9: Infections in the returned traveller

David F M Looke and Jennifer M B Robson

Remember to consider serious yet treatable diseases, such as malaria

STUDIES SHOW that almost 50% of travellers returning to Europe and North America from the tropics experience health problems related to their travel, and that 8% consult doctors either abroad or on return.[1] Figures are not available for Australian travellers but are probably similar. The most common diseases in travellers to the tropics are travellers' diarrhoea (35% incidence per month of travel), followed by acute respiratory infections (1.4%), giardiasis (0.7%) and other infections (including hepatitis, amoebiasis and gonorrhoea).[1] Australian travellers increasingly visit tropical and developing countries and may present with infections that are rare in Australia.

Pre-travel health assessment and planning can prevent or ameliorate some of these problems (Box 1). Useful information about travel-related infections can be found at the websites of the World Health Organization (www.who.int/ith), United States Centers for Disease Control and Prevention (www.cdc.gov/travel) and the Department of Public Health and Tropical Medicine at James Cook University, Townsville (www.jcu.edu.au/school/phtm/PHTM/putravel.htm).

Clinical presentations

Over 90% of infections related to short-term travel present within six months of return. Diseases with long latent periods or potential for lifetime persistence are rare after short-term travel, but more common in those who have lived abroad or were born overseas. The usual presentation of a returned traveller is with a particular syndrome — fever, respiratory infection, diarrhoea, eosinophilia, or skin or soft tissue infection — or for screening for asymptomatic infection.

When assessing a returned traveller, it is important to obtain:

■ a complete travel history, including dates and places visited, and potential exposures to exotic diseases (eg, travel to rural areas, freshwater exposure, insect bites and sexual contacts); and

Abstract

■ The usual presentation of a returned traveller is with a particular syndrome — fever, respiratory infection, diarrhoea, eosinophilia, or skin or soft tissue infection — or for screening for asymptomatic infection.

■ Fever in a returned traveller requires prompt investigation to prevent deaths from malaria; diagnosis of malaria may require up to three blood films over 36–48 hours.

■ Diarrhoea is the most common health problem in travellers and is caused predominantly by bacteria; persistent diarrhoea is less likely to have an infectious cause, but its prognosis is usually good.

■ While most travel-related infections present within six months of return, some important chronic infections may present months or years later (eg, strongyloidiasis, schistosomiasis).

■ Travellers who have been bitten by an animal require evaluation for rabies prophylaxis.

MJA 2002; 177: 212-219

■ time of symptom onset in relation to travel, which may help eliminate diseases with different incubation periods (eg, fever beginning over 10 days after departure from an endemic area is unlikely to be dengue, which has a short incubation period). Incubation periods of common travel-related infections are shown in Box 2.

Fever

Between 2% and 12% of travellers suffer from a febrile illness while away or on return.[1,3] Malaria is the most common diagnosis[3-5] and is particularly frequent in travellers to West Africa who have taken no prophylaxis (2%).[1] Among people arriving in Australia, the incidence of malaria is highest in those who have been in Nigeria (1.3%), the Solomon Islands (1.1%), Ghana (0.6%) and Papua New Guinea (0.4%).[6] Other causes of fever are shown in Box 3. Younger travellers are more likely to have an exotic infection than the elderly, as their travel tends to be more adventurous. Older travellers are more likely to have a febrile complication of underlying disease, such as endocarditis or pneumonia.

Evaluation and initial management of fever in a returned traveller is outlined in Box 4. It is important to exclude falciparum malaria, which is potentially fatal but treatable. Once this is excluded, patients require hospital admission only if severely ill. Viral haemorrhagic fevers (eg, Lassa fever, and Marburg and Ebola virus infections) usually present as undifferentiated fever, but are rare in returned travellers. If suspected (recent travel to an African country with endemic

Series Editors: M Lindsay Grayson, Steven L Wesselingh

Infection Management Services – Southern Queensland, Princess Alexandra Hospital, Woolloongabba, QLD.
David F M Looke, FRACP, FRCPA, MMedSci (Clin Epidemiol), Infectious Diseases Physician.

Sullivan Nicolaides Pathology, Taringa, QLD.
Jennifer M B Robson, FRACP, FRCPA, FACTM, Microbiologist.
Reprints will not be available from the authors. Correspondence: Dr J M B Robson, Sullivan Nicolaides Pathology, 134 Whitmore Street, Taringa, QLD 4068. jrobson@snp.com.au

<div style="border:1px solid">

1: Pre-travel health assessment and planning

This is recommended at least six weeks before departure and should include:

Assessment of fitness to travel: pre-existing conditions (eg, diabetes, heart disease, pregnancy, immunocompromise); psychological state (eg, depression, seeking "way-out" of problems, alcohol, drugs); need for specialised medications, with doctor's letter specifying this.

Full travel history and risk assessment

Update of routine vaccinations: measles–mumps–rubella; diphtheria; pertussis; tetanus; hepatitis B; poliomyelitis; influenza; and pneumococcal vaccines.

Routine vaccinations for travel to developing countries: hepatitis A and (if travelling for more than two weeks) typhoid.

"Special circumstance" vaccinations: yellow fever; meningococcus; rabies; and Japanese B encephalitis.

Prophylactic drugs when indicated: antimalarials (mefloquine, doxycycline, chloroquine, proguanil or malarone); and antibiotics for travellers' diarrhoea (if immunocompromised or other special circumstances).

Advice on prevention: travellers' diarrhoea; schistosomiasis and fresh-water exposure in Africa; traffic-accident injuries; sexually transmitted diseases; sunburn and sunstroke; insect bites; scuba-diving accidents; deep venous thrombosis; and jet lag.

Advice and drugs for medical or first-aid kit: including diarrhoea kit (loperamide, antibiotic [norfloxacin], thermometer and [for long-term traveller or trekker] tinidazole).

Advice on travel health insurance and assistance

</div>

2: Incubation periods of travel-related infections[2]

Short (<10 days)	Intermediate (10–21 days)	Long (>21 days)
Influenza	Malaria	Malaria
Dengue	Viral haemorrhagic fevers	Hepatitis A, B, C, E
Yellow fever	Typhoid fever	Rabies
Plague	Scrub typhus	Schistosomiasis
Paratyphoid fever	Q fever	Leishmaniasis
Mediterranean spotted fever	Relapsing fever (*Borrelia* spp.)	Amoebic liver abscess
African tick-bite fever	African trypanosomiasis	Tuberculosis
Rocky Mountain spotted fever		Filariasis
		Brucellosis

3: Causes of fever in Canadian and Australian studies of returned travellers

	Percentage of fever cases	
Diagnosis	Canada (*n*=587)[4]	Australia (*n*=232)[5]
Undiagnosed	25	9
Malaria	32	27
Respiratory infection*	11	18
Hepatitis	6	3
Diarrhoeal illness	5	14
Pyelonephritis	4	1
Dengue	2	8
Enteric fever	2	3
Epstein–Barr virus infection	2	0.4
Rickettsial infection	1	2
Amoebiasis	1	1
Tuberculosis	1	0.4
Acute HIV infection	0.3	0.4
Other infections	4	10
Other causes	4	3

* Including upper respiratory tract infection, bronchitis and pneumonia.

disease or a known outbreak), then public health authorities must be notified to allow appropriate action.[7]

Malaria

Malaria caused by *Plasmodium falciparum* generally presents within six weeks of return from an endemic area, although onset may be delayed by prophylactic mefloquine.[8] In contrast, malaria caused by *Plasmodium vivax* may present many months after exposure. No signs or symptoms are specific to malaria, although fever is invariable. Occasionally, malaria mimics acute gastroenteritis, acute abdomen, pneumonia and meningoencephalitis. As prophylactic antimalarials do not eliminate the possibility of malaria, appropriate testing should always be done.

Malaria is diagnosed by detecting the parasite in a blood film or circulating malarial antigen. Initial blood films may be negative, and repeat films should be taken every six to 12 hours for 36–48 hours before malaria can be confidently excluded. As untreated falciparum malaria can be fatal within 24–48 hours of presentation, particularly in children, the diagnosis should be pursued urgently (case history, Box 5).

Patients with falciparum malaria require hospital admission until the disease is clearly under control. All should be treated as if they have chloroquine-resistant disease. Uncomplicated disease is treated with oral quinine plus either doxycycline or pyrimethamine–sulfadoxine, or, alternatively, mefloquine as a single agent, or the combination of atovaquone and proguanil.[9] Severe malaria requires intravenous quinine.

Malaria caused by the *Plasmodium* species *vivax, ovale* and *malariae* can still usually be treated effectively with oral chloroquine followed by primaquine to eradicate the hepatic stages of *P. vivax* and *P. ovale*. Patients receiving primaquine should have prior testing for glucose-6-phosphate dehydrogenase deficiency, as the drug may cause severe haemolytic anaemia if this is present. However, as chloroquine-resistant *P. vivax* has now been reported throughout South-East Asia,[10] specialist advice may be required, particularly for relapsing disease.[9]

Dengue

Infected travellers have periodically introduced this common mosquito-borne flavivirus disease to northern Australia. Its range is currently spreading as one of its vectors, *Aedes albopictus,* becomes acclimatised to the urban environment.[11]

Clues to diagnosis of dengue are the short incubation period (four to seven days), maculopapular rash, thrombo-

4: Evaluation and initial management of fever in a returned traveller*

Suspected febrile illness in a returned traveller

↓

Confirm fever

↓

Severe sepsis
(confusion, collapse, cyanosis, tachypnoea, hypotension, neck stiffness, peritonism or digital gangrene)

No features of severe sepsis

Resuscitation if shocked
Blood cultures
Malaria films
Penicillin or ceftriaxone
(if meningococcal disease likely)

History: Travel and fever onset (compare with typical incubation periods)
Pattern of fever: Occasionally helpful (eg, second-daily paroxysm in vivax malaria)
Focal features: Neck stiffness, cellulitis, abdominal tenderness, pulmonary consolidation
Investigations: Full blood count, liver function tests, blood cultures (two), chest x-ray, urine microscopy and culture, baseline serological tests, specific investigations for focal disease

Malaria possible†

Thick and thin malaria films (if initially negative, repeat 3 times)

↓

Plasmodium vivax, ovale or *malariae*

Plasmodium falciparum

Urgent hospital transfer

Rash

Consider dengue or rickettsial disease
• Serological tests
• Consider empirical doxycycline for rickettsia

Consider influenza
• Rapid antigen or PCR test

Respiratory symptoms

Return within 3 days from country with acute influenza

Pulmonary consolidation

Consider unusual causes of pneumonia (eg, Legionnaire's disease, melioidosis)
• If severe, give empirical treatment, including macrolide or quinolone

Fever >7 days, malaria ruled out

Consider enteric fever
• Blood, stool and urine cultures
• Consider empirical quinolone or third-generation cephalosporin

Jaundice

Consider
• Acute hepatitis (eg, A, B, C, E, Epstein–Barr virus, dengue, Q fever): serological tests
• Acute cholangitis (stones, liver fluke): blood cultures, ultrasound and stool examination
• Liver abscess (amoebic, pyogenic): blood cultures, serological tests

PCR = polymerase chain reaction.
*Evaluation should also include the differential diagnoses that would be considered in a non-traveller with fever.
†Travel to high-risk area, rural or prolonged travel, non-compliance with prophylaxis.

---

cytopenia and leukopenia. The last three features also occur in some rickettsial diseases (eg, scrub typhus), HIV seroconversion (Box 6), Q fever, meningococcal disease, toxic shock syndrome, measles, secondary syphilis and rubella. Diagnosis depends on virus isolation from blood, amplification of viral nucleic acid or serological results (dengue IgM or IgG seroconversion).

There is as yet no effective antiviral therapy, and supportive treatment is all that can be offered. Spontaneous resolution is usual. Occasionally, severe depression complicates the recovery phase.

Enteric fever (typhoid and paratyphoid)

Enteric fever is the clinical syndrome caused by *Salmonella typhi* or "paratyphi" *Salmonella* species. Fever is the dominant symptom, with gastrointestinal symptoms variably present. Typhoid vaccine confers about 70% protection against *S. typhi*, so does not rule out the diagnosis. Diagnosis depends on culture, as serological testing is unreliable, particularly if vaccine has been given.

In a patient with prolonged, undifferentiated fever, empirical therapy for enteric fever with quinolones (eg, ciprofloxacin) can be considered once malaria has been ruled out. Quinolone-resistant strains of *Salmonella* have now been reported, and, in children, third-generation cephalosporins (eg, ceftriaxone or cefotaxime) may be required.[9]

Rickettsial diseases

These include scrub typhus, African tick bite fever and Mediterranean and Rocky Mountain spotted fever. All are transmitted by arthropod (mostly tick) bites, although many patients have not noted a bite. Rickettsial disease should be suspected in patients with fever and a rash (particularly if an eschar is present) who have travelled to an endemic area. Diagnosis is by serological testing. As acute serological testing is usually negative, empirical therapy with doxycycline should be considered while awaiting results of tests on convalescent sera.

Respiratory infections

About 20%–40% of travellers have respiratory symptoms while away or on return.[12,13] The most common causes are allergy and viral infection of the upper respiratory tract.

Tuberculosis (defined as skin test conversion) occurs in an estimated 2% of long-term travellers to high risk areas, such as sub-Saharan and North Africa, South and East Asia, the Middle East and Central and South America.[14] Risk is lower during short-term holidays. Infants and children staying in these areas for more than three months are recommended to have bacille Calmette–Guérin (BCG) vaccination, as it reduces disease severity and mortality. For adults, the recommendations are less clear. Possible strategies include

<div style="border:1px solid">

5: Case history — fever and confusion in a traveller to Papua New Guinea

History: A 42-year-old geologist presented 14 days after return from a 6-week field trip to Papua New Guinea. He had a six day history of high fevers and rigors. On the day of presentation, he had become vague and confused. He had taken antimalarials as prophylaxis, but ceased when he found that local people did not take them.

Examination: His temperature was 40°C, pulse rate 140 bpm, respiratory rate 28 per minute, and blood pressure 100/60 mmHg. He had dry mucous membranes, mild jaundice, pallor, spleno-megaly and generalised crackles in both lungs. He was drowsy and disoriented but had no meningism.

Investigations: Full blood examination revealed reduced haemo-globin concentration (65 g/L; reference range [RR], 130–180 g/L), leukopenia (2.5×10^9/L; RR, 3.5–10×10^9/L) and thrombocytopenia (10×10^9/L; RR, 150–400×10^9/L). Malaria films were positive for *Plasmodium falciparum*, with 18% of red blood cells parasitised. Liver function tests revealed raised levels of bilirubin (60 μmol/L; RR, 3–20 μmol/L) and lactate dehydrogenase (489 U/L; RR, 100–225 U/L). Serum creatinine level was also raised (0.28 mmol/L [RR, 0.04–0.12 mmol/L]). Blood gas measurement revealed pH 7.1, P_{O_2} 110 mmHg (RR, 70–80 mmHg) and P_{CO_2} 15 mmHg (RR, 36–45 mmHg).

Management: Severe falciparum malaria was diagnosed. The patient was admitted to the intensive care unit, treated with ventilation, renal dialysis, intravenous quinine and exchange transfusion. Despite therapy and full support, he died on Day 5 of the admission.

- *Malaria should be excluded in any traveller with fever, even if prophylactic antimalarials have been taken, as their efficacy is less than 100%.*
- *Severe malaria is defined by any degree of altered consciousness, focal neurological signs, jaundice, oliguria, severe anaemia, hypoglycaemia, hypotension, >2% of red blood cells parasitised or absolute parasite count >100000/mL, vomiting or acidosis.*
- *Severe malaria requires treatment with intravenous quinine and admission to an intensive care unit, as complications may occur suddenly, and quinine therapy must be monitored closely. Even with intensive-care treatment, mortality is high.*

</div>

<div style="border:1px solid">

6: Case history — fever with rash after a tropical holiday

History: A 34-year-old man presented 10 days after returning from a six-week holiday in South-East Asia. He had an eight-day history of malaise, chills, headache, sore throat and generalised rash. He had stayed mostly at five-star hotels, but reported many mosquito bites.

Examination: He had fever, a macular rash and generalised lymphadenopathy with mild splenomegaly, but no meningism and no eschar present.

Investigations: Full blood examination revealed lymphocytosis with numerous atypical lymphocytes and thrombocytopenia. Blood cultures and malaria films were negative. Liver function tests revealed marginally elevated serum transaminase levels. Serological testing revealed past infection with Epstein–Barr virus and cytomegalovirus and was negative for Q fever, dengue, rubella, measles and rickettsial infection.

Management: The presumptive diagnosis was dengue, and supportive treatment was instituted. However, symptoms persisted for the next three weeks.

Dengue serological testing was repeated and found to be still negative.

A repeat sexual history revealed unprotected intercourse with a number of men during the holiday. HIV antibody tests were positive on enzyme immunoassay and indeterminate on western blot. A p24 antigen test was positive. HIV seroconversion illness was diagnosed, and appropriate counselling and therapy offered.

- *Acute HIV infection may mimic several tropical diseases, including dengue and typhus, as well as infectious mononucleosis.*
- *A sexual history is important in assessing infection risk in any traveller with a febrile illness.*
- *Early diagnosis of HIV infection is important in preventing transmission, as well as allowing the correct timing of antiretroviral therapy.*

</div>

<div style="border:1px solid">

7: Causes of travellers' diarrhoea (% of cases)[16]

Bacteria (> 80%)	*Viruses (0–36%)*
Salmonella spp.	Rotavirus
Campylobacter spp.	Adenovirus
Shigella spp.	Caliciviruses
Aeromonas spp.	Astroviruses
Plesiomonas spp.	Norwalk virus
Yersinia spp.	*Parasites (0–20%)*
Vibrio cholerae	*Giardia lamblia*
Vibrio parahaemolyticus and other non-cholera vibrios	*Cryptosporidium parvum*
Escherichia coli (eg, enterotoxigenic strains)	*Cyclospora cayetanensis*
Clostridium perfringens	*Entamoeba histolytica*
Clostridium difficile	*Isospora belli*
Edwardsiella tarda	Microsporidia
	Blastocystis hominis (pathogenicity controversial)[17]

</div>

pre-travel BCG vaccination or Mantoux screening before and after travel, followed by prophylactic isoniazid for those whose skin test has converted. However, a recent analysis suggested that, given the problems of compliance and adverse effects with these strategies, it is more rational to await the rare cases of clinically overt travel-associated tuberculosis and treat appropriately as they arise.[15]

Travellers' diarrhoea

Acute diarrhoea is common in travellers to developing countries.[16] Despite the advice "cook it, boil it, peel it or forget it", dietary transgressions are usually unavoidable. Most cases of travellers' diarrhoea are caused by bacterial contamination of food, particularly with enterotoxigenic *Escherichia coli* (ETEC). Other causes are shown in Box 7. It is rarely life-threatening. Mean duration of symptoms is four days. Up to 60% of people complain of cramps, 15% of bloody stools, and 10% of fever or vomiting.

Preventive strategies include education about safe food and beverages, water purification, and chemoprophylaxis with antibiotics (eg, trimethoprim–sulfamethoxazole or nor-

floxacin administered once daily). Antibiotics are 70%–95% effective in preventing travellers' diarrhoea,[16] but should be considered only in selected high-risk, short-term travellers — those who cannot tolerate a brief illness (eg, athletes, business and political travellers) and those with increased susceptibility (eg, because of achlorhydria, gastrectomy, history of repeated severe travellers' diarrhoea, immuno-compromise or chronic illness). Prophylaxis is not recom-mended for healthy travellers. As most travellers' diarrhoea

occurs during travel, patients should be instructed in self-management (Box 8).

When diarrhoea persists for 14 days or more (1%–3% of cases[18]), bacterial causes are less likely. Parasite infestations are more common, but the spectrum of causes is much wider and includes non-infective causes, such as lactose intolerance, irritable-bowel syndrome, post-infectious malabsorption, bile-salt enteritis, inflammatory bowel disease, malignancy, coeliac disease and drugs. An approach to evaluation of persistent diarrhoea in travellers is shown in Box 9. It is important to consult with the pathology laboratory, as tests for some potential causes may not be routine.

Some patients have continuing symptoms (loose stools, urgency, and sensitivity to certain foods resulting in flatus or diarrhoea, similar to irritable-bowel syndrome) despite empirical therapy and negative results on gastroenterological workup. They are best treated symptomatically and reassured that the prognosis is good.[18]

Eosinophilia

Eosinophilia (blood eosinophil count $\geqslant 0.6 \times 10^9/L$) in a returned traveller may be an isolated finding or associated with symptoms such as cough, fatigue, skin lesions (urticaria), abdominal discomfort and diarrhoea. A recent German study of 14 000 travellers returning from the tropics found eosinophilia in almost 5%, and a definite diagnosis was made in a third of these.[19] The higher the grade of eosinophilia, the more likely a travel-related diagnosis, particularly helminth infestation (eg, strongyloidiasis, filariasis, hookworm, schistosomiasis, cutaneous larva migrans and ascariasis).[19] However, less than half of those with helminth infestation in the total population had blood eosinophilia. The absence of eosinophilia does not exclude parasites, as eosinophilia generally occurs only during the tissue invasive stages of worm development.
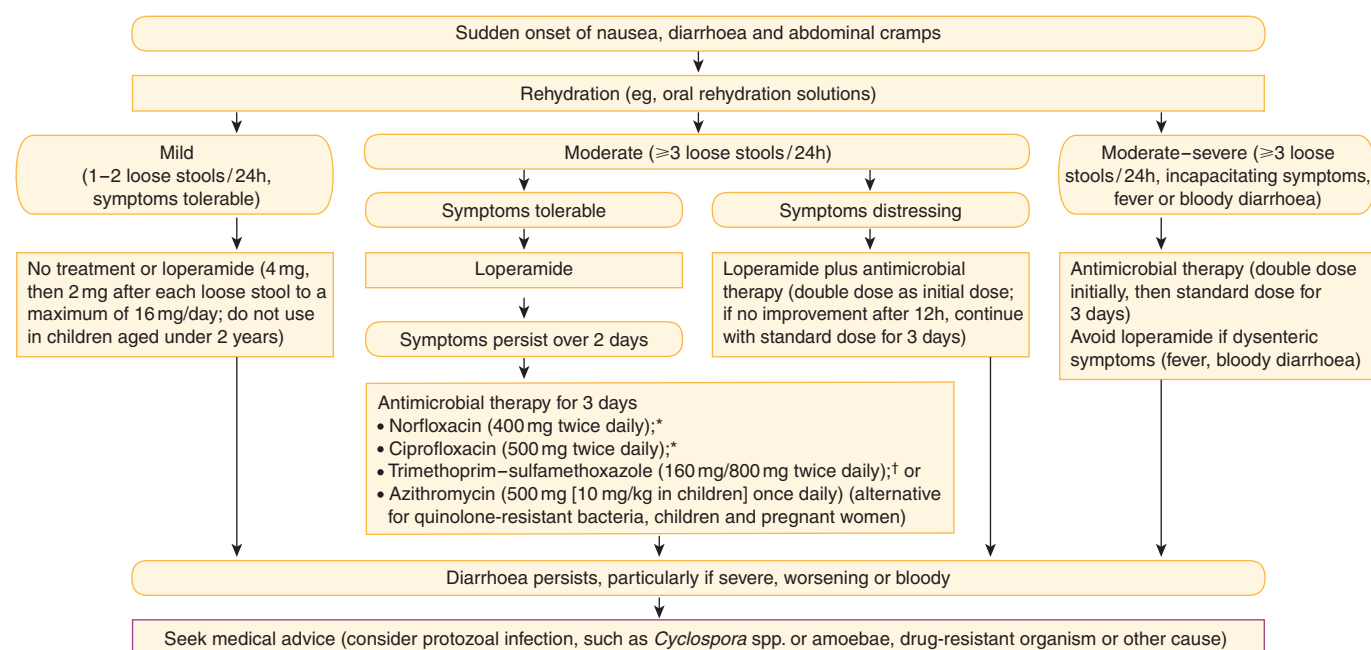
Initial investigation of eosinophilia should include three stool examinations for ova, cysts and parasites to detect the more common gastrointestinal helminths, whose eggs may be excreted intermittently. Patients may report passing worms in faeces or coughing them up, and any macroscopically visible worms (likely to be ascarids or tapeworm) should be sent for laboratory identification. Specific serological testing is available for schistosomiasis, strongyloidiasis, filariasis, echinococcosis, toxocariasis and angiostrongyliasis.

Initial empirical treatment with a broad-spectrum anthelmintic is reasonable after stool collection. Options include mebendazole, pyrantel and albendazole.[9] As the first two are not effective for strongyloidiasis, tapeworm infection or schistosomiasis, a specific diagnosis should be attempted if the eosinophil count does not return to normal and treated appropriately. Albendazole is available from the Pharmaceutical Benefits Scheme on authority for specific indications.

Strongyloidiasis

Infection is acquired by penetration through intact skin of filariform larvae of *Strongyloides stercoralis* in faecally con-

---

8: Self-management of acute travellers' diarrhoea

Sudden onset of nausea, diarrhoea and abdominal cramps

Rehydration (eg, oral rehydration solutions)

Mild (1–2 loose stools/24h, symptoms tolerable)

No treatment or loperamide (4 mg, then 2 mg after each loose stool to a maximum of 16 mg/day; do not use in children aged under 2 years)

Moderate (≥3 loose stools/24h)

Symptoms tolerable

Loperamide

Symptoms persist over 2 days

Antimicrobial therapy for 3 days
• Norfloxacin (400 mg twice daily);*
• Ciprofloxacin (500 mg twice daily);*
• Trimethoprim–sulfamethoxazole (160 mg/800 mg twice daily);† or
• Azithromycin (500 mg [10 mg/kg in children] once daily) (alternative for quinolone-resistant bacteria, children and pregnant women)

Symptoms distressing

Loperamide plus antimicrobial therapy (double dose as initial dose; if no improvement after 12h, continue with standard dose for 3 days)

Moderate–severe (≥3 loose stools/24h, incapacitating symptoms, fever or bloody diarrhoea)

Antimicrobial therapy (double dose initially, then standard dose for 3 days)
Avoid loperamide if dysenteric symptoms (fever, bloody diarrhoea)

Diarrhoea persists, particularly if severe, worsening or bloody

Seek medical advice (consider protozoal infection, such as *Cyclospora* spp. or amoebae, drug-resistant organism or other cause)

*Contraindicated in children under 16 years and pregnant women. However, for children with severe diarrhoea, the benefits of quinolones used for 1–3 days may outweigh the risks.
†Although resistance to trimethoprim–sulfamethoxazole is widespread in some areas, prescription is less restricted for these antibiotics than for quinolones.

9: Suggested investigation and management of persistent diarrhoea in a returned traveller

Diarrhoea persisting over 14 days

History and examination
- Travel history and symptom onset in relation to travel
- Antimicrobial therapy in previous month (consider *Clostridium difficile*), other medications, laxative abuse
- Underlying conditions (eg, HIV infection)
- Fever (consider malaria)
- Stool quality (eg, semiformed, bulky, greasy and malodorous suggests malabsorption; bloody stools suggest amoebiasis, inflammatory bowel disease)
- Relationship of symptoms to food (eg, lactose, fatty foods)
- Weight loss
- Associated symptoms (eg, extraintestinal manifestations of inflammatory bowel disease)

Investigations
- Microscopy and culture of three stool samples
- Test for *Clostridium difficile* toxin
- Full blood count, blood film and differential, erythrocyte sedimentation rate, serum electrolyte levels, renal and liver function tests
- Consider serological tests for parasites (strongyloidiasis, amoebiasis, schistosomiasis) and coeliac disease; blood cultures; malaria blood films; thyroid function tests

Positive test results*

Appropriate treatment

Negative test results

Empirical therapy
- Antibacterial: norfloxacin (400 mg twice daily for 5 days)† or
- Antigiardial: tinidazole (2 g [50 mg/kg in children] as single dose) or metronidazole (400 mg [5–10 mg/kg in children] three times daily for 5-7 days)
  (Administer antibacterial therapy first if both are to be tried)

No response

Modify diet (avoid all lactose or pre-treat with lactase; reduce caffeine intake; increase dietary bulk)

Symptoms persist

Refer for gastrointestinal assessment to exclude non-infectious causes (eg, bowel malignancy, especially if patient aged over 50 years)

No cause found

Treat symptomatically and reassure of good long-term prognosis

* Often *Blastocystis hominis* is the only positive finding, but its pathogenicity is controversial. If symptoms persist after other causes have been excluded, a trial of therapy for this organism may be indicated: metronidazole 400 mg (10 mg/kg in children) three times daily for 7–10 days or trimethoprim–sulfamethoxazole 160/800 mg orally twice daily for 7 days.

† In children, trimethoprim–sulfamethoxazole (2.5–10 mL [concentration, 40/200 mg per 5 mL] twice daily) or azithromycin (10 mg/kg once daily) for 5 days.

10: Case history — genital ulceration two years after a trip across Africa

Presentation: A 28-year-old woman presented with a non-healing genital ulcer. She had travelled overland through Africa two years previously.
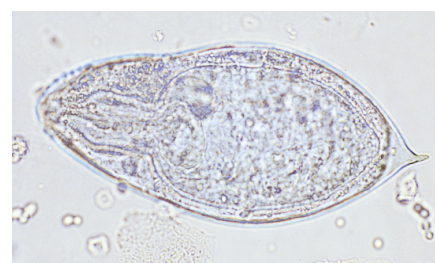
Examination: An indurated 1 cm ulcer was present on the inner aspect of the left labia majoris.

Investigations: Polymerase chain reaction tests were negative for herpes simplex, gonorrhoea and chlamydia; syphilis serological testing and a swab for *Haemophilus ducreyi* (chancroid) were also negative. Skin biopsy of the lesion revealed a granuloma surrounding a schistosome egg (pictured). *Schistosoma haematobium* eggs were detected in terminal urine collected between midday and 2 pm (pictured). Eosinophil count in blood was 1.2 x 10⁹/L (reference range, < 0.6 x 10⁹/L).

Serological testing by indirect hemagglutination assay was positive for schistosomiasis (titre, 512).

Management: She was treated with praziquantel and six months later remained well. Her asymptomatic travelling companions were found to be positive for schistosomiasis on serological screening and were also treated.
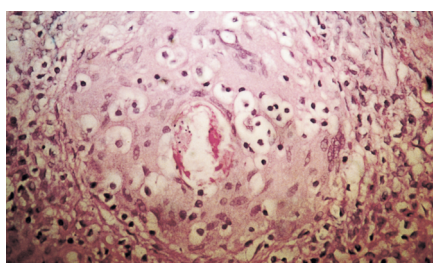
Biopsy of genital ulcer, showing granulomatous reaction surrounding a schistosome egg (haematoxylin and eosin stain; original magnification, x 400).

- Schistosomal infestation may persist and present long after leaving an endemic area.
- Attack rates for infection are high, and diagnosis in a traveller should prompt screening of all fellow travellers, regardless of presence or absence of symptoms.
- Serological tests are the most sensitive method of screening, but are not species-specific. Indirect hemagglutination titres ≥ 64 suggest infection, although antibodies may take months or years to fall to low or undetectable levels.

Schistosoma haematobium *egg in urine sediment (phase contrast; original magnification x 100).*

- Diagnosis is complicated by the long pre-patent interval (time between infection and detection of eggs in urine or faeces). As antibodies develop against egg antigens, not adult worms, antibody testing gives false negative results if done too early. Tests may need to be repeated for up to six months after exposure.
- Identification of schistosome eggs in terminal urine or faeces is required to differentiate the species causing infection. At least two specimens are recommended.

taminated soil. Autoinfection may occur, and no intermediate host is necessary. Infection can persist for decades and occasionally presents as hyperinfection syndrome after immunosuppression.

Strongyloidiasis may be diagnosed with stool microscopy and special culture techniques, as well as serological testing. Effective treatment includes ivermectin, albendazole and thiabendazole.[9] Repeat or prolonged treatment may be necessary in patients who are immunosuppressed.

Schistosomiasis

Schistosomiasis detection is increasingly common in Australian travellers.[20] Although the parasite is endemic in Africa, the Middle East, Latin America, and limited areas in Asia, the greatest risk of infection appears to come from exposure to freshwater in Africa, especially Lake Malawi. Infection results from penetration of intact skin by larvae liberated from snail intermediate hosts.

Most infected travellers are asymptomatic and at low risk of complications because of low parasite burdens, although end-organ damage may result from egg deposition. Other presentations include swimmers' itch (a papular pruritic dermatitis at the time of exposure) and Katayama fever, which is associated with the migration of schistosome larvae throughout the body (symptoms include fever, chills, malaise, headache, cough, abdominal pain, diarrhoea, urticaria, and occasionally neurological disorders).

Once egg deposition begins, clinical features include haematuria, haematospermia, urgency, frequency, terminal dysuria, salpingitis, prostatitis and genital ulcers (case history, Box 10). More serious but rare complications are paraparesis, paraplegia and mass cerebral lesions. Immigrants and refugees from endemic countries are likely to have much heavier infection loads and may present with the complications of chronic fibrosis, such as ureteric obstruction and portal hypertension.

The standard treatment is praziquantel (20 mg/kg orally for two doses, four hours apart). About 10%–15% of patients require re-treatment.

Skin and soft tissue infections

Although not usually serious or life-threatening, skin and soft tissue infections are common. Most common are the infections also seen in non-travellers, such as cellulitis, furunculosis, folliculitis and dermatophyte infections. Other infections are more exotic. For example, among 269 patients who presented to a Paris tropical disease unit with travel-associated dermatosis, 53% had an imported tropical disease.[21] Most common among these were cutaneous larva migrans (25%; Box 11), pyodermas (18%), pruritic arthropod-reactive dermatitis (10%), myiasis (9%), tungiasis (6%), urticaria (5%), fever and rash (eg, dengue) (4%) and cutaneous leishmaniasis (3%; Box 12).

Non-healing skin lesions and furuncles in travellers from Africa and South America should be examined closely, as myiasis or infestation with fly larvae (eg, *Cordylobia* or African tumbu or putsi fly) is possible. The larvae are best removed by applying petroleum jelly in a toothpaste cap.

11: Cutaneous larva migrans in a traveller to Malaysia

Cutaneous larva migrans is caused by the penetration through intact skin of larval animal hookworms. Diagnosis is predominantly clinical. Treatment is often necessary because of intense pruritus, long duration (over a year) and complications, such as impetigo and allergic reactions. Therapy comprises ivermectin, albendazole or thiabendazole.[22]

12: Mucocutaneous leishmaniasis acquired in South America

Cutaneous leishmaniasis is relatively common after sandfly bites in travellers returning from South and Central America, the Mediterranean and the Middle East. Mucous membranes and viscera may be involved.

They burrow into the cap and can then be extracted with forceps, the whole process usually taking less than an hour.

Sandfleas, or "jiggers", usually burrow into the skin of the soles of the feet and around toenails, causing itchy lumps. Prevention is by wearing shoes, avoiding sandals and bare feet. Jiggers are best shelled out, being careful not to break the developing egg sac of the female flea.

The asymptomatic returned traveller

Returned travellers often present requesting a "check-up". Cost-effectiveness studies have yet to demonstrate the benefits of widespread screening for returned travellers.[23]

Evidence-based recommendations

- Fever in a traveller within three months of departure from a malaria-endemic area is a medical emergency and should be investigated with thick and thin blood films to exclude malaria; films should be repeated at least twice if negative and symptoms persist[5] (E3).
- The most important factors determining survival in falciparum malaria are early diagnosis and prompt initiation of appropriate treatment[5] (E3).
- Antimotility agents, such as loperamide, are safe and efficacious for mild to moderate cases of travellers' diarrhoea in adults[16] (E1); most acute cases of this diarrhoea respond to a single dose or three-day course of antimicrobial therapy[16] (E3).
- Persistent diarrhoea in returned travellers is less likely to have an infective cause than acute diarrhoea and require investigation[18] (E3).
- Post-exposure rabies treatment is effective and should be considered for all travellers with potential exposure[24] (E1).

A careful history of potential exposures should include illnesses while away, sexual exposure, food, swimming in rivers and lakes, contact with animals, use of illicit drugs, compliance with antimalarial prophylaxis, and pre-travel vaccinations. Physical examination depends on history, and more directed tests for follow-up of disease experienced while away may be required.

Risk wanes with time for most infections but persists for life for some diseases, including:

- Bacteria — *Mycobacterium leprae*, *Mycobacterium tuberculosis*, *Treponema pallidum*, *Rickettsia prowazekii* and *Salmonella typhi*;
- Viruses — hepatitis B, C and delta viruses, herpes simplex viruses, HIV 1 and 2 and HTLV-1;
- Protozoa — *Plasmodium malariae*, *Toxoplasma gondii*, *Trypanosoma cruzi* (Chagas' disease);
- Helminths — *Echinococcus granulosis*, *Strongyloides stercoralis*, *Taenia solium*, *Schistosoma* spp.; and
- Fungi: *Coccidioides immitis*, *Histoplasma capsulatum*.

Some of these infections may be latent and reactivated during immunosuppression.

Rabies

The incubation period of rabies is usually two to eight weeks but ranges from five days to 10 years. Although many animals can carry the virus, dogs are the most important vector for travellers. As rabies is fatal once symptoms develop, expert advice should be sought to determine whether post-exposure prophylaxis (available from public health units) is required in a returned traveller who reports a bite or scratch from a mammal in a rabies-endemic area. If doubt remains, rabies immunoglobulin and five doses of vaccine should be administered. If the person has had pre-exposure rabies vaccination, no rabies immunoglobulin and only two doses of vaccine are required. Many travellers are unaware of the need to obtain post-exposure prophylaxis within 24 hours if at all possible.

References

1. Steffen R, DuPont HL. Manual of travel medicine and health. Hamilton, BC: Decker, 1999.
2. Yung AP, Ruff T. Infections in returned travellers and immigrants. In: Yung AP, McDonald MI, Spelman DW, et al. Infectious diseases: a clinical approach. Melbourne: Royal Melbourne Hospital, 2001: 366-377.
3. Doherty JF, Grant AD, Bryceson ADM. Fever as the presenting complaint of travellers returning from the tropics. *Q J M* 1995; 88: 277-281.
4. MacLean JD, Lalonde RG, Ward B. Fever from the tropics. *Travel Med Advisor* 1994; May: 27.1-27.14.
5. O'Brien D, Tobin S, Brown G, Torresi J. Fever in returned travelers: review of hospital admissions for a 3-year period. *Clin Infect Dis* 2001; 33: 603-609.
6. Bryan J, Fa'afoi E, Forsyth S. Report of the Australian Malaria Register for 1992 and 1993. *Commun Dis Intell* 1998; 22: 237-245.
7. Isaacson M. Viral hemorrhagic fever hazards for travelers in Africa. *Clin Infect Dis* 2001; 33: 1707-1712.
8. Reyburn H, Behrens RH, Warhurst D, Bradley D. The effect of chemoprophylaxis on the timing of onset of Falciparum malaria. *Trop Med Int Health* 1998; 3: 281-285.
9. Therapeutic Guidelines Writing Group. Therapeutic guidelines: antibiotic. 11th ed. Melbourne: Therapeutic Guidelines Limited, 2000.
10. Barat LM, Bloland PB. Drug resistance among malaria and other parasites. *Infect Dis Clin North Am* 1997; 11: 969-987.
11. Jelinek T. Dengue fever in international travelers. *Clin Infect Dis* 2000; 31: 144-147.
12. Looke DFM, Mills DJ, Kass RB, et al. The "welcome home" letter and questionnaire as a valuable quality assurance tool for an Australian traveller's medical clinic. In: Lobel HO, Steffen R, Kozarsky PE. Travel medicine 2. Proceedings of the Second Conference On International Travel Medicine; Atlanta, Ga USA, 1991 May 9-12. Atlanta: International Society of Travel Medicine, 1991: 287-289.
13. Hill DR. Health problems in a large cohort of Americans travelling to developing countries. *J Trav Med* 2000; 7: 259-266.
14. Cobelens FGJ, van Deutekom H, Draayer-Jansen IWE, et al. Risk of infection with *Mycobacterium tuberculosis* in travellers to areas of high endemicity. *Lancet* 2000; 356: 461-465.
15. Rieder HA. Risk of travel-associated tuberculosis. *Clin Infect Dis* 2001; 33: 1393-1396.
16. Ericsson CD, DuPont HL. Travelers' diarrhea: approaches to prevention and treatment. *Clin Infect Dis* 1993; 16: 616-624.
17. Shlim DR, Hoge CW, Rajah R, et al. Is *Blastocystis hominis* a cause of diarrhea in travellers? A prospective controlled study in Nepal. *Clin Infect Dis* 1995; 21: 97-101.
18. DuPont HL, Capsuto EG. Persistent diarrhea in travellers. *Clin Infect Dis* 1996; 22: 124-128.
19. Schulte C, Krebs B, Jelinek T, et al. Diagnostic significance of blood eosinophilia in returning travelers. *Clin Infect Dis* 2002; 34: 407-411.
20. Robson JMB, Htut T. Schistosomiasis — a need for increasing vigilance. *Commun Dis Intell* 1994; 18: 652-654.
21. Caumes E, Carriere J, Guermonprez G, et al. Dermatoses associated with travel to tropical countries. A prospective study of the diagnosis and management of 269 patients presenting to a tropical disease unit. *Clin Infect Dis* 1995; 20: 542-548.
22. Caumes E. Treatment of cutaneous larva migrans. *Clin Infect Dis* 2000; 30: 811-814.
23. MacLean JD, Libman M. Screening returned travellers. *Infect Dis Clin North Am* 1998; 12: 431-433.
24. World Health Organization. Recommendations on rabies postexposure treatment and the correct technique of intradermal immunization against rabies. Geneva: WHO, 1996.   ❏