and in Central and South America.

Pathogenesis

Pathogenesis is discussed in detail for each bacterial cause.

Incubation

Incubation is 4 to 14 days after arrival in a developing nation.

Symptoms

Common symptoms include malaise, anorexia, abdominal pain and cramping, watery diarrhea, nausea and vomiting, and low-grade fever. If caused by *Campylobacter jejuni* or *Shigella*, symptoms may progress to colitis, bloody diarrhea, and tenesmus.

Duration

Duration is 1 to 5 days and generally self-limited, but, in 8% to 15% of cases, symptoms last longer than 1 week.[15] If bloating, nausea, or other gastrointestinal symptoms persist for more than 14 days, consider alternative diagnoses, such as parasitic infection.

Diagnosis

The diagnosis is often clinical and confirmation is usually not pursued because traveler's diarrhea is self-limited. Stool cultures may be useful in patients with severe symptoms, prolonged illness, bloody diarrhea, and fever. Stool cultures, however, do not differentiate between nonpathogenic *E coli* and ETEC or enteroaggregative *E coli*.

Treatment

- Fluid replacement is the mainstay of symptomatic treatment, plus or minus diet restrictions. There is limited information about whether a clear liquid diet versus an unrestricted diet significantly changes the duration or severity of symptoms because traveler's diarrhea is usually self-limited, lasting 3 to 5 days. Oral rehydration is ideal, but intravenous hydration may be necessary in the setting of dehydration.
- Antibiotics may shorten the course by 1 to 2 days. Travelers often request a prescription for antibiotics that may be taken at the onset of symptoms. Ciprofloxacin (500 mg as a single dose or twice a day for 1–2 days) is commonly sufficient, although resistance to quinolones is increasing, especially for *Campylobacter jejuni.* Quinolones are not Food and Drug Administration approved for pregnancy

or for treating traveler's diarrhea in children. Azithromycin is appropriate in these groups. In adults, a single 1-g dose is effective. In children, recommended dosing is 10 mg/kg as a single dose, not to exceed 1 g. Rifaximin (200 mg 3 times a day) has been shown effective and, with increasing quinolone resistance, it is increasingly used.[16]

- Antimotility agents, such as loperamide or diphenoxylate, can decrease stool frequency but do not alter the course of the infection. Their use should be avoided in cases of fever or rectal bleeding.
- *Lactobacillus GG*, a specific probiotic, has been shown to decrease diarrhea caused by the pathogens that typically cause traveler's gastroenteritis. Other *Lactobacillus* preparations, however, using nonviable probiotics, have not.[17,18]

Prevention

In 2001, the Infectious Diseases Society of America (IDSA) published guidelines to assist travelers in decreasing their chances of contracting traveler's diarrhea:

- Water must be boiled for 3 minutes to kill pathogens. Two drops of bleach or 5 drops of iodine kill pathogens in water within 30 minutes.
- Freezing does not kill pathogens. Avoid ice, request bottled beverages, and use a straw versus a glass.
- Fruit that must be peeled is safe. Fruit that is not peeled or raw vegetables should be avoided.
- Steam table buffets pose a high risk of contracting traveler's gastroenteritis.
- Communal condiments are frequently contaminated and should be avoided.

Medications, such as H_2 blockers and proton pump inhibitors, can increase susceptibility to traveler's diarrhea. These medications lower gastric acidity and can increase the chance of contracting traveler's diarrhea by allowing more pathogens to survive transit to the small bowel. Similarly, conditions or medications that slow gastric motility allow the number of pathogens to accumulate.

Foodborne Acute Gastroenteritis

The CDC estimate that 48 million cases of foodborne bacterial gastroenteritis occur annually in the United States, leading to 125,000 hospitalizations, 3000 deaths, and costs greater than $150 billion.[2] The Foodborne Disease Active Surveillance Network (or FoodNet program) was established in 1996 by the CDC to track foodborne gastrointestinal illnesses in the United States. Data from this 10-site study that covers 46 million cases suggests that 1 in 5 episodes of gastroenteritis are caused by foodborne pathogens. Data from 2010 show little significant overall change in the known foodborne causes of acute gastroenteritis over the past 4 years. The data did, however, show a decline in Shiga toxin–producing *E coli* O157:H7 and *Shigella*. *Vibrio* gastroenteritis increased over this time period and Salmonella incidence was unchanged, despite increasing awareness and efforts to decrease these infections. In general, treatment of foodborne gastroenteritis can range in cost from $78 in Montana to $162 in New Jersey. The total cost per case, including productivity losses, can be as high as $1506, as noted in Connecticut.[3] There is also research suggesting, however, a significant presence of unspecified agents causing 38.4 million cases of foodborne acute gastroenteritis.[19] Reasons for this include a limited amount of data because not all cases of foodborne gastroenteritis are reported nor is a specific etiology identified; other microbes or chemicals in food could cause or contribute to illness; and, finally, new causes being discovered and known causes, such as *C difficile*, not thought to be transmitted by food, have been detected in retail meat products,[19] suggesting a new route of transmission.

Pathogenesis

The pathogenesis of foodborne gastroenteritis can be broken down into 3 mechanisms:

1. Pathogens that make a toxin in the food before it is consumed (preformed toxin)
2. Pathogens that make a toxin in the gastrointestinal tract, after the food is ingested
3. Pathogens that invade the bowel wall and directly break down the epithelial lining, releasing factors that cause an inflammatory diarrhea.

1. Preformed toxins: *Staphylococcus aureus* and *Bacillus cereus* produce heat-stable enterotoxins in the food before it is consumed.

Transmission: These pathogens are usually transmitted by a food handler and often found in summer picnic foods.
S aureus: grows well in dairy, meat, eggs, and salads
Bacillus cereus: grows in starchy foods, such as rice, but is also found in beef, pork, and vegetables

Incubation: 1–6 hours. Ingestion of preformed toxins leads to rapid onset of symptoms.

Pathophysiology: These bacteria usually affect the small intestine, causing nausea, profuse vomiting, and abdominal pain/cramping. The emetic enterotoxin can be found in vomitus and the food. Testing is rarely conducted, however, because illnesses are self-limited. In cases of preformed toxins, there is no risk of person-to-person spread.

Symptoms: Sudden onset of nausea and vomiting after eating suggests ingestion of a preformed toxin.

Diagnosis: Stool studies are not contributory. Diagnosis is usually made based on history and food diary.

Treatment: No antibiotics needed because it is a preformed enterotoxin.
Supportive care and parenteral antiemetics help control vomiting.

Prognosis: Rapid spontaneous recovery in 1 day is typical.

2. Pathogens that transmit illness by making a toxin after consumption

a. *C perfringens*

Transmission: ingestion of spores that have germinated in food products, such as beef, pork, home canned foods, and poultry[1]

Pathophysiology: Once spores reach the small intestine, they produce an enterotoxin, leading to watery diarrhea.

Incubation: 6–48 hours

Symptoms: frequent watery stools and abdominal cramping; rarely, fever, nausea, and vomiting

Duration: usually less than 24 hours

Treatment: Rarely does a patient need intravenous fluids. Antibiotics are of no use given the short duration of symptoms.

Diagnosis: Usually unnecessary given the short lived nature of this illness, but fecal leukocytes are present because this is an inflammatory gastroenteritis.

Prognosis: Self-limited, rarely lasting more than 24 hours. Ingestion of type C strain of these bacteria, however, can lead to a serious illness, enteritis necroticans (pigbel). Symptoms include severe abdominal pain, vomiting, diarrhea, and possible shock and can be rapidly fatal.

Prevention: Do not keep foods that have already been cooked warm for long periods of time.

b. ETEC

Transmission: ingestion of food or water contaminated by infected fecal matter

Pathophysiology: Bacteria attach to the wall of the small bowel and enterotoxins are released, drawing fluid and electrolytes from the mucosa into the lumen, causing profuse watery diarrhea.
Incubation: 24–72 hours after ingestion
Symptoms: wide-ranging, from mild to severe diarrhea
Duration: 48–72 hours
Treatment: hydration plus ciprofloxacin (500 mg twice daily × 3 days) or Bactrim DS (twice daily × 3 days)
Prevention: safe preparation of food and the avoidance of keeping foods that have already been cooked warm for long periods of time

3. Pathogens that directly invade the bowel wall causing inflammatory diarrhea

a. Enterohemorrhagic *E coli* (EHEC) (Shiga toxin producing)
E coli O157:H7 is 1 of at least 30 serotypes of *E coli* that make shiga-like toxin. It was discovered in 1982, after 2 outbreaks traced to undercooked beef. In May 2011, another serotype, O104:H4, was discovered in Germany.[20] The CDC estimate 110,000 cases and 2100 hospitalizations annually in the United States.[1]
Transmission: These bacteria are present in the intestines of cows and transferred initially through processing and then ingested through undercooked animal food products. Transmission can also occur through contaminated water, raw milk, unpasteurized apple cider, petting zoos, and day care centers.[1]
Pathophysiology: Bacteria attack epithelial cells of the cecum and the large bowel. The shiga-like toxins, called verotoxins, destroy the cells, leading to hemorrhagic colitis.
Incubation: 1–9 days, with 3–4 days typical
Symptoms: Watery diarrhea develops that quickly becomes bloody. Elevated white cell count, abdominal pain, cramping, and vomiting are also commonly seen. The absence of fever (or only a low-grade fever) helps differentiate EHEC from other bacterial causes of bloody acute gastroenteritis.
Duration: 1 week for uncomplicated EHEC infection
Diagnosis: The CDC recommend all stool cultures be screened for *E coli* O157:H and certainly all bloody stool samples. Fecal leukocytes are present in 50% of cases. *E coli* O157:H7 can be screened for using a sorbitol MacConkey agar. Both stool cultures and toxin assays are recommended.
Complications: Hemolytic uremic syndrome (HUS) is associated with Shiga toxin 2 and is a complication seen in 6% to 9% of EHEC causes of acute gastroenteritis.[21] The CDC estimate that greater than 90% of HUS is associated with *E coli* O157:H7. HUS is often seen in children younger than 4 years old and the elderly. There is some concern that empiric antibiotic use may increase the risk of developing HUS.[22] Long-term sequelae caused by this complication include, hypertension, proteinuria, decreased glomerular filtration rate, and, less commonly, seizure, coma, or motor deficits.[23]
Thrombotic thrombocytopenia purpura, which shares many similar features with HUS, presents with prominent neurologic findings rather than renal failure. Rarely, pseudomembranous colitis is associated with *E coli* O157:H7.
Treatment: Treatment is largely supportive. Antibiotics do not shorten the duration of illness and should be avoided. There is some thought that empiric antibiotics or antiperistaltics may increase the chance of developing complications.[24]

Prognosis: Uncomplicated cases resolve spontaneously in 7 to 10 days. A carrier state may last an additional 1 to 2 weeks. Hospitalization is required for 23% to 47% of patients, median length of stay 6 to 14 days. Mortality rate is 1% to 2% and is highest in the elderly population.[1]

Prevention: The best prevention is practicing good hand hygiene and fully cooking meat. In addition, the Department of Agriculture has been improving and continues to improve the slaughter process.

b. Salmonella

Transmission: Salmonella is transmitted through the consumption of contaminated raw or undercooked eggs, meats, raw milk, ice cream, peanuts, fruits, and vegetables. Transmission also occurs through contact with infected animals, such as turtles and pet ducklings.[11]

Pathophysiology: bacteria that survive the acidity of the stomach, colonize the intestine, and move across the intestinal epithelium, either by direct invasion of enterocytes or through dendritic cells inserted into epithelial cells. Once present, the inflammatory process begins releasing cytokines, neutrophils, macrophages, and T cells and B cells. This inflammatory response decreases normal intestinal flora and allows the pathogen to proliferate. The nontyphoid Salmonella produce a more localized response and the typhi serotype (the cause of typhoid fever) tends to be more invasive and more often results in bacteremia.[25]

Incubation: 6–48 hours[11]

Duration: 1–7 days

Symptoms: nausea, vomiting, fever, cramping abdominal pain, possibly bloody diarrhea

Treatment: not usually recommended. Exceptions include severe illness, extremes of age, valvular heart disease, uremia, or malignancy. In the case of these exceptions, a third-generation cephalosporin or fluoroquinolone for 5 to 7 days is indicated.

Complications: Antibiotic use can increase carrier state. Additional complications include transient reactive arthritis, which can be seen in up to 30% of adult patients, and Reiter syndrome, which occurs in 2% of patients.

Prognosis: Most patients recover in 2 to 5 days. Sustained or intermittent bacteremia may occur in immunocompromised patients.

c. *Campylobacter jejuni*

Population: usually under 5 years of age

Transmission: handling or eating raw or undercooked poultry or raw milk or cheeses, by contaminated drinking water, or by handling infected animals[1]

Pathophysiology: direct invasion of epithelial cells of the colon inducing inflammation

Incubation: 1 to 10 days

Duration: 5 to 14 days

Symptoms: Usually rapid onset with fever, chills, headache, and malaise followed by abdominal pain, nausea, vomiting, and diarrhea. Diarrhea may be grossly bloody or melanotic in 60% to 90% of patients.

Treatment: Empiric antibiotics are not recommended in healthy patients. Stool culture is appropriate. Antibiotics shorten the illness by 1 to 1.5 days. Erythromycin or azithromycin $\times$ 5 days (resistance to fluoroquinolones).

Complications: *Campylobacter jejuni* gastroenteritis is associated with postinfectious Guillain-Barré syndrome, incidence 1 per 1000. In cases of more severe symptoms, this can be less reversible.[26]

Prognosis: Most patients recover within 1 week. Relapses are common but tend to be milder than the original infection. Fatalities are rare.

d. *Vibrio parahaemolyticus*

It is not common in the United States, but worldwide this pathogen is the most common cause of bacterial gastroenteritis.[1]

Transmission: eating contaminated seafood, crabs, oysters, or clams or by exposure of an open wound to contaminated seawater (Gulf of Mexico). It has been transmitted through airline food.

Pathophysiology: production of a heat-stable enterotoxin, inducing a secretory diarrhea and hemolysis

Incubation: 6 hours to 4 days

Duration: self-limited up to 3 days, commonly 24 to 48 hours

Symptoms: abrupt onset of severe watery diarrhea, abdominal cramping, nausea, and vomiting are common symptoms. Fever occurs less commonly.

Diagnosis: can be cultured on thiosulfate citrate–bile salts sucrose if ingestion of contaminated seafood within 3 days before testing[1]

Treatment: tetracycline × 3 days, ciprofloxacin × 1 dose, or chloramphenicol

e. Shigella

Population: usually has an impact on children less than 5 years of age. It is rare in the United States.

Transmission: consumption of contaminated food or water or by person-to-person or fecal-oral route

Pathophysiology: invades colonic epithelia cells; Shiga toxin causes inflammation and results in hemorrhagic colitis.[1]

Incubation: 1 to 6 days

Duration: self-limiting, lasting 2 to 5 days

Symptoms: Fever, cramping abdominal pain, and diarrhea that is often bloody. Infants may not have bloody diarrhea.

Treatment: ciprofloxacin (500 mg twice a day × 3–5 days), trimethoprim/sulfamethoxazole (160 mg twice a day × 3–5 days), or azithromycin (500 mg once daily for 3 days).

Prognosis: Most patients recover in 1 week. Untreated patients shed bacteria in stool for 2 weeks. Relapse occurs in 10% of patients if not treated with antibiotics.

Antibiotic-Associated Diarrhea

Antibiotic-associated diarrhea is also called *C difficile* colitis. This infection often occurs in hospitalized patients, with increasing risk correlating with length of hospital stay. The use of multiple antibiotics and duration of antibiotic are associated with an increased risk of *C difficile* infection. Patients older than 65 years of age and those who are immunocompromised are at an increased risk of developing *C difficile* colitis, likely related to comorbid conditions.[27] The prevalence of *C difficile* associated colitis is increasing in the United States, both in pediatric and adult admissions. From 2001 to 2006, pediatric *C difficile* admissions increased from 2.6 to 4 cases per 1000.[28] The National Hospital Discharge Survey found the rate for *C difficile* colitis increased from 31 per 100,000 in 1996 to 61 per 100,000 in 2003.[29]

Antibiotics most often associated with *C difficile* infection are flouroquinolones, clindamycin, cephalosporins, and penicillins. Those least associated with *C difficile* infection include doxycycline, aminoglycosides, vancomycin, and metronidazole. Proton pump inhibitors have also been associated with increased susceptibility to *C difficile*

infection. Studies found that the use proton pump inhibitors increased the risk 1.4 to 2.75 times compared with those without proton pump inhibitor use.[30]

Transmission

Transmission occurs by fecal-oral route and colonization occurs because antibiotic use has disturbed the normal flora of the intestinal tract.

Pathophysiology

C difficile is an anaerobic bacterium that forms spores capable of producing exotoxins. The spores are heat resistant, acid resistant, and antibiotic resistant. They are also resistant to alcohol-based hand sanitizer, so caregivers must wash their hands in soap and water. Once in the colon, the bacteria become functional and produce toxin A (enterotoxin) and toxin B (cytotoxin). Both toxins lead to inflammation, mucosal injury, and secretory diarrhea.[31] Although toxin B is more virulent than toxin A, they both inactivate regulatory pathways, causing cell apoptosis, mucosal ulceration, and neutrophil chemotaxis to produce the pseudomembranes, common in this infection.[32] Pseudomenbranes are composed of neutrophils, fibrin, epithelial debris, and mucin. Pseudomembranes are not found in all patients, for example, those with ulcerative colitis or who are on immunosuppressive agents, such as steroids or cyclosporine.[33] The hypothesized reason for this is that pseudomembranes develop because of the host immunoreactions.[33]

A new strain of *C difficile*, hypervirulent North American pulsed-field type 1 (NAP1/027/III), has been suspected in epidemic outbreaks since the early 2000s. It produces a binary toxin in addition to larger quantities of toxin A and toxin B and is associated with increasing incidence and severity of illness. It is resistant to fluoroquinolones.[1] It is associated with community onset and there is concern for transmission via animals and retail meat.[34]

Incubation and duration

Symptom onset may start during use of antibiotics or up to 3 to 4 weeks after antibiotic completion. Symptoms can resolve after stopping the offending antibiotic or follow a complicated and prolonged course.

Symptoms

Patients can present with abdominal pain and mild to moderate watery diarrhea. *C difficile* can also present with fever, nausea, severe abdominal pain, profuse diarrhea, and, possibly, bloody diarrhea.

Diagnosis

C difficile toxin assay is widely used and available. It must be done on liquid or unformed stool. Stool cultures are sensitive but not clinically useful because results are not rapid. Also, *C difficile* is present in stool of healthy people and infants. Fecal leukocyte testing is not diagnostic. Sigmoidoscopy and colonoscopy is occasionally used but the risk of perforation is possible. A complete blood cell count to identify leukocytosis and thrombocytosis, albumin level, and lactate may also be useful.

Treatment

Discontinuation of the offending antibiotic is one of the first steps in treatment. According to IDSA treatment guidelines, mild to moderate disease should be treated with metronidazole (500 mg 3 times daily $\times$ 10–14 days) and severe disease should be treated with vancomycin (125 mg 4 times daily for 10–14 days). For a first recurrence, treat the same as the initial episode. For a second recurrence, however, use of vancomycin in a tapered or pulsed dose is recommended.

A Cochrane review from 2008 concluded that there is inconclusive evidence supporting the benefit of probiotics in the treatment of *C difficile*. Stool transplantation in patients with recurrent or refractory *C difficile* colitis may be useful.[35] Antiperistaltic medications should be avoided, because they increase the risk for toxic megacolon.

Complications

Complications include toxic megacolon.

Prevention

Use contact precautions—isolate patients in private rooms and gown and glove all visitors and health care workers. Mandate that everyone wash hands with soap and water (**Table 3**).

EVALUATION OF PATIENTS PRESENTING WITH SIGNS AND SYMPTOMS OF ACUTE GASTROENTERITIS, ETIOLOGY UNKNOWN

History

Important questions to consider when exploring the history of acute gastroenteritis are listed in (**Box 1**).

Physical Examination Findings

1. Abnormal vital signs: fever and/or orthostatic blood pressure, and/or tachycardia, and/or pain
2. Clinical signs of dehydration include the following: dry mucus membranes, decreased skin turgor, absent jugular vein pulsations, mental status changes

These and other physical examination findings, such as abdominal pain, have poor predictive value but contribute to the diagnosis and help with appropriate management of the illness.

Diagnostics

Test if symptoms are prolonged or severe or if the patient was recently hospitalized or has fever, bloody stool, systemic illness, recent antibiotic use, or day care center attendance. Assess serum electrolytes, serum urea nitrogen, creatinine to evaluate hydration, and acid-base status. A complete blood cell count is nonspecific but, if eosinophils are elevated, a parasitic infection should be considered.

Table 3
Onset, duration, and symptoms as caused by specific bacteria

Bacteria	Onset	Duration	Signs
Salmonella	6–48 h	1–7 d	N, V, F, P, ± blood
Campylobacter	1–10 d	5–14 d	F, H, P, N, V ± blood
Vibrio	6 h–4 d	SL (up to 3 d)	N, V, D
Shigella	1–6 d	SL (2–3 d)	F, P, D, ± blood
ETEC	1–3 d	2–3 d	D
C perfringens	8–16 h	Less than 24 h	P, D
EHEC	1–9 d	1 wk	N, P, D + blood
C difficile	4–5 d	Variable	F, N, P, D ± blood

Abbreviations: D, diarrhea; F, fever; H, headache; N, nausea; P, abdominal pain; SL, self-limiting; V, vomiting.

Box 1
Questions to consider in the evaluation of patient with signs and symptoms of acute gastroenteritis

1. Abrupt or gradual onset of symptoms. In cases of foodborne illness, how many hours after eating before symptoms onset?
2. Duration of symptoms
3. Characteristics of stool: watery, bloody, mucus, and color
4. Frequency and quantity of bowel movements.
5. Presence of fever, tenesmus, nausea, vomiting, headache, abdominal pain, malaise
6. Recent hospitalization, recent antibiotic use
7. Recent travel, pets, occupational exposures
8. Food history, specifically consumption of raw milk, cheese, undercooked beef, pork, poultry
9. Immunocompromised
10. Family members, coworkers, or other close contacts with similar symptoms
11. Evidence of dehydration: thirst, tachycardia, decreased urine output, lethargy, orthostasis

1. Fecal leukocytes and occult blood: The presence of these suggests a bacterial cause of the acute gastroenteritis. The sensitivity of fecal leukocyte testing varies tremendously. A meta-analysis reported that at 70% sensitivity, fecal leukocytes were only 50% specific for an inflammatory process.[36]
2. Fecal lactoferrin: Use when an inflammatory process is considered or when there is fever, tenesmus, or bloody stool. It is a more sensitive test for fecal leukocytes, because lactoferrin is a marker for fecal leukocytes, with sensitivity and specificity between 90% and 100%. Test is not readily available.[5]
3. Stool cultures: The IDSA published guidelines for diagnosis and management of infectious gastroenteritis in 2001, but controversy remains as to when stool cultures are most useful. This controversy is not helped by the low rate of positive stool cultures.[1]
   - According to IDSA recommendations, stool cultures are appropriate if symptoms do not quickly resolve, if fever or bloody stool are present, if patients' comorbidities put them at risk for complications, or if patients are immunocompromised. Culture for Salmonella, shigella, campylobacter, *E coli* O157:H7 (also do Shiga toxin assay if blood in stool).
   - Food handlers may require negative cultures to return to work.
4. *C difficile* assay: if hospitalized or if recent antibiotics or chemotherapy
5. Stool ova and parasites: Generally, testing stool for ova and parasites is low yield and not cost effective. It is appropriate if symptoms and exposure history support a parasitic or protozoal etiology, bloody diarrhea without fecal leukocytes, or persistent diarrhea in day care centers or aer associated with a community waterborne outbreak. In these cases, 3 samples, taken on 3 consecutive days, should be sent to catch parasite excretion.

Treatment

General recommendations

Guidelines emphasize hydration or rehydration plus diet changes and bowel rest. Oral rehydration is best, if possible, and is often underutilized in the United States. In

Box 2
WHO rehydration recommendations

Manufactured 1-L solutions contain

- 3.5 g Sodium chloride
- 2.5 g Sodium bicarbonate
- 1.5 g Potassium chloride
- 20 g Glucose

Home 1-L solutions contain[37]

- ½ Teaspoon salt
- ½ Teaspoon baking soda
- 4 Teaspoons sugar

diarrheal illnesses that involve the small intestine, oral rehydration is effective because the small bowel can still absorb water but requires sodium-glucose cotransport. To provide the glucose and electrolytes, the World Health Organization recommends rehydration with water containing salt, sodium bicarbonate, and glucose. Gatorade and other sports drinks do not contain sufficient salt (**Box 2**).

Antibiotics

Empiric antibiotics should be used with caution. IDSA treatment guidelines from 2001 suggest empiric treatment of moderate to severe traveler's gastroenteritis; those with more than 8 stools per day, dehydration, symptoms more than a week; or immunocompromised patients. Empiric treatment can also be considered with the presence of fever and bloody stools. Empiric treatments include ciprofloxacin (500 mg twice a day for 3 to 5 days), norfloxacin (400 mg twice a day for 3–5 days), or levofloxacin (500 mg daily for 3–5 days). In areas where fluoroquinolone resistance is a problem, azithromycin (500 mg daily for 3 days) is recommended. Specific treatments of other pathogens are discussed previously. These treatment guidelines, however, are for immunocompetent patients. For immunocompromised hosts, antibiotic treatment should be extended for 7 to 10 days and may be considered when not recommended for immunocompetent patients and there is a lower threshold for hospitalization.

Dietary modifications

A short period of clear liquids with adequate electrolyte replacement is generally ideal. In patients with watery diarrhea, boiled rice, potato, noodles or oats with salt, soup, crackers, or bananas are recommended. This is often referred to as the BRAT diet—bananas, rice, applesauce, and toast. Avoid high-fat foods until normal bowel function returns. Secondary lactose malabsorption or intolerance occurs after infectious gastroenteritis and may last for several weeks, so avoiding lactose-containing foods during this time is appropriate.[38]

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