

Traveller's diarrhoea

'Travel broadens the mind but opens the bowels'

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ABSTRACT Traveller's diarrhoea is a common problem. This article features the diagnosis and management of diarrhoea in returned travellers to the UK. Treatment is essentially fluid replacement, bed rest if there is much colic, exclusion from work in certain infections, and antibiotics in certain situations.

KEYWORDS Travel, diarrhoea, infection, investigation, treatment, screening

LIST OF ABBREVIATIONS Enterotoxigenic (ETEC), *Escherichia coli* (*E. coli*), oral rehydration solution (ORS)

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SUMMARY

Diarrhoea is recognised as a frequent accompaniment to foreign holidays. At any one time about 300,000 people are airborne, about 5% of journeys are to countries with significant risk of gastroenteritis, and about 40% of travellers develop diarrhoea.

In developing countries, and in some developed countries, travellers may be exposed to impure (meaning faecally contaminated) water and food, and are thus at risk of infection from a broad spectrum of pathogens. Prevention may be better than cure, but widespread use of antibiotics for prevention would be ill-advised, and advice aimed at avoiding exposure may be difficult in practice. Antibiotics can be used to prevent and treat diarrhoea, but widespread use may be counterproductive and they may also cause diarrhoea.

Treatment rests upon adequate fluid replacement, bed rest if there is much colic, exclusion from work for certain occupations, and antibiotics in selected patients.

OVERVIEW

Introduction

The main risk factor is a country of acquisition where sewage disposal may be suspect, where water supplies are not guaranteed uncontaminated, or where kitchen hygiene is not rigorously supervised. Travellers to Latin America, Africa, some of the Middle East, the Dominican Republic, Haiti, and Asia have a 20–50% incidence of diarrhoea whereas southern Europe has a risk of 8–20%.

Most travellers fall ill and recover in the country visited. With the exception of symptomatic amoebic colitis,

giardiasis and tropical sprue, most infective diarrhoeas tend to be of rapid onset and rarely persist for more than two weeks. This overview deals mostly with those who have not recovered. The major causes of diarrhoea are listed in Table 1 and some relevant characteristics are detailed in Table 2.

Clinical pathophysiology of diarrhoea

The small intestine is second only to the kidney as the organ responsible for fluid balance. Small intestinal diarrhoea comprises large amounts of watery diarrhoea, which rarely contains blood, mucus, or pus. Direct invasion of the small bowel wall is one mechanism but toxins often act by stimulating production of cyclic adenosine monophosphate (the 'second messenger') to induce the cells to secrete. This is the mechanism of cholera in which there may be a net secretion of fluid into the small bowel lumen without significant bowel wall invasion. Alternatively, malabsorptive-type small intestinal 'porridge' diarrhoea can occur in giardiasis and tropical sprue. With giardia it was thought that the trophozoites lining the bowel caused malabsorption but now it is known that the syndrome can be produced by only a few organisms and that the pathology must depend on other, currently unknown, mechanisms.

Large intestinal diarrhoea is often caused by processes that invade or irritate the large intestinal wall and thus the large intestine cannot fulfil its normal function as a reservoir from which water and electrolytes are absorbed. Often, small intestinal function is unaffected by large intestinal disease, so large intestinal diarrhoea usually comprises frequent passage of small amounts of stool which may contain blood, mucus or pus. Blood in or on the stool, faecal urgency, or incontinence usually implies large intestinal problems.

TABLE 1 Microbial causes of diarrhoea in returning travellers**Brief duration diarrhoeas**

Staphylococcal and *Bacillus cereus* food poisoning
Campylobacter
Salmonella
Cholera
 Enterotoxin-producing *E. coli*
 Enteroinvasive *E. coli*
Shigella
 Antibiotic-related (including *Clostridium difficile* infection)

Persisting diarrhoeas

Giardia lamblia
Entamoeba histolytica
 Schistosomiasis
 Tropical sprue

Clinical features

Traveller's diarrhoea is defined by the passage of unformed stool twice as frequently as the normal bowel habit. Most pass 4–5 stools daily. Recovery occurs within a week in 90% of cases, and <1% have symptoms at 3 months. Usually there is an abrupt onset with diarrhoea and cramps, malaise, nausea, and possibly fever. Abdominal pain is occasionally severe (Table 2). Signs of dehydration can occur in more severe cases.

Microbiology

Shigella and *amoebae* are almost exclusively large bowel pathogens whereas *Giardia lamblia* and *Vibrio cholerae* are exclusively small bowel pathogens. Some pathogens, including *Campylobacter jejuni* and *Salmonella*, may produce a sequential mixed picture, with small bowel diarrhoea initially, followed by large bowel diarrhoea. Invasive pathogens often produce fever, whereas toxin-mediated illness usually does not produce a febrile response. Dysentery is diarrhoea with blood and usually implies an invasive pathogen rather than a purely toxin-mediated illness.

Bacteriological diagnosis may be suspected from symptomatology. A standard 'stool for culture' will not reveal non-bacterial pathogens; examination for ova, cysts, and parasites has to be requested specifically. Suspected amoebiasis is the only indication for hot stools (meaning either 'instant microscopy' or very rapid transport of the stool sample to the laboratory in a thermos flask). Occasionally viral examination is required. Viral examination would rarely be necessary for isolated instances of bacteriologically culture-negative diarrhoea, but may be important if there is an outbreak of bacteriologically negative diarrhoea – on cruise ships for example.

TABLE 2 Infections in which diarrhoea is a predominant feature

Organism	Nature of illness	Usual incubations	Blood in stool	Abdominal pain
<i>Amebic colitis</i>	Invasion of bowel wall	Variable 5–7 days	Usually (with mucus)	Possible: large bowel type
<i>Campylobacter</i>	Penetration of bowel wall	5–7 days (3–10 days possible)	In about 40%	Possibly very severe
<i>Non-typhoidal Salmonellae</i>	Invasion of bowel wall	some toxins 12–48 hrs 6–72 hrs	About 30%	Possible
<i>Clostridium perfringens</i> Type A	Toxin mediated	8–16 hrs	No	Mild
Enterotoxin-producing <i>E. coli</i>	Enterotoxin	A few days	No	Possible: usually mild
<i>Giardia lamblia</i>	Upper small bowel dysfunction	Variable: large range	No	Possible: small intestinal
Rotavirus	Infection of bowel wall	1–2 days usually	Not usually	Possible: mild
<i>Shigella sonnei, flexneri, boydii, dysenteriae</i>	Invasion of large bowel wall	3–4 days (1–7 days possible)	Very common (with mucus)	Large bowel type colic
<i>Vibrio cholerae</i>	Toxin-mediated	6–72 hrs	No	Colicky

Brief duration, infection-related diarrhoeas

Staphylococcal and Bacillus cereus

These causes of food poisoning have such short incubation periods, 3–8 hours and 6–24 hours, respectively, that they are almost always acquired during the return journey. Both produce vomiting and diarrhoea of less than 24 hours duration, and are toxin-mediated.

Campylobacter

Fever and severe abdominal pain often accompany this cause of diarrhoeal illness. Occasionally abdominal pain is so severe that peritonitis or perforation is wrongly diagnosed. A significant clue to the correct diagnosis is that patients with peritonitis or perforation usually have absent bowel sounds whereas patients with invasive *Campylobacter* (or *Salmonella*) often have increased bowel sounds. Infection is usually from animal sources. Antibiotics (usually an erythromycin) are only indicated if the illness is severe or if symptoms are not improving once the diagnosis is confirmed.

Salmonella

There are three main clinical syndromes but there may be some overlap.

- The first, and most common type of illness ('gastroenteritis', 'food poisoning') is produced by infection which usually remains confined to the gut and causes diarrhoea and vomiting, abdominal pain, and flu-like symptoms. Infection is usually acquired from undercooked animal carcasses. Antibiotic therapy is not indicated unless patients have additional risk factors such as cardiovascular disease and immunodeficiency.
- The second type of illness is caused by bloodstream invasion with possible focal sepsis in which gastrointestinal symptoms and signs may be prominent, minimal, or absent. Fever may be high and constitutional symptoms may be marked with rigors. Antibiotic therapy is indicated, largely in an attempt to prevent seeding of infection, particularly into bones, joints, or pre-existing cardiovascular lesions
- The third type of illness is caused by strains that are strict human pathogens which usually invade the bloodstream to produce typhoid or paratyphoid fever. Initial symptoms, other than feverishness, may be vague but abdominal discomfort, splenomegaly, constipation (*not* diarrhoea), and dry cough are suggestive. Later in the illness, which may last for four weeks or so, 'pea soup' diarrhoea occurs when the organism relocates to the terminal ileum.

Cholera

This has such a short incubation period (6–72 hours) and such a brief, although possibly fatal, course that it usually begins and ends in the country of acquisition.

E. coli

Is a normal resident of the large gut but certain strains are associated with diarrhoeal illnesses:

- Enterotoxigenic strains are the most common cause of self-limiting traveller's diarrhoea;
- Enteroinvasive strains produce a shigella-like illness (indeed *Shigella* and *E. coli* are close bacterial relatives);
- Verocytotoxin-producing strains of *E. coli* O157, in particular, produce a toxin that can damage red blood corpuscles and cause kidney failure (haemolytic uraemic syndrome) or a predominantly nervous system illness (thrombotic thrombocytopenic purpura). Both these syndromes tend to appear as the diarrhoea is improving. Often patients look systemically unwell and often have dysentery. The role of antibiotics is uncertain.
- Enteropathogenic strains mostly cause watery diarrhoea in children by causing dysfunction of the intestinal brush border and microvilli.

Shigella

These organisms invade the large intestine only and cause classical large intestinal diarrhoea ('bacillary dysentery'). Patients often look toxic and ill whereas those with amoebic dysentery often look relatively well. Antibiotics may have a role if patients are unwell.

Antibiotic-related diarrhoea

This is usually caused by infection with *Clostridium difficile* and has a wide spectrum of severity, ranging from mild or no symptoms through to fulminant pseudomembranous enterocolitis.

Infections that can produce persisting diarrhoea

Giardia lamblia

This infection is the most common cause of persistent traveller's diarrhoea. It produces a malabsorption-type diarrhoea with giardia trophozoites present in the upper small bowel. The trophozoites are not invasive and essentially provoke a malabsorptive reaction (a suggestive feature) with bloating after food because undigested food passes through the upper small bowel producing osmotically mediated distention. Anorexia and nausea are associated features. Giardia stools are often foul, both in smell and appearance. The diagnosis can be made by finding cysts in the stool – a stool need not be freshly passed if searching for cysts. Metronidazole or tinidazole is effective treatment and patients should be made aware that interaction of the treatment with alcohol causes vomiting. If stools are negative for cysts a therapeutic trial may be given; duodenal aspiration should be reserved for those who do not respond to treatment. Other protozoa that may cause persistent diarrhoea include cryptosporidium and cyclospora, both of which may affect patients with normal immunity to give a self-limiting, if protracted, illness. In the immunocompromised, especially those

with AIDS, symptoms may last for months and weight loss may be severe.

Entamoeba histolytica

This is an infection usually acquired in the tropics. The organisms invade the large gut to cause typical large bowel-type diarrhoea ('amoebic dysentery'). Amoebae may produce acute dysentery, but infection often presents as insidious onset chronic diarrhoea, which may be confused with ulcerative colitis. Diagnosis is by finding cysts in the stool or by finding actively motile trophozoites on stool or rectal mucus examination. Suspected amoebiasis is the only indication for a hot stool examination (see Microbiology above). Metronidazole followed by furamide (to eradicate intraluminal parasites) is required.

Schistosomiasis (Bilharzia)

This is caused by three main nematodes: *Schistosoma mansoni* and *Schistosoma japonicum* both have an affinity for the human gut and other viscera whereas *Schistosoma haematobium* mostly affects the human bladder. The distribution depends on that of the snails in which the schistosomal life cycle occurs. *Schistosoma mansoni* is found in Africa, Central and South America and in the Caribbean whereas *S. japonicum* is found in the Far East. Larvae penetrate the skin in still-water bathers, the larvae mature, and the adults mate and lay eggs in the gut (and elsewhere) which may cause acute or chronic fibrosing inflammation possibly leading to intestinal ulceration and narrowing. Chronic diarrhoea can occur in patients who have repeated long-term infections. Short-term bathers in a schistosomiasis endemic area may acquire infection but chronic diarrhoea is unlikely.

Tropical sprue

This produces chronic malabsorption, weight loss, and multiple deficiencies particularly of iron and folate. Sprue is often associated with small bowel colonisation with Gram-negative bacteria. Sprue is found in those who stay in certain geographically well-defined tropical areas for longer than one month and is presumed to have an infection-related pathology causing malabsorption, steatorrhoea, and folate and vitamin B12 deficiency. There are highly endemic areas in India and the Far East and areas of low endemicity in South and Central America, and Africa. Treatment is with antibiotics (usually tetracyclines) and folic acid.

Lactase deficiency

This may take months to recover from and may occur in those who have had severe gastroenteritis. A trial of a lactose-free diet may be helpful.

Irritable bowel syndrome

This occurs frequently after bacterial gastroenteritis and may last for several months. Antispasmodics should be tried.

The vulnerable traveller

Patients with pre-existing bowel disease may be at increased risk of infection. Those with inflammatory bowel disease may also suffer relapses after minor traveller's diarrhoea (see also S Ghosh. Recognition and management of inflammatory bowel disease. *J R Coll Physicians Edinb* 2005; **35**:50–54). Those with hypochlorhydria or those receiving acid-reduction therapies lose the protection of gastric acid, which reduces the number of most ingested pathogens (but notably not *Shigella*) that pass onward into the small bowel. Immunosuppressed patients may be at increased risk of acquiring infection in at-risk countries, as they may have more severe and/or protracted gastroenteritis, and may excrete the organism(s) for longer.

Prophylaxis

In at-risk countries, the most important measures for prevention are self-protection against enteric infection. The main steps are to avoid tap water, ice, undercooked meat, seafood, fruit not needing to be peeled, salads, uncooked vegetables, fresh cheeses, unpasteurised milk or butter, and buffet food at room temperature. Above all, avoid street vendors. Fruits requiring to be peeled, piping hot foods, cooked vegetables, carbonated or boiled water, and hot teas or coffee are generally safe. Drug prophylaxis, apart for antibiotics (see below), with agents such as bismuth subsalicylate or antimotility agents is of no value and may be dangerous.

Antibiotic prophylaxis can be effective but is limited by the resistance patterns of the organisms in countries visited. These are seldom known before travel. Prophylaxis for all travellers would inevitably increase resistance rates and limit the use of those antibiotics. The cost in the UK, if all visitors to higher risk areas were prescribed antibiotics, would be about £24 million a year! Antibiotic prophylaxis is best reserved for those visiting high-risk areas for brief periods during which they will be performing important tasks. They can also be given to immunocompromised or immunodeficient individuals. Antibiotics used included ciprofloxacin, trimethoprim, co-trimoxazole, norfloxacin, and doxycycline (now often given for malaria prophylaxis) and it will be interesting to see if bacterial resistance in Gram-negative bacilli increases. Various dosages have been used but one tablet daily seems to be effective. Ciprofloxacin produces a protection rate of up to 95%. Antibiotics are of no value in preventing viral or parasitic diarrhoea.

Specific treatments

Rehydration

Treatment depends on adequate fluid replacement (ORS), colic relief, sometimes anti-diarrhoeal agents, and sometimes antibiotics. Oral rehydration solution does *not*

relieve diarrhoea – its purpose is to replace fluid and electrolyte losses rather than relieve diarrhoea. It contains water, sodium, glucose (sodium absorption requires glucose), potassium, and an alkali to combat the acidosis resulting from an alkaline diarrhoea. Glucose is necessary to promote sodium absorption but the amount present is small and of little nutritional value. However, lack of nutrition in a previously well patient with diarrhoea of short duration is not critical. The aim should be to replace fluid losses over about 3–4 hours followed by sufficient fluid to replace continuing losses, usually given on an empirical basis. Severe continuing diarrhoea, particularly in children, should lead to hospital admission. Malnourished children require continued feeding during treatment and also need hospital admission. Bed rest is a much neglected intervention for relieving colic and settling diarrhoea.

Antimotility drugs

Antimotility drugs such as loperamide are useful in controlling acute symptoms in adults. The manufacturer's instructions should be followed and the maximum dose not exceeded. Antimotility drugs should be avoided if there is a possibility of dysentery or inflammatory bowel disease.

FURTHER READING

- Cairo J-P, DuPont HL. Management of travellers' diarrhoea. *Drugs* 1998; **56**(1):73–80.
- Casburn-Jones AC, Farthing MJ. Traveler's diarrhea. *J Gastroenterol Hepatol* 2004; **19**(6):610–18.
- Centers for Disease Control and Prevention. *Travelers' Health*.
- De Bruyn G, Hahn S, Borwick A. Antibiotic treatment for

Antibiotics

Antibiotics, notably quinolones, shorten diarrhoea by about 1–2 days and reduce the severity to some extent. Not all gut pathogens, however, are sensitive to quinolones, and, indeed, the *therapeutic* use of antibiotics after diarrhoea develops is controversial. If diarrhoea is mild then ORS should suffice, if diarrhoea is moderate an antibiotic plus loperamide should be used, and if diarrhoea is severe (especially with fever, dysentery, or incapacitating symptoms) then an antibiotic for 3–5 days would be reasonable without an antimotility agent, which may worsen the situation. The role of probiotics in prevention and treatment is under investigation.

HIGHLIGHTS

- Rehydration therapy is advised for all patients
- Travel destination(s) should be chosen with care, particularly for those with pre-existing bowel disease and immunosuppressed patients.
- Increased bowel sounds in a diarrhoeal illness with severe abdominal pain speak against a diagnosis of perforation or peritonitis.
- Giardia is the most common cause of persistent traveller's diarrhoea.
- Antibiotic prophylaxis is best used only for those visiting high-risk areas to perform important tasks.

travellers' diarrhoea (Cochrane review). *From The Cochrane Library, Issue 3, 2004*. Chichester, UK: John Wiley & Sons, Ltd.

- Rodriguez LA, Ruigomez A. Increased risk of irritable bowel syndrome after bacterial gastroenteritis: cohort study. *BMJ* 1999; **318**(7183):565–6.
- The Travel Doctor. *Travellers' Diarrhoea*.
- Thielman NM, Guerrant RL. Clinical practice. Acute infectious diarrhoea. *N Engl J Med* 2004; **350**(1):38–47.

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