

## Travelers' diarrhea

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**INTRODUCTION** — Traveler's diarrhea is the most common illness in persons traveling from resource-rich to resource-poor regions of the world [1]. The fear of developing diarrhea while traveling is common among travelers to any part of the developing world. This concern is realistic; 40 to 60 percent of travelers to these countries may develop diarrhea. Episodes of travelers' diarrhea (TD) are nearly always benign and self-limited, but the dehydration that can complicate an episode may be severe and pose a greater health hazard than the illness itself. Nevertheless, it is possible to educate a traveler to manage a diarrheal episode without compromising either their trip or their health.

**DEFINITIONS** — TD is frequently categorized into three forms: classic, moderate, and mild [2]. For epidemiologic studies, the three types can be grouped together to estimate a total number of cases of TD. These forms of TD are defined as follows [2]:

- \* Classic — passage of three or more unformed stools in a 24 hour period plus at least one of these other symptoms: nausea, vomiting, abdominal pain or cramps, fever, blood in stools

- \* Moderate — passage of one or two unformed stools in 24 hours plus at least one of the above symptoms or more than two unformed stools in 24 hours without other symptoms

- \* Mild — passage of one or two unformed stools in 24 hours without other symptoms

These definitions allow some uniformity in studies of the epidemiology and etiologies of TD. TD should also be in the differential diagnosis when diarrhea develops within 10 days after the individual returns home. (See "Evaluation of fever in the returning traveler").

**EPIDEMIOLOGY** — Diarrheal disease in travelers may be caused by a variety of bacterial, viral, and parasitic organisms, which are most often transmitted by food and water [3-5]. More than 90 percent of illnesses in most geographic areas are caused by bacteria; the most common organism is enterotoxigenic *Escherichia coli* (ETEC) [3,6,7]. In one series of 30,369 travelers to Jamaica, the attack rate for TD was 24 percent; 12 percent of these cases were the classic form [8]. Departing travelers surveyed at the airport reported incapacity for a mean of 11.6 hours from the illness; fewer than three percent stated that they had attempted to avoid potentially high-risk foods or drinks.

The epidemiology of TD does vary from location to location and with the season of the year [9,10]. Spices in food and changes in climate do not cause TD, although variations in diet, temperature, or even time zones can alter the way a traveler feels and the stresses of travel may exacerbate diarrheal symptoms.

The world can be divided into three regions by risk for the development of TD [3]:

- \* Low risk (<10 percent) — Northern Europe, Australia and New Zealand, the United States, Canada, Singapore, Japan

- \* Moderate risk (10 to 20 percent) — Caribbean Islands, South Africa, and countries bordering the Mediterranean Ocean including Israel

- \* High risk (>30 percent) - Asia (with the exception of Singapore), Africa (outside of South Africa), South and Central America, and Mexico

Travelers should be aware that food items on aircraft will often be obtained at the city of departure [11]. (See "Travel advice").

**Risk factors** — The development of diarrhea is related to the number of ingested organisms that reach the intestine alive. Thus, any factor which enhances the ability of bacteria to survive ingestion and transit to the intestine will increase the risk for the development of diarrheal disease. As an example, an individual who is taking histamine blockers for ulcer disease will be at increased risk for developing diarrhea since the reduction of gastric acid will allow ingested pathogens prior to their entry into the small bowel. Similarly, an individual who has altered upper

gastrointestinal (GI) anatomy (eg, after ulcer surgery, or with a blind loop syndrome) or motility may be at increased risk for the development of diarrheal disease while traveling in more contaminated environments. However, it is not clear what factors beyond exposure may influence the acquisition of parasites or viruses.

Ingestion of parasites that cause diarrhea requires a more contaminated environment than is usually frequented by the average traveler. Thus, parasitic pathogens rarely cause TD [4,12,13]. However, there are a few locations where travelers are more likely to acquire parasites, including Nepal (where both *Giardia lamblia* and *Cyclospora cayetanensis* are common) and St. Petersburg (where *G. lamblia* remain hyperendemic). The mountainous regions of the West and Northeast United States are also highly endemic for *G. lamblia*, but travelers to these locations rarely request advice prior to travel. In these situations, it may be that environmental factors such as the juxtaposition of the water supply with the habitat of a certain animal species predispose the area to a hyperinfestation with the parasite.

**ETIOLOGY** — As noted above, a variety of bacterial, viral, and parasitic organisms can cause TD (show table 1), although bacterial pathogens, especially ETEC, predominate. In the series of travelers to Jamaica, 322 individuals had stool specimens processed and an etiologic agent was identified in 32 percent [8].

**Bacteria** — Bacterial pathogens predominate as the cause of TD. In the series of 322 patients cited above, ETEC accounted for 12 percent of cases due to bacteria followed by *Salmonella* spp., *Campylobacter jejuni*, and *Shigella* spp. at 8, 6, and 0.3 percent, respectively [8]. In another study of 636 travelers to Guadalajara Mexico, Ocho Rios Jamaica, and Goa India, the more newly described enteroaggregative *E. coli* (EAEC) were responsible for 26 percent of cases, second only to ETEC with 30 percent [14]. The identification of EAEC in these stool specimens reduced the number of cases with an undiagnosed etiology from 51 to 37 percent. (See "Diarrheagenic *Escherichia coli*").

Other organisms (*Salmonella* spp., *Shigella* spp., *C. jejuni*, *Vibrio* spp., *Aeromonas hydrophila*, *Plesiomonas shigelloides* as well as rotavirus and the parasites *Entamoeba histolytica*, *Cryptosporidium parvum*, and *G. lamblia*) accounted for 7 percent of cases [14]. Twenty percent also had infection with more than one enteric organism.

Patients taking malaria prophylaxis [15] or other antibiotics may also occasionally develop antibiotic-associated diarrhea due to *Clostridium difficile*. However, this is not a common cause of TD.

Viruses — Viruses can also cause TD. Rotaviruses are the most common among the viral pathogens, accounting for 9 percent of cases in the series from Jamaica [8]. It is not always clear that the individual acquires the virus while traveling rather than incubating the infection prior to departure, with symptoms developing during the trip.

Parasites — Although parasitic traveler's diarrhea is rare, *C. parvum*, microsporidia, and *Isospora belli*, in addition to *G. lamblia* and *C. cayetanensis*, may contribute to diarrhea in travelers [16]. *E. histolytica* can produce intestinal infection but is not a common pathogen in TD, perhaps because the time spent in the endemic area is short. (See "Intestinal amebiasis"). Other parasites, such as *Ascaris lumbricoides* or *Strongyloides stercoralis*, are not usually associated with diarrheal symptoms.

CLINICAL MANIFESTATIONS — Most episodes of TD occur between 4 and 14 days after arrival [8], but can occur within a much shorter time frame if the concentration of bacteria ingested is sufficiently high. The illness is generally self-limited with symptoms lasting for approximately one to five days. However, 8 to 15 percent of patients experience symptoms for more than one week and as many as two percent for more than one month [17]. While it is common to be unable to proceed with planned activities [8], only approximately 20 percent of patients report requiring bedrest for one to two days [17].

The symptoms of TD depend upon the microbial etiology. The classic "turista" due to ETEC generally produces malaise, anorexia, and abdominal cramps followed by the sudden onset of watery diarrhea. Nausea and vomiting also may occur. Typically there are no symptoms of colitis such as blood or pus in the stool. Patients may develop a low grade fever.

Even when other bacterial agents such as *C. jejuni* and *Shigella* spp. are implicated, the symptoms initially experienced by the traveler may be similar to those seen with ETEC. However, infections with these organisms may progress to include symptoms of colitis, such as tenesmus, urgency, cramping and bloody diarrhea. (See "Clinical features and treatment of *Campylobacter* infection" and see "Clinical manifestations and diagnosis of *Shigella* infection in adults").

Belching and other upper intestinal symptoms are typical of giardiasis, while profuse watery diarrhea is characteristic of cryptosporidiosis and *C. cayetanensis* infection. The symptoms of microsporidiosis may be more subtle with bloating and intermittent diarrhea. (See "Epidemiology, clinical

manifestations, and diagnosis of giardiasis", see "Cryptosporidiosis", see "Microsporidiosis", and see "Cyclospora infections").

**DIAGNOSIS** — Since TD is generally self-limited, treatment is often symptomatic and initiated without documenting an etiologic agent. However, if symptoms are severe and associated with toxicity or if they persist beyond 48 to 72 hours, intervention may be necessary. Routine stool cultures are rarely warranted routine since ETEC and EAEC cannot be distinguished from nonpathogenic E. coli on stool culture and viral agents would not be identified with stool cultures. A stool culture should be sent in a patient with fever and colitic symptoms. In patients with predominantly upper GI symptoms (eg, bloating, gas, nausea), stool examination for G. lamblia and cyclospora should be undertaken. The itinerary of the traveler should be considered when deciding which patients to culture or obtain special stains for parasites. Examination for C. parvum, microsporidium, or other less common organisms should only be initiated when diarrhea has persisted for more than 10 to 14 days. (See "Approach to the adult, in the United States and other developed countries, with acute diarrhea").

**TREATMENT** — The treatment of TD may include three different modalities:

- \* Fluid replacement
- \* Antibiotics
- \* Antimotility agents

Fluid replacement is essential; antibiotics and antimotility agents may be required depending upon the circumstances. Most cases are self-limited and resolve on their own within three to five days of treatment with fluid replacement only. Antimicrobial therapy shortens the disease duration to about one day and antimotility agents may limit symptoms to a period of hours.

**Fluid replacement** — The primary and most important treatment of traveler's (or any other) diarrhea is fluid replacement since the most significant risk is volume depletion [18,19]. Patients with mild diarrhea may combine alternating sips of fluids with both salt and sugar to replete and maintain hydration. Broth, fruit juice, or similar fluids may be used. Pedialyte is frequently useful in children.

Severe diarrhea should be treated with oral rehydration solution; this replaces needed electrolytes in the appropriate concentrations. These solutions were developed following the realization that intestinal glucose linked sodium absorption remains intact in most small bowel diarrheal

illnesses. Thus, in diarrheal disease caused by any organism that activates small bowel secretory processes (eg, cholera toxin turning on cAMP), the intestine remains able to absorb water if glucose and salt are also present to assist in the transport of water from the intestinal lumen.

Packets of oral rehydration solution are available in the pharmacies of most countries and can be mixed with clean drinking water [20]. Alternatively, a similar solution can be made by adding 1/2 teaspoon of salt, 1/2 teaspoon of baking soda, and 4 tablespoons of sugar to one liter of water. The electrolyte concentrations of fluids used for sweat replacement (eg, Gatorade) are not equivalent. If available, racecadotril, an enkephalinase inhibitor, may be an effective adjunct to oral rehydration solutions [21]. (See "Approach to the adult, in the United States and other developed countries, with acute diarrhea", section on Oral rehydration solutions).

For mild diarrhea, the use of fluids is the critical factor; the fluid need not be oral rehydration solution. One study showed no difference in outcome between treatment with oral rehydration solution plus loperamide versus generic fluids and loperamide [22].

Diet — The optimal dietary intake has not been resolved. Controversy exists about such issues as partial fasting, the composition of the diet, and the time at which solid food intake should be resumed. A restricted diet (eg, beginning with only clear liquids to match diarrheal losses during the acute phase of diarrhea) is often recommended.

A pilot randomized trial compared the effects of this restricted diet to an unrestricted diet in which the only specific recommendation was to match fluid intake to diarrheal losses [23]. The study subjects were healthy American college students being treated with an antimicrobial agent in Mexico. The mean duration of diarrhea (37 versus 33 hours) and the course of clinical symptoms were similar in the two groups.

The general applicability of these observations is uncertain. Furthermore, diet other than hydration is not likely to be important since disease duration is only about one to two days with antibiotic therapy.

Antibiotics — Antibiotics are warranted to treat diarrhea in those who develop moderate to severe diarrhea as characterized by more than four unformed stools daily, fever, blood, pus, or mucus in the stool. In addition, some travelers desire antibiotic treatment for milder disease if the illness is a large burden on a business trip or vacation. Travelers may be given a prescription for antibiotics that can be taken if diarrhea develops rather than as prophylaxis.

Travelers generally should medicate themselves rather than seek medical advice while traveling. However, medical help may be needed in patients who develop high fever, abdominal pain, bloody diarrhea, or vomiting and empiric antibiotics have not been of benefit. For most patients while traveling or after returning home, medical consultation is not needed unless symptoms persist without abating for 10 to 14 days.

Quinolones — When antibiotics are indicated, therapy with a quinolone antibiotic should be started as soon as possible after the diarrhea begins. Most commonly, ciprofloxacin (500 mg twice daily) is given for one or two days, although any of the newer, once a day quinolones should be effective. Quinolones are not approved for use in pregnant women or children. (See "Use of fluoroquinolones in the treatment of gastrointestinal and abdominal infections").

The quinolones will lead to resolution of diarrheal symptoms in the majority of travelers within one day [7,10,24-26]. In two randomized trials, for example, ciprofloxacin (500 mg twice daily) resulted in a mean duration of diarrhea of 1.5 days compared to 2.9 days with placebo [25] and norfloxacin (400 mg twice daily for three days) resulted in a mean duration of diarrhea of 1.2 days compared to 3.3 days with placebo [10]. Although two to three days should be sufficient for the majority of episodes of TD, a single dose of ciprofloxacin or norfloxacin may also be effective [26].

All of the quinolones can be expected to have similar activity against the organisms that cause TD; the most readily available, easiest to tolerate, and most inexpensive quinolone should be prescribed. When ciprofloxacin is used by an individual who drinks caffeine containing beverages, the drug may increase caffeine levels and cause jitteriness. The newer once daily quinolones (eg, levofloxacin and moxifloxacin) would be expected to be active but have not been approved for use in infectious diarrhea.

The quinolones are active against the majority of ETEC strains and also have activity against less common but potential pathogens such as *Campylobacter* spp., *Salmonella* spp., *V. parahaemolyticus*, and, although rarely a cause of TD, *Vibrio cholerae* [3,27]. One concern is the frequent resistance to quinolones among *Campylobacter jejuni* isolates worldwide, particularly in Southeast Asia, [28-31]. Azithromycin is a possible alternative.

Azithromycin — Azithromycin is an effective drug for the treatment of TD and evidence of efficacy has been provided by studies from Mexico [32], Turkey [33], and Thailand [34,35]. In randomized controlled trials of American adults with TD in Mexico and Turkey, a single 1000 mg oral

dose of azithromycin was as effective as a single 500 mg dose of levofloxacin [32,33]. In the trial from Turkey, azithromycin was associated with a greater likelihood of nausea in the 30 minutes after dosing (8 versus 1 percent) with levofloxacin [33].

Azithromycin also may have a role in the treatment of travelers' diarrhea in southeast Asia where, as noted in the previous section, quinolone-resistant *Campylobacter jejuni* is a common cause. A randomized trial performed in Thailand compared azithromycin, given as a single 1 g dose or 500 mg/day for three days, to levofloxacin (500 mg/day for 3 days) in 156 United States military personnel [35]. *C. jejuni* was responsible for 64 percent of cases and was quinolone-resistant in 50 percent.

The cure rate at 72 hours was highest with 1 g of azithromycin (96 percent versus 85 percent) with three days of azithromycin and 71 percent with levofloxacin. The rate of microbiologic eradication was much higher with azithromycin (96 to 100 percent versus 38 percent with levofloxacin), but this difference correlated poorly with outcome.

**Rifaximin** — Rifaximin (200 mg three times daily for three days), a nonabsorbed rifamycin drug, has been demonstrated to be effective in the treatment of TD caused by noninvasive strains of *E. coli*; in controlled trials, rifaximin was associated with more rapid cessation of diarrhea than placebo [36] and has equal efficacy to ciprofloxacin [37,38]. It is attracting increasing interest because of concerns about quinolone resistance.

However, rifaximin is not effective against invasive infections associated with fever or blood in the stool, such as *Campylobacter* [38]. The absence of broad activity against the pathogens responsible for TD may limit its use.

**Other** — Widespread antibiotic resistance to drugs such as ampicillin and trimethoprim-sulfamethoxazole (TMP-SMX) have made these agents less useful for the treatment of TD in much of the world [34,39,40]. Resistance has developed among many routine enteric pathogens. In addition, organisms such as *Campylobacter* spp. or any of the vibrios would not be expected to be sensitive to these agents.

**IDSA treatment recommendations** — The 2006 guidelines on travel medicine from the Infectious Diseases Society of America recommended the following oral agents for the treatment of travelers' diarrhea [1]:

- \* Norfloxacin — 400 mg twice daily
- \* Ciprofloxacin — 500 mg twice daily
- \* Ofloxacin — 200 mg twice daily

- \* Levofloxacin — 500 mg once daily
- \* Azithromycin — 1000 mg once daily
- \* Rifaximin — 200 mg three times daily

In terms of the duration of therapy, the guidelines recommended that the patient be given enough pills for three days of therapy [1]. Patients who are not completely well at 24 hours have the option of completing the three day course or stopping sooner if they are well.

Other agents — Bismuth subsalicylate can also be used to treat 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.

An antisecretory agent derived from plants (SP-303 [Provir]) was tested in a double-blind placebo-controlled study of TD in 184 travelers from the United States to Jamaica or Mexico [41]. The duration of TD was reduced by 21 percent among those taking SP-303, and the incidence of treatment failure was significantly decreased compared to placebo. This may be another promising approach.

Antimotility agents — Antimotility agents such as loperamide (Imodium) or diphenoxylate (Lomotil) are frequently used by travelers to reduce the rate of stooling; they do not treat the cause of diarrhea. They have been used in combination with antibiotics, although the improvement associated with their use in this setting is limited [24,42]. In one study, for example, 104 patients with TD were treated with ciprofloxacin 500 mg twice daily for three days [24]. They were then randomly assigned to receive loperamide (4 mg first dose and 2 mg for every loose stool up to 16 mg/day) or placebo. After 24 hours, symptoms had improved or fully recovered in 82 percent of the loperamide group compared with 67 percent of those receiving placebo. After 48 hours, the symptoms of 90 percent of both groups had improved or fully recovered. The authors concluded that the addition of loperamide did not confer a significant advantage.

In addition to issues about efficacy, there continues to be some concern that antimotility agents can prolong some types of dysenteric illnesses (eg, Shigella) [43]. Some studies suggest that antimotility drugs can be safely used in dysenteric illnesses as long as they are combined with antibiotic therapy [24,42]. Nevertheless, caution should be exercised in using these agents in travelers with bloody diarrhea [24,42].

Despite these concerns, travelers often elect to take antimotility agents in certain circumstances (eg, a prolonged bus or car trip). Particular vigilance about hydration is important in these patients since the antimotility drugs 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.

Recommendation — We do not recommend antimotility agents for mild to moderate TD. If used for more severe symptoms, they should be administered only in conjunction with empiric antibiotic treatment of the offending diarrheal pathogen. Antimotility agents should be stopped if abdominal pain or other symptoms worsen or if the diarrhea continues to be intractable after two days.

POSTINFECTIOUS IRRITABLE BOWEL SYNDROME — The development of irritable bowel syndrome following infectious enteritis is discussed separately. (See "Pathophysiology of irritable bowel syndrome" section on Postinfectious).

PREVENTION — There are several means by which travelers can reduce their risk of developing a diarrheal illness, including the following [7,44]:

- \* Improving food and drink selection
- \* Water purification
- \* Prophylactic medications

The following discussion is consistent with the 2006 guidelines on travel medicine from the Infectious Diseases Society of America [1].

Improving food and drink selection — Educated choices in selecting food and drinks can result in a lower incidence of diarrheal disease. Travelers should be aware of the following observations regarding transmission of diarrhea-causing organisms:

- \* 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 [45]. 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 but still in a number in Houston (66 versus 40 percent) [46]. 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.

These observations are also pertinent in expensive resorts or hotels; price does not guarantee appropriate hygiene.

Hot tea or coffee are usually safe alternatives to boiled water. Bottled drinks should be requested without ice and should be drunk from the bottle with a straw rather than from a glass. Fruits that can be peeled are safe as long as they are peeled just prior to eating.

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 living in rustic circumstances overseas will need to make arrangements for a safe water supply depending upon their circumstances. 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.

Prophylactic medications — Both antibiotics and certain other drugs have been evaluated for the prevention of TD.

Antibiotics — Prophylactic antibiotics prevent the majority of diarrheal disease in travelers, but cannot be recommended unless the complications of diarrhea or an underlying medical condition make the consequence of dehydration so severe that the benefits of using antibiotic prophylaxis outweigh the risks [17]. Daily antibiotics are expensive and have potential side effects that may exact a medical cost that is unacceptable. The side effects include sun sensitivity, allergic reactions, altered GI flora with colonization by resistant bacteria, yeast infections such as candidal vaginitis, and a small but real risk of *C. difficile* colitis.

Some situations in which it might be reasonable to consider prophylactic antibiotics include: known severe inflammatory bowel disease which could be exacerbated by an episode of infectious diarrhea; severe vascular, cardiac, or renal disease which would be seriously compromised by dehydration; or severe immunocompromise such as advanced HIV disease, or after a complicated organ transplant such as a liver or cardiac transplant. Studies with prophylactic antibiotics were predominantly performed with older agents such as TMP-SMX or doxycycline. However, these drugs are generally not used since susceptibility among the bacteria causing TD have changed.

Most travelers requiring prophylaxis are given a quinolone antibiotic at the same doses used for treatment (see "Quinolones" above). A number of studies, particularly with norfloxacin, showed that quinolones had a protective efficacy of 80 to 100 percent [17]. However, emerging resistance among *Campylobacter* spp. to the quinolones, especially in Southeast Asia, raise questions about how long prophylaxis with these drugs will continue to be effective.

Concerns regarding the development of fluoroquinolone resistance have led to increased interest in the use of rifaximin, which is not absorbed. In a randomized, double-blind placebo-controlled trial in Mexico, 210 American adults received either rifaximin (doses included 200 mg daily, 200 mg twice daily, or 200 mg three times daily) or placebo for two weeks [47]. The following findings were noted:

\* There was a significant reduction in TD with rifaximin therapy (15 versus 54 percent with placebo).

\* Protection from illness was similar at all rifaximin doses.

\* The rates of adverse events were comparable in all treatment and placebo arms.

\* Rifaximin therapy was associated with minimal changes in intestinal flora.

Other — Nonantibiotic preventive methods have also been studied. Bismuth subsalicylate (30 mL or two tablets four times daily with meals) can prevent a significant number of cases of TD [7]. However, the doses required are inconvenient for the traveler, and the same cautions about salicylate toxicity apply when used for prevention as well as therapy. (See "Other agents" above).

Probiotics such as *Lactobacillus GG* have been shown to decrease the incidence of diarrhea in travelers in randomized controlled trials [48]. However, another lactobacillus preparation, nonviable *Lactobacillus acidophilus* (LA) showed no beneficial effect compared to placebo in a randomized, double-blind, controlled trial in 174 travelers [49]. The authors speculate that the lack of benefit compared to that seen with *Lactobacillus GG* may be due to either the strain selected for the trial or the fact that the bacteria were nonviable.

These studies indicate that there are probably important differences in efficacy between probiotics. It is necessary to think of individual probiotics (like individual antibiotics) rather than to generalize results to the whole class of agents.

*Saccharomyces boulardii* also had some protective effect in travelers to North Africa and Turkey [17]. Prevention of TD without using systemic antibiotics is highly appealing; further work on probiotics is needed. It must be recognized that all probiotics are not identical and results of studies done with a particular agent should not be generalized to indicate that any probiotic agent would be successful in the same clinical situation.

IDSA prophylaxis recommendations — The 2006 guidelines on travel medicine from the Infectious Diseases Society of America recommended the following oral agents for prophylaxis against travelers' diarrhea, even though no antibiotic has been approved for such use by the Food and Drug Administration in the United States [1]:

- \* Norfloxacin — 400 mg once daily
- \* Ciprofloxacin — 500 mg once daily
- \* Rifaximin — 200 mg once or twice daily
- \* Bismuth subsalicylate — two tablets chewed four times daily

The guidelines noted that other fluoroquinolones are likely to be effective but have not been studied for prophylaxis and that there is no antibiotic with proven efficacy for prophylaxis against *Campylobacter* species, which are a more common cause of travelers' diarrhea in south and southeast Asia [1]. (See "IDSA treatment recommendations" above),

With respect to bismuth subsalicylate, the doses required are inconvenient for the traveler, and salicylate toxicity is a potential complication. (See "Other agents" above).

Travelers' diarrhea cholera vaccine — Administration of a cholera vaccine is not routinely recommended for travelers. (See "Immunizations for travel", section on Cholera).

However, a number of trials suggest that the oral, killed whole-cell vaccine given with the nontoxic B subunit of cholera toxin (Dukoral) provides protection for travelers against enterotoxigenic *E. coli* (ETEC) infection [50-52]. 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, the killed whole-cell vaccine combined with the B subunit of cholera toxin reduced the incidence of diarrhea caused by ETEC by 67 percent in a trial in Bangladesh and 52 percent among travelers to Morocco [50,51].

The Dukoral vaccine was approved in the United States in late 2006 for use as a travelers' diarrhea vaccine. A conservative estimate that took into account the incidence of ETEC infection throughout the world and the efficacy of the vaccine suggested that less than or equal to 7 percent of travelers might benefit from use of the vaccine [53]. The 2006 guidelines on travel medicine from the Infectious Diseases Society of America concluded that the decision to use the vaccine to prevent travelers' diarrhea must balance its cost, adverse effects, and limited utility against the known effectiveness and costs of self-treatment as described above [1].

**INFORMATION FOR PATIENTS** — Educational materials on this topic are available for patients. (See "Patient information: General travel advice"). We encourage you to print or e-mail this topic review, or to refer patients to our public web site, [www.patients.uptodate.com](http://www.patients.uptodate.com), which

includes this and other topics.

## SUMMARY

\* Traveler's diarrhea is a common entity and can be induced by a variety of bacteria, viruses, and parasites.

\* It is uncommon to have to make an etiologic diagnosis. Stool cultures or examination for ova and parasites should generally be reserved for cases that last beyond 10 to 14 days, except for patients with fever and colitis, those with upper intestinal symptoms in whom giardiasis is more likely, or immunocompromised patients.

\* The mainstay of therapy for traveler's diarrhea is fluid replacement. Attention to fluids including those with sugar and salt is sufficient for mild diarrhea but severe diarrhea should be treated with oral rehydrating solution. Packets, which can be reconstituted in clean drinking water, are available for sale in most countries.

\* Travelers should be given a prescription for antibiotics to fill and take with them in case diarrhea develops. The usual choice is a fluoroquinolone. Antibiotics should be taken by the traveler if unformed stools occur more than four times a day or for fever, or blood, pus or mucous in stools.

\* Medical care should be sought if fevers persist beyond 10 to 14 days or if fevers become higher, or abdominal pain, bloody diarrhea, or vomiting ensue.

\* Antimotility agents are usually not necessary for mild to moderate diarrhea and should not be used except for severe diarrhea in association with antibiotic therapy. These agents should be discontinued promptly if abdominal pain develops, other symptoms worsen, or diarrhea persists.

\* Attention to choices of food and drink, water purification, and antibiotic prophylaxis are all means of attempting to prevent traveler's diarrhea. Antibiotic prophylaxis is usually reserved for patients in whom dehydration would put them at severe risk.

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