Travelers' diarrhea: Treatment and prevention

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INTRODUCTION

Travelers' diarrhea is the most common illness in persons traveling from resource-rich to resource-limited regions of the world [1,2]. Among travelers to such areas, 40 to 60 percent develop diarrhea [3]. Episodes of travelers' diarrhea are nearly always benign and self-limited, but symptoms may disrupt planned activities and result in health care visits for some travelers [4]. There is a growing recognition that travelers' diarrhea and its self-treatment abroad are associated with the acquisition of organisms harboring antibiotic resistance [5-10].

The treatment and prevention of travelers' diarrhea are discussed here. The epidemiology, microbiology, clinical manifestations, and diagnosis of travelers' diarrhea are discussed separately. (See "Travelers' diarrhea: Epidemiology, microbiology, clinical manifestations, and diagnosis".)

MANAGEMENT

Clinical approach — Management of travelers' diarrhea depends on the severity of illness. Fluid replacement is an essential component of treatment for all cases of travelers' diarrhea. Most cases are self-limited and resolve on their own within three to five days of treatment with fluid replacement only. Antimotility agents can provide symptomatic relief but should not be used when bloody diarrhea is present. Antimicrobial therapy shortens the disease duration, but the benefit of antibiotics must be weighed against potential risks, including adverse effects and selection for resistant bacteria. These issues are discussed in the sections that follow.

When to seek care — Travelers from resource-rich settings who develop diarrhea while traveling to resource-limited settings generally can treat themselves rather than seek medical advice while traveling. However, medical evaluation may be warranted in patients who develop high fever, abdominal pain, bloody diarrhea, or vomiting. Otherwise, for most patients while traveling or after returning home, medical consultation is generally not warranted unless symptoms persist for 10 to 14 days.

Fluid replacement — The primary and most important treatment of travelers' (or any other) diarrhea is fluid replacement, since the most significant complication of diarrhea is volume depletion [11,12]. The approach to fluid replacement depends on the severity of the diarrhea and volume depletion. Travelers can use the amount of urine passed as a general guide to their level of volume depletion. If they are urinating regularly, even if the color is dark yellow, the diarrhea and volume depletion are likely mild. If there is a paucity of urine and that small amount is dark yellow, the diarrhea and volume depletion are likely more severe.

- Mild cases – Patients with mild diarrhea may combine alternating sips of fluids that contain salt and fluids that contain sugar to replete and maintain hydration. Broth, fruit juice, or similar fluids may be used. Pedialyte is frequently useful in children. For mild diarrhea, the use of fluids is the critical factor; the fluid need not be oral rehydration solution (ORS). One study showed no difference in outcome between treatment with ORS plus loperamide versus generic fluids and loperamide [13].

- Severe cases – Severe diarrhea should be treated with ORS; this replaces needed electrolytes in the appropriate concentrations. Packets of ORS are available in the pharmacies of most countries and can be mixed with clean drinking water [14]. ORS should be used until the individual is urinating regularly.

  Alternatively, a similar solution can be made by adding 0.5 teaspoon of salt, 0.5 teaspoon of baking soda, and 4 tablespoons of sugar to 1 liter of water. The electrolyte concentrations of fluids used for sweat replacement (eg, Gatorade) are not equivalent. (See "Approach to the adult with acute diarrhea in resource-abundant settings", section on 'Fluid repletion' and "Oral rehydration therapy", section on 'Clinical management'.)

Dietary guidance — The optimal dietary intake during diarrheal illnesses has not been established. Controversy exists about issues such as partial fasting, the composition of the diet, and the time at which solid food intake should be resumed. Ultimately, apart from hydration, diet is not likely to be important, since disease duration is only a few days. The most important intervention for someone with travelers' diarrhea is to maintain hydration. In general, we advise individuals to eat or not as they choose, depending on how hungry they are. Often someone

with diarrhea will not feel hungry, but if they do choose to eat, will prefer a bland diet such as rice or toast.

Limited role for antibiotics — We suggest not treating most cases of travelers' diarrhea with antibiotics, as symptoms typically resolve spontaneously. Antibiotics can shorten the duration of travelers' diarrhea compared with placebo. However, the cost, potential adverse effects, and antibiotic resistance among many routine enteric pathogens (including the presence of extended-spectrum beta-lactamases in diarrheagenic *E. coli*) largely outweigh the modest benefits of antibiotic treatment for a self-limited condition [15,16]. Self-administration of antibiotics for diarrhea while traveling has also been associated with gut colonization by multidrug-resistant bacteria, suggesting that use of antibiotics by international travelers plays a role in the global spread of antimicrobial resistance [5,9].

- **Restrict use to select cases** – We reserve antibiotic treatment for select travelers with severe diarrhea, particularly when it is characterized by fever and blood, pus, or mucus in the stool. Thus, we do not routinely prescribe antibiotics to travelers for self-treatment of travelers' diarrhea. For certain high-risk travelers (eg, those with an immunocompromising condition), we prescribe antibiotics to have on hand in the event of severe diarrhea and advise them to seek medical care in conjunction with their use. Caution should also be used when treating a patient who has grossly bloody diarrhea with antibiotics, particularly if there is no or minimal fever. Although an uncommon cause of travelers' diarrhea, bloody diarrhea can reflect infection with enterohemorrhagic *E. coli*, for which antibiotic treatment has been associated with an increased risk of hemolytic-uremic syndrome, especially in children. (See "Shiga toxin-producing Escherichia coli: Clinical manifestations, diagnosis, and treatment", section on 'Antibiotics'.)

- **Antibiotic selection** – There are several antibiotic options for treatment of severe travelers' diarrhea (table 1). We suggest azithromycin for most travelers. Rifaximin and rifamycin are alternatives for travelers' diarrhea suspected to be caused by noninvasive strains of *E. coli*, but their effectiveness against invasive pathogens is unknown, and they should not be used in patients with fever or bloody diarrhea.

  - Azithromycin – The most practical dose for travelers' diarrhea is a single 1 g dose (table 1); however, it can cause nausea in some individuals. A three-day course of 500 mg daily is also effective [17]. Azithromycin is active against pathogens that cause dysentery (bloody or mucoid diarrhea) and retains activity in some locations where antibiotic-resistant pathogens are prevalent (such as Southeast Asia, where quinolone-resistant *C. jejuni* is a common cause of travelers' diarrhea). It can be used safely in pregnant women and children. In randomized trials, azithromycin was as effective as

fluoroquinolones, which had previously been shown to reduce the duration of traveler's diarrhea by about one to two days [17-20].

- Rifaximin **and** rifamycin – Rifaximin (200 mg three times daily for three days for children ≥12 years of age and adults) and rifamycin (two 194 mg tablets twice daily for three days for adults) are poorly absorbed drugs from the rifamycin class that are alternatives to azithromycin for travelers' diarrhea likely caused by noninvasive strains of *E. coli*. In randomized trials, rifaximin was associated with more rapid cessation of diarrhea than placebo (33 versus 60 hours) [21] and had equal efficacy to fluoroquinolones [20,22,23]. Rifaximin combined with loperamide may provide more rapid symptomatic improvement than either agent alone [24]. When used for treatment of travelers' diarrhea, novel formulations of rifamycin are also less associated with subsequent colonization with multidrug-resistant bacteria compared with ciprofloxacin [25].

Most of the trials evaluating these agents had been performed prior to widespread prevalence of multidrug-resistant diarrheagenic bacteria, and their contemporary effectiveness is thus uncertain. In a review of studies evaluating resistance in diarrheagenic *E. coli* among travelers, rates of resistance to azithromycin and rifaximin ranged from 0 to 61 percent and 0 to 20 percent, respectively, with the more recent studies reporting the higher rates; rates of extended-spectrum beta-lactamase production have also increased [16].

Fluoroquinolones had previously been the first choice of treatment for travelers' diarrhea (table 1). In several placebo-controlled randomized trials, fluoroquinolones reduced the duration of travelers' diarrhea by one to two days [26-30]. However, increasing resistance to quinolones among diarrheal pathogens worldwide, particularly *C. jejuni* isolates in Southeast Asia [31-34] and diarrheagenic *E. coli* [35], makes the use of fluoroquinolones almost obsolete. Furthermore, adverse effects associated with fluoroquinolones dampens enthusiasm for their use. Specifically, in the United States, the Food and Drug Administration released a statement about disabling and potentially permanent side effects of the tendons, muscles, joints, nerves, and central nervous system related to fluoroquinolone use [36] and advised that they not be prescribed unless the benefits outweigh the risks. Fluoroquinolones should also not be used for travelers' diarrhea in pregnant women or children.

- **Antimicrobial resistance** − Antimicrobial resistance is increasing among bacterial pathogens that cause travelers' diarrhea. Among 1726 travel-associated infections reported during 2004 to 2014, 56 percent were quinolone nonsusceptible; most resistant

bacteria were *Campylobacter* species [37]. Resistance to quinolones among enteroaggregative *E. coli* (EAEC) and enterotoxigenic *Escherichia coli* (ETEC) strains causing travelers' diarrhea has also increased steadily over decades, particularly among travelers to Southeast Asia [35]. Extended-spectrum beta-lactamase production has been identified in up to 15 percent of EAEC and ETEC isolates [16].

Symptomatic therapy — Nonantibiotic symptomatic management (eg, bismuth or antimotility agents such as loperamide or diphenoxylate) can be used for mild or moderate diarrhea. For travelers with severe diarrhea, we suggest that antimotility agents only be taken in conjunction with antibiotics.

Probiotic use in adults with acute infectious gastroenteritis is unproven.

Antimotility agents — Antimotility agents, such as loperamide (Imodium) or diphenoxylate (Lomotil), can be used by travelers to reduce the rate of stooling; they do not treat the cause of diarrhea. Antimotility agents can be used alone (ie, without antibiotics) in mild to moderate travelers' diarrhea. They should be avoided in individuals with dysentery (bloody stool and/or fever) and should only be used in conjunction with antibiotics for individuals with severe watery diarrhea. Antimotility agents should be stopped if abdominal pain or other symptoms worsen or if the diarrhea continues to be intractable after two days.

Particular vigilance about hydration is important in patients who take antimotility agents for travelers' diarrhea, as the agents do not kill the pathogen causing the diarrhea or stop the secretory process in the intestine. Patients may be unaware of how much fluid they are losing into their intestine since they are no longer having frequent bowel movements.

Additionally, there continues to be some concern that antimotility agents can prolong some types of dysenteric illnesses (eg, *Shigella*) [38]. While some studies suggest that antimotility drugs can be safely used in dysenteric illnesses as long as they are combined with antibiotic therapy, none of the studies in a 2008 meta-analysis evaluating the benefit of antimotility agents included patients with bloody diarrhea or symptoms suggestive of dysentery [28,39,40].

The antisecretory drug, racecadotril, which is not available in the United States, may be useful in travelers' diarrhea.

Bismuth — Bismuth subsalicylate can also be used to treat the symptoms of diarrhea, although large doses are required. Sixty mL (or four tablets) should be taken every one-half hour until the diarrhea resolves or eight doses have been taken. The two major disadvantages of this type of treatment are the potential for salicylate toxicity (especially in those who take

aspirin for any reason, pregnant women, and children) and the need to carry large quantities of bismuth subsalicylate.

Patients with persistent diarrhea — For patients with diarrhea that has persisted for more than 10 to 14 days or for those whose diarrhea does not improve with antibiotic therapy, less common or drug-resistant pathogens may be causative. In a study of 7442 returning travelers who sought care at a GeoSentinel Network site and were diagnosed with an infectious gastrointestinal disease (not limited to diarrhea), 2092 cases had a pathogen identified on testing [41]. In 65 percent of those cases, a parasite was isolated. The most commonly isolated pathogens were *Giardia* spp (28 percent), *Campylobacter* spp (13 percent), *Entamoeba histolytica* (13 percent), *Shigella* spp (6 percent), and *Strongyloides* (6 percent). *Cyclospora*, *Isospora*, *Cryptosporidium*, and microsporidia are also thought to be important causes, but may be underestimated because of difficulty in identifying them [42]. In travelers who had taken antibiotics, *C. difficile* is another possibility.

For such patients, evaluation focuses on identifying the infecting pathogen so that therapy can be targeted. In addition to a stool culture, this includes examination of stool for ova and parasites. Specialized staining techniques, such as a modified acid fast or trichome stain, may be required for certain organisms, such as *Cryptosporidium parvum*, microsporidia, *Cyclospora*, and *Isospora*. Stool antigen testing is also available for some parasites, such as *Giardia* and *Entamoeba* spp. Multiplex polymerase chain reaction (PCR) assays for identification of a variety of enteropathogens are also available, but interpretation may be confounded by the identification of more than one pathogenic organism. Diagnosis and treatment of these organisms are discussed in the dedicated topic reviews.

In some cases, persistent diarrhea may be representative of a previously undiagnosed noninfectious cause or a postinfectious irritable bowel syndrome. The approach to this is discussed in detail elsewhere. (See "Approach to the adult with chronic diarrhea in resource-abundant settings" and "Clinical manifestations and diagnosis of irritable bowel syndrome in adults".)

PREVENTION

The most important strategy to prevent travelers' diarrhea is prudent selection of food and drink while traveling. Water purification can be used if sanitary water is not otherwise available. Prophylactic medications (mainly antibiotics) are generally not indicated.

Food and drink selection — Educated choices in selecting food and drinks might result in a lower incidence of diarrheal disease. Basic advice for travelers to moderate or high-risk regions for travelers' diarrhea includes eating only food that has been thoroughly cooked and served hot, fruits that the traveler peels just prior to eating, and pasteurized dairy products. Beverages should be bottled or disinfected. Bottled drinks should be requested without ice. Hot tea and coffee are usually safe alternatives to boiled water.

Travelers should be aware of additional observations regarding food safety and the transmission of diarrhea-causing organisms. These observations are also pertinent in expensive resorts or hotels; price does not guarantee appropriate hygiene:

- Freezing does not kill the organisms that cause diarrheal disease. Thus, ice in drinks is not safe unless made from adequately boiled or filtered water.
- Alcohol does not sterilize water or ice; mixed drinks may still be contaminated.
- Outbreaks of diarrheal disease have been associated with bottled water (including carbonated water with insufficient carbonation) on rare occasions [43]. However, the presence of carbonation when a bottle is opened (eg, carbonated water or soft drinks) can reassure the traveler that the drink was processed in a proper fashion and is usually safe.
- Fruit salads, lettuce, or chicken salads are examples of unwise food choices; the ingredients may have been improperly washed and/or may have been sitting for some time without proper refrigeration.
- Condiments on the table can frequently become contaminated. One study of Mexican sauces in restaurants in Guadalajara and Houston found *E. coli* in more sauces in Mexico than in Houston (66 versus 40 percent); it is important to note that significant levels of contamination was not limited to Mexico [44]. Guacamole was the most frequently contaminated and was second only to pico de gallo for the highest colony count of bacteria.
- Steam table buffets that offer the traveler a variety of foods from the local region are risky since the temperature of the food can promote the growth of bacteria.
- Food provided on international airline flights can also be at risk of contamination.

Although common sense would suggest that following such dietary guidance can decrease the risk of travelers' diarrhea, this has been difficult to demonstrate in formal studies. The minority of travelers are able to strictly abide by all safe food and beverage restrictions [45]. As an

example, in a series of over 30,000 travelers to Jamaica, less than 3 percent stated that they had attempted to avoid potentially high-risk foods or drinks [45].

Water purification — It is usually safe to assume that the traveler will be able to find bottled water or soft drinks unless travel is to a rather remote area. Travelers who are going to be staying in rustic circumstances overseas will need to make arrangements for a safe water supply. Water can be purified in one of several ways:

- Boiling for 3 minutes followed by cooling to room temperature (do not add ice) to kill bacteria, parasites, and viruses.
- Adding two drops of 5 percent sodium hypochlorite (bleach) to a quart of water will kill most bacteria in 30 minutes.
- Adding five drops of tincture of iodine to a quart of water will kill bacteria within 30 minutes.
- Compact water filters in which the filters are impregnated with iodine remove parasitic pathogens and kill viral and bacterial pathogens; they provide a reasonable alternative for those who expect to be traveling under rustic circumstances. These are available commercially at camping or wilderness supply stores.

Boiling water is usually the most palatable solution to water purification if sanitary storage is feasible. The addition of iodine or chlorine to water can impart an unpleasant taste.

Chemoprophylaxis

Limited role for antibiotics — Antibiotic chemoprophylaxis should not be used routinely for travelers [2]. Use of daily antibiotics is expensive, has potential side effects, can disrupt normal gastrointestinal flora that may be beneficial, and can promote bacterial resistance [8]. For most travelers, such drawbacks are not outweighed by the prevention of a self-limiting diarrheal illness.

Antibiotic chemoprophylaxis may be appropriate in short-term (eg, <2 weeks) travelers who have an underlying medical condition that would increase the risk of complications from diarrhea or would be severely exacerbated by dehydration from diarrhea such that the benefits of using antibiotic prophylaxis outweigh its risks [2,46]. Such situations include known severe inflammatory bowel disease that could be exacerbated by an episode of infectious diarrhea; severe vascular, cardiac, or renal disease that would be seriously compromised by dehydration; or a severe immunocompromised state.

If antibiotic chemoprophylaxis is used, we suggest rifaximin, a non-absorbed antibiotic with a favorable safety profile that has been effective at preventing travelers' diarrhea in several trials. The optimal dose is uncertain, as various doses have been evaluated and there is no clear evidence that one is superior to the others. We favor a dose of 200 mg three times daily to try to maximize efficacy in the high-risk patient who warrants antibiotic prophylaxis, as there was a non-statistically significant trend towards better outcomes than other doses in a small trial; we generally advise prophylactic rifaximin for the duration of the trip. In the United States, rifaximin is not US Food and Drug Administration (FDA) approved for children younger than 12 years old.

In a meta-analysis of four placebo-controlled randomized trials that included over 500 travelers to Mexico or Turkey, rifaximin (total daily dose ranging from 550 to 1100 mg) reduced the rate of travelers' diarrhea to 16 percent compared with 40 percent with placebo (relative risk 0.41, 95% CI 0.30-0.56) during the time of administration [47]. Rifaximin did not result in excess adverse events and was associated with minimal changes in intestinal flora. One of the randomized trials in Mexico had compared several rifaximin doses (200 mg daily, 200 mg twice daily, or 200 mg three times daily) with placebo for two weeks [48]. Rifaximin at all doses reduced the rate of travelers' diarrhea, although the highest dose may have been associated with slightly lower rates of travelers' diarrhea that warranted antibiotic therapy (only the highest dose was included in the meta-analysis) [48]. Rifaximin also prevented travelers' diarrhea, although to a more moderate degree, in a subsequent randomized, double-blind trial of 258 German adults who were travelling to South or Southeast Asia for 6 to 28 days [49]. During travel and the week following, 25 percent of patients who received rifaximin (200 mg twice daily for the duration of the trip) reported symptoms consistent with travelers' diarrhea compared with 41 percent of those who received placebo. Of note, there was a trend toward lower effectiveness among travelers to Southeast Asia; this finding may be related to the decreased activity and efficacy of rifaximin for *Campylobacter* species [50], which predominate in Southeast Asia.

Although fluoroquinolones are effective in preventing travelers' diarrhea, we agree with an expert panel that has recommended against their use for this purpose due to increasing resistance of enteric pathogens and the potential for harm to the peripheral and central nervous system, tendons, muscles, and joints from fluoroquinolones [2].

Nonantibiotic agents — Nonantibiotic agents have also been studied for the prevention of travelers' diarrhea. Bismuth subsalicylate (30 mL or two tablets four times daily with meals) can prevent a significant number of cases of travelers' diarrhea [26]. However, the doses required

are inconvenient for the traveler, and salicylate toxicity is a potential complication (particularly in pregnant women, infants, and those taking aspirin for other reasons).

The highly appealing prospect of preventing travelers' diarrhea without systemic antibiotics has fueled interest in probiotics for this purpose. However, all probiotics are not identical and results of studies done with a particular agent cannot be generalized to indicate that any probiotic agent would be successful in the same clinical situation. Probiotics such as Lactobacillus GG have been shown to decrease the incidence of diarrhea in travelers in randomized controlled trials [51]. In contrast, another *Lactobacillus* preparation, nonviable *Lactobacillus acidophilus* showed no benefit compared with placebo in a randomized, double-blind, controlled trial in 174 travelers [52]. The reasons for this were unclear but could have been related to the bacteria not being viable or a particularity about the strain selected for the trial.

Vaccination — Effective vaccination to protect against travelers' diarrhea is hindered by the varied pathogens that can cause it. Although enterotoxigenic *E. coli* (ETEC) predominates as an etiology of travelers' diarrhea, vaccination strategies that have focused on this pathogen as a target have been suboptimal.

As an example, despite initial promising data on vaccination with heat-labile enterotoxin from ETEC via a skin patch, it was not effective in decreasing the incidence of moderate to severe diarrhea due to either ETEC or any cause in a randomized, placebo-controlled trial that included 1644 individuals who traveled to Mexico or Guatemala [53]. In a subgroup analysis, the vaccine provided modest protection against ETEC that produced only heat-labile enterotoxin (vaccine efficacy 61 percent [95% CI, 7 to 84 percent]), but not ETEC that produced heat-stable toxin or both. This highlights the limitations of a single-antigen vaccine for travelers' diarrhea.

A number of trials suggest that the oral, killed whole-cell cholera vaccine, which includes a nontoxic B subunit of cholera toxin (Dukoral), provides protection for travelers against ETEC infection [54-56]. The rationale for such protection is that the B subunit of cholera is antigenically similar to the heat-labile enterotoxin of ETEC. In two randomized trials, this vaccine reduced the incidence of diarrhea caused by ETEC by 67 percent in a trial in Bangladesh and by 52 percent among travelers to Morocco [54,55]. However, a conservative estimate that took into account the incidence of ETEC infection throughout the world and the efficacy of the vaccine suggested that it may prevent ≤7 percent of travelers' diarrhea cases [57]. Dukoral is not licensed or available in the United States.

While toxigenic *Vibrio cholerae* is a rare cause of travelers' diarrhea, sporadic but potentially life-threatening diarrhea does occur in travelers to endemic areas. A single-dose live oral cholera

vaccine CVD 103-HgR (Vaxchora) is approved by the FDA for use in individuals 2 through 64 years of age traveling to affected areas. This does not include all individuals traveling to countries where cholera occurs (because not all regions in each country where cholera is endemic are experiencing active transmission). However, vaccination should be considered for individuals who are at high risk for exposure, including health care workers, individuals who are traveling to provide humanitarian assistance, cholera outbreak response workers, and individuals who are traveling for extended periods to areas with active or recent cholera transmission.

The use of vaccination to prevent cholera and typhoid is discussed elsewhere.

Pretravel guidance — For travelers who present for a pre-travel evaluation, the risk of travelers' diarrhea based on the destination and the clinical manifestations of travelers' diarrhea should be discussed. The traveler should be advised about prudent food and beverage choices and the options for water purification if traveling to very remote locations. Travelers should also be counseled on self-diagnosis and management of travelers' diarrhea.

Other details of travel advice are found elsewhere. (See "Travel advice".)

SOCIETY GUIDELINE LINKS

Links to society and government-sponsored guidelines from selected countries and regions around the world are provided separately. (See "Society guideline links: Acute diarrhea in adults" and "Society guideline links: Acute diarrhea in children" and "Society guideline links: Travel medicine".)

INFORMATION FOR PATIENTS

UpToDate offers two types of patient education materials, "The Basics" and "Beyond the Basics." The Basics patient education pieces are written in plain language, at the 5th to 6th grade reading level, and they answer the four or five key questions a patient might have about a given condition. These articles are best for patients who want a general overview and who prefer short, easy-to-read materials. Beyond the Basics patient education pieces are longer, more sophisticated, and more detailed. These articles are written at the 10th to 12th grade reading level and are best for patients who want in-depth information and are comfortable with some medical jargon.

Here are the patient education articles that are relevant to this topic. We encourage you to print or e-mail these topics to your patients. (You can also locate patient education articles on a variety of subjects by searching on "patient info" and the keyword(s) of interest.)

- Basics topic (see "Patient education: Travelers' diarrhea (The Basics)")
- Beyond the Basics topics (see "Patient education: General travel advice (Beyond the Basics)" and "Patient education: Foodborne illness (food poisoning) (Beyond the Basics)" and "Patient education: Giardia (Beyond the Basics)")

SUMMARY AND RECOMMENDATIONS

- **Management**
  - **Fluid replacement** – Travelers can generally treat themselves rather than seek medical advice while traveling. The primary and most important treatment of travelers' (or any other) diarrhea is fluid replacement, since the most significant risk of diarrhea is volume depletion. Fluid replacement can be done with general fluids or with oral rehydration solutions (ORS), depending on the severity of the illness. (See 'Fluid replacement' above.)
  - **Limited role for antibiotics** – For most individuals with travelers' diarrhea, we suggest not treating with antibiotics (**Grade 2C**). The adverse effects and promotion of bacterial resistance with antibiotics generally outweigh the modest reduction in diarrhea duration. Antibiotic therapy is appropriate for travelers with severe diarrhea characterized by fever and blood, pus, or mucus in the stool.

    For patients who warrant antibiotic therapy for travelers' diarrhea, we suggest azithromycin (**Grade 2C**). Rifaximin and rifamycin are alternative agents but should be avoided in patients with features of invasive diarrhea (eg, bloody or mucoid stool).
  - **Symptomatic therapy** – Nonantibiotic symptomatic management (eg, bismuth or antimotility agents such as loperamide or diphenoxylate) can be used for mild or moderate diarrhea. However, we suggest that travelers with dysentery (bloody stool and/or fever) avoid antimotility agents and that travelers with severe watery diarrhea use them only in conjunction with antibiotics (**Grade 2C**). Because they address the symptoms but not the cause, antimotility agents can mask the amount of fluid lost into the intestine. Additionally, there is concern that they can prolong or exacerbate dysentery. If used, these agents should be discontinued promptly if abdominal pain

develops, other symptoms worsen, or diarrhea persists. (See 'Symptomatic therapy' above.)

- **Persistent symptoms** – For patients with diarrhea that has persisted for more than 10 to 14 days, or for those whose diarrhea does not improve with antibiotic therapy, less common or drug-resistant pathogens may be causative. For such patients, evaluation focuses on identifying the infecting pathogen so that therapy can be targeted. In addition to a stool culture, this includes examination of stool for ova and parasites. (See 'Patients with persistent diarrhea' above.)

- **Prevention**

  - **Guidance for food and water** − The most important strategy to prevent travelers' diarrhea is prudent selection of food and drink while traveling. Basic advice includes eating only food that has been thoroughly cooked and served hot, fruits that the traveler peels just prior to eating, and pasteurized dairy products. Beverages should be bottled. Water purification can be used if sanitary water is not otherwise available. (See 'Food and drink selection' above and 'Water purification' above.)

  - **Role of prophylaxis** − For individuals traveling from resource-rich to resource-limited settings, we suggest not routinely administering chemoprophylaxis to prevent travelers' diarrhea (**Grade 2B**). While effective, agents used for chemoprophylaxis have known and potential drawbacks that outweigh the benefit of preventing a self-limited illness.

  - **Pretravel guidance** − Issues related to pre-travel guidance are discussed further separately. (See "Travel advice".)

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GRAPHICS

Oral antibiotics for treatment of travelers' diarrhea in adults

Agent	Dose	Duration	Comment
Azithromycin	1000 mg once	Single dose*	▪ Preferred for dysentery or febrile diarrhea, travelers from Southeast Asia, and pregnant women. ▪ The 1000 mg dose may be associated with nausea.
	500 mg once daily	3-day course	
Rifaximin	200 mg 3 times daily	3-day course	▪ Not for use with dysentery or febrile diarrhea.
Rifamycin	2 (194 mg) tablets twice daily	3-day course	
Levofloxacin	500 mg once daily	Single dose* or 3-day course	▪ Fluoroquinolones ar associated with multiple adverse events. ▪ Resistance to fluoroquinolones in enteric pathogens is increasing worldwide, limiting their utility.
Ciprofloxacin	750 mg once	Single dose*	
	500 mg twice daily	3-day course	
Ofloxacin	400 mg once daily	Single dose* or 3-day course	

* If symptoms have not resolved after 24 hours, the regimen can be extended to complete a 3-day course (using the dosing listed for the 3-day course).

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