



THEME

Travel medicine



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The returned traveller with diarrhoea

BACKGROUND

Traveller's diarrhoea is among the most frequently reported problems for travellers. Prevention remains a challenge in travellers and the appropriate management of traveller's diarrhoea remains paramount.

OBJECTIVE

This article provides an overview of the general approach to diarrhoea in the returned traveller, including identification of common causes and management.

DISCUSSION

The most common causes of traveller's diarrhoea are bacterial contamination of food and water, particularly with enterotoxigenic *Escherichia coli*. Most cases of traveller's diarrhoea are mild, are of short duration and do not require antibiotic treatment. Where the diarrhoea is severe, bloody and/or prolonged, then laboratory investigation is necessary. Where the patient is severely ill and possibly septicaemic, blood culture is mandatory. Presently, one of the most useful groups of the antibiotics routinely available for treatment is the fluoroquinolones.

At the First Conference on International Travel Medicine held in Zurich almost 20 years ago, DuPont and Ericsson¹ stated that: 'Among persons from highly industrialised areas of northwestern Europe and the United States, acute diarrhoea represents the most common medical complaint during travels to the developing countries of Africa, Latin America and southeastern Asia.'

This remains true today and applies equally to travellers from Australia visiting such developing areas and to quote DuPont and Ericsson¹ again: 'Diarrhoea continues to be an important problem among persons travelling from low risk regions to developing areas where enteric infection is hyperendemic in the local population'. Therefore, about 30–50% of travellers will suffer from diarrhoea – in about half of these travellers it will be short lived (3–5 days), and about 30–40% will require confinement to bed.^{2–6} About 12% will present with diarrhoea on their return home.⁷

Causes of diarrhoea in travellers

While the causes of infectious diarrhoea in travellers are many and varied (*Table 1, 2*) enterotoxigenic *Escherichia coli* (ETEC) are the cause in up to 80% of cases.^{6,7} Most

cases of traveller's diarrhoea are mild and have a duration of about 3 days.

It should be noted that typhoid and paratyphoid are septicaemic illnesses and infected people do not usually present initially with diarrhoea – in fact they often suffer from constipation in the initial stages of the disease and develop diarrhoea in the later stages. It is important to remember that vaccination against typhoid is not 100% protective and vaccine failures occur.⁸

A clinical approach

History

A careful history must be taken from the traveller, covering past illnesses, countries visited and when, possible sources of infection (eg. foods consumed while away), time of commencement and duration of the diarrhoea, medications taken before and since, and immunisation history. It should be remembered that *Plasmodium falciparum* can present with severe diarrhoea!

Assessment

The patient should be assessed in relation to overall physical condition, including:

Table 1. Common causes of diarrhoea in travellers⁵

Pathogen	% traveller's diarrhoea	Usual incubation period	Average duration of illness
Virus			
Norovirus	Unknown	18–48 hours	24–48 hours
Rotavirus	Unknown	<48 hours	Up to 5 days
Bacteria (noninvasive)			
Enterotoxigenic <i>E. coli</i>	50%	12 hours to 3 days	1 week
<i>Vibrio parahaemolyticus</i>	2%	12–24 hours	1–3 days
Enterotoxigenic <i>S. aureus</i>	Common cause of food poisoning	2–6 hours	8–12 hours
Bacteria (invasive)			
<i>S. enteritica</i>	5%	6–48 hours	3–4 days
<i>Shigella</i> spp.	15%	1–3 days	3 days
<i>Campylobacter jejuni</i>	10%	1–7 days	1–7 days
<i>Yersinia enterocolitica</i>	Unknown	4–7 days	Weeks to months
Enterohaemorrhagic <i>E. coli</i>		1–3 days	
Protozoa			
<i>Giardia duodenalis</i>	<3%	12–15 days	Weeks to months
<i>Entamoeba histolytica</i>	<2%	4–6 weeks	Can be prolonged to years
<i>Cryptosporidium</i> spp.	1–5%	5–10 days	Particularly in children and patients with AIDS
<i>Cyclospora cayetanensis</i>	Unknown	2–11 days	7–21 days

- associated symptoms (especially abdominal pain, nausea, fever)
- nature and severity of the diarrhoea (mild: <4 stools per day or moderate-severe: 5+ stools per day), and
- the presence of blood in the faeces.

This assessment will determine:

- management
- any laboratory studies needed, and
- whether treatment is necessary and if so what drugs should be considered.

Mild diarrhoea

Most cases of diarrhoea in the returned traveller are mild and short lived. In these cases, laboratory investigations are usually unnecessary – and are often not helpful – and antibiotic treatment is usually not required.

Moderate to severe diarrhoea

In moderate to severe diarrhoea, the patient has a more severe or persistent (longer than 2 weeks) diarrhoea but is

not passing blood and is not febrile. The patient may require antidiarrhoeal medication, and laboratory investigations may reveal a parasitic aetiology in cases of prolonged diarrhoea.

Severe, bloody diarrhoea

In severe, bloody diarrhoea, laboratory investigations, and in most cases antimicrobial treatment, will be required. An excellent syndromic approach to the patient with diarrhoea has been given by Keddy et al⁹ and is reproduced in modified form in *Table 3*.

It is worth noting in relation to the need for both laboratory investigation and specific treatment, that while all the pathogens listed in *Table 1* and *2* can cause diarrhoea, only some may be associated with bloody diarrhoea (dysentery): *Shigella* spp., *Salmonella* spp., *E. coli* 0157, *Campylobacter* spp., and *Entamoeba histolytica*.

Similarly, a prolonged diarrhoea (in excess of 2 weeks or longer) is often associated with a protozoan aetiology, ie. giardiasis, cryptosporidiosis, cyclosporidiosis, and isosporiasis.

In immunocompromised patients (especially those with HIV), microsporidia and organisms from the *Mycobacterium avium* complex might be involved additional to the agents mentioned above, particularly *Cryptosporidium* spp. and *Isospora belli*.

Intestinal worm infections, with a few notable exceptions (*Table 2*) are not usually associated with diarrhoea.

Laboratory investigations

For the patient with short duration, mild diarrhoea, laboratory investigations are usually unhelpful and unnecessary.

Where the diarrhoea is severe, bloody and/or prolonged, then laboratory investigation is necessary. In some cases however, laboratory tests might not be available from routine diagnostic laboratories (eg. specific tests for diarrhoeagenic pathotypes of *E. coli* other than *E. coli* 0157:H7). Routine tests used in most laboratories would include enrichment, culture, biochemical identification, serotyping, antigen detection and/or polymerase chain reaction (PCR) as appropriate.¹⁰

Where the patient is severely ill and possibly septicemic, as in typhoid or paratyphoid, then blood culture is mandatory.

Table 2. Other less common causes of diarrhoea

Pathogen	Comments
Virus	
Hepatitis A, hepatitis E	
Bacteria	
<i>Aeromonas</i> spp.	Can be dysenteric and/or persistent
<i>Plesiomonas shigelloides</i>	Can sometimes cause dysenteric illness
<i>Vibrio cholerae</i> 01:0139	Rare in returned travellers
Noncholera vibrios	Some associated with seafood
<i>Bacillus cereus</i>	Food poisoning – often associated with rice
<i>Yersinia enterocolitica</i>	Mesenteric lymphadenitis; may cause bloody diarrhoea
Enterohaemorrhagic <i>E. coli</i> (EHEC)	May cause a bloody diarrhoea; can proceed to haemolytic uraemic syndrome (especially serotype 0157:H7)
Enteroinvasive <i>E. coli</i> (EIEC)	May cause bloody diarrhoea
Enteroaggregative <i>E. coli</i> (EAggEC)	May cause persistent diarrhoea
<i>Clostridium perfringens</i> type A	Food poisoning
<i>C. perfringens</i> type C	Enteritis necroticans
<i>C. botulinum</i>	May get diarrhoea in early stages
<i>C. difficile</i>	Antibiotic associated, may be bloody in pseudomembranous colitis
Enterotoxigenic <i>S. aureus</i>	Food poisoning intoxication
<i>Listeria monocytogenes</i>	Occasional cause of diarrhoea
<i>Salmonella typhi</i>	Presents initially with constipation but may develop diarrhoea later in infection
<i>S. paratyphi</i>	
Protozoa	
<i>Dientamoeba fragilis</i>	Requires permanent faecal stained smear
<i>Blastocystis hominis</i>	If large numbers present in faecal specimen and no other cause of diarrhoea detected
<i>Balantidium coli</i>	Zoonotic – causes colitis and dysentery
<i>Isospora belli</i>	Watery diarrhoea in children and patients with AIDS
<i>P. falciparum</i>	The initial presentation of complicated malaria may be diarrhoea-like illness
Helminths	
<i>Schistosoma mansoni</i>	Occasionally in early stages of infection
<i>S. japonicum</i>	Occasionally in early stages of infection
<i>Strongyloides stercoralis</i>	Especially in cases of internal autoinfection
<i>Taenia</i> spp.	Beef and pork tapeworms occasionally
<i>Trichuris trichiura</i>	With very heavy worm loads, may be bloody
<i>Trichinella</i> spp.	In early infection

Table 3. A clinical approach to the possible aetiology of diarrhoea⁷

Clinical presentation	Anatomic consideration	Potential pathogen
Few, voluminous stools; may be watery and severe in cholera; pale, fatty and smelly in giardiasis	Diarrhoea of small bowel origin	<i>Vibrio cholerae</i> , ETEC, early shigellosis, <i>Giardia</i> , <i>V. parahaemolyticus</i>
Many small volume stools	Diarrhoea of large bowel origin	<i>Shigella</i> , <i>Salmonella</i> , <i>Campylobacter</i> , diarrhoeagenic pathotypes of <i>E. coli</i> , <i>Yersinia enterocolitica</i> , <i>Entamoeba histolytica</i>
Tenesmus, faecal urgency, dysentery	Colitis	<i>Shigella</i> , <i>Salmonella</i> , EIEC, EHEC, <i>Campylobacter</i> , <i>E. histolytica</i> , <i>V. parahaemolyticus</i> (rarely)
Predominance of vomiting	Gastroenteritis	Viral (eg. rotavirus, calicivirus, norovirus) or intoxication (eg. <i>S. aureus</i> food poisoning)
Predominance of fever	Mucosal invasion	<i>Shigella</i> , <i>Salmonella</i> (especially enteric fever group), <i>Campylobacter</i> , viral agents, EIEC
Prolonged diarrhoea (>2 weeks)	Small/large bowel	<i>Giardia</i> , <i>E. histolytica</i> , <i>Cryptosporidium</i>

Where parasitic infections are involved, then a direct smear in saline of a fresh stool specimen, stained faecal smears, concentration techniques, antigen detection or PCR might be used. If the patient has been on antidiarrhoeals, this can make microscopic identification of protozoan pathogens more difficult. Based on scientific observation, three repeat stools (eg. Monday, Wednesday, Friday) for parasitic protozoa should suffice, as *Giardia* sheds cysts in irregular 'showers' and *E. histolytica* sheds cysts in 8–10 day cycles.

Inglis¹⁰ has made the important point that with enteric infections, more than one pathogen might be isolated – a fact even more relevant when dealing with returned travellers.

Treatment

Fluid replacement remains the first essential in the treatment of diarrhoea.⁴ While patients with mild diarrhoea of short duration do not usually require specific antimicrobial treatment, the duration of traveller's diarrhoea in adults can be shortened by the use of ciprofloxacin.^{6,7} With short term, uncomplicated diarrhoea, antimotility/antisecretory agents such as loperamide or agents such as bismuth subsalicylate might be considered. Dietary recommendations might be helpful in these patients, especially in children, and they should be encouraged to drink fluids/oral rehydration solution as indicated and take in salt with soups or crackers. The 'BRAT' diet (bananas, rice, apple sauce and toast) is sometimes suggested with avoidance of milk products often recommended due to possible transient lactose deficiency.¹¹

Where patients present with severe, persistent diarrhoea or they are febrile and/or passing blood in their faeces, then attempts need to be made to identify the cause of the illness in order that specific treatment can be prescribed. In general

terms, antimicrobial treatment should be considered where the patient has bloody diarrhoea (dysentery); the patient is suffering from cholera with severe dehydration; where the diarrhoea/dysentery has a proven parasitic aetiology; and where there is laboratory proven enteropathogenic *E. coli* infection.⁶ The actual treatment depends on the species of pathogen and in most bacterial diarrhoeas, on the sensitivities of the isolated organism. In general, the antimicrobials in use are given in *Table 4* and the topic of antimicrobial drug use in traveller's diarrhoea has been well summarised by Kass⁷, Thielman and Guerrant,¹¹ and Looke and Robson.¹³ Kass further advises that antisecretory agents should not be used when treating bloody diarrhoea or where the patient is febrile,⁷ although this widely held concern about the use of antisecretory/antimotility agents is largely allayed in a review by Ericsson.¹² Useful flow charts relating to the management of diarrhoea are given by Thielman and Guerrant,¹¹ and Looke and Robson.¹³

Where the diarrhoea appears to be related to taking antibiotics (ie. antibiotic associated diarrhoea due to *C. difficile*) then withdrawal of antibiotics may be necessary.

Summary of important points

- Enterotoxigenic *E. coli* is the most common cause of traveller's diarrhoea.
- Most cases of traveller's diarrhoea are mild and have a duration of about 3 days and laboratory investigation tends to be unhelpful in these cases.
- Where the diarrhoea is severe, bloody and/or prolonged, then laboratory investigation is necessary.
- Where the patient is severely ill and possibly septicaemic, then blood culture is mandatory for diseases such as typhoid.

Table 4. Antimicrobial agents for treatment of infectious diarrhoea

Pathogen/disease	Antimicrobial agents to be considered (depending on sensitivities)	Comments on treatment
Viral		
Rotavirus, norovirus, calicivirus	None	Mostly symptomatic treatment
Bacterial		
Cholera	Ampicillin, cotrimoxazole, furazolidone, doxycycline, erythromycin, azithromycin, ciprofloxacin	Rehydration is the most important measure. Antibiotics may shorten duration of illness and help limit spread
Uncomplicated bacterial gastroenteritis	Rarely indicated	Symptomatic if needed. Ciprofloxacin or rifaximin (not yet available in Australia) can shorten duration of severe ETEC
Bacillary dysentery	Ampicillin, cotrimoxazole, naladixic acid, ciprofloxacin, ceftriaxone	
Typhoid fever	Ampicillin, chloramphenicol, cotrimoxazole, ciprofloxacin, azithromycin	This is a septicemic illness and always requires antibiotic treatment
Salmonella gastroenteritis	Not usually recommended	Prolongs excretion of bacteria and is not recommended unless evidence of septicemic spread is noted
Campylobacteriosis	Erythromycin, ciprofloxacin, azithromycin	
Protozoal		
Giardiasis	Metronidazole/tinidazole	Treat entire family
Amoebiasis	Diloxanide furoate if asymptomatic (ie. infection confined to gut lumen), metronidazole, tinidazole	
Blastocystosis	Metronidazole	Often difficult to treat even with high dose regimen
Cryptosporidiosis	Azithromycin, paromomycin	
Cyclosporidiosis	Cotrimoxazole	
Microsporidiosis	Albendazole, ocreotide	
Isosporiasis	Cotrimoxazole	
Dientamoebiasis	Doxycycline, metronidazole	
Helminthic		
Schistosomiasis	Praziquantel	
Taeniasis	Praziquantel	
Strongyloidiasis	Ivermectin, albendazole	
Trichuriasis	Albendazole	
Trichinellosis	Albendazole	

- Malaria may also need to be excluded. Any patient returning from a tropical area who presents with diarrhoea AND fever should have a blood smear examined for malaria (and *P. falciparum* testing if available).
- Fluid replacement is the most important aspect of treatment for diarrhoea.
- When treatment is indicated, one of the most useful groups of antibiotics is the fluoroquinolones, with the addition of antimotility/antisecretory agents

(eg. loperamide) in troublesome, uncomplicated traveller's diarrhoea.

Resources

- Cohen J. Traveller's pocket medical guide and international certificate of vaccination. Available at www.travelclinic.com.au/pocket-guide.asp
- Leggat PA, Goldsmid JM, editors. Primer of travel medicine. 3rd edn. Available at www.tropmed.org
- Mills D. Travelling well. Available at www.travellingwell.com.au
- Yung A, Ruff T, Torresi J, Leder K, O'Brien D. The manual of travel medicine: a pre-travel guide for health care professionals. 2nd

- edn. Melbourne: IP Communications, 2004
- Centres for Disease Control and Prevention. Health information for international travel 2005–2006. Available at www.cdc.gov/travel
 - Travel Health Advisory Group, Australia. Available at www.welltogo.com.au
 - World Health Organisation. International travel and health. Available at <http://who.int/ith>.

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References

1. DuPont HL, Ericsson CD. Travelers' diarrhoea: its prevention and treatment. In: Steffen R, et al, editors. Travel medicine. Berlin: Springer-Verlag, 1989;291–5.
2. Jong EC, Kleger MM, McMullen R. Approach to infectious diarrhea in the returned traveller. In: The tropical and travel medicine manual. 2nd edn. Philadelphia: Saunders, 1995;295–312.
3. Keystone JS, Kozarsky PE. Health advice for international travel. In: Guerrant RL, et al, editors. Essentials of tropical infectious diseases. Philadelphia: Churchill-Livingstone, 2001;128–40.
4. Leggat PA, Goldsmid JM. Travellers' diarrhoea: health advice for travellers. *Travel Med Inf Dis* 2004;2:17–22.
5. Leggat PA, Goldsmid JM. Travellers' diarrhoea. In: Leggat PA, Goldsmid JM, editors. Primer of travel medicine. 3rd (revised) edn. Brisbane: ACTM, 2005.
6. Penny M. Diarrhoeal diseases. In: Eddleston M, et al, editors. Oxford: Handbook of tropical medicine. 2nd edn. Oxford: Oxford University Press, 2005;117–68.
7. Kass, R. Traveller's diarrhoea. *Aust Fam Physician* 2005;34:243–5.
8. Fuller D, Hasnat M, Marks MK, Curtis N. Fever in a returned traveller. *J Paediatr Child Health* 2004;40:315–6.
9. Keddy K, Goldsmid JM, Frean J. Tropical gastrointestinal infections. In: Goldsmid, JM, Leggat PA, editors. Primer of tropical medicine. 1st edn. Brisbane: ACTM, 2005.
10. Inglis TJJ. Clinical microbiology. Edinburgh: Churchill-Livingstone, 1997.
11. Thielman NM, Guerrant RL. Acute infectious diarrhoea. *New Engl J Med* 2004;350:38–47.
12. Ericsson CD. Travelers' diarrhea. *Int J Antimicrob Agents* 2003;21:116–24.
13. Looke DFM, Robson JMB. Infection in the returned traveller. *Med J Aust* 2002;177:212–9.