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Chapter 2
The Pre-Travel Consultation
Self-Treatable Diseases

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TRAVELERS' DIARRHEA

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Description

Travelers' diarrhea (TD) is the most predictable travel-related illness. Attack rates range from 30% to 70% of travelers, depending on the destination. Traditionally, it was thought that TD could be prevented by following eating rules, but studies have found that people who follow the rules still get ill. Poor hygiene practice in local restaurants is likely the largest contributor to the risk for TD.

TD itself is a clinical syndrome that can result from a variety of intestinal pathogens. Bacterial pathogens are the predominant risk, thought to account for 80%–90% of TD. Intestinal viruses have been isolated in studies of TD, but they usually account for 5%–8% of illnesses. Protozoal pathogens are slower to manifest symptoms, and collectively account for about 10% of diagnoses in longer-term travelers. What is commonly known as "food poisoning" involves the ingestion of preformed toxins in food. In this syndrome, vomiting and diarrhea may both be present, but symptoms usually resolve spontaneously within 12 hours.

Infectious Agent

- Bacteria are the most common cause of TD. The most common pathogen is enterotoxigenic *Escherichia coli*, followed by *Campylobacter jejuni*, *Shigella* sp., and *Salmonella* sp. Enteroadherent and other *E. coli* species have been found to also be common pathogens in bacterial diarrhea.
- Viral diarrhea can be caused by a number of viral pathogens, including norovirus, rotavirus, and astrovirus.
- *Giardia* is the main protozoal pathogen found in travelers. *Entamoeba histolytica* is a relatively uncommon pathogen in travelers. *Cryptosporidium* is also relatively uncommon. The risk for *Cyclospora* is highly geographic and seasonal, with the most well-known risks in Nepal, Peru, Haiti, and Guatemala. *Dientamoeba fragilis* is a low-grade but persisent pathogen that is occasionally diagnosed in travelers.
- The individual pathogens are each discussed in their own sections in Chapter 5 (/travel/yellowbook/2010/table-of-contents.aspx#16) , and persistent diarrhea is discussed in Chapter 4 (/travel/yellowbook/2010/table-of-contents.aspx#15) .

Occurrence

- The most important determinant of risk is travel destination, and there are regional differences in both the risk for and etiology of diarrhea.
- The world is generally divided into three grades of risk: low, intermediate, and high.
    - Low-risk countries include the United States, Canada, Australia, New Zealand, Japan, and countries in Northern and Western Europe.
    - Intermediate-risk countries include those in Eastern Europe, South Africa, and some of the Caribbean islands.
    - High-risk areas include most of Asia, the Middle East, Africa, Mexico, and Central and South America.

Risk for Travelers

Travelers' diarrhea occurs equally in male and female travelers and is more common in young adults than in older people. In short-term travelers, bouts of TD do not appear to protect against future attacks, and more than one episode of TD may occur during a single trip. A cohort of expatriates taking up residence in Kathmandu, Nepal, experienced an average of 3.2 episodes of TD per person in their first year. In more temperate regions, there may be seasonal variations in diarrhea risk. In South Asia, for example, during the hot months preceding the monsoon, much higher TD attack rates are commonly reported.

In environments where large numbers of people do not have access to plumbing or outhouses, the amount of stool contamination in the environment will be higher and more accessible to flies. Inadequate electrical capacity may lead to frequent blackouts or poorly functioning refrigeration, which can result in unsafe food storage and an increased risk for disease. Inadequate water supplies can lead to the absence of sinks for handwashing by restaurant staff. Poor training in handling and preparation of food may lead to cross-contamination from meat and inadequate sterilization of food preparation surfaces and utensils. In destinations in which effective food handling courses have been provided, the risk for TD has been demonstrated to decrease. It should be noted, however, that pathogens that cause TD are not unique to developing countries. The risk of TD is associated with the hygiene practices in specific destinations and the handling and preparation of food in restaurants in developed countries as well.

Clinical Presentation

- Bacterial diarrhea presents with the sudden onset of bothersome symptoms that can range from mild cramps and urgent loose stools, to severe abdominal pain, fever, vomiting, and bloody diarrhea.
- Viral enteropathogens present in a similar fashion to bacterial pathogens, although with norovirus vomiting may be more prominent.
- Protozoal diarrhea, such as that caused by *Giardia intestinalis*, or *Entamoeba histolytica*, generally has a more gradual onset of low-grade symptoms, with 2–5 loose stools per day.
- The incubation period of the pathogens can be a clue to the etiology of TD.
    - Bacterial and viral pathogens have an incubation period of 6–48 hours.
    - Protozoal pathogens generally have an incubation period of 1–2 weeks and rarely present in the first few weeks of travel. An exception can be *Cyclospora cayetanensis*, which can present quickly in areas of high risk.
- Untreated bacterial diarrhea lasts 3–5 days. Viral diarrhea lasts 2–3 days. Protozoal diarrhea can persist for weeks to months without treatment.
- An acute bout of gastroenteritis can lead to persistent gastrointestinal symptoms, even in the absence of continued infection (see the Persistent Travelers' Diarrhea (/travel/yellowbook/2010/chapter-4/persistent-travelers-diarrhea.aspx) section in Chapter 4). Other postinfectious sequelae include reactive arthritis and Guillain–Barré syndrome.

Preventive Measures for Travelers

- For travelers to high-risk areas, several approaches may be recommended that can reduce but never completely eliminate the risk for TD. These include—
    - Instruction regarding food and beverage selection
    - Use of agents other than antimicrobial drugs for prophylaxis
    - Use of prophylactic antibiotics
- Carrying small containers of hand-sanitizing solutions or gels (containing at least 60% alcohol) may make it easier for travelers to clean their hands before eating.

Food and Beverage Selection

Care in selecting food and beverages for consumption might minimize the risk for acquiring TD. Travelers should be advised that foods that are

freshly cooked and served piping hot are safer than foods that may have been sitting for some time in the kitchen or in a buffet. Care should be taken to avoid beverages diluted with nonpotable water (reconstituted fruit juices, ice, and milk) and foods washed in nonpotable water, such as salads. Other risky foods include raw or undercooked meat and seafood, and unpeeled raw fruits and vegetables. Safe beverages include those that are bottled and sealed, or carbonated. Boiled beverages and those appropriately treated with iodine or chlorine may also be safely consumed. Although food and water precautions continue to be recommended, travelers may not always be able to always adhere to the advice. Furthermore, many of the factors that ensure food safety, such as restaurant hygiene, are out of the traveler's control.

Nonantimicrobial Drugs for Prophylaxis

The primary agent studied for prevention of TD, other than antimicrobial drugs, is bismuth subsalicylate (BSS), which is the active ingredient in Pepto-Bismol. Studies from Mexico have shown this agent (taken daily as either 2 oz of liquid or two chewable tablets four times per day) reduces the incidence of TD from 40% to 14%. BSS commonly causes blackening of the tongue and stool and may cause nausea, constipation, and rarely tinnitus. BSS should be avoided by travelers with aspirin allergy, renal insufficiency, and gout, and by those taking anticoagulants, probenecid, or methotrexate. In travelers taking aspirin or salicylates for other reasons, the use of BSS may result in salicylate toxicity. Caution should be used in administering BSS to children with viral infections, such as varicella or influenza, because of the risk for Reye syndrome. BSS is not recommended for children <3 years of age. Studies have not established the safety of BSS use for periods >3 weeks.

The use of probiotics, such as Lactobacillus GG and *Saccharomyces boulardii*, has been studied in the prevention of TD in limited numbers of subjects. Results are inconclusive, partially because standardized preparations of these bacteria are not reliably available.

Prophylactic Antibiotics

Prophylactic antibiotics have been demonstrated to be quite effective in the prevention of TD. Controlled studies have shown that diarrhea attack rates are reduced from 40% to 4% by the use of antibiotics. The prophylactic antibiotic of choice has changed over the past few decades as resistance patterns have evolved. Agents such as trimethoprim-sulfamethoxazole and doxycycline are no longer considered effective antimicrobial agents against enteric bacterial pathogens. The fluoroquinolones have been the most effective antibiotics for the prophylaxis and treatment of bacterial TD pathogens, but increasing resistance to these agents, mainly among *Campylobacter* species, may limit their benefit in the future. A nonabsorbable antibiotic, rifaximin, is being investigated for its potential use in TD prophylaxis. In the only study published to date, rifaximin reduced the risk for TD in travelers to Mexico by 77%. At this time, prophylactic antibiotics should not be recommended for most travelers. In addition to affording no protection against nonbacterial pathogens, the use of antibiotics may be associated with allergic or adverse reactions in a certain percentage of travelers. The use of prophylactic antibiotics should be weighed against the result of using prompt, early self-treatment with antibiotics when TD occurs, which can limit the duration of illness to 6–24 hours in most cases.

Prophylactic antibiotics may be considered for short-term travelers who are high-risk hosts (such as those who are immunosuppressed) or are taking critical trips during which even a short bout of diarrhea could impact the purpose of the trip.

Treatment

Antibiotics are the principal element in the treatment of TD. Adjunctive agents used for symptomatic control may also be recommended.

Antibiotics

As bacterial causes of TD far outnumber other microbial etiologies, empiric treatment with an antibiotic directed at enteric bacterial pathogens remains the best therapy for TD. The benefit of treatment of TD with antibiotics has been proven in numerous studies. The effectiveness of a particular antimicrobial depends on the etiologic agent and its antibiotic sensitivity. Both as empiric therapy or for treatment of a specific bacterial pathogen, first-line antibiotics include those of the fluoroquinolone class, such as ciprofloxacin or levofloxacin. Increasing microbial resistance to the fluoroquinolones, especially among *Campylobacter* isolates, may limit their usefulness in some destinations such as Thailand, where *Campylobacter* is prevalent. Isolated anecdotal case reports of resistant *Campylobacter* diarrhea occur periodically from other destinations. An alternative to the fluoroquinolones in this situation is azithromycin. Rifaximin has been approved for the treatment of TD caused by noninvasive strains of *E. coli*. However, since it is often difficult for travelers to distinguish between invasive and noninvasive diarrhea and since they would have to carry a back-up drug in the event of invasive diarrhea, the overall usefulness of rifaximin as empiric self-treatment remains to be determined.

Single-dose or 1-day therapy for TD with a fluoroquinolone is well established, both by clinical trials and clinical experience. The best regimen for azithromycin treatment is not yet established. One study used a single dose of 1,000 mg, but side effects (mainly nausea) may limit the acceptability of this large dose. Azithromycin, 500 mg per day for 1–2 days, appears to be effective in most cases of TD.

Antimotility Agents

Antimotility agents provide symptomatic relief and serve as useful adjuncts to antibiotic therapy in TD. Synthetic opiates, such as loperamide and diphenoxylate, can reduce bowel movement frequency and enable travelers to ride on an airplane or bus while awaiting the effects of antibiotics. Loperamide appears to have antisecretory properties as well. The safety of loperamide when used along with an appropriate antibiotic has been well established, even in cases of invasive pathogens. Loperamide can be used in children, and liquid formulations are available. In practice, however, these drugs are rarely given to small children.

Oral Rehydration Therapy

Fluids and electrolytes are lost in cases of TD, and replenishment is important, especially in young children or adults with chronic medical illness. In adult travelers who are otherwise healthy, severe dehydration resulting from TD is unusual unless prolonged vomiting is present. Nonetheless, replacement of fluid losses remains an important adjunct to other therapy and helps the traveler feel better more quickly. Travelers should remember to use only beverages that are sealed or carbonated, or otherwise known to be purified. For more severe fluid loss, replacement is best accomplished with oral rehydration solutions (ORS), such as the WHO ORS solutions, which are widely available at stores and pharmacies in most developing countries (see Table 2-25 for details). ORS is prepared by adding one packet to the appropriate volume of boiled or treated water. Travelers may find most ORS formulations to be relatively unpalatable, due to their saltiness. In most cases, rehydration can be maintained with any palatable liquid.

Treatment of TD Caused by Protozoa

The most common parasitic cause of TD is *Giardia intestinalis*, and treatment options include metronidazole, tinidazole, and nitazoxanide. Although cryptosporidiosis is usually a self-limited illness in immunocompetent persons, nitazoxanide can be considered as a treatment option. Cyclosporiasis is treated with trimethoprim–sulfamethoxazole. Treatment of amebiasis is with metronidazole or tinidazole, followed by treatment with a luminal agent such as paromomycin.

Treatment for Children

Children who accompany their parents on trips to high-risk destinations may be expected to have TD as well. There is no reason to withhold antibiotics from children who contract TD. In older children and teenagers, treatment recommendations for TD follow those for adults, with possible adjustments in the dose of medication. Macrolides such as azithromycin are considered first-line antibiotic therapy in children, although some experts now use short-course fluoroquinolone therapy for travelers <18 years of age. Rifaximin is approved for use starting at 12 years of age.

Infants and younger children are at higher risk for developing dehydration from TD, which is best prevented by the early use of ORS solutions. Breastfed infants should continue to nurse on demand, and bottle-fed infants can continue to drink their formula. Older infants and children may eat a regular diet, depending on the level of their appetite while they are ill. Infants in diapers are at risk for developing a painful, ecxematous rash on their buttocks in response to the liquid stool. Hydrocortisone cream will quickly improve this rash. More information about diarrhea and dehydration are discussed in the Traveling Safely with Infants and Children section in Chapter 7.

Table 2-25. Composition of WHO oral rehydration salts (ORS) for diarrheal illness[1]

Ingredient	Amount
Sodium chloride	2.6 g/L
Potassium chloride	1.5 g/L
Glucose, anhydrous	13.5 g/L
Trisodium citrate, dihydrate	2.9 g/L (or 2.5 g/L)
Water	1.0 L

[1] World Health Organization. Oral Rehydration Salts (ORS): Production of the new ORS. Geneva: WHO; 2006: p. 2–4.

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