Travelers' diarrhea: Epidemiology, microbiology, clinical manifestations, and diagnosis

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INTRODUCTION

Travelers' diarrhea refers to development of unformed stools during or within 10 days of returning from travel; it commonly occurs in association with travel to a setting where sanitation and hygienic practices are poor and there is limited access to safe drinking water. Travelers' diarrhea is typically self-diagnosed.

For epidemiologic purposes, travelers' diarrhea may be defined as passage of three or more unformed stools in a 24-hour period, accompanied by at least one of these other symptoms: nausea, vomiting, abdominal pain or cramps, fever, or blood in the stool.

Episodes of travelers' diarrhea are nearly always benign and self-limited, but dehydration may be severe and pose a greater health hazard than the illness itself. Nevertheless, travelers can be educated to manage a diarrheal episode without compromising their trip or their health.

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

EPIDEMIOLOGY

Frequency — Travelers' diarrhea is the most common illness among individuals traveling to settings where sanitation and hygienic practices are poor and there is limited access to safe drinking water. The attack rate for travelers' diarrhea ranges between 10 and 70 percent; estimates vary greatly between studies [1-5].

In one study including 390 travelers from the Netherlands to subtropical and tropical regions, 41 percent reported travelers' diarrhea (defined as three or more unformed stools within a 24-hour period) on post-travel questionnaires [5]. Of those, 86 percent reported watery stools, 77 percent reported abdominal discomfort or cramps, 71 percent reported fecal urgency, 20 percent reported vomiting, and only 11 percent had fever. Most had three to five stools per day; 3 percent had >10 stools per day.

Travel risk factors — The organisms that cause travelers' diarrhea are most often transmitted by food and water; therefore, the risk of travelers' diarrhea is the highest in regions where sanitation and hygienic practices are poor and there is limited access to safe drinking water. Also, settings with inadequate electricity resulting in poor refrigeration can result in unsafe food storage and increased risk for disease.

The risk of travelers' diarrhea varies considerably based on destination [6]. Southeast Asia is commonly identified as the region with the highest incidence rate [6]. The risk of travelers' disease also varies by season; the risk is higher during warmer and wetter seasons [7-9].

The risk of travelers' diarrhea is highest during the first month of travel, then decreases with time [6]. Activities associated with development of travelers' diarrhea include buying food from street vendors, traveling to visit friends and relatives, and staying in "all-inclusive" lodging [10]. (See "Travel advice", section on 'Food and water'.)

Host risk factors — The likelihood of developing diarrheal illness correlates with the number of live organisms that reach the intestine. Any factor that enhances the ability of bacteria to survive ingestion and transit to the intestine may increase the risk for the development of diarrheal disease. As an example, individuals taking histamine blockers for ulcer disease or gastrointestinal reflux disease are at increased risk for travelers’ diarrhea, since the reduction of gastric acid enables more pathogens to enter the small bowel. Similarly, individuals with altered upper gastrointestinal anatomy or motility may be at increased risk for travelers’ diarrhea.

Travelers from higher risk regions are less likely to develop travelers' diarrhea when they travel to other high-risk regions, suggesting some degree of protective immunity from prior exposure [11]. In addition, some genetic factors may be associated with an increased risk of travelers' diarrhea [11].

MICROBIOLOGY

Travelers' diarrhea may be caused by a variety of organisms; these include bacteria, viruses, and parasites (table 1). Identifying a microbial etiology is not necessary for most cases of travelers' diarrhea but this may be warranted in certain circumstances. (See 'Clinical approach' below.)

Bacterial pathogens are the most frequent cause in patients with acute illness. In a systematic review of publications between 1990 and 2015, 62 percent of tested cases of travelers' diarrhea were due to bacterial pathogens [6,12].

Spices in food and changes in climate do **not** cause travelers' diarrhea; however, variations in diet, temperature, or even time zones can alter the way a traveler feels, and the stresses of travel may exacerbate diarrheal symptoms.

- **Bacteria** – Enterotoxigenic *Escherichia coli* (ETEC), enteroaggregative *E. coli*, and *Campylobacter* predominate as the bacterial causes of travelers' diarrhea [6,13-16]. *Shigella* spp, *Salmonella* spp, *Vibrio* spp, *Aeromonas hydrophila,* enteropathogenic *E. coli*, enterohemorrhagic *E. coli*, and *Plesiomonas* are less commonly identified [1]. (See "Pathogenic Escherichia coli associated with diarrhea".)

  There is geographic variation to the microbial distribution of travelers' diarrhea. In Southeast Asia, *Campylobacter* species are the most common cause of travelers' diarrhea, whereas ETEC is the predominant pathogen in travelers to Latin America/Caribbean, Africa, and the Middle East [6,16,17].

  Additional causes of microbial food-borne illness are discussed separately. (See "Causes of acute infectious diarrhea and other foodborne illnesses in resource-abundant settings".)

  Occasionally, travelers taking malaria prophylaxis or other antibiotics develop antibiotic-associated diarrhea due to *Clostridioides difficile* [18].

- **Viruses** – Norovirus has increasingly been identified as a cause of traveler's diarrhea with broader availability of molecular diagnostic techniques [19,20]. One review of the etiology of diarrhea among United States military personnel found norovirus to be the most commonly detected pathogen (24 percent of cases), followed by ETEC (16 percent), and *Campylobacter jejuni* (14 percent) [21]. However, prolonged shedding of norovirus can complicate interpretation of diagnostic tests.

Rotaviruses have also been identified as a common viral pathogen [14]. (See "Clinical manifestations and diagnosis of rotavirus infection" and "Norovirus".)

- **Parasites** – Most travelers are not exposed to environments with significant risk for parasite infection [22-24].

  Regions with risk for parasitic infection among travelers include Nepal (where both *Giardia lamblia* and *Cyclospora cayetanensis* are common) and St. Petersburg (where *G. lamblia* remains hyperendemic). The mountainous regions of the West and Northeast United States are also highly endemic for *G. lamblia.* In these settings, environmental factors (such as the juxtaposition of the water supply with the habitat of certain animal species) may predispose to parasite infection.

  Uncommonly, other parasitic infections implicated in travelers' diarrhea include *Cryptosporidium parvum*, microsporidia, and *Cytoisospora belli* [25].

  Entamoeba histolytica can produce intestinal infection; it is not a common pathogen in travelers' diarrhea but can be associated with persistent diarrhea. (See "Intestinal Entamoeba histolytica amebiasis".)

  Blastocystis spp are protozoan parasites found in the human gastrointestinal tract; there is controversy regarding whether *Blastocystis* spp represent a commensal organism, a marker of intestinal dysbiosis, or a true pathogen. This is discussed further separately. (See "Blastocystis species".)

CLINICAL MANIFESTATIONS

Typical signs and symptoms — Travelers' diarrhea refers to diarrheal illness that develops among individuals during or within 10 days of returning from travel to a setting where sanitation and hygienic practices are poor and there is limited access to safe drinking water.

For epidemiologic purposes, travelers' diarrhea may be defined as passage of three or more unformed stools in a 24-hour period, accompanied by at least one of the following: nausea, vomiting, abdominal pain or cramps, fever, or blood in the stool.

- **Timing** – Most episodes of travelers' diarrhea occur between 4 and 14 days after arrival [14], but travelers' diarrhea can occur within a shorter time frame if the concentration of bacteria ingested is sufficiently high.

- **Manifestations** – The symptoms of travelers' diarrhea may vary depending on the microbial etiology.

  Illness due to enterotoxigen*ic E. coli* (ETEC) generally produces malaise, anorexia, and abdominal cramps followed by sudden onset of watery diarrhea. Very frequent stools are uncommon. Nausea and vomiting also may occur. Symptoms of colitis (such as blood or pus in the stool) are rare. Patients may develop a low-grade fever.

- **Categorizing severity** – The severity of travelers' diarrhea can be categorized according to a classification scheme suggested by an expert panel of the International Society of Travel Medicine, which uses functional impact to define severity [26]:

  - Mild – Diarrhea that is tolerable, is not distressing, and does not interfere with planned activities.

  - Moderate – Diarrhea that is distressing or interferes with planned activities.

  - Severe – Diarrhea that is incapacitating or completely prevents planned activities; dysentery (passage of grossly bloody stools) is considered severe.

- **Duration of illness** – Travelers' diarrhea is generally self-limited; symptoms usually last for approximately one to five days. It is common to be unable to proceed with planned activities. In one series including more than 30,000 travelers to Jamaica (travelers' diarrhea attack rate 24 percent), incapacity was reported for a mean of 11.6 hours from illness onset [14].

  Patients experience symptoms for more than one week in 8 to 15 percent of cases, and as many as 2 percent of patients experience symptoms for more than one month [27].

Manifestations associated with specific etiologies — The initial symptoms are generally similar to those seen with ETEC, even when other bacterial agents such as *C. jejuni* and *Shigella* spp are implicated. However, infections with these organisms may progress to include symptoms of colitis, such as fever, tenesmus, urgency, cramping, and bloody diarrhea. (See "Campylobacter infection: Clinical manifestations, diagnosis, and treatment" and "Shigella infection: Epidemiology, clinical manifestations, and diagnosis", section on 'Clinical manifestations'.)

Upper gastrointestinal symptoms (bloating, gas, nausea) are typical of giardiasis, while profuse watery diarrhea is characteristic of cholera, cryptosporidiosis, and *C. cayetanensis* infection. Symptoms of microsporidiosis may be more subtle, with bloating and intermittent diarrhea. (See "Giardiasis: Epidemiology, clinical manifestations, and diagnosis" and "Cryptosporidiosis:

Epidemiology, clinical manifestations, and diagnosis" and "Microsporidiosis" and "Cyclospora infection".)

Long-term sequelae — Subsequent development of chronic gastrointestinal symptoms, and in particular irritable bowel syndrome, has been reported in a sizable minority of patients following travelers' diarrhea. Postinfectious irritable bowel syndrome is discussed separately. (See "Pathophysiology of irritable bowel syndrome", section on 'Postinfectious'.)

DIAGNOSIS AND EVALUATION

Clinical approach — The diagnosis of travelers' diarrhea is established in an individual who develops unformed stools during or within 10 days after returning from travel to a setting where sanitation and hygienic practices are poor and there is limited access to safe drinking water. Travelers' diarrhea is typically self-diagnosed. (See 'Clinical manifestations' above.)

For patients who present with uncomplicated travelers' diarrhea after returning home, determination of the microbiologic agent is generally unnecessary [28]. Management of travelers' diarrhea is often symptomatic and should be initiated without regard to the specific offending agent. (See "Travelers' diarrhea: Treatment and prevention".)

Circumstances in which we favor pursuing microbiologic workup include:

- **Symptoms of colitis** (bloody or mucoid stools, abdominal cramping) – In such cases, a stool culture should be performed (to evaluate for *Campylobacter*, *Shigella* spp, pathogenic *E. coli*, and *Salmonella* spp including *Salmonella* Typhi). Stool should also be sent for additional studies including Shiga toxin and *C. difficile*. In addition, blood cultures should be obtained. (See "Campylobacter infection: Clinical manifestations, diagnosis, and treatment", section on 'Diagnosis' and "Shigella infection: Epidemiology, clinical manifestations, and diagnosis", section on 'Diagnosis' and "Pathogenic Escherichia coli associated with diarrhea" and "Shiga toxin-producing Escherichia coli: Clinical manifestations, diagnosis, and treatment" and "*Clostridioides difficile* infection in adults: Clinical manifestations and diagnosis".)

- **Presence of fever** – In such cases, blood and stool cultures should be obtained to evaluate for *Salmonella* species, including *S.* Typhi. (See "Nontyphoidal *Salmonella* bacteremia and extraintestinal infection" and "Enteric (typhoid and paratyphoid) fever: Epidemiology, clinical manifestations, and diagnosis", section on 'Diagnosis'.)

- **Presence of predominantly upper gastrointestinal symptoms** (eg, bloating, gas, nausea) – In such cases, diagnostic testing for *G. lamblia, Cyclospora,* and *Cystoisospora* should be undertaken. Diagnostic tools include stool antigen tests, nucleic acid detection, and stool examination. (See "Giardiasis: Epidemiology, clinical manifestations, and diagnosis", section on 'Diagnosis' and "Cyclospora infection", section on 'Diagnosis'.)

- **Recent antibiotic use** – For patients with antibiotic use in the preceding 8 to 12 weeks, testing for *C. difficile* diarrhea is warranted. (See "*Clostridioides difficile* infection in adults: Clinical manifestations and diagnosis", section on 'Diagnosis'.)

- **Persistent diarrhea** – For patients with persistent diarrhea beyond 10 to 14 days, further workup may be warranted, including testing for intestinal parasitic infections [28]. (See "Travelers' diarrhea: Treatment and prevention", section on 'Patients with persistent diarrhea'.)

Diagnostic tools

- **Stool culture** – Stool cultures are warranted in the circumstances outlined above (see 'Clinical approach' above). Routine stool cultures are rarely informative, since enterotoxigenic *E. coli*, enteroaggregative *E. coli*, and enteropathogenic *E. coli* cannot be distinguished from nonpathogenic *E. coli*; in addition, stool culture cannot identify viral or parasitic agents.

- **Multiplex molecular testing** – Culture-independent diagnostic methods, such as multiplex polymerase chain reaction tests, are increasingly available yet expensive [6]. Multiplex molecular testing is useful for providing rapid results and may allow detection of viral infections such as norovirus, avoiding unnecessary antibiotics [29]. In addition, for chronic diarrhea due to protozoa, molecular testing can be very helpful [30].

  Clinical interpretation of molecular test results can be complex, since multiple pathogens may be detected. As an example, in one study including more than 100 patients with travelers' diarrhea, use of a multiplex molecular panel identified multiple pathogens in 76 percent of cases; in contrast, use of conventional stool culture identified a pathogen in 24 percent of cases [31].

DIFFERENTIAL DIAGNOSIS

The differential diagnosis of travelers’ diarrhea includes:

- **Systemic infections** – Systemic infections that may include diarrhea among the clinical manifestations include:

  - **Malaria** – Malaria is characterized by fever, malaise, nausea, vomiting, abdominal pain, diarrhea, myalgia, and anemia. The diagnosis of malaria is established by rapid antigen test on blood or by visualization of parasites on peripheral smear. (See "Malaria: Clinical manifestations and diagnosis in nonpregnant adults and children".)

  - **Dengue fever** – Manifestations of dengue include fever, hemorrhagic manifestations, and thrombocytopenia, and occasionally diarrhea. The virus is transmitted by *Aedes aegypti* mosquitoes, which have broad epidemiologic distribution; the incubation period is four to seven days (range 3 to 10 days). The diagnosis is established via polymerase chain reaction of blood or serologic testing. (See "Dengue virus infection: Clinical manifestations and diagnosis".)

  - **Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2)/COVID-19** – Patients with coronavirus disease 2019 (COVID-19) may present with gastrointestinal manifestations [32]. The diagnosis of COVID-19 is established via nucleic acid amplification testing or antigen testing on respiratory tract samples. (See "COVID-19: Clinical features" and "COVID-19: Diagnosis".)

- **Food poisoning syndromes** – Noninfectious food poisoning syndromes include shellfish or mushroom poisoning. These other syndromes can be differentiated from travelers' diarrhea by distinguishing clinical features and/or specific diagnostic testing. (See "Overview of shellfish, pufferfish, and other marine toxin poisoning", section on 'Diarrheic shellfish poisoning' and "Clinical manifestations and evaluation of mushroom poisoning", section on 'Acute gastroenteritis'.)

  Infectious food poisoning syndromes, such as those caused by *Staphylococcus aureus* and *Bacillus cereus*, may present with acute gastroenteritis symptoms. These conditions usually present with vomiting as the predominant symptom; diarrhea occurs in a minority of patients. (See "Causes of acute infectious diarrhea and other foodborne illnesses in resource-abundant settings".)

- **Medications** – New medications may be a cause of acute diarrhea in travelers; comparing the timing of drug initiation with onset of diarrhea can help evaluate for this noninfectious etiology of diarrhea.

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: 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.)

- 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)" and "Patient education: Travelers' diarrhea (The Basics)")

SUMMARY

- **Definition** – Travelers' diarrhea refers to development of unformed stools among individuals during or within 10 days of returning from travel to a setting where sanitation and hygienic practices are poor and there is limited access to safe drinking water. Travelers' diarrhea is typically self-diagnosed. (See 'Introduction' above.)

- **Epidemiology** – Travelers' diarrhea is the most common illness travel-associated illness. The attack rate ranges between 10 and 70 percent. Organisms causing travelers’ diarrhea are transmitted via contaminated food and water. The risk is the highest in regions where sanitation and hygienic practices are poor. Risk factors include buying food from street vendors, traveling to visit friends and relatives, and staying in "all-inclusive" lodging. (See 'Epidemiology' above.)

- **Microbiology** – Travelers' diarrhea may be caused by a variety of organisms, including bacteria, viruses, or parasites (table 1). Bacterial pathogens are the most frequent cause in patients with acute illness. (See 'Microbiology' above.)

- **Clinical manifestations** – Most episodes of travelers' diarrhea occur between 4 and 14 days after arrival. The classic "turista" due to enterotoxigen*ic Escherichia coli* generally produces malaise, anorexia, and abdominal cramps followed by sudden onset of watery diarrhea. Very frequent stools are uncommon. Nausea and vomiting also may occur. Symptoms of colitis (such as blood or pus in the stool) are rare. Patients may develop a low-grade fever. Symptoms usually last for one to five days. (See 'Clinical manifestations' above.)

- **Evaluation** – Identifying a microbial etiology is not necessary for most cases of travelers' diarrhea. We pursue microbiologic workup for patients with symptoms of colitis (bloody or mucoid stools, abdominal cramping), fever, predominantly upper gastrointestinal symptoms (bloating, gas, nausea), recent antibiotic use, and persistent diarrhea beyond 10 to 14 days. (See 'Clinical approach' above.)

- **Diagnostic tools** – Diagnostic tools include stool culture and molecular testing. Multiplex molecular testing is increasingly available yet expensive. This tool is useful for providing rapid results and may allow detection of viral infections, avoiding unnecessary antibiotics. Clinical interpretation of the results can be complex, since multiple pathogens may be detected. (See 'Diagnostic tools' above.)

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GRAPHICS

Pathogens causing travelers' diarrhea

Bacteria
▪ Enterotoxigenic *Escherichia coli* (ETEC) ▪ Enteroaggregative *E. coli* (EAEC) ▪ Enteropathogenic *E. coli* (EPEC) ▪ Enterohemorrhagic *E. coli* (EHEC) ▪ *Campylobacter jejuni* ▪ *Salmonella* species ▪ *Shigella* species ▪ *Clostridioides difficile* ▪ *Vibrio parahaemolyticus* (*V. cholerae* less common) ▪ *Aeromonas hydrophila* ▪ *Plesiomonas shigelloides* ▪ *Yersinia enterocolitica*
Viruses
▪ Norovirus ▪ Rotavirus ▪ Enteric adenovirus ▪ Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2)/coronavirus disease 2019 (COVID-19)
Parasites
▪ *Giardia lamblia* ▪ *Cryptosporidium parvum* ▪ *Cyclospora cayetanensis* ▪ Microsporidia ▪ *Cystoisospora belli* ▪ *Entamoeba histolytica* (not common)

There is geographic variation to the microbial distribution of travelers' diarrhea. In Southeast Asia, Campylobacter species are the most common cause of travelers' diarrhea, whereas ETEC is the predominant pathogen in travelers to Latin America/Caribbean, Africa, and the Middle East.

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