Educational Objectives

Goal: The goal of this activity is to review the various risk factors, etiologies, and treatments of diarrhea as well as the pharmacist’s role in its management.

After participating in this activity, pharmacists will be able to:

- Discuss the different causes of and risk factors for diarrhea including IBS-D, infectious diarrhea (including CDAD), and non-infectious diarrhea
- Describe the available non-prescription and prescription agents for the treatment of diarrhea, including the mechanism of action, indications, side effects, onset of effect, duration of therapy, and clinical usage considerations for each agent
- Outline the pharmacist’s role in providing recommendations to treat diarrhea and referral to a physician for inadequate response to OTC therapies

After participating in this activity, pharmacy technicians will be able to:

- Recall the basic definition of diarrhea
- Recall the risk factors for diarrhea
- List available OTC and prescription drug therapies for diarrhea
- Recognize when to refer patients to the pharmacist for recommendations on diarrhea management

The Rundown: Management of Acute and Chronic Diarrhea

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Abstract

Diarrhea is a common complaint seen in patients worldwide and can be caused by either infectious or noninfectious sources, including bacteria, viruses, protozoa, food intolerances, and irritable bowel syndrome. Management strategies for the adult patient with diarrhea depend on the underlying cause but may include hydration, over-the-counter products, and prescription medications. Pharmacists and pharmacy technicians must be familiar with the characteristics of the various types of diarrhea and with the appropriate treatment options, and they should recognize when it is appropriate to refer patients for medical evaluation.

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**Introduction**

Diarrhea affects nearly all patients at some point in their lives. Although diarrhea is commonly categorized as merely a bothersome symptom in the United States (US), the consequences of diarrhea can be fatal if not properly managed. Each year, an estimated 2 billion cases of diarrheal disease and 2.5 million deaths due to diarrhea-related illness occur worldwide.\(^1,2\)

Diarrhea, in its most basic definition, is a variation from normal bowel movements with stools of increased frequency and/or decreased consistency. Normal bowel habits vary among individuals, with frequency ranging from three times per week to three times per day, and these variations must be considered when clinicians are evaluating patients and recommending treatments for symptom management. To help guide treatment recommendations, diarrhea can be classified by suspected or proven etiology (infectious or noninfectious), duration, and pathophysiologic mechanism. Diarrhea is defined as acute, persistent, or chronic based on the duration of symptoms, and the pathophysiologic mechanism may fall into one or more of the following clinical groups: secretory, osmotic, exudative, or motor (Table 1).\(^2,4\)

Treatment recommendations vary greatly depending on the etiology, duration, and pathophysiologic mechanism of diarrhea; therefore, an attempt should be made to classify a diarrheal episode upon presentation. Pharmacists and pharmacy technicians play an integral role in the management of diarrhea through self-treatment recommendations or referrals for medical evaluation. Thus, it is critical for pharmacists and technicians to be familiar with the various classifications of diarrhea and the prescription and over-the-counter (OTC) products available for treatment and symptom management. This review will focus on treatment and management of diarrhea in immunocompetent adults.

**Noninfectious diarrhea**

Diarrhea is classified as noninfectious when symptoms worsen or become chronic in the absence of an identifiable infectious organism (virus, bacterium, protozoan). Infectious etiologies may be ruled out with a negative stool culture and testing for ova and parasites.\(^5\) Noninfectious diarrhea can occur acutely due to medication and food intolerance or chronically due to primary gastrointestinal (GI) disease, such as inflammatory bowel disease.

**Hydration and diet management**

The main component of treatment for acute noninfectious diarrhea is hydration therapy to maintain water and electrolyte balances despite the loss of important salts in the stool. The World Health Organization (WHO) defines oral rehydration therapy (ORT) as the administration of appropriate solutions by mouth to prevent or correct dehydration related to diarrhea. ORT solutions recommended by the WHO contain the following per 1 L of solution: 2.6 g sodium chloride, 2.9 g trisodium citrate, 1.5 g potassium chloride, and 13.5 g glucose.\(^6\) ORT has been found to be a cost-effective means of managing acute diarrhea and reducing hospitalizations.\(^2\) ORT solutions such as Pedialyte are not interchangeable with sports drinks and more closely resemble the WHO ORT recommendations for replenishment during diarrheal illness. However, in otherwise healthy patients who present without dehydration, adequate fluid intake may...

<table>
<thead>
<tr>
<th>FREQUENCY CLASSIFICATION</th>
<th>CHRONICITY</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acute</td>
<td>≤14 days in duration</td>
</tr>
<tr>
<td>Persistent</td>
<td>&gt;14 days in duration</td>
</tr>
<tr>
<td>Chronic</td>
<td>&gt;30 days in duration</td>
</tr>
</tbody>
</table>

**Mechanistic classification**

<table>
<thead>
<tr>
<th>Mechanism</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Secretory</td>
<td>Occurs when a substance either decreases absorption or increases secretion of large quantities of water and electrolytes in the gastrointestinal tract</td>
</tr>
<tr>
<td></td>
<td>• Leads to large stool volume (&gt;1 L/d)</td>
</tr>
<tr>
<td></td>
<td>• Fasting does not alter stool volume</td>
</tr>
<tr>
<td></td>
<td>• May be caused by bacterial toxins, laxatives, or excess bile salts</td>
</tr>
<tr>
<td>Osmotic</td>
<td>Occurs when a poorly absorbed substance retains intestinal fluids and leads to a flux of water and electrolytes into the lumen as the gut adjusts to the osmolality of the plasma</td>
</tr>
<tr>
<td></td>
<td>• Unlike other mechanisms, fasting causes diarrhea to stop</td>
</tr>
<tr>
<td></td>
<td>• May be caused by lactose intolerance or ingestion of magnesium-containing antacids or poorly soluble carbohydrates (lactulose)</td>
</tr>
<tr>
<td>Exudative</td>
<td>Occurs when an inflammatory process in the GI tract causes discharge of mucous, serum proteins, and blood into the gut, and discharged substances are excreted in the stool</td>
</tr>
<tr>
<td></td>
<td>• Absorption, secretory, or motility functions are altered to accommodate large stool volume</td>
</tr>
<tr>
<td>Motor</td>
<td>Occurs when altered intestinal motility leads to reduction in contact time of chyme (semiliquid combination of gastric fluids and partially digested food) in the small intestine; premature emptying of the colon; and bacterial overgrowth. Diarrhea may also be caused by increased contact time, which leads to overgrowth of fecal bacteria and rapid dumping of chyme into the colon that is unable to absorb water</td>
</tr>
<tr>
<td></td>
<td>• May occur with bypass surgery, intestinal resection, or administration of metoclopramide</td>
</tr>
</tbody>
</table>

Source: Refs 2, 4
Noninfectious diarrhea can occur acutely due to medication and food intolerance or chronically due to primary GI disease, such as inflammatory bowel disease.”

Many people have food intolerances to vegetables (e.g., onions, peppers), fruits, and various spices and experience diarrhea after eating these foods. When consumed in excess, high-salt beverages, high-fiber foods, and foods containing sugars that cannot be completely absorbed by the body (e.g., sorbitol and fructose) can also cause diarrhea.17,18 In the case of food intolerances, patients should be advised to not rely on OTC antidiarrheal medications and to instead avoid the offending food product to prevent future occurrences of diarrhea.

Diarrhea is also a side effect of many medications such as magnesium-containing antacids, chemotherapeutic agents, antihypertensives, nonsteroidal anti-inflammatory drugs, metformin, protease inhibitors, and proton pump inhibitors.4 When a medication is suspected as the causative agent, the patient should be evaluated to
DOSING COMMON ADVERSE REACTIONS DRUG-DRUG INTERACTIONS AMERICAN COLLEGE OF GASTROENTEROLOGY RECOMMENDATIONS COST (AWP)

<table>
<thead>
<tr>
<th>DRUG</th>
<th>MECHANISM OF ACTION</th>
<th>DOSING</th>
<th>COMMON ADVERSE REACTIONS</th>
<th>INTERACTIONS</th>
<th>RECOMMENDATIONS</th>
<th>COST (AWP)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Eluxadoline</td>
<td>Mu-opioid receptor agonist</td>
<td>100 mg twice daily with food</td>
<td>Abdominal pain, Constipation, Nausea</td>
<td>Cyclosporine increases exposure to eluxadoline, Eluxadoline may increase exposure to rosvastatin, Strong CYP inhibitors may increase exposure to eluxadoline</td>
<td>Approved after guideline monograph issued</td>
<td>$1152.00 (30-day supply)</td>
</tr>
<tr>
<td>Rifaximin</td>
<td>Rifamycin antibacterial</td>
<td>550 mg three times daily for 14 days; maybe repeated for 2 additional courses</td>
<td>Increased ALT, Nausea</td>
<td>Cyclosporine increases exposure to rifaximin</td>
<td>Weak recommendation for use to decrease bloating and other symptoms in IBS-D</td>
<td>$1539.31 (14-day supply)</td>
</tr>
</tbody>
</table>

**New Agents for the Treatment of IBS-D**

40% of patients with IBS may be characterized as IBS-D.19 Loperamide has demonstrated efficacy in decreasing fecal urgency and frequency of stools as well as increasing the number of formed stools in patients with IBS-D.23 However, it does not provide relief from other symptoms such as pain and bloating. Current American College of Gastroenterology treatment guidelines do not recommend the use of loperamide for IBS-D because of lack of strong evidence.22

Tricyclic antidepressants may be useful in relieving symptoms of IBS-D because of their ability to slow transit through the GI tract.23 Guidelines include a weak recommendation for the use of tricyclic antidepressants but recognize that limited evidence is available and that patients may find the anticholinergic adverse effects intolerable.22

Eluxadoline is a mu-opioid receptor agonist and delta-opioid antagonist that reduces the symptoms of IBS-D by slowing motility and relieving pain in the GI tract.24 Eluxadoline became available in December 2015 and is classified as a Schedule IV controlled substance by the Drug Enforcement Administration.25 Decreases in abdominal pain, stool frequency, and urgency have been associated with eluxadoline therapy in conjunction with improved consistency of stools.23 Furthermore, eluxadoline has shown benefit in patients whose symptoms are not adequately relieved with loperamide.23,24 Common adverse effects associated with this agent include nausea and constipation (Table 2).22,23,26-28

Rifaximin is a rifamycin antibiotic similar to rifampin that is not significantly absorbed into systemic circulation.24 Its efficacy in IBS-D is attributed to alterations in GI flora.23 Rifaximin has been shown to decrease many symptoms of IBS-D, including abdominal discomfort/pain, unformed stools, and bloating.23,24 Patients whose condition relapsed after an initial course of rifaximin achieved statistically significant benefits with up to two additional courses.24 Rifaximin is generally well tolerated; the most common adverse effects include GI and upper respiratory symptoms.23,24 Current guidelines include a weak recommendation for the use of rifaximin for the relief of bloating and other symptoms of IBS-D.22

Serotonergic antagonists are believed to provide benefit in IBS-D through modulation of secretion and motility in the GI tract.23 Alosetron, which was removed from the US market in 2001 because of a risk of ischemic colitis, has been available since 2002 with access currently restricted by a Risk Evaluation and Mitiga-
In the United States alone, there are more than 200 million cases of infectious diarrheal illness annually; worldwide, infectious diarrhea is the second most common cause of morbidity and mortality.”

**Infectious diarrhea**

Infectious diarrhea is defined by the Infectious Disease Society of America (IDSA) guideline as diarrhea due to infectious etiology, which is commonly associated with symptoms of nausea, abdominal cramps, and vomiting. It is a common disease worldwide, with incidence varying by age group and country for each causative agent. In the US alone, there are more than 200 million cases of infectious diarrheal illness annually; worldwide, infectious diarrhea is the second most common cause of morbidity and mortality. Those at risk for infectious diarrhea include immunocompromised patients, those at the extremes of age, travelers, military personnel with overseas assignments, patients in chronic care facilities, and those with altered GI physiology (including patients taking proton pump inhibitors and antibiotics). Causative agents for this infection include viral, bacterial, and protozoal sources, which may be passed through contaminated food and drinks or by fecal-oral contamination via sexual intercourse, community pools, poor water sanitation, gardening, and other sources.

Infectious diarrhea can be subclassified as either watery or bloody diarrhea. Watery diarrhea tends to be less severe than bloody diarrhea, or dysentery, with norovirus commonly causing watery diarrhea. Dysentery is associated with more severe complications and is commonly caused by Shigella species and Salmonella bacteria. Some species such as *Escherichia coli* may cause either watery or bloody presentations; for instance, *enterotoxigenic E coli* (ETEC) is associated with watery diarrhea, whereas *enterohemorrhagic E coli* is associated with bloody diarrhea.

The cause of the diarrhea can often be determined based on symptoms, incubation period, and the frequency and volume of stool. For example, both viral gastroenteritis and foodborne illness are commonly associated with nausea and diarrhea, but foodborne illness has a shorter incubation period than viral gastroenteritis. A patient history should be obtained to assess for risk factors. Stool cultures often have a low yield for positive results; therefore, cultures should be performed only for patients with severe diarrhea, diarrhea associated with fever, or persistent diarrhea; for patients with dehydration or dysentery; for patients who are immunocompromised, elderly, and/or hospitalized; and when outbreak is a concern.

Prevention of these infections is focused on patient education, proper hand hygiene, and safe food preparation. Common management of infectious diarrhea includes supportive therapy with fluids and electrolytes to prevent and treat dehydration. Loperamide should be avoided in patients with bloody diarrhea and in those presenting with fever because of a risk of complications. Infections for which specific prevention or treatment modalities have been identified will be discussed in the following sections.

**Viral diarrhea**

Viral sources are the leading cause of diarrhea worldwide. Viral gastroenteritis affects the stomach and small intestine and commonly presents with diarrhea and nausea.

Rotavirus is the primary source of gastroenteritis in infants and children and historically has caused 20 to 60 deaths, 55,000 to 70,000 hospitalizations, 200,000 emergency room visits, and 400,000 physician office visits per year. Cases of rotavirus tend to occur from the late fall to early spring. This virus is transmitted via the fecal-oral route and through food and water contamination. The infection lasts for approximately three to seven days and is commonly associated with fever, nausea, vomiting, watery diarrhea, and abdominal pain. The rotavirus vaccine, available as either a two- or three-dose vaccine series depending on the brand, is now recommended for infants as...
a standard vaccination procedure in the US. Use of this vaccine has led to a reduction in emergency department visits and hospitalizations. These vaccines (Rotarix and RotaTeq) should not be used in patients with an allergy to the vaccine, patients with severe combined immunodeficiency syndrome (bubble boy disease), or patients with intussusception.33

Norovirus, also known as the Norwalk-like virus, is the principle cause of gastroenteritis in the US and is the leading cause of viral gastroenteritis worldwide, with outbreaks occurring on cruise ships, in dormitories, in restaurants, and in healthcare facilities as some examples.31,34 Norovirus outbreaks tend to occur during the winter months by similar modes of transmission as rotavirus. The infection lasts approximately two to three days in immunocompetent hosts but may last weeks to years in immunocompromised individuals.34 Norovirus infection is associated with muscle aches, abdominal cramps, nausea, vomiting, and watery diarrhea.

Other potential causes of viral gastroenteritis may include (but are not limited to) coronavirus and adenovirus; however, information about these causes is beyond the scope of this review. As these infections are viral in nature, management is focused on supportive care with fluids and electrolytes.

**Bacterial diarrhea**

Bacteria are another common cause of acute gastroenteritis in the US; ETEC and Vibrio cholera are the leading causes of watery diarrhea. Dysentery is commonly caused by nontyphoid Salmonella species, Shigella species, and Campylobacter species. Diarrhea can be caused by either the bacteria themselves or by toxins the bacteria produce. Antibiotic therapy is recommended for severe cases of diarrhea, febrile dysentery, culture-positive bacterial diarrhea, and moderate-to-severe traveler’s diarrhea (TD), with the preferred agent specific to each causative organism.30

**Clostridium difficile.** Clostridium difficile is an anaerobic gram-positive bacillus that is both toxin and spore forming. It is the causative organism of *C. difficile* associated diarrhea (CDAD), which is spread via the fecal-oral route.35 According to the IDSA and Society for Healthcare Epidemiology of America guidelines, CDAD is defined by the presence of diarrhea and histopathologic or colonoscopic findings of pseudomembranous colitis or a stool test positive for toxigenic *C. difficile* or its related toxins.36 CDAD can be further stratified by its etiology as being community- or hospital-acquired or by its level of severity (Table 3).35-36 Although CDAD is primarily hospital acquired, up to one-third of cases may be community acquired, which is defined as a new infection occurring in a patient who has not been in a healthcare facility overnight in the past three months.35,37 *C. difficile* is a common cause of nosocomial infections, with risk factors for infection including immunosuppression, treatment with chemotherapy, GI surgery, advanced patient age, presence of severe underlying disease or chronic kidney disease, environmental contamination, and use of medications such as proton pump inhibitors and antibiotics. Fluoroquinolones, clindamycin, cephalosporins, and aminopenicillins are the antibiotics most commonly associated with CDAD.35 Prevention of CDAD focuses on proper hygiene and antibiotic stewardship.

> **Although CDAD is primarily hospital acquired, up to one-third of cases may be community acquired.”**

Management of CDAD is focused on proper rehydration, cessation of causative antibiotic therapy as appropriate, and initiation of pharmacologic treatment with metronidazole, vancomycin, or fidaxomicin. Medications that inhibit GI motility should be avoided if CDAD is suspected because of the potential for toxic megacolon.36

Metronidazole is a nitroimidazole antibiotic used for the management of a number of parasitic and anaerobic conditions.38 Metronidazole is associated with GI side effects such as nausea, diarrhea, metallic taste, and abdominal discomfort. Major drug interactions include disulfiram.

### TABLE 3

**Preferred Management of *C. difficile* Infection**

<table>
<thead>
<tr>
<th>TYPE OF INFECTION</th>
<th>TREATMENT OPTIONS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mild to moderate severity</td>
<td>Metronidazole 500 mg by mouth every 8 h for 10-14 days</td>
</tr>
<tr>
<td>Severe severity</td>
<td>Vancomycin 125 mg by mouth every 6 h for 10-14 days or fidaxomicin 200 mg by mouth twice daily for 10 days</td>
</tr>
<tr>
<td>Severe complicated severity</td>
<td>Vancomycin 500 mg by mouth 4 times daily + intravenous metronidazole 500 mg every 8 h + vancomycin 500 mg per rectum in cases of complete ileus</td>
</tr>
<tr>
<td>First recurrence</td>
<td>Same as initial preferred therapy for the stratified disease severity or fidaxomicin 200 mg by mouth twice daily for 10 days</td>
</tr>
<tr>
<td>Second recurrence</td>
<td>Vancomycin pulse or tapered dose; fidaxomicin 200 mg by mouth twice daily for 10 days; alternative therapy; stool transplant</td>
</tr>
</tbody>
</table>

Source: Refs 25-36

### PAUSE AND PONDER

Which patient-specific factors would help you decide which therapy to use for the treatment of CDAD?
and alcohol. The use of alcohol while taking metronidazole can lead to a reaction similar to that seen with disulfiram, which may include nausea, vomiting, headache, and abdominal cramps. As such, patients should abstain from alcohol while they are taking metronidazole and for three days after treatment. Vancomycin is a bactericidal glycopeptide antibiotic that works by inhibiting the formation of the bacterial cell wall. Because this agent has minimal systemic absorption, orally administered vancomycin is indicated only for the management of CDAD and enterocolitis secondary to Staphylococcus aureus, and routine monitoring of vancomycin levels is unnecessary. The most common adverse effects of vancomycin are nausea, abdominal pain, flatulence, diarrhea, and vomiting. Vancomycin-resistant Enterococcus is a concern with overuse of oral vancomycin therapy. Zar et al completed a prospective, randomized, double-blind, placebo-controlled trial comparing metronidazole 250 mg by mouth four times daily to vancomycin 125 mg by mouth four times daily for 10 days in patients stratified by CDAD disease severity. In patients with mild disease, 90% of patients taking metronidazole (37/41) and 98% of those taking vancomycin (39/40) achieved clinical cure (P = 0.36). For those with severe disease, a significant difference was found between the two groups, with 76% (29/38) achieving clinical cure in the metronidazole group compared to 97% (30/31) in the vancomycin group (P = 0.02), suggesting the benefit of preferential use of vancomycin in this population. No significant difference was found in the rate of relapse between the two groups (14% in the metronidazole group; 7% in the vancomycin group; P = 0.27). This led the IDSA to recommend that mild to moderate disease should be managed with oral metronidazole therapy, whereas vancomycin should be used for severe CDAD (Table 3).

Fidaxomicin is a macrocyclic antibiotic indicated for the management of CDAD-associated diarrhea in patients at least 18 years of age. This agent maintains bactericidal activity by inhibiting RNA synthesis. The FDA-approved dose is 200 mg by mouth twice daily for 10 days. The most common side effects associated with fidaxomicin include GI adverse effects such as nausea and diarrhea. Because of its high cost, fidaxomicin is not used as a first-line agent. In studies comparing fidaxomicin with vancomycin, fidaxomicin was found to be noninferior to vancomycin for clinical cure rates but was associated with significantly lower rates of recurrence.

The first recurrence of CDAD can be managed with the same preferred therapy, whereas a second recurrence may be managed with pulsed or tapered dose vancomycin. Alternative management strategies, including stool transplants, may also be considered at this point. Traveler’s diarrhea. TD affects individuals who live in developed countries and travel to less developed or more tropical areas of the world. Afflicted patients experience at least three loose stools within a one-day period accompanied by at least one of the following symptoms: elevated temperature, cramping or pain in the abdomen, urgency to defecate, stools containing mucus or blood, nausea, or vomiting. It is estimated that one in two people who travel to developing areas will experience diarrhea. TD develops within the first seven days of the trip and often runs its course in seven days or fewer without medication. However, one in five patients with TD may experience symptoms significant enough to limit activities, and one in 100 patients may experience severe illness requiring hospital admission.

Bacteria cause eight of 10 cases of TD; therefore, bacterial pathogens will be the focus of this review. The most frequently implicated bacteria are ETEC, followed by other common pathogens such as Shigella species, Campylobacter, Aeromonas species, Salmonella species, and Plesiomonas species, with prevalence varying by location. Other important causative agents include parasites such as Giardia (comprising approximately 10% of TD cases) and viruses such as norovirus and rotavirus (comprising <10% of TD cases). Information about the management of viral diarrhea can be found in the “infectious diarrhea” section of this article. TD is transmitted by the consumption of food or beverages contaminated with pathogenic bacteria. Commonly implicated food carriers include salads, raw vegetables, unpeeled fruits, and seafood or meat products that are not thoroughly cooked. Activities such as hiking and camping are particularly risky because of the limited ability to properly clean and cook foods. Travelers should be aware of the possibility of contracting TD based on the region to which they will be venturing. Mexico, Central and South America, Africa, most of Asia, and the Middle East are considered to be the highest risk. Conversely, the lowest risk regions are Australia, New Zealand, North and West Europe, Canada, and Japan. Timing of travel is an important consideration, as most cases of TD occur during hot and rainy seasons.

“Antibiotics are the mainstay of pharmacologic therapy for TD and should be initiated after a patient passes three or more unformed stools in 24 hours.”

Patients may consult a pharmacist regarding strategies to prevent TD before travel. Antibiotic prophylaxis is very effective but is generally not recommended because of increased risk of adverse effects and antibiotic resistance. Furthermore, changes to normal GI flora precipitated by antibiotic use may in fact increase a patient’s susceptibility to infection by more virulent pathogens. Additionally, antibiotic prophylaxis may lead patients to have a false sense of protection and be less cautious when selecting food and beverages. Bismuth subsalicylate has been shown to decrease the risk of TD by half when used prophylactically. However, patients must take two tablets four times daily, and pill burden limits the usefulness of this regi-
**Management of Acute and Chronic Diarrhea**

Diarrhea is a common complaint with a higher incidence of morbidity and mortality in patients at the extremes of age and in immunosuppressed populations. Hydration is the primary treatment modality for both noninfectious and infectious diarrhea. Noninfectious diarrhea may be caused by food intolerances, in which case patients should be counseled to avoid the offending foods, or by IBS-D, for which newer treatment modalities may be employed. Other management options for noninfectious diarrhea include bismuth subsalicylate and loperamide. Infectious diarrhea may be caused by bacterial, viral, or protozoal sources; the management of these cases depends on the underlying cause of infection. Preventive therapy for infectious diarrhea is focused on vaccinations when appropriate, proper hand hygiene, antibiotic stewardship, and proper food preparation to prevent cross-contamination. Because loperamide monotherapy has the potential to worsen disease and cause complications, this treatment option should be avoided in most cases of infectious diarrhea.

**References**

References are available online at www.drugtopics.com/cpe. •

**Controlling high risk groups**

Patients should be counseled that the most effective strategies for preventing TD are proper hand hygiene and selection of foods and beverages. Before eating, patients should clean their hands thoroughly with soap and water or alcohol-containing sanitizers if clean water is not available. Travelers should seek fruits and vegetables that can be peeled or that have been rinsed with clean water. They should only eat meals that have been recently cooked. Beverages should be bottled if possible or boiled before consumption if not bottled.

If a patient does contract TD, the first step is to adequately replace fluids and electrolytes. Parents traveling with young children should be counseled to carry ORT. ORT must be prepared by combining the contents of the packet with a specified amount of sterile water. Many patients, especially children, may find the salty taste of ORT to be unpleasant; however, ORT should be replaced with more palatable sports drinks only in cases of mild diarrhea. Beverages with high sugar content such as fruit juice and cola have the potential to exacerbate diarrhea through osmotic effects and should therefore be avoided. Antibiotics are the mainstay of pharmacologic therapy for TD and should be initiated after a patient passes three or more unformed stools in a 24-hour period. Fluoroquinolones, specifically levofloxacin and ciprofloxacin, are the antibiotics of choice, and a one-day course of these agents is usually sufficient. In areas where resistance to fluoroquinolones is increasing among TD pathogens, azithromycin 500 mg may be used for one to three days. Rifaximin is not approved for empiric therapy but may be used when the causative pathogen is known to be noninvasive E coli. Antimotility agents such as loperamide are generally considered safe and effective when used in conjunction with antibiotics to provide additional symptom relief.

**Foodborne illness**

There are approximately 9.4 million episodes, 56,000 hospitalizations, and more than 1000 deaths due to foodborne illnesses each year in the US. These may be caused by bacterial, parasitic, or viral sources. The most common of these infectious etiologies include Salmonella species, Shigella species, S aureus, Campylobacter species, and norovirus; Salmonella species are associated with the highest annual rates of illnesses, hospitalizations, and deaths. Symptoms of foodborne illness occur within hours to days of infection depending on the causative organism and are short in duration. Foods commonly associated with foodborne illnesses include meats, poultry, water, unpasteurized dairy products, and vegetables. An assessment of foodborne illness causes in the US from 1998 to 2008 found that norovirus was associated with the most outbreaks of foodborne illnesses. Produce commodities, including fruits, vegetables, and nuts, accounted for many of the illnesses (46%), and leafy vegetables accounted for more illnesses than any other commodity (22%). Poultry-based infections (19%) were primarily caused by Listeria monocytogenes or Salmonella species.

Preventive strategies include avoidance of undercooked seafood or meat, prevention of cross-contamination, and avoidance of unpasteurized dairy products. Treatment strategies include supportive care with fluids and electrolytes. Foodborne illnesses caused by Bacillus cereus, Clostridium perfringens, and S aureus do not benefit from antimicrobial therapy management; the management of other infectious causes of foodborne illnesses has been discussed in previous sections.

**The pharmacist’s role and self-care exclusions**

When assessing a patient with diarrhea, pharmacists should first determine whether a patient is in need of medical evaluation, such as those patients at risk for dehydration and other complications. Patients who are at high risk for dehydration include those with diarrhea lasting more than two days, diarrhea occurring at least six times per day, those who are experiencing frequent vomiting in addition to diarrhea, and those with fever (temperature of at least 101.3°F/38.5°C). Individuals who are less than two years old or older than 65 years should be referred because of an increased risk of complications resulting in hospitalization or death. Pregnant women, patients taking immunosuppressive medications, and those with immunocompromising diseases should be treated under the care of a provider. Patients who report severe pain in the abdomen and those who observe pus or blood in the stool should be referred to rule out more serious illnesses. Technicians may play a role in collecting information about patient symptoms and severity in preparation for referral to the pharmacist.

Those patients who are eligible for self-care with OTC products should be counseled that use of these agents is not recommended beyond 48 hours after the onset of acute diarrhea symptoms, regardless of when OTC products are initiated. Chronic and persistent diarrhea should be further evaluated by a provider before continued use of self-care interventions.

**Conclusion**

Diarrhea is a common complaint with a higher incidence of morbidity and mortality in patients at the extremes of age and in immunosuppressed populations. Hydration is the primary treatment modality for both noninfectious and infectious diarrhea. Noninfectious diarrhea may be caused by food intolerances, in which case patients should be counseled to avoid the offending foods, or by IBS-D, for which newer treatment modalities may be employed. Other management options for noninfectious diarrhea include bismuth subsalicylate and loperamide. Infectious diarrhea may be caused by bacterial, viral, or protozoal sources; the management of these cases depends on the underlying cause of infection. Preventive therapy for infectious diarrhea is focused on vaccinations when appropriate, proper hand hygiene, antibiotic stewardship, and proper food preparation to prevent cross-contamination. Because loperamide monotherapy has the potential to worsen disease and cause complications, this treatment option should be avoided in most cases of infectious diarrhea.

References are available online at www.drugtopics.com/cpe. •
TEST QUESTIONS

For Pharmacists:

1. Which of the following medications for IBS-D is only available through a Risk Evaluation and Mitigation Strategy program?
   a. Alosetron
   b. Eluxadoline
   c. Loperamide
   d. Rifaximin

2. Which of the following medications for IBS-D is a schedule IV controlled substance?
   a. Alosetron
   b. Eluxadoline
   c. Loperamide
   d. Rifaximin

3. Which of the following patients should be referred for medical evaluation?
   a. 45-year-old man with a 36-hour history of diarrhea and a temperature of 101°F regardless of the patient’s baseline consistency from baseline
   b. 18-year-old woman with a three-day history of diarrhea and a temperature of 99.6°F
   c. 12-year-old boy with four loose stools occurring in the past 24 hours and a temperature of 100.4°F
   d. 56-year-old man with three loose stools and one episode of vomiting in the past 18 hours and a temperature of 98.5°F

4. Which of the following bacteria are most commonly implicated in traveler’s diarrhea?
   a. Enterotoxigenic Escherichia coli
   b. Salmonella species
   c. Shigella species
   d. Campylobacter species

5. Which of the following is a cause of infectious diarrhea?
   a. Bacteria
   b. Viruses
   c. Protozoa
   d. All of the above

6. In the management of noninfectious diarrhea, which of the following OTC agents is associated with tinnitus?
   a. Bismuth subsalicylate
   b. Loperamide
   c. Pedialyte
   d. Omeprazole

7. Which of the following antibiotics is commonly associated with causing Clostridium difficile associated diarrhea (CDAD)?
   a. Fluoroquinolones
   b. Cephalosporins
   c. Amoxicillin
   d. All of the above

8. In a patient with mild CDAD, which of the following agents is considered first-line therapy?
   a. Metronidazole
   b. Vancomycin
   c. Rifaximin
   d. Fidaxomicin

9. Based on epidemiologic studies, which of the following food substances was most commonly associated with foodborne illnesses?
   a. Fruits
   b. Poultry
   c. Leafy vegetables
   d. Shellfish

10. Which of the following is the primary cause of gastroenteritis in the United States?
    a. Rotavirus
    b. Norovirus
    c. Salmonella species
    d. Escherichia coli

For Pharmacy Technicians:

1. Diarrhea is defined as which of the following means:
   a. The production of more than one stool per day regardless of the patient’s baseline
   b. The production of more than two stools per day regardless of the patient’s baseline
   c. An increase in stool frequency or a decrease in stool consistency from baseline
   d. A decrease in stool frequency or an increase in stool consistency from baseline

2. Diarrhea can be classified by which of the following etiologies:
   a. Etiology: Infectious versus noninfectious etiology
   b. Duration: Acute, persistent, or chronic
   c. Pathophysiologic mechanism: secretory, osmotic, exudative, or motor
   d. All of the above

3. Which of the following oral liquids is preferred in patients most at risk for dehydration in the outpatient setting?
   a. Bottled water
   b. Sports drinks
   c. ORT (e.g., Pedialyte)
   d. None of the above, as dehydration is not a concern

4. Which of the following factors has the potential to cause acute noninfectious diarrhea?
   a. Overconsumption of fructose
   b. Consumption of magnesium-containing antacids
   c. Lactose intolerance
   d. All of the above

5. Which of the following is a correctly matched brand and generic OTC product for symptom management of diarrhea?
   a. Bismuth subsalicylate - Lactaid
   b. Loperamide - Imodium
   c. Pedialyte - Pepto-Bismol
   d. Bismuth subsalicylate - Imodium

6. At what point in time should patients be referred for further evaluation when they are self-treating for noninfectious diarrhea?
   a. >48 hours after the first OTC dose
   b. >48 hours after the onset of symptoms
   c. One week after first OTC dose
   d. None of the above

7. Which of the following is an antibiotic used in the treatment of IBS-D?
   a. Rifaximin
   b. Loperamide
   c. Bismuth subsalicylate
   d. Alosetron

8. Which of the following may put patients at the highest risk for traveler’s diarrhea?
   a. Drinking only bottled water
   b. Traveling during cold and dry seasons
   c. Traveling within the United States
   d. Eating raw vegetables and unpeeled fruit

9. Which of the following diagnoses requires the use of antibiotics for treatment?
   a. Acute noninfectious diarrhea
   b. Lactose intolerance
   c. C difficile
   d. None of the above

10. Which of the following medication classes is associated with an increased risk of C difficile?
    a. Proton pump inhibitors (e.g., omeprazole)
    b. B-lactam antibiotics (e.g., amoxicillin)
    c. Both A and B
    d. None of the above
References


