The returning traveller with diarrhoea

Introduction

Between 1950 and 2012 worldwide international tourist arrivals increased from 25 million to over 1.1 billion. A large proportion (48%) of this travel is to tropical and subtropical destinations (United Nations World Tourism Organisation, 2013). From the UK 56.8 million people travelled abroad in 2012, with 8.9 million of these visits outside Europe or North America (Office for National Statistics, 2012).

With increased travel, there will be an increasing burden of communicable disease, including diarrhoeal disease, in those returning. Travellers are a heterogeneous group with different categories including short and long haul tourists, those visiting friends and relatives, business travellers, immigrants and military personnel.

The risks of acquiring infections vary among different groups of travellers. Those travelling for longer periods of time on a restricted budget will have different exposures to business travellers staying a western style hotel in a capital city. In assessing people presenting with diarrhoeal illnesses it is important to take a travel history. General physicians are poor at taking a travel history, as re-enforced in north west England, with only 19% of over 130 travellers assessed in acute medical units undergoing a travel history (Price et al, 2011). This article describes the epidemiology, aetiologies and a pragmatic approach to managing returned travellers presenting with diarrhoea.

Epidemiology: defining the risk

Epidemiological studies of travel-related infection were patchy until the mid-2000s when the GeoSentinel survey started to provide a more comprehensive global survey of incidence. In 2006, the first major publication from the survey covered some 17 000 travellers in over 40 travel clinics worldwide. Diarrhoeal disease was the commonest clinical presentation (335 per 1000 cases), with a significant association between diarrhoea and visiting the Indian sub-continent (Freedman et al, 2006). Expansion of site numbers and travel-related data is ongoing.

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Defining diarrhoea

Diarrhoea has been classified according to its aetiology, pathogenesis and clinical presentation. Traditionally, small bowel diarrhoea is said to be watery and of high volume whereas colonic diarrhoea is small volume and frequent, sometimes with blood; however, this can be of limited use in the clinical setting. A pragmatic approach, recommended by the World Health Organization, is the passage of three or more loose-to-watery stools in any 24-hour period (Al-Abri et al, 2005).

Defining traveller's diarrhoea

Traveller's diarrhoea is diarrhoea starting during or shortly after a period of foreign travel, with or without blood or other gastrointestinal symptoms (cramping, nausea, vomiting). It can be acute (lasting less than 4 weeks) or chronic (lasting longer than 4 weeks). Some describe diarrhoea lasting 14–28 days as persistent.

Risk

Traveller's diarrhoea is common, as shown by the GeoSentinel data. However, not all those affected will seek medical attention and estimates of incidence vary worldwide; it affects between 20% and 60% of returning travellers, particularly in resource-poor settings (Cobelens et al, 1998; Hill, 2000; Steffen et al, 2004). A business traveller staying in a five star hotel for 3 days of meetings may be much less likely to suffer a gut infection than a backpacker who is using basic accommodation and for whom costs are a limiting factor.

Destination

Destination of travel is the major determinant of risk. In declining order of frequency: southern and south east Asia, south and central America and sub-Saharan Africa are considered high risk (20–90% risk over 2 weeks). The middle east, southern and eastern Europe and central Asia carry a moderate risk (8–20%), and Europe, north America and Australasia a low risk (<8%) (Steffen, 2005). Lower income countries have a greater risk (Greenwood et al, 2008).

Alongside the region visited, other risk factors are well defined. The choice of eating establishment and eating in restaurants (Shlim, 2005) increase the risk of traveller's diarrhoea. Younger age and female sex (Swaminathan et al, 2009) are risk factors. It is also clear that travellers from a high income country (Steffen, 2005) are more likely to suffer with traveller's diarrhoea. Single nucleotide polymorphisms in lactoferrin, osteoprotegerin and IL-10 genes (Hill and Beeching, 2010) also confer an increased risk of traveller's diarrhoea. The traditional advice given to travellers is to 'boil it, cook it, peel it or forget it' but there is no evidence that adhering to these rules reduces the rates of diarrhoea (Shlim, 2005).

Clinical course

Duration

For the majority of patients, traveller's diarrhoea runs a benign course beginning within the first week of travel and resolving spontaneously, with a mean duration of 4 days. Over 60% of cases will have improved by 48 hours. Chronic diarrhoea is less common; 10% of cases will last for a week, and around 2% for a month or longer (Cobelens et al, 1998; Hill, 2000; Steffen, 2005). Chronic diarrhoea has different causes to acute diarrhoea – malignancy, inflammatory bowel disease, protozoal infections, HIV, endocrine or autoimmune causes are in the differential diagnosis. This often warrants a more complex assessment beyond the scope of this article (Thomas et al, 2003).

Presentation

Acute diarrhoea is usually associated with abdominal discomfort or cramping pain, nausea and vomiting. Fever can also occur. Bloody diarrhoea (dysentery) is a marker of

invasive and more severe gut infection occurring in less than 10% (Steffen, 2005). Incapacity, usually for less than a day, occurs in 20–30% of patients before recovery (Cobelens et al, 1998; Hill, 2000; Steffen, 2005), and hospitalization is rare (<1%) (Steffen et al, 2004). However, people who are old, very young or immunosuppressed may experience more severe illness.

Complications

Post-infectious complications of traveller's diarrhoea are increasingly being described. Irritable bowel syndrome is most common, affecting between 10 and 17% of patients, and can persist for months or years after infection (Connor and Riddle, 2013).

Guillain–Barré syndrome, a rare, acute, ascending motor neuropathy, is associated with enteric infection; *Campylobacter* spp. is thought to be the cause of up to 40% of cases of Guillain–Barré syndrome, but the prevalence in traveller's diarrhoea is not established (Connor and Riddle, 2013). Reactive arthritis has been described in 1–62% of enteric infections, but there are no data on prevalence in traveller's diarrhoea (Connor and Riddle, 2013).

Dysentery caused by *Escherichia coli* O157 and *Shigellae* spp. (among others) can be associated with the haemolytic-uraemic syndrome, which warrants specialist referral. There are few data as to how common this is in traveller's diarrhoea. Invasive bacterial infections can cause toxic dilatation and perforation, although this is rare in traveller's diarrhoea (Steffen, 2005).

Aetiology: what causes traveller's diarrhoea?

The common enteric pathogens, areas of risk and treatments are summarized in *Table 1*.

Viruses

Viruses account for a minority of cases of traveller's diarrhoea, up to 20% in some studies. Rotavirus and norovirus are the most commonly isolated pathogens; norovirus is often responsible for outbreaks in resorts and on cruise ships (Al-Abri et al, 2005; Shah et al, 2009).

Bacteria

The enteric pathogens causing traveller's diarrhoea vary with location and season. The pathogen will not be identified in over 50% of cases. Nevertheless, since the 1970s, bacteria have been recognized as the commonest isolated cause. Enterotoxigenic *E. coli* are responsible for up to 45% of traveller's diarrhoea worldwide. These organisms secrete an enterotoxin that stimulates a secretory diarrhoea (Al-Abri et al, 2005; Shah et al, 2009).

Campylobacter spp. accounts for up to 30% of traveller's diarrhoea, and is more prevalent in South Asia. Non-typhoidal *Salmonellae* spp. and *Shigellae* spp. account for around 15% each. Enteroinvasive and enteroaggregative *E. coli* – which in contrast to enterotoxic *E. coli* can cause inflammatory bloody diarrhoea – are also increasingly being recognized as enteric pathogens (Hill and Ryan, 2008; Hill and Beeching, 2010).

Protozoa

Parasitic infections are responsible for only a small proportion of cases of traveller's diarrhoea – less than 10%. However, chronic diarrhoea is significantly more likely to have a parasitic cause (McGregor et al, 2012). Of the identifiable enteric pathogens causing gastrointestinal disease from the GeoSentinel data, 65% were parasitic (Ross et al, 2013), although this likely reflects the chronicity of symptoms of the patients presenting to specialist travel clinics. However, the introduction of molecular methods for diagnosis may show that protozoan infection is more common.

Giardia lamblia, a protozoa, is the commonest identified parasitic cause, and is more common in travellers in South Asia (Al-Abri et al, 2005; Ross et al, 2013). *Cryptosporidia* spp. and *Entamoeba* spp. are also isolated, but less frequently than *Giardia* spp.

Approach to the management of traveller's diarrhoea

The aims of treatment of diarrhoea in the returning traveller are to correct any dehydration and to treat causes of the diarrhoeal illness. The majority of sufferers do not seek medical attention (Steffen et al, 2004) and can manage at home with increased oral fluid intake and perhaps oral rehydration solutions. Self-treatment with antibiotics is also sometimes recommended. However, this review will focus on a management approach for those seeking medical attention.

Assessment

A thorough history, including detailed travel history, is essential. Indeed, all patients presenting with diarrhoea should be asked about travel. The travel history, site of exposure, environmental risk, and

Table 1. Pathogens causing traveller's diarrhoea

Enteric pathogen		High-risk area	Incubation period	Symptoms	Adult treatment
Bacteria	Enterotoxogenic *Escherichia coli*	Latin America	1–2 days	Watery diarrhoea, abdominal pain	Ciprofloxacin, azithromycin, rifaximin
	Campylobacter	South Asia, south east Asia	1–5 days	Watery diarrhoea, sometimes bloody, fever	Azithromycin
	Salmonella (non-typhoidal)	South east Asia, Oceania	12–36 hours	Watery diarrhoea	Ciprofloxacin, azithromycin
	Shigella	North Africa, south and south east Asia	1–7 days	Bloody diarrhoea, fever	Ciprofloxacin
Viral	Norovirus	Worldwide	1–2 days	Acute vomiting and diarrhoea	Supportive
	Rotavirus	Worldwide	2–6 days	Acute vomiting and diarrhoea	Supportive
Parasitic	Giardia	South Asia, middle East, south America	7–10 days	Abdominal pain, nausea, chronic diarrhoea	Tinidazole, metronidazole
	Entamoeba histolytica	South and south east Asia, middle East, south America	11–21 days	Watery or bloody diarrhoea, abdominal pain, fever	Tinidazole, metronidazole
	Cryptosporidium	South Asia	1–12 days	Watery diarrhoea	Usually supportive

Adapted from Ross et al (2013)

determining the incubation period may help identify the causative pathogen (*Table 1*).

Asking about the frequency of bowel action is a guide to fluid loss from the body and, along with thirst and dizziness on standing, may suggest significant fluid depletion. If a patient gets up at night for bowel action this is a red flag symptom, prompting a careful search for the cause. The presence of blood in the stools, abdominal pain, vomiting and fever are also important features to ask about. Duration of symptoms identifies acute *vs* chronic diarrhoea. A thorough review of systems is mandatory as diarrhoea can also be a presentation of systemic disease, both infectious and non-infectious; notably, malaria can present with diarrhoea. Any immunosuppressive comorbidities or medications may increase the severity of illness.

Mild disease is defined as 1–2 loose stools per day, moderate as greater than 2 stools and severe disease as greater than 2 stools with blood, fever or incapacitating symptoms (Al-Abri et al, 2005).

Examination should focus on assessing the level of dehydration, assessing nutritional status (body mass index) and ruling out signs of severe colitis by looking for signs of severe abdominal tenderness and/or peritonism. Dehydration manifests as dry mucous membranes, reduced skin turgor and postural hypotension. More severe dehydration manifests as cool peripheries, tachycardia, shock and reduced conscious level.

Digital rectal examination can exclude constipation with overflow, allows assessment of other causes such as rectal tumours and may show the presence of blood on the examining glove. Fever can be a marker of invasive disease.

If there is evidence of colitis or possible cancer, fibreoptic sigmoidoscopy or colonoscopy may be needed.

Blood tests will provide a biochemical assessment of hydration status and renal function, although this will not be necessary in mild disease. Inflammatory markers, white cell count, C-reactive protein and serum albumin level are useful to help classify the severity of disease. Patients with chronic diarrhoea should have a coeliac screen.

Malaria films should be performed for any at-risk traveller who complains of fever or has a fever. Plain abdominal X-rays can show signs of colitis, such as mucosal thickening or 'thumb-printing', and any dilated bowel implies development of a toxic megacolon and should trigger prompt surgical review.

Stool should be sent for bacterial culture, for *Clostridium difficile* toxin and microscopy for parasites. Bloodstaining of stools, fluid stool and bloodstained mucus should be examined for the presence of amoebic trophozoites. Microscopy of unformed stools for the presence of cellular exudate, white cells and red cells is important as it can give valuable information about the possibility of an invasive bacterial infection of the gut. Stool can also be sent for norovirus polymerase chain reaction if it is a possible cause.

Treatment

Correcting dehydration remains the priority in the treatment of traveller's diarrhoea. For those with mild disease who are able to drink, oral fluids – in particular oral rehydration solutions – may be appropriate. If there are markers of severe dehydration (shock, cool peripheries, reduced mental status) or if the patient is vomiting, physiologically matched intravenous fluids such as Hartmann's, Ringer's lactate or normal saline should be administered.

Anti-motility drugs – in particular loperamide – are often used by travellers to self-treat, and reduce stool frequency, especially in conjunction with antibiotics (Riddle et al, 2008). However, they should not be used in dysenteric disease where there is concern that they can worsen outcome (DuPont and Hornick, 1973), particularly in the very young and the elderly. Up to date data are lacking and care needs to be exercised with their use.

Antibiotic therapy reduces the duration of traveller's diarrhoea (de Bruyn et al, 2000) but, given the self-limiting nature of the majority of cases, it is necessary to balance the risks of antibiotic therapy against any benefits, including development of resistant organisms.

Mild disease should be treated with rehydration only; if the patient can drink, and there are no signs of severe dehydration, oral fluids should be used. Moderate to severe disease can be treated with antimicrobials, especially if any signs of invasive disease are present – any of bloody diarrhoea, severe abdominal pain or abdominal signs, fever or shock.

Quinolones are active against the majority of bacterial pathogens, and ciprofloxacin is historically the antibiotic of choice. Unfortunately, ciprofloxacin-resistant *Campylobacter* is an increasing problem in the developing world, especially in south and south-east Asia. Azithromycin should be considered for travellers from this area (Tribble et al, 2007), and also in children, for whom quinolones are contraindicated. Single dose ciprofloxacin is as effective as a longer course in the absence of features of invasive infection (Salam et al, 1994), otherwise a 3-day course is usually adequate. An algorithm for the treatment of traveller's diarrhoea is shown in *Figure 1* (adapted from Al-Abri et al, 2005).

A number of agents are effective against giardiasis and amoebiasis. Tinidazole (or metronidazole) can be used first line for giardiasis, and metronidazole is usually preferred for amoebiasis (followed by a luminal agent such as paromomycin or diloxanide). Discussion with an infectious diseases physician should follow identification of *Giardia* or *Entamoeba* spp. Failure of improvement of diarrhoea should prompt consideration of infectious and non-infectious causes of chronic diarrhoea, and referral to an appropriate specialist centre.

Conclusions

Traveller's diarrhoea is common and largely self-limiting. Indeed all patients presenting with diarrhoea should be asked about travel. Mostly, traveller's diarrhoea can be managed as an outpatient with simple measures to ensure hydration, and anti-biotic therapy is indicated only in moderate to severe disease. There is increasing understanding of the global distribution of pathogens that cause traveller's diarrhoea, host characteristics that predispose to it, and treatment strategies. Work continues on vaccines and prophylactic regimens. However, rates of enteric disease in those travelling to low-income countries have largely remained static over the last 30 years, and, given the boom in international travel, health-care professionals will likely be increasingly presented with this common condition. **BJHM**

Conflict of interest: none.

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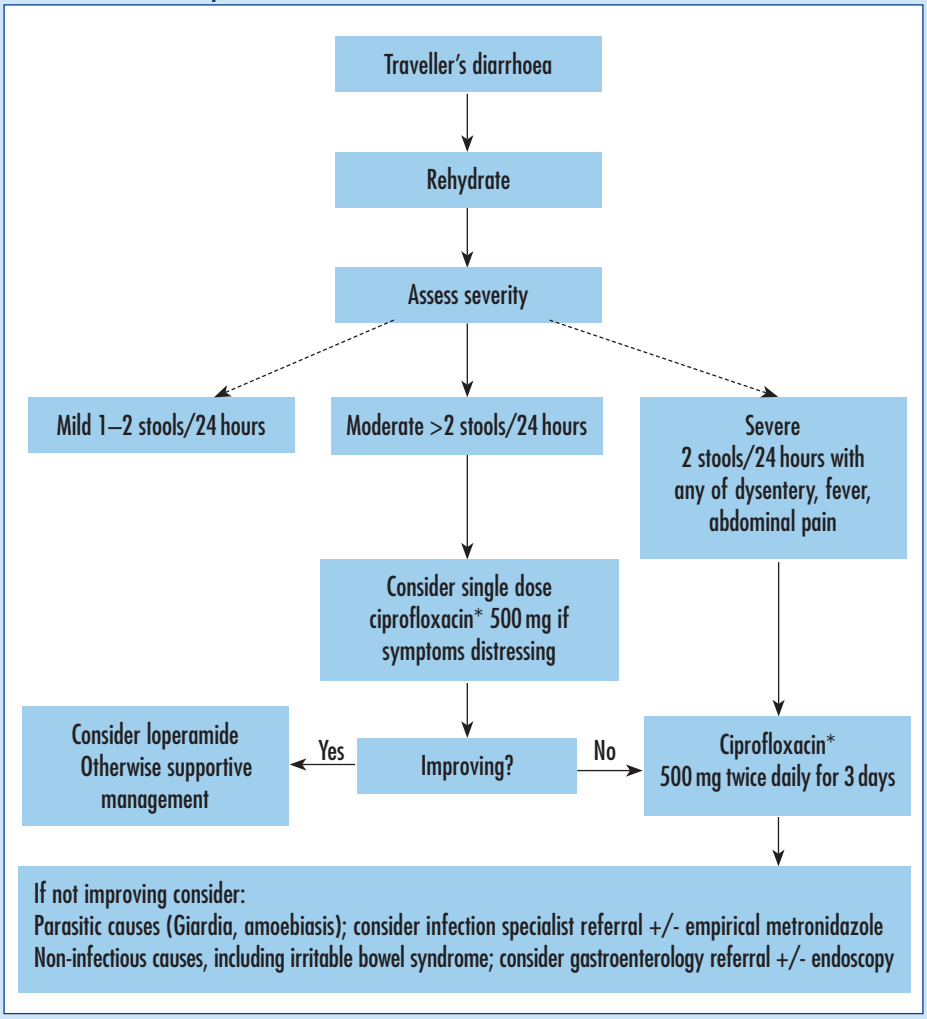
Figure 1. Algorithm for the treatment of traveller's diarrhoea. *Replace ciprofloxacin with azithromycin if the patient's travel was to an area of high prevalence of resistant campylobacter (south and south east Asia) or in children. Adapted from Al-Abri et al (2005).



KEY POINTS

- If you do not take a travel history, then you do not know if the patient has travelled.
- Traveller's diarrhoea affects up to 60% of visitors to low-income countries.
- Bacteria, in particular enterotoxic *Escherichia coli*, are thought to be the commonest cause.
- The majority of cases of traveller's diarrhoea are self-limiting and do not require antimicrobial therapy.
- Maintaining hydration is the key intervention.
- Antibiotics should be given if there are signs of moderate or severe disease, in particular fever, abdominal pain or dysentery.
- Loperamide should be avoided if there is blood, abdominal pain or fever.
- Post-infectious irritable bowel syndrome is increasingly recognized as a consequence of traveller's diarrhoea.