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TRAVELER'S DIARRHEA

Stanley L. Giddings, MD[1], **A. Michal Stevens, MD, MPH**[1], and **Daniel T. Leung, MD, MSc**[1,2,*]

[1] Division of Infectious Diseases, Department of Medicine, University of Utah School of Medicine, Salt Lake City, UT

[2] Division of Microbiology & Immunology, Department of Pathology, University of Utah School of Medicine, Salt Lake City, UT

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1. INTRODUCTION

Over 68 million Americans traveled abroad in 2014,[1] and the annual number of international tourist arrivals worldwide has reached more than 1 billion.[2] In data collected by GeoSentinel, a global surveillance network of international travelers, acute diarrhea was the most common amongst travel-related diagnostic groupings.[3] In this article, we will review the epidemiology, etiology, and strategies to prevent and treat traveler's diarrhea (TD).

1.A. Definition, Incidence and risk factors

TD is defined as the passage of 3 or more unformed stools per day with 1 or more associated enteric symptom, such as abdominal pain or cramps, occurring in a traveler after arrival, usually in a resource-limited destination.[4]

Recent studies have shown that approximately 25% of travelers develop TD in the first 2 weeks abroad, with the highest rates occurring in travel to Africa and South, Central and West Asia.[5,6] Factors that influence the incidence of TD vary based on the study design and location (Table 1).[5,6,7]

1.B. Etiology

TD is predominantly a fecal-orally transmitted disease and can be caused by bacterial, viral or protozoal pathogens, with helminths being uncommon. Many of the etiologies for TD (Table 2) are similar to those causing acute diarrhea in young children of low- and middle-income countries.[8] The frequency of each pathogen varies by geographic location and the

*Corresponding author: Daniel T. Leung, MD, MSc, Division of Infectious Diseases, University of Utah School of Medicine, 30 N 1900 E, SOM Room 4C416B, Salt Lake City, UT 84132, Tel: (801) 581-8804, Fax: (801) 581-8509, Daniel.leung@utah.edu.

etiology may be unknown in 40-50% of cases despite microbiologic evaluation,[9,10] though with increasing use of multiplex molecular testing,[11] this will likely change. Globally, enterotoxigenic *Escherichia coli* (ETEC) and enteroaggregative *E. coli* (EAEC) are the most common bacterial pathogens,[9] with the exception of Southeast Asia, where *Campylobacter* is more common, a high proportion of which are fluoroquinolone resistant.[9,12] Norovirus and rotavirus are the most common viral etiologies of TD. Of the protozoa, *Giardia duodenalis* and *Entamoeba histolytica* are the main pathogens considered, depending on the region of travel. In some instances, TD may be due to more than one pathogen.

1.C. Impact on the traveler

The median duration of TD is 3 days, and symptoms are usually mild, with approximately 4 bowel movements per day.[13] Unfortunately, TD can lead to significant limitation of activity. This incapacity typically lasts for 1-2 days,[14] resulting in loss of vacation or business days,[6] though data from one post-travel survey suggests that the majority with TD do not need to alter their planned programs.[15] Approximately 10% of travelers with TD seek medical care and up to 3% of them require hospitalization.[14,16]

2. PRE-TRAVEL PREPARATION

The goals of pre-travel consultation are to identify travelers at increased risk of travel-related illness, and provide counseling, vaccinations and medications for prophylaxis or self-treatment. Application of these principles at a pre-travel consultation may decrease the incidence of TD.

2.A. PREVENTION

2.A.i. IMPACT OF FOOD AND WATER HYGIENE MEASURES—Given that most cases of TD are caused by ingestion of contaminated food and water, it is thought that counseling on food and water hygiene measures reduces the risk of TD. However, there is little evidence that such precautions decrease the incidence of TD,[6, 17] and it is likely that factors outside of a traveler's control, such as poor restaurant hygiene, may have a higher impact. [17] Despite this, travelers should be educated on appropriate food and water precautions (Table 3),[18] including frequent hand washing with soap.

2.A.ii. VACCINES—There are no vaccines available against TD in the United States at this time. The oral killed whole-cell cholera vaccine, Dukoral, which is available in Canada and Europe, contains a recombinant cholera toxin B subunit, which is homologous with the heat-labile toxin (LT) of ETEC and by extension provides partial protection against TD. Unfortunately, worldwide, only approximately 25% of ETEC strains are LT-only (most express or co-express the heat-stable toxin, ST).[19] In a recent non-randomized evaluation, the vaccine was found to provide 28% protection against TD.[20] Several vaccine candidates against ETEC are in various phases of development, including consideration of a combined ETEC/*Shigella* vaccine, targeting both travelers and children living in endemic countries.[21]

2.A.iii. PROBIOTICS—The use of probiotics for the prevention of TD is controversial and suffers from a lack of well- controlled studies. The challenges with using probiotic products

include the diversity of probiotic strains, the need for adequate quality control of products, defined optimal dose and duration of therapy, and specific storage requirements of some products. Attempts at systematic review of available studies have produced mixed results. One pooled meta-analysis of 12 randomized controlled trials showed that probiotics may be safe and effective at preventing TD,[22] with *Saccharomyces boulardii* and a mixture of *Lactobacillus acidophilus* and *Bifidobacterium bifidum* found to be efficacious. A subsequent review found that *S. boulardii* afforded a dose- related protection for travelers to North Africa and *Lactobacillus rhamnosus strain GG* provided 12-45% protection against TD.[23] In contrast, a meta-analysis that reviewed 5 randomized controlled trials did not find any benefit from probiotic use.[24] More data are needed before definitive recommendations can be made on the use of probiotics for prevention of TD.

2.A.iii BISMUTH SUBSALICYLATE—Bismuth subsalicyclate (BSS) has been shown to provide up to 65% protection against TD when taken as 2 tablets 4 times per day for a maximum of 3 weeks.[25] It is usually well tolerated in young healthy adults. However, clinicians must warn travelers about blackening of the stool or tongue when taking this drug. BSS can decrease absorption of doxycycline, which may be used concomitantly for malaria prophylaxis.[26] A careful review of the traveler's medication list should be performed to look for potential drug-drug interactions. Although BSS provides moderate protection against TD, the need for frequent administration decreases the overall compliance and makes it a less attractive choice for most travelers.

2.A.iv. ANTIBIOTIC CHEMOPROPHYLAXIS—Antibiotic chemoprophylaxis can provide up to 90% protection against TD.[27] Fluoroquinolones are effective prophylactic agents and they provide a broad spectrum of activity against many common travel-related enteropathogens including ETEC and EAEC. In a meta-analysis, they were shown to provide 88% protection against TD.[27] However, the risks of long term quinolone therapy, including tendon rupture (especially in those with pre-existing kidney disease or on systemic corticosteroids), QTc prolongation, and *Clostridium difficile* infection limit their usefulness as prophylaxis and should be discussed with the traveler.

Prophylactic rifaximin can provide up to 77% protection against TD,[28] though its effectiveness in SE Asia is lower (48% efficacy).[29] It is poorly absorbed from the gastrointestinal tract, and thus systemic side effects are rare. However, rifaximin has poor activity against many enteroinvasive pathogens, and this is reflected in its decreased efficacy in SE.[29] Thus, the potential need for use of a second antimicrobial agent in case of invasive disease, as well as its high cost relative to quinolones (Table 4), makes rifaximin a less attractive candidate.

For travelers to areas of SE Asia where there are high rates of quinolone resistance, it is reasonable to consider prophylaxis with azithromycin but there is minimal data for its use in travelers and the safety of prophylactic use of azithromycin is extrapolated from studies in cystic fibrosis and HIV patients.

The advantages and efficacy of antibiotic prophylaxis are tempered by the risks of side effects, *C. difficile* infection, acquisition of antimicrobial resistant organisms, and cost.

Thus, we recommend that its use only be reserved for high risk travelers such as those who are immunosuppressed or those in whom an episode of TD may lead increased morbidity.[27] While chemoprophylaxis may also be considered in travelers with little flexible time, such as politicians, athletes or performers, early self-treatment (discussed below) may be more appropriate.

2.B. TRAVELER-INITIATED SYMPTOMATIC TREATMENT

Self-treatment upon initial symptoms is the mainstay of traveler's diarrhea management, the backbone of which is oral rehydration therapy. Adding to that backbone, for mild cases, the use of bismuth and loperamide is effective and sufficient. For moderate or severe TD, use of empiric oral antibiotics has been found to be effective in shortening the duration of symptoms, though there is increasing evidence that this practice may have societal and personal health costs.

2.B.i. ORAL REHYDRATION—Adequate oral fluid intake is essential to both prevent and treat dehydration related to TD. For mild dehydration, simply increasing the amount of oral fluid intake with clean water and/or readily available fluids is adequate. For moderate or severe dehydration, and particularly in children, elderly and those with chronic medical conditions, we recommend WHO-formulated oral rehydration salts (ORS),[30] which have been shown to be similar in efficacy as IV fluids in children presenting to a US ER.[31] ORS can be prepared at home (Box 1),[32] or it is available as packaged commercial products sold in pharmacies and stores worldwide. Commonly used beverages such as Gatorade, apple juice or soft drinks may not be appropriate for repletion of moderate or severe dehydration due to their high sugar and low salt content, though data comparing their use with ORS is lacking.

2.B.ii. ANTI-DIARRHEAL MEDICATION—Loperamide is safe and effective for treatment of nondysenteric TD.[33] It can be used alone for mild cases and as an adjunct with antibiotics (see below) for moderate or severe TD. A meta- analysis found that compared to antibiotic therapy alone, adjunctive loperamide decreased the duration of illness and increased the probability of cure.[33]

Apart from BSS being used to prevent TD, it can also be used to treat TD. It has been shown to reduce the passage of unformed stools and it may be useful for treatment of mild TD.[34] However, when compared to loperamide, it has a delayed onset of action and it is less effective, with estimates of loperamide providing just over 50% reduction in passage of unformed stools compared to BSS providing a 16-18% reduction.[34]

2.B.iii. EARLY ANTIBIOTIC SELF TREATMENT—Early self-treatment of TD with antibiotic therapy has been shown to be effective at reducing the duration of symptoms.[35] In a randomized placebo-controlled trial, early self-treatment of TD with ciprofloxacin reduced the duration of symptoms from 81 to 29 hours.[35] We recommend offering travelers a prescription of antibiotics for early self-treatment, but emphasizing its use only for moderate to severe TD and for dysentery. Antibiotics can be given as a single dose regimen or as a

multiple dose regimen for up to 3 days (Table 5). For travelers on the multiple dose regimens, if the symptoms resolve after 1 or 2 doses the antibiotic therapy can be stopped.

The antibiotic agent selected should be tailored to the region of travel and the prevalence of multi-drug resistant pathogens in that region. Either ciprofloxacin or rifaximin may be used for most global destinations, but travelers to South and Southeast Asia should receive azithromycin, given the high incidence of quinolone resistant enteropathogens.[12] Rifaximin use is often limited by cost. Notably, azithromycin and levofloxacin (though not ciprofloxacin) has been associated with increased risk of ventricular arrhythmia and cardiovascular death,[36] and given the risk of electrolyte imbalances during severe diarrhea, a high level of caution should be used when prescribing these agents in patients with pre-existing heart disease, and should be avoided in those with known QT-prolongation.

A number of recent reports have associated the use of antibiotics for TD with an increased risk of acquisition of extended-spectrum beta-lactamase (ESBL) enterobacteriaceae organisms.[37,38] While the persistence of ESBL colonization in returning travelers appears to be relatively short, and no infection has been directly linked to such colonization, the longterm societal and personal health consequences are not known. Thus, we recommend education and discussions regarding appropriate use of antibiotics, including mention of the self-resolving nature of most cases of TD, and the risks associated with antibiotic use, including their side effects, *C. difficile* infection, and acquisition of multidrug-resistant bacteria. Other factors to be considered are the availability of appropriate medical care, and the safety and purity of antibiotics, in the destination country.

2.B.iv. WHEN TO SEEK MEDICAL CARE—A TD pre-travel kit (Box 2) is a useful tool that can limit the duration of TD and its impact on the traveler. Travelers should be encouraged to carry this kit during their trip and they should be counseled on how to use it effectively. However, they should seek medical care for persistent fever, chills, bloody diarrhea, moderate to severe abdominal pain, intractable vomiting, if they are unable to retain oral fluid intake, or if their symptoms worsen or persist despite early self- treatment. Special traveler populations are more at risk for severe and complicated TD and these travelers should have a low threshold to seek medical attention. Information on clinics in destination countries specializing in travel medicine can be obtained from the International Society of Travel Medicine (http://www.istm.org/AFCstmClinicDirectory.asp), or the International Association for Medical Assistance to Travellers (https://www.iamat.org)

3. SPECIAL POPULATIONS

3.A. PREGNANT WOMEN

Pregnant women may be more prone to TD due to reduced gastric acidity and slowed intestinal motility.[39] In one study, TD occurred in 11% of pregnant travelers to developing countries.[40] The main pre-travel advice for pregnant women are counseling on food and water hygiene as well as ensuring adequate fluid hydration.[39] Antimicrobial chemoprophylaxis is not recommended for pregnant travelers. Clinicians must be wary of medication use and their potential for adverse pregnancy outcome, fetal harm and secretion of medications into breast milk. BSS and fluoroquinolones are not recommended in

pregnancy, and loperamide and rifaximin are pregnancy class C drugs. Azithromycin, which is pregnancy class B, is the drug of choice for early self-treatment of TD.

3.B. CHILDREN

Infants and young children with TD have a more severe and prolonged course of disease, and are more likely to present with fever and bloody diarrhea.[41,42] The mainstay of treatment is rehydration and parents should be advised on appropriate oral rehydration solution. Antimicrobial chemoprophylaxis, loperamide and BSS are usually not recommended for this population and parents should have a low threshold to seek medical care if the child develops bloody diarrhea, fever with temperature > 101.5 F, moderate to severe dehydration, persistent vomiting, or for any changes in mental status. For antibiotic self-treatment, azithromycin is the drug of choice.[42] While trimethoprim/sulfamethoxazole has been used in the past, due to increasing resistance worldwide, we recommend cefixime or other third-generation cephalosporins as second-line agents, though they may be ineffective against campylobacter.[43] Fluoroquinolones are not recommended in children less than 18 years due to potential for cartilage damage based on animal studies, but there is ongoing review on the safety of this drug in children, and it may have a role in targeted treatment of multidrug-resistant enteropathogens.[44]

3.C. IMMUNOCOMPROMISED HOST

The immunocompromised host would benefit from a multidisciplinary evaluation prior to travel so that travel related issues including prevention and management of TD can be discussed.[45] Antimicrobial chemoprophylaxis for TD should be considered,[45] though there is increased potential for drug-drug interactions in this population. Immunocompromised host travelers also need to have a contingency plan in case of a medical emergency, this plan should include medical contact both locally and abroad.

3.D. COMORBID DISEASE

Travelers with comorbid disease such as insulin dependent diabetes mellitus, heart failure or renal insufficiency may not be able to tolerate an episode of TD, as it can lead to severe electrolyte imbalance and dehydration with subsequent exacerbation of their underlying medical condition. The importance of ensuring adequate hydration must be stressed to these travelers. Antimicrobial chemoprophylaxis and early self-treatment options must be discussed in relation to their comorbidities and careful attention to their home medication list and potential drug-drug interactions must be noted. The risk of ventricular arrhythmia and cardiovascular death with azithromycin and levofloxacin are important considerations.[36]

4. POST-TRAVEL MANAGEMENT

TD can occur, or persist, after the traveler has returned home. The time to onset of symptoms would depend on the incubation period of the pathogen. Typically this would be up to 2 weeks after return from travel but this incubation period may be longer when protozoa or helminths are the etiologic agents.

4.A. PERSISTENT DIARRHEA AFTER TRAVEL

Infectious gastrointestinal disease accounts for approximately 30% of diagnoses of returning travelers who present for medical care.[46] Common pathogens associated with diarrheal illness in returned travelers include bacterial causes with longer incubation periods (such as *Campylobacter*, *Shigella*, *Salmonella*), protozoa (Giardia, cryptosporidium, cyclospora, *Entamoeba histolytica*, and *Dientamoeba fragilis*), as well as helminthes such as Ascaris, Strongyloides, and hookworms. In particular, if there is a history of antibiotic use, *Clostridium difficile* infection should also be considered.[47]

4.A.i. EVALUATION—A detailed history and physical examination should be performed in all travelers seeking medical care for diarrhea on return home. This should include information on areas visited during their trip and specific exposures that may provide clues to the etiology. Drug resistant pathogens must also be considered, taking into account the region of travel and prior antibiotic therapy Consultation with a travel medicine expert may be useful and work up may include a complete blood count (CBC) with differential (eosinophilia may suggest helminthic infection), and stool for microscopy (ova and parasites), and antigen-based testing. *Clostridium difficile* testing may also be warranted. Serological investigation for *Strongyloides* and *Schistosoma* may also be obtained when clinically indicated. Recent advances in molecular diagnostics have led to the development and marketing of a number of stool multiplex PCR panels for gastrointestinal pathogens (Table 6). There is a lack of published studies examining the utility of such panels in returning travelers, though there may be benefits with respect to their sensitivity, cost-effectiveness, and timeliness, compared to traditional methods. However, results from such panels in returning travelers need to be interpreted with caution, given the likelihood of multiple pathogens identified.

4.B. POST-INFECTIOUS SEQUELAE

4.B.i. POST-INFECTIOUS IRRITABLE BOWEL SYNDROME (PI-IBS)—Travel-associated diarrhea afflicts a relatively large proportion of international travelers, and the majority experience complete recovery without further symptoms. In some, however, despite clearance of the infectious pathogen from the gut, there is persistence or recurrence of abdominal symptoms, similar to that described for irritable bowel syndrome (IBS).[48,49] It is unclear whether the pathogenesis of travel-related IBS, especially that experienced by longterm travelers,[48] is the same as that of non-travel-associated PI-IBS. Possible mechanisms include a reversible small intestinal enteropathy such as described in the 1970s in Peace Corp Volunteers returning from Pakistan,[50] also known as “tropical enteropathy” in residents of low-income countries,[51] tropical sprue, or the unmasking of an underlying gastrointestinal disorder.[52] Nevertheless, many patients do meet Rome III diagnostic criteria for irritable bowel syndrome, and overall, approximately 3-20% of travelers develop post-infectious irritable bowel syndrome (PI-IBS), with most cases being diarrhea-predominant.

Known risk factors for developing post-infectious IBS (PI-IBS) include duration of initial illness, severity of initial illness, smoking, degree of gut inflammation, female gender, presence of stress at the time of the initial illness.[53] Gulf War Veterans in particular seem to have increased risk of developing PI-IBS.[54]

It is possible that treatment modalities commonly used for traveler's diarrhea, such as antibiotics and anti-motility agents, may not only alter the course of traveler's diarrhea, but may also impact its potential to develop PI-IBS. However, these associations are poorly understood and not well studied. Despite recent studies showing the efficacy of rifaximin for IBS,[55] it has not been evaluated in PI-IBS, and at this point we do not recommend its use in returning travelers. Further investigation into the microbiota and mucosal immune correlates of post-travel IBS are warranted.

While the prognosis of post-travel PI-IBS is unknown, a recent study of post-Shigella IBS patients showed that roughly half of patients with PI-IBS recovered by 5 years after onset, but also that patients with a history of IBS prior to infection were more likely to have a prolonged course of illness beyond 5 years.[56]

4.B.ii. REACTIVE ARTHRITIS—Reactive arthritis can occur 1 to 4 weeks after an episode of TD.[49,57] It is an oligoarthritis that is asymmetric and typically involves the lower limbs or sacroiliac joint. It can have an acute self- limited course lasting months or lead to chronic (refractory) symptoms for years.[49,57] Several TD pathogens, including Shigella, Campylobacter, Salmonella and E.coli, have been associated with reactive arthritis, and host factors such as HLA B27 are also implicated.[49]

4.B.iii. GUILLAIN-BARRE SYNDROME—Guillain-Barre syndrome may also develop 1 to 4 weeks after a bout of TD.[49] The preceding enteric infection is usually due to *Campylobacter*, although other enteric gram-negative bacteria can trigger this phenomenon, in which an autoimmune response is mounted against peripheral nerves leading to peripheral neuropathy or acute neuromuscular failure.[49] There is a bimodal peak in incidence with young adults and the elderly most commonly affected. This disease can result in permanent disability or even death.

5. SUMMARY

TD is the most common travel-related illness. Pre-travel consultation by the healthcare provider is an excellent opportunity to educate the traveler and provide them with resources to decrease the incidence and impact of the disease. Early self-treatment is an effective strategy for moderate to severe TD, though its benefits must be weighed against risks of adverse effects and acquisition of antimicrobial resistant bacteria. Persistent diarrhea and post infectious sequelae of TD can present after return from travel, and such travelers may benefit from specialist referral.

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Box 1

Recipe for ORS

½ small spoon of salt + 6 level small spoons of sugar + 1 L of safe water (water that is bottled and sealed or disinfected)

OR

Lightly salted rice water

Data from World Health Organization. WHO position paper on Oral Rehydration Salts to reduce mortality from cholera. Available at: http://www.who.int/cholera/technical/en/. Accessed Jul 1 2015.

Box 2

Traveler's diarrhea pre-travel kit

Instructions on food safety and water hygiene

Oral rehydration salt (ORS) recipe

Anti-diarrheal medication (loperamide)

Self-treatment antibiotics (fluoroquinolone, azithromycin or rifaximin) with instructions on use

OR antimicrobial chemoprophylaxis for select travelers

Emergency medical contacts locally and abroad

KEY POINTS

-Traveler's diarrhea (TD) is the most common travel related illness.

-Pre-travel consultation is an opportunity to provide the traveler with education and therapeutic options to decrease the incidence and impact of TD.

-Early self-treatment of TD is effective, though its use must be balanced by consideration of medication side effects, acquisition of antimicrobial resistant organisms through disturbance of gut flora, and potential for *Clostridium difficile* infection

-Post-infectious sequelae of TD may result in presentation for care weeks or months after return from travel

SYNOPSIS

TD is the most common travel related illness and it can have a significant impact on the traveler. Pre-travel consultation provides an excellent opportunity for the clinician to counsel the traveler and discuss strategies such as food and water hygiene, vaccinations and medications for prophylaxis or self-treatment that may decrease the incidence and impact of TD. Post-infectious sequelae such as post-infectious irritable bowel syndrome, reactive arthritis and Guillain-Barre syndrome may develop weeks or months after return.

Table 1

Risk factors for traveler's diarrhea

Host related factors	Country of origin (higher incidence if the traveler is from a highly industrialized country) Age (higher incidence in young adults 15 to 30)
Travel related factors	Destination (higher incidence in travel to Africa and South, Central and West Asia) Duration of stay (incidence increases until day 12 or day 14)

Data from Refs[5,6,7]

Table 2

Etiologies of traveler's diarrhea

Pathogen	Organisms	Comments
Bacteria	Enterotoxigenic *Escherichia coli* (ETEC) Enteroaggregative *Escherichia coli* (EAEC) *Campylobacter spp.* *Shigella spp.* *Salmonella spp.* Enteropathogenic *Escherichia coli* (EPEC) *Aeromonas spp* *Plesiomonas shigelloides* *Vibrio spp* Enterotoxigenic *Bacteroides fragilis* *Acrobacter butzleri*	SE Asia has significant fluoroquinolone resistant campylobacter isolates
Viral	Norovirus Rotavirus Astrovirus Sapovirus Adenovirus 40/41	Norovirus is associated with outbreaks on cruise ships
Protozoa	*Giardia duodenalis* *Cryptosporidium parvum* *Entamoeba histolytica* *Cyclospora cayetanensis* *Dientamoeba fragilis*	
Unknown	No organism identified	Up to 50% of cases
Multiple pathogens	2 or more pathogens identified	Not uncommon, varying prevalence

Data from Shah N, DuPont HL, Ramsey DJ. Global etiology of travelers' diarrhea: systematic review from 1973 to the present. Am J Trop Med Hyg 2009;80(4):609-14; and Jiang ZD, Dupont HL, Brown EL, et al. Microbial etiology of travelers' diarrhea in Mexico, Guatemala, and India: importance of enterotoxigenic Bacteroides fragilis and Arcobacter species. J Clin Microbiol 2010;48(4):1417-19.

Table 3

Food and water precautions

High risk foods	Strategies to avoid high risk foods
Salads	Consume peeled fruits and vegetables
Uncooked meat, fish or eggs	Consume cooked food
Unpasteurized dairy products	Consume pasteurized dairy products
Tap or well water Products made using tap water or well water such as ice or juice	Consume water that is bottled and sealed or water that is disinfected (boiled, filtered, treated)
Food from street vendors	Be wary of food and water hygiene at eating establishment
Food served at room temperature	Ensure meals are piping hot prior to consumption

Data from Centers for Disease Control and Prevention. Food and water safety. Available at: http://wwwnc.cdc.gov/travel/page/food-water-safety. Accessed Jun 26 2015.

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Table 4

Chemoprophylaxis options for TD

Drug	Dosing	Average cost for a 2-week trip*
Bismuth	2 tabs QID	$14.56
Ciprofloxacin	500 mg daily	$44.52
Rifaximin	200 mg daily or bid	$246.96 - $493.92

* **Cost is based on average wholesale price.**

Table 5

Antibiotic self-treatment options for TD in healthy adults

Drug	Dosing	Average cost for 3 days of therapy*
Azithromycin	500 mg daily × 3 days or 1 g single dose	$25.32 - $46.71
Ciprofloxacin	500 mg bid × 3 days or 750 mg single dose	$19.08
Rifaximin	200 mg 3 times daily × 3 days	$158.76

* **Cost is based on average wholesale price.**

Table 6

Comparison of pathogens tested by various multiplex PCRs

	FilmArray™ Gastrointestinal Panel (BioFire Diagnostics, Inc., Salt Lake City, UT)	**xTag ® Gastrointestinal Pathogen Panel (Luminex Corporation, Austin,TX)**	**Verigene® Enteric Pathogen test (Nanosphere, Northbrook, IL)**
Bacteria and bacterial toxins			
Campylobacter spp.[*]	x	x	x
Salmonella spp.	x	x	x
Vibrio cholerae	x		
Vibrio spp.	x		x
Yersinia entercolitica	x		x
Clostridium difficile (toxin A/B)	x	x	
Plesiomonas Shigelloides	x		
Enteroinvasive *E. coli /Shigella spp.*	x	x	x
E. coli O157	x	x	
Enterotoxigenic *E. coli* (ETEC) lt/st	x	x	
Enteroaggregative *E. coli* (EAEC)	x		
Enteropathogenic *E. coli* (EPEC)	x		
Shiga toxin producing *E. coli* (STEC) stx1/stx2	x	x	x
Viruses			
Adenovirus 40/41	x		
Astrovirus	x		
Norovirus	x	x	x
Rotavirus	x	x	x
Sapovirus	x		
(I,II,IV and V)			
Parasites			
Cryptosporidium	x	x	
Cyclopora cayetanesis	x		
Entamoeba histolytica	x		
Giardia lamblia	x	x	

** test for vibrio cholera

[*] Campylobacter spp. varies with test performed