Management of Acute Infectious Diarrhea
Crenguta Stepan, MD, Iris Liou, MD, and Christina M. Surawicz, MD

Worldwide, acute infectious diarrhea remains a major cause of morbidity and mortality among children younger than 5 years. Recent estimates suggest that diarrhea accounts for 1.4 to 2.5 million deaths per year in children worldwide [1] and about 500 every year in the United States. In U.S. adults, the incidence of diarrhea is still high, with 0.72 episodes per person-year, but the mortality is low, with the elderly at greatest risk. A study from 1991 showed that most diarrheal deaths were among those older than 74 years (51%), followed by adults 55 to 74 years (27%) and young children (11%) [2]. Age is also an important risk factor for death following hospitalization for gastroenteritis, with a case-fatality ratio higher in the elderly than in children [3]. Traveler’s diarrhea is another challenge in treatment and prevention, with a risk of about 7% in travelers to developed countries and 20% to 50% in travelers to the developing world [4]. Thus, it is important for clinicians to understand the management of acute diarrhea with respect to evaluation, treatment, and prevention [5].

Etiology and Clinical Presentation
Acute diarrhea is defined as 3 or more stools per day (or at least 200 g of stool/day) lasting 14 days or less. In most cases, the etiology is infectious (Table 1). Estimates show that pathogens are identified in less than 20% of cases because many patients do not seek medical attention and stool tests are not sensitive in identifying pathogens [6–8].

Most acute infectious diarrhea is self-limited, lasting less than 3 days, with approximately 80% attributed to viruses. Viruses causing acute diarrheal illnesses are noroviruses (formerly Norwalk agent), rotaviruses, caliciviruses, astroviruses, and enteric adenoviruses. Viral illnesses are typically associated with watery stools, nausea, vomiting, myalgia, fatigue, and low-grade fever. In these cases, supportive fluid therapy to maintain hydration is generally sufficient.

The most common causes of bacterial diarrhea are Salmonella, Campylobacter, and Shigella species. Other pathogens are Yersinia, Aeromonas, and Plesiomonas species. Bacteria can cause watery diarrhea that can turn into bloody diarrhea, sometimes with tenesmus and fever.
Among the protozoa, *Giardia*, *Cryptosporidium*, *Entamoeba histolytica*, and *Cyclospora* are the most common, and can have a prolonged course in immunosuppressed patients.

**Evaluation**

Most cases of infectious diarrhea in developed countries are self-limited, so diagnostic evaluation is generally not indicated. Further evaluation for invasive pathogens is indicated in patients younger than 2 years or older than 70 years or when there is blood or mucus in the stool, signs of dehydration, immunocompromised status, or high fever.

Evaluation begins with a careful patient history (onset, duration, the character of the stool, frequency, amount, associated symptoms). Epidemiologic factors (travel, ill family members, day care, history of contact with pets, consumption of “unusual” food items) and incubation period may provide clues to etiology of the diarrheal illness. Medication history is also important, especially recent antimicrobial therapy. Certain underlying medical conditions (eg, AIDS), immunosuppressive medications, or prior gastrectomy can predispose to infectious diarrhea [11]. The predictive value of any clinical feature, however, is relatively low for any particular pathogen. Based on the history and physical examination, the clinician should be able to determine the severity of the diarrhea and choose an appropriate treatment approach (Figure).

The next step in the management of acute diarrhea, if needed, includes diagnostic testing: stool culture, fecal leukocyte test, and/or stool lactoferrin. These tests are usually positive in patients infected with *Shigella*, *Salmonella*, *Campylobacter*, *Aeromonas*, *Plesiomonas*, noncholera vibrios, and *Clostridium difficile* [12].

Because stool cultures are often inappropriately ordered, they are one of the most inefficient and costly tests (about $900 per positive result). Stool culture typically takes at least 2 days to yield results, and positive results occur in only 1.5% to 5.8% of specimens [5]. In cases of bloody diarrhea, however, pathogens can be identified in up to 20% of cases. Given these considerations, stool culture for invasive pathogens is appropriate when there is a history of bloody diarrhea, fever, and recent travel to high-risk areas. Other indications for stool culture are a positive fecal leukocyte test or stool lactoferrin, which indicate an inflammatory process. When the presence of inflammation is demonstrated, the yield of stool culture for invasive pathogens will be increased [13]. However, inflammation can be seen in inflammatory bowel disease and other colitis as well.

Microscopic examination for fecal leukocytes has long been used to screen for inflammatory diarrhea. The test is limited by the need for fresh specimens and experienced microscopists, difficulties present especially in developing countries. An alternative to fecal leukocyte test is latex agglutination test for detection of fecal lactoferrin. This is more sensitive than fecal leukocyte examination but is more expensive and may have false-positive results in breast-fed infants [14]. In addition, patients infected with *Escherichia coli* O157:H7 often have bloody diarrhea and negative or low levels of lactoferrin, and thus need a specialized approach to diagnosis [15]. Some suggest a positive fecal lactoferrin test be used as an indication for immediate empiric therapy in the elderly and travelers, whereas a negative test makes an invasive infection unlikely. Other tests may be used when pathogens not identified by usual stool culture are suspected (Table 2).

If the patient is moderately to severely ill, a general evaluation is needed in order to assess severity of disease, dehydration, or possible complications; evaluation may also include serum chemistry analysis, complete blood count, blood cultures, and abdominal radiography.

**Treatment**

**Rehydration**

If the patient is able to drink, oral hydration is the first choice. This can be accomplished with an oral glucose or

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**Table 1. Common Causes and Associated Risk Factors for Infectious Diarrhea**

<table>
<thead>
<tr>
<th>Etiology</th>
<th>Annual Cases by Stool Culture per 100,000 Population (U.S.)</th>
<th>Risk Factors</th>
</tr>
</thead>
<tbody>
<tr>
<td>Norovirus</td>
<td>8500 [9]</td>
<td>Winter outbreaks in adults, raw oyster consumption, cruise ships</td>
</tr>
<tr>
<td>Rotavirus</td>
<td>1100 [9]</td>
<td>Winter outbreaks in children under 2 years</td>
</tr>
<tr>
<td>Giardia</td>
<td>750 [9]</td>
<td>Contaminated water; recreational exposure in lakes, rivers, or swimming pools; day care centers</td>
</tr>
<tr>
<td>Salmonella</td>
<td>14.7 [10]</td>
<td>Raw eggs, undercooked poultry and turkey, unrefrigerated dressing, pet reptiles, family members with <em>Salmonella</em></td>
</tr>
<tr>
<td>Campylobacter</td>
<td>12.9 [10]</td>
<td>Undercooked poultry, contaminated milk, tuna salad</td>
</tr>
<tr>
<td>Shigella</td>
<td>5.1 [10]</td>
<td>Contaminated water and vegetables</td>
</tr>
<tr>
<td>E. coli O157:H7</td>
<td>0.9 [10]</td>
<td>Undercooked beef, unpasteurized milk, apple cider, visits to animal farms or petting zoos</td>
</tr>
<tr>
<td><em>C. difficile</em></td>
<td>NA</td>
<td>Antibiotic use</td>
</tr>
</tbody>
</table>

NA = not available.

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Infectious diarrhea

starch-containing electrolyte solution. Studies have shown that glucose-containing solutions help the absorption of sodium and water through a mechanism of cotransport of electrolytes. This simple measure is superior to administration of intravenous fluids for persons who are able to take oral fluids. More severe diarrhea (with dizziness, orthostatic hypotension, or reduced urinary output) requires the use of intravenous fluids.

Dietary changes are also part of the management, because a better nutritional status helps to decrease intestinal permeability and hasten recovery. Food should be reintroduced as soon as possible, and breastfeeding should be continued in infants. It is recommended that fruits (especially bananas, rich in potassium), salty food (rich in sodium), and bread and rice (sources of carbohydrates) be increased. Milk products can be eliminated from the diet during the first days of a diarrheal bout, even though transient lactose intolerance is usually not significant [16]. Recently, consumption of yogurt has been associated with a clinically relevant decrease in stool frequency and duration of diarrhea in children who have reducing sugars in stools [17].

The introduction of hypo-osmotic solution, resistant starch and glutamine [18] incorporating nutrition therapy are promising new approaches to diarrheal management.

**Antidiarrheal Medications**

When rehydration and dietary changes do not improve symptoms, antidiarrheal medication is the next step. There are 3 types of antidiarrheal agents: antisecretory (bismuth subsalicylate, racecadodril, provir), adsorbents (kaolin pectin, attapulgite), and antimotility (loperamide, opioids).

Among antimotility agents, loperamide is the drug of choice for self-treatment of mild diarrhea. Loperamide decreases the intestinal transit and has some antisecretory properties, reducing the passage of loose stools by about 50%. Loperamide combined with antibiotics reduces the duration of traveler’s diarrhea or bacillary dysentery by 1 day [19]. Other antimotility drugs are opioid-based (eg, diphenoxylate, codeine, and paregoric); their use is limited by the neurologic side effects. Antimotility agents should be avoided in children and infants and in patients with severe bloody diarrhea and suspected *C. difficile* disease.
Among the antisecretory agents, bismuth subsalicylate is most commonly used in adults and children. It works by multiple mechanisms: inhibition of intestinal secretion, anti-inflammatory action and anti-bacterial effects. In children, bismuth subsalicylate shortens illness and leads to significant weight gain and has been shown to improve viral gastroenteritis with less vomiting and shorter median duration [20]. In adults, it can be used for the treatment of watery diarrhea and traveler’s diarrhea with a significant reduction in the passage in loose stool [21]. Pregnancy and immunosupression are contraindications to its use.

The adsorbents, such as kaolin pectin or attapulgite, are also antisecretory agents, but their use in the management of infectious diarrhea needs further investigation related to efficiency and safety.

New Agents

Racecadotril is a promising new antisecretory agent, which potentiates the action of enkephalins in the gastrointestinal tract. It can reduce stool frequency and volume, and is safe even in children. However, in 1 study itching was described in 28% of those treated. Compared with loperamide, the clinical success is just slightly better, but the benefit is related to the lower incidence of treatment-related constipation for racecadotril [22].

SP 303 (Provir) is a chloride channel blocker that has been used for more than 10 years and has been proved to be safe and effective in management of AIDS-related diarrhea, reducing stool volume and frequency [23]. It was shown effective in treatment of traveler’s diarrhea in Jamaica and Mexico, shortening duration by 21% and with no risk of invasive diarrhea or posttreatment constipation [24]. It is not commercially available.

Antimicrobial Therapy

Routine use of antimicrobial agents for acute infectious diarrhea is not recommended because of the self-limited nature of most cases (about 80%), the cost, and the potential antibiotic resistance of enteric pathogens. There are 2 types of antimicrobial therapy: empiric and targeted.

Empiric antimicrobial therapy is recommended in the following situations: in moderate to severe forms of traveler’s diarrhea, in moderate to severe invasive diarrhea (with temperature > 38°C, positive stool test for leukocytes and/or lactoferrin, and/or blood), in patients with high risk of diarrhea-related complications, and in severe nosocomial diarrhea in highly suspicious cases of C. difficile infection. The Centers for Disease Control and Prevention has reported on recent emergence of nonantibiotic-associated severe C. difficile diarrhea in peripartum women.

Approximately 80% of traveler’s diarrhea cases with an identified pathogen are caused by bacteria, including enterotoxigenic E. coli (ETEC), enteroaggregative E. coli (EAEC), Salmonella spp., Shigella spp., Campylobacter spp., Plesiomonas shigelloides, Aeromonas spp., and noncholeria vibrios. Usually at the time of therapeutic decision, no microbial isolation is done, so the chosen antibiotic needs to cover most of the possible spectrum. Antibiotics decrease severity and duration of diarrheal episodes (the number of patients free of traveler’s diarrhea 72 hours after starting treatment was 84.4% compared with 50.3% taking placebo) [25].

Fluoroquinolones are the drugs of choice for traveler’s diarrhea in most regions of the world. Their advantages are good absorption with a high fecal concentration, excellent spectrum of activity and effectiveness in shortening of duration of diarrhea from 3 to 4 days to 1.5 days. Treatment with fluoroquinolones can be a single dose or a 3-day course; both have the same efficacy [26]. For invasive diseases, with bloody diarrhea or fever, and for persistent diarrhea with symptomatic treatment, a 3-day course of fluoroquinolone is recommended. The drug of choice in children is trimethoprim-sulfamethoxazole (TMP/SMX), long used for empiric therapy in the general population, but lately restricted because of increasing prevalence of resistance. Both options (fluoroquinolone and TMP/SMX) are highly effective for E.coli, Shigella and Vibrio cholerae infections but their efficacy against Salmonella and Campylobacter is modest.

Thus, in case of antimicrobial empiric treatment, the clinicians should be aware of the importance of taking stool samples for stool culture before starting antibiotics.

### Table 2. Diagnostic Tests for Specific Pathogens

<table>
<thead>
<tr>
<th>Pathogen</th>
<th>Diagnostic Test</th>
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<tbody>
<tr>
<td>E. coli O157:H7</td>
<td>EIA kit for Shiga toxin, confirmed by culture on sorbitol-MacConkey agar</td>
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<tr>
<td>Vibrio cholera</td>
<td>Dark field microscopy, confirmed by culture on thiosulphate-citrate-bile salts medium</td>
</tr>
<tr>
<td>Salmonella, Campylobacter, V. parahemolyticus</td>
<td>RT-PCR</td>
</tr>
<tr>
<td>Campylobacter spp., Salmonella</td>
<td>Stool assay for toxin</td>
</tr>
<tr>
<td>C. difficile</td>
<td>Stool antigen test</td>
</tr>
<tr>
<td>Giardia</td>
<td>Immunofluorescent antibody test</td>
</tr>
<tr>
<td>Giardia, Cryptosporidum</td>
<td>Stool ova and parasites</td>
</tr>
<tr>
<td>Giardia, Cryptosporidum, Enterotoxigenic E. coli (ETEC), enterotoaggregative E. coli (EAEC), Salmonella spp., Shigella spp., Campylobacter spp., Plesiomonas shigelloides, Aeromonas spp., and noncholeria vibrios. Usually at the time of therapeutic decision, no microbial isolation is done, so the chosen antibiotic needs to cover most of the possible spectrum. Antibiotics decrease severity and duration of diarrheal episodes (the number of patients free of traveler’s diarrhea 72 hours after starting treatment was 84.4% compared with 50.3% taking placebo) [25]. Fluoroquinolones are the drugs of choice for traveler’s diarrhea in most regions of the world. Their advantages are good absorption with a high fecal concentration, excellent spectrum of activity and effectiveness in shortening of duration of diarrhea from 3 to 4 days to 1.5 days. Treatment with fluoroquinolones can be a single dose or a 3-day course; both have the same efficacy [26]. For invasive diseases, with bloody diarrhea or fever, and for persistent diarrhea with symptomatic treatment, a 3-day course of fluoroquinolone is recommended. The drug of choice in children is trimethoprim-sulfamethoxazole (TMP/SMX), long used for empiric therapy in the general population, but lately restricted because of increasing prevalence of resistance. Both options (fluoroquinolone and TMP/SMX) are highly effective for E.coli, Shigella and Vibrio cholerae infections but their efficacy against Salmonella and Campylobacter is modest. Thus, in case of antimicrobial empiric treatment, the clinicians should be aware of the importance of taking stool samples for stool culture before starting antibiotics.</td>
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</table>
Worldwide, antibiotic resistance has increased for several classes of antimicrobials. Recently, more studies report an increase of partially fluoroquinolone-resistant strains of ETEC especially in India, Cambodia, Nepal, and Egypt (from 3.4% in 1996 to 15.8% in 1999) [27]. No high-level fluoroquinoline-resistant strain of ETEC has been reported, but careful monitoring of the antimicrobial susceptibility pattern worldwide is needed.

Resistance to fluoroquinolones has been also reported for *Campylobacter* (in Thailand and Spain), *Shigella* (India, Japan, and Bangladesh), and *Salmonella* (Taiwan, Spain, Southeast Asia, and Japan) [28]. Azithromycin is an alternative to fluoroquinolones, with a good activity against most enteric pathogens and comparable efficacy to fluoroquinolones for traveler’s diarrhea, shortening EAEC infection in adults and children, and efficacy in quinolone-resistant *Campylobacter* [29] or *Shigella dysenteriae* [30]. Also, its advantage compared with fluoroquinolones is a lower potential for interaction with other medication.

In May 2004, the U.S. Food and Drug Administration (FDA) approved the use of rifaximin for treatment of traveler’s diarrhea in patients older than 12 years infected with noninvasive *E. coli* strains. Rifaximin is a nonabsorbable antibiotic that is very well tolerated with no significant adverse effects. It has been showed to be as effective as ciprofloxacin for traveler’s diarrhea treatment and for diarrhea caused by EAEC infection. Its efficacy has not been shown for invasive pathogens such as *Campylobacter, Salmonella, or Shigella* [31]. Rifaximin should not be used in pregnant women, lactating women, or children younger than 12 years.

For moderate to severe invasive diarrhea, empiric antibiotic treatment should be indicated only when there is no suspicion of *E. coli* O157:H7 (eg, bloody diarrhea in an afibrile patient). The drugs of choice are fluoroquinolones in adults and TMP/SMX in children; when there is a strong suspicion for fluoroquinolone resistance, azithromycin is recommended. Stool tests results may determine if a specific antimicrobial therapy is needed.

Watery diarrhea that lasts for more than 7 days should raise the concern of a protozoal infection such as *Giardia* or *Cryptosporidium*. Metronidazole efficacy against *Giardia* is about 90% [32], but cases of resistance have been reported worldwide. It is contraindicated in pregnant women when the treatment should be postponed until the stool test results. *C. difficile* causes about 20% of cases of antibiotic-associated diarrhea, following the use of clindamycin, the second- and third-generation cephalosporins, and quinolones. Diarrhea is usually mild, and stopping the antibiotic resolves the illness in 2 to 3 days. For severe forms, metronidazole is the drug of choice. In case of failure, the option is vancomycin. In case of severe nosocomial diarrhea with high suspicion of *C. difficile* infection, the empiric antibiotic treatment can be started pending the results for toxin assay test. For relapse, a second course of metronidazole is recommended or tapering courses of vancomycin or probiotics. Antimotility agents such as loperamide are contraindicated for the treatment of *C. difficile* colitis because of the risk of toxic megacolon.

### Targeted Antimicrobial Treatment

The use of specific antimicrobial agents may be necessary in some cases due to an increase in antimicrobial resistance among some enteropathogens. Once the stool culture and sensitivity are available, treatment can be continued, changed, or discontinued accordingly.

*Salmonella* gastroenteritis does not require antibiotic treatment because of the risk of a carrier state. There are a few exceptions, such as in severe forms, very old or young patients, and immunocompromised or other patients with high risk of complications. Fluoroquinolones usually cover the *nontyphi Salmonella* infection, but the appearance of multidrug resistance may warrant the use of ceftriaxone in some parts of the world. Most cases of *Campylobacter* enteritis do not require antimicrobial treatment. However, in severe and prolonged cases of enteritis, septicemia, and other extraintestinal infections, antibiotics are needed. Antibiotics do not alter the course of the illness when started after 4 days after the onset of symptoms. Starting earlier than 3 days, erythromycin might reduce the severity of illness and the carriage of pathogens. Fluoroquinolones are also an option in case of susceptible *Campylobacter*; unfortunately, the use of fluoroquinolones in poultry feeds has increased resistance [28]. Azithromycin remains the best alternative in case of resistance to fluoroquinolones, although in Thailand, azithromycin resistance was reported in 7% to 15% of *Campylobacter* isolates [33]. A new treatment option that arises is tigecycline; its high in vitro activity against ciprofloxacin-resistant strains suggests a potential therapeutic role in the treatment of infections that involve *Campylobacter* spp [34].

*Shigella* is a highly infectious agent, and antibiotic treatment is required for all patients with confirmed shigellosis. Antibiotics are necessary to reduce fecal excretion preventing further transmission, to manage infection (shortening the duration of fever, diarrhea, and toxemia), and to reduce the risk of complications. *S. sonnei* is at present the predominant species in the United States and other developed countries, but in developing countries and low socioeconomic conditions, *S. flexneri* is still the predominant serotype [35]. The drug of choice for shigellosis is fluoroquinolones but lately, resistance to fluoroquinolones has been reported, especially among *S. flexneri* and *S. dysenteriae*. Alternative drugs like azithromycin, pivmecillin, and ceftriaxone should further be evaluated for treatment of shigellosis [30]. Because of increased resistance to TMP/SMX (80%–94%) in children with shigellosis, the options are azithromycin or parenteral ceftriaxone, especially in those who are hospitalized [36].
The most common protozoal infections are caused by *Giardia* and *Cryptosporidium*. For *Giardia*, the drug of choice is metronidazole. In refractory cases, a combination of quinacrine and metronidazole can be used with good results [37]. *Cryptosporidium* infection requires treatment only in immunocompromised patients and in children. The FDA approved nitazoxanide for treatment of *Cryptosporidium* diarrhea and *Giardia* infection in children and also for the treatment of *Giardia* in adults. Nitazoxanide demonstrates a 67% and 71% rate of eradication of *Cryptosporidium* and *Giardia*, respectively, 7 to 10 days after initiation of a 3-day course of treatment [38]. Amebiasis is treated with metronidazole or iodoquinolide with the addition of paromomycin or tinidazole for the luminal phase.

**Prevention**

With 2 billion cases of acute diarrhea per year worldwide, prevention is important. Prevention should be focused on infection control and medical prevention.

Infection control by public health measures and improved sanitation are very important to decreased infectious diarrhea. A study conducted in Pakistan showed a decreased incidence of diarrhea among children living in households that received hand washing promotion with soap (53% lower incidence than in control group and 39% fewer days of diarrhea) [39]. In adults, sanitation is important in prevention of traveler's diarrhea and includes hand washing, careful choice of food, and drinking bottled or boiled water. “Boil it, cook it, peel it, or forget it” is the best advice for any traveler, but data on the effectiveness of dietary precautions in preventing traveler's diarrhea are inconclusive.

Medical prevention includes prophylactic drugs (absorbable/nonabsorbable antibiotics, bismuth subsalicylate), probiotics, and vaccines.

Antibiotic therapy is generally reserved for curative treatment of diarrhea caused by invasive pathogens. During recent years, the increasing number of traveler’s diarrhea cases (46% of the Americans traveling to developing countries [40]) has required more effective prophylactic measures, and antibiotic therapy has been the most accessible method. Although the CDC does not recommend antibiotic prophylaxis, it can be used in some instances, such as inflammatory bowel disease, renal diseases, and severe immunocompromised with high-risk illnesses [41]. Quinolones are the first choice with an efficacy of 80% to 100% [41]. The drawbacks are antibiotic-induced diarrhea and the possibility of developing resistant pathogens (an increased resistance to quinolone for *Campylobacter* has been recognized in many areas of Asia).

Rifaximin has been approved for prophylaxis of traveler’s diarrhea. A randomized study in Mexico has showed that rifaximin offers protection in 72% to 77% of cases in dosages of 200 mg/day, 400 mg/day, and 600 mg/day [42]. The results are limited by the fact that in Mexico, most of the cases of traveler’s diarrhea are caused by *E. coli*. Therefore, further studies are needed to assess its efficacy with other invasive pathogens.

The increasing incidence of antibiotic resistance pathogens is a good incentive for investigating other prevention options. Bismuth subsalicylate is a nonantimicrobial agent that can provide a rate of protection of 65% for high-dose (2 tablets 4 times daily) and 40% for low-dose (1 tablet 4 times daily) against traveler's diarrhea for periods up to 3 weeks [43]. It is less effective than rifaximin for the prevention of travelers’ diarrhea and the required doses are less convenient. In terms of safety, the product is well tolerated, with side effects such as blackening of tongue and stool and very low incidence of tinnitus. Because bismuth subsalicylate interferes with the absorption of doxycycline, it should not be taken by travelers using doxycycline for malaria prophylaxis [44]. Bismuth subsalicylate is not considered a recommendable option for prophylaxis in Europe because it is frequently administered and provides only moderate protection.

Probiotics are another alternative to conventional prophylaxis. Different members of the Lactobacillus genus have been used in controlled trials to assess their effectiveness in prevention of traveler’s diarrhea and antibiotic-associated diarrhea. In 1 study, the probiotic Lactobacillus GG was found to provide 49% protection against traveler’s diarrhea, but results with this agent and other probiotics as well have been variable and inconsistent [45]. Lactobacilli and *S. boulardii* are both effective in preventing antibiotic-associated diarrhea, but *S. boulardii* seems to be the first choice [46]. Treatment with probiotics is relatively safe but not risk-free. Several reports describe patients with fungemia in whom the probiotic origin was proven by DNA fingerprinting, and bacteriemia with lactobacillus GC [47]. Recombinant probiotics capable of binding the toxin have showed a considerable potential and may be the next step for the prophylaxis of ETEC-induced traveler's diarrhea [48].

**Vaccination**

The most effective way to prevent infectious diseases is vaccination. For some pathogens there are already available vaccines, for other it is a work in progress.

**Rotavirus.** Given the rotavirus burden, developing a vaccine against rotavirus is a high priority. RotaShield was the first rotavirus vaccine approved in the United States but because of a presumable association with intussusception, it was taken off the market after a year. In 2006, RotaTeq, a new live reassortant virus vaccine, was approved by the FDA to prevent rotavirus gastroenteritis in infants. The vaccine was found to prevent 74% of all rotavirus gastroenteritis cases.
and 98% of the severe cases [49]. RotaTeq also prevents approximately 96% of hospitalizations due to rotavirus gastroenteritis. It seems to be well tolerated and is not associated with increased risk of intussusception.

**Norovirus.** There are undergoing studies on oral vaccine against norovirus, but the results show modest antibody titers; further studies are needed to evaluate its protective value.

**Salmonella typhi.** Typhoid fever, causing more than half a million deaths annually, is of great risk to travelers in South Asia and South America. There are 2 vaccines commercially available but the recommendation is just for international travelers. The attenuated Ty21a is administrated orally and the liquid protection is of 77% over 7 years [50]. The purified Vi PS is a parenteral vaccine, demonstrating a 69% protective efficacy. Live vaccines are also undergoing clinical studies.

**Cholera.** Currently, there are 2 types of vaccines available. The inactivated vaccines confer 50% to 53% protection over 3 years. The live attenuated vaccine, CVD 103-HgR, shows efficacy of 80% against all diarrheas and 90% against severe diarrhea 3 months after vaccination [50]. The recommendation is for travelers and prevention of cholera outbreaks in developing countries.

Although many studies are in process at this point, there are no available vaccines against *E. coli*, *Shigella*, or *Campylobacter*.

**Conclusion**

There are 2 to 4 billion cases of food-borne and diarrheal disease annually worldwide, resulting in 3.1 million deaths, mostly among children living in developing countries. Despite increasing in knowledge of pathogenesis and pathogens detection, most are of unknown etiology. Most cases of acute infectious diarrhea are self-limited and supportive therapy with oral rehydration is usually enough for recovery. It is important to identify the patients at risk for developing complications and patients who may benefit from empiric or targeted antibiotic therapy. Targeted antibiotic treatment should be considered after stool test culture and sensitivity where an increased incidence of resistant enteropathogens is described. In recent years, a global effort has tried to decrease the burden of this disease by prevention through hygiene, vaccine development, and prophylaxis guidelines. However, diarrheal disease is still a challenge.

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**Author contributions:** conception and design, CMS; drafting of the article, CS, IL; critical revision of the article, CMS.

**References**


1. A 5-year-old girl is brought to a clinic by her parents, who report that she has had 2 days of nonbloody diarrhea, intermittent fever, and abdominal cramping, and began vomiting and having bloody stools last night. She is afebrile and appears lethargic on examination. The physician initially orders a fecal leukocyte test, which is negative. Along with rehydration, what is the appropriate next step in management?

(A) Initiate empiric antibiotic therapy with 10 mg/kg/d of trimethoprim and 50 mg/kg/d of sulfamethoxazole divided twice daily for 5 days

(B) Perform fecal lactoferrin test

(C) Order stool cultures, to include special medium for *E. coli* O157:H7

(D) Use loperamide to alleviate patient’s diarrhea and limit further dehydration

2. A 30-year-old pregnant woman presents with moderate watery diarrhea for the past 3 days. For symptomatic management of her diarrhea, the most appropriate agent to use is:

(A) Loperamide

(B) Diphenoxylate with atropine

(C) Codeine

(D) Bismuth subsalicylate

3. A 50-year-old man is planning a 7-day safari trip in Ghana. What is the most appropriate prophylactic regimen for traveler’s diarrhea?

(A) Trimethoprim/sulfamethoxazole 160/800 mg daily

(B) Bismuth subsalicylate two 262-mg tablets with meals and at bedtime

(C) Ciprofloxacin 500 mg daily

(D) *Shigella* inactivated whole cell vaccine

4. Antibiotic therapy is most clearly indicated for which of the following patients?

(A) A 35-year-old woman who developed fever, abdominal pain, and diarrhea 1 day after eating egg salad at a company picnic but with improving diarrhea for the past 3 days. Stool cultures are positive for *Salmonella enteritidis*.

(B) A 24-year-old female day care worker with fever, abdominal pain, and watery diarrhea that has become bloody and mucoid. She states that there is a known outbreak of *Shigella* where she works.

(C) An 18-year-old man with a 2-day history of watery diarrhea upon return from vacationing in Guatemala. He states he has been drinking plenty of liquids.

(D) A 58-year-old man, who has just returned from a Caribbean cruise, describes a 2-day history of myalgias, vomiting, and watery diarrhea. His wife and 2 children have similar symptoms.

5. A 20-year-old man presents with a 2-day history of severe watery diarrhea following return from a spring break trip to Mexico. He is afebrile and appears pallid. He is also tachycardic and hypotensive. In addition to rehydration and obtaining stool cultures, the physician should prescribe empiric antibiotic therapy with:

(A) Trimethoprim/sulfamethoxazole 160/800 mg twice daily × 3 days

(B) Ciprofloxacin 500 mg twice daily × 3 days

(C) Metronidazole 500 mg thrice daily × 7 days

(D) Doxycycline 300 mg single dose
EVALUATION FORM: Management of Acute Infectious Diarrhea

Participants may earn 1 credit by reading the article named above and correctly answering at least 70% of the accompanying test questions. A certificate of credit and the correct answers will be mailed within 6 weeks of receipt of this page to those who successfully complete the test.

Circle your answer to the CME questions below:

1. A   B   C   D
2. A   B   C   D
3. A   B   C   D
4. A   B   C   D
5. A   B   C   D

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