

Fever in the returning traveller

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Abstract

Travel-related infections are becoming more common as travel abroad becomes easier. Whilst most imported infections will have recognisable features some of the more obscure will be less familiar to the clinician. A detailed travel history including all stopovers is vital as is a thorough examination. Falciparum malaria is a medical emergency and prompt treatment is essential. Emerging infections such as SARS and avian influenza provide new challenges in diagnosis for the admitting team.

Key words

Fever, travel, infection

Key Points

- 1 Identify and treat the potentially fatal diseases
- 2 Most causes will not require immediate action and time can be taken to make a diagnosis
- 3 A travel history does not automatically mean a travel-related illness
- 4 Fever is not always caused by infections
- 5 Some infections are highly contagious and need immediate isolation

Introduction

Travel abroad is not only becoming more common but people are travelling further, more regularly and being more adventurous. In 2003 more than 61 million trips abroad were made by UK residents.¹ Travel has become more accessible over recent years with cheaper flights and package deals encouraging groups of travellers such as the disabled and immunocompromised to visit places that were previously inaccessible.² Some groups are vulnerable for other reasons such as Haj pilgrims who have experienced meningococcal disease outbreaks.³ Antibiotic resistance patterns may also vary: For example the frequency of meningitis due to penicillin-resistant *Streptococcus pneumoniae* has increased in recent years⁴ and these are seen more commonly outside of the UK.

Between 2% and 12% of travellers suffer from a febrile illness while away or on return,⁵ with traveller's diarrhoea affecting over 50% of travellers to some destinations.⁶ Gastrointestinal illness is the most commonly reported travel-associated infection in England, Wales, and Northern Ireland¹ though many

people who return from abroad unwell never present to a doctor. A returning traveller with fever may not necessarily have an exotic infection. Some, however, may have acquired an infection not commonly encountered in the UK. The list of possible causes of infection in a returning traveller is long. This review aims to highlight the serious and a few of the more recent problems.

Clinical assessment

As with any illness the history and examination remain vitally important. A range of diagnostic tests may be available but they often take time and treatment may need to be initiated before the results become available.

In establishing a travel history a number of key questions should be asked:

- Which country (or countries) has been visited and what are the dates of arrival and departure?
- Was the visit to an urban or rural setting?
- What kind of accommodation?
- Any significant pastimes – e.g. healthcare, animals, water-sports?
- Any precautions taken – vaccines, prophylaxis?

Timing is very helpful in establishing a diagnosis (see table I). Over 90% of infections related to short-term travel present within six months of return.⁷ However, a travel history may be relevant in someone who has not travelled for months or even years. In many cases it is also essential to take a sexual history; people often behave differently on holiday than they would at home.⁸

Immunosuppression associated with HIV infection or following transplantation increases susceptibility to central nervous system (CNS) infections and in the context of travel this could represent an increased risk of acquiring malaria, microsporidiosis, leishmaniasis, or African trypanosomiasis.⁹

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Fever in the returning traveller

Short	Incubation range	Time most infections clinically apparent
Anthrax	1 – 7 days	
Cholera	4hrs – 5 days	2-3 days
Diphtheria	2-5 days	Occasionally longer
Dengue	3-14 days	4-7 days
Food poisoning	4hours – 10 days	
Gonorrhoea	2-7 days	
Haemorrhagic fevers		
Ebola	2-21 days	
Lassa	6-21 days	
Marburg	3-9 days	
Influenza	1-3 days	
Legionnaires disease	2-10 days	5-6 days
- Non-pneumonic- (Pontiac fever)	5-66 hours	24-48 hrs
Lyme Disease – EM	3-32 days	7-10 – May present late
Melioidosis	2 days – many years	
Polio	3-35 days	7-14 days
SARS	4-6 days	
Travellers diarrhoea	10hrs – 10 days	3-4 days
Typhoid/paratyphoid	3 – 30 days	8-14 days
West Nile fever	3-12 days	
Yellow fever	3-6 days	
Medium		
Amoebiasis	Days – months	2-4 weeks
Brucella	4 – 8 weeks	Occasionally several months
Chlamydia	1-2 weeks	
Hepatitis A	2-7 weeks	28-30 days
Hepatitis E	2-8 weeks	26-42 days
Leishmaniasis – cutaneous	1 week - months	
-visceral	1 week – years	
Malaria –		
<i>P. falciparum</i>	1 - 2 weeks	May be much longer, eg if prophylaxis taken
<i>P. vivax/ovale</i>	1 – 2 weeks	
<i>P. malariae</i>	1 – 4 weeks	
Syphilis	1 - 14 weeks	3 weeks
Tuberculosis	2-10 weeks	
Typhus	1-22 weeks	
Long		
Filiariasis	12 – 52 weeks	
HIV seroconversion	4 – 12 weeks	
Hepatitis B	7 – 12 weeks	8-13 weeks

Table I. Incubation periods of selected infectious diseases

Although any prophylaxis or prior immunisations should be noted, an infection should not be ruled out entirely on this basis as 100% efficacy is rarely achieved. In terms of prophylaxis, the actual amount taken, rather than the amount prescribed should be established. Past medical history such as diabetes may be relevant as is a history of drinking excess alcohol, smoking and injected substances. Fever can present in many different forms such as high or low grade, constant, swinging or circadian.

Other associated features such as sweats, rash, nausea, vomiting, diarrhoea, constipation, meningism, cough, myalgia or arthralgia should be noted.

A thorough examination must be carried out and will obviously focus on any areas highlighted by the history. If there are no clues from the history, this should include examining for rashes, lymphadenopathy and organomegaly (spleen and liver in particular).

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Investigations

All patients should have a full blood count, routine chemistry, blood and urine cultures. Other useful tests will depend on the clinical features but include liver function tests, malaria screen, stool culture, chest X-ray and specific serology if a diagnosis is suspected. In any case it may be worth taking blood for serology that can be processed at a later date along with convalescent sera when potential diagnoses are clearer. Ultrasound and CT scanning may be helpful for abdominal pathology such as amoebic liver abscesses.

Arthropod-borne diseases

Malaria

Occurrence

Africa, Asia, Latin America, and regions of the South Pacific. Has also been reported in people who have not travelled but have been near to an airport.¹⁰

Causative organisms

Members of the *Plasmodium* species. *Falciparum* is the most serious of the human malarias. Spread by *Anopheles* mosquitoes.

Clinical Features

Fever, cough, diarrhoea, respiratory distress and headache. Later, coagulation defects, shock, liver failure, acute encephalopathy, pulmonary and cerebral oedema, coma and death may be encountered.

Diagnosis

Demonstration of malaria parasites in blood thick and thin films. Repeat films should be taken every six to 12 hours for 36–48 hours before malaria can be confidently excluded from a patient with a fever from an endemic region.⁷ Antigen detection dipstick methods are not yet commonly available, but are becoming more so.

Treatments

Quinine remains the most widely used anti-malarial drug in the treatment of *falciparum* malaria. If the patient is seriously ill or has a parasite count >2%, quinine should be given intravenously. Current regimens can be found in the British National Formulary.

Notes

There are approximately 2000 cases of malaria imported into the UK each year. Prophylactic medications are recommended for individuals travelling to endemic regions but compliance is poor and it is possible to acquire malaria despite appropriate prophylaxis. Case-fatality rates among untreated children and non-immune adults can be 10–40% or higher. The non-*falciparum* human malarias (*vivax*, *malariae* and *ovale*) are not generally life-threatening. 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.

Further information

http://www.hpa.org.uk/infections/topics_az/malaria/men u.htm

Dengue

Occurrence

Most tropical countries, rarely in Queensland, Australia¹¹

Causative organism

An arbovirus spread by *Aedes* mosquitoes

Clinical Features

Sudden onset, fever, headache, arthralgia, myalgia, retro-orbital pain, anorexia, GI disturbance and rash. Mortality is low except in Dengue Haemorrhagic Fever.

Diagnosis

Serologic testing

Treatments

No specific antiviral therapy is available, treatment is supportive

Notes

Dengue haemorrhagic fever is characterised by increased vascular permeability, hypovolaemia and abnormal blood clotting mechanisms.

West Nile fever

Occurrence

Africa, Europe, the Middle East, west and central Asia, and more recently, North America.

Causative organism

An arbovirus spread by *Culex* spp mosquitoes.

Clinical Features

Sudden onset of malaise, headache, anorexia, nausea, vomiting, retro-orbital pain, myalgia, lymphadenopathy and rash. Self-limiting in the majority.

Diagnosis

Serology

Treatments

Supportive

Notes

Symptoms typically last 3–6 days.¹² The virus is transmitted from birds to man by mosquitoes.

Further information:

http://www.hpa.org.uk/infections/topics_az/west_nile/men u.htm

Yellow fever

Occurrence

Sub-Saharan Africa and tropical South America

Causative organism

An arbovirus spread by various mosquitoes including *Aedes* spp.

Clinical Features

Sudden onset of fever and headache, which may be followed by widespread haemorrhage and jaundice. Case-fatality up to 40% in outbreaks.

Diagnosis

Virus isolation in the blood or serology.

Treatments

Supportive

Notes

Rare in returning travellers.

Food, water-borne and close association diseases**Traveller's diarrhoea****Occurrence**

Almost anywhere. Especially common where standards of hygiene are low.

Causative organism

Many possible including *Escherichia coli*, *Shigella* spp., *Salmonella* spp., *Campylobacter* spp., *Vibrio parahaemolyticus* (in Asia), rotavirus and protozoa (*Giardia*, *Cryptosporidium* and *Cyclospora* spp., and *Entamoeba histolytica*)

In 50% no cause will be identified.¹³

Clinical Features

Diarrhoea, may be bloody, abdominal cramps

Diagnosis

Stool culture

Treatments

Rehydration is usually the only treatment required but severe dehydration is rarely encountered.¹⁴ In severe or prolonged cases a fluoroquinolone with or without loperamide can be used.¹³

Notes

1. It should be noted that there is increasing resistance to the fluoroquinolones in some parts of the world, and that in some cases, for example diarrhoea caused by VTEC *E. coli* antibiotics may actually worsen the clinical situation.
2. Typhoid and Paratyphoid are very common in some parts of the world eg Nepal and commonly present with headache, malaise, anorexia and constipation.

Cholera**Incubation**

4 hours – 5 days

Occurrence

Africa, Asia, the Middle East, Peru and some countries of Central America.

Causative organism

Some serogroups of *Vibrio cholerae*

Clinical Features

Sudden onset of profuse painless watery diarrhoea with nausea and vomiting early in the course. Severe life-threatening dehydration and circulatory collapse can follow.

Diagnosis

Stool culture

Treatments

Rehydration is the mainstay of therapy.

Notes

The oral vaccine does not give complete protection.

Legionnaires' disease**Incubation**

2 – 10 days

Occurrence

Seen in UK and abroad but commonly holiday accommodation where there is intermittent use of facilities such as showers or air conditioning systems

Causative organism

Most commonly caused by *Legionella pneumophila* serogroup 1.

Clinical Features

Anorexia, malaise, myalgia, headache, confusion and non-productive cough.

Diagnosis

Send urine for *Legionella* antigen and take a serology sample for antibody testing.

Treatments

Fluoroquinolones such as ciprofloxacin or levofloxacin are now treatment of choice,¹⁵ although erythromycin is still commonly used.

Notes

More common in males and people with pre-existing lung disease.

Viral haemorrhagic fevers**Occurrence**

Mainly confined to outbreaks seen in central Africa but also seen in South America and Asia.

Causative organism

Filoviridae viruses – Marburg and Ebola, Arenavirus – Lassa

Clinical Features

Severe illness, starts with fever, malaise, myalgia and headache followed by vomiting, diarrhoea and a rash.

Diagnosis

Serology

Treatments

Supportive for Ebola and Marburg.

Tribavirin reduces mortality in Lassa Fever.

Notes

Very rare in returning travellers. Immediate isolation if suspected; only take blood if absolutely essential.

Further information:

http://www.hpa.org.uk/infections/topics_az/VHF/ACDP_VHF_guidance.pdf

Blood-borne and sexually transmitted

5-67% of travellers engage in sexual activities with local inhabitants or fellow travellers who are not their regular sexual partners.^{16,17} Unprotected sexual intercourse puts travellers at an increased risk of acquiring HIV, hepatitis B, and hepatitis C infections and other sexually transmitted diseases. Acute hepatitis B is seen in less than 50% of those infected and presents with insidious onset of malaise, abdominal discomfort, nausea and vomiting. Jaundice frequently appears late.

New and emerging infections**SARS**

Severe Acute Respiratory Syndrome (SARS) was first seen in Guangdong Province in China in November 2002, and spread worldwide before being contained by 5 July 2003. It is caused by the SARS coronavirus (SARS CoV). As of January 2006 there have been no reported cases since May 2004. Patients with suspected or probable SARS need to be isolated, ideally in a negative pressure side room, and all healthcare workers who come into close contact with, examine or take samples from a potential SARS case should wear gloves, and a respirator or, if not available, a surgical mask.

Further information:

http://www.hpa.org.uk/infections/topics_az/SARS/men u.htm

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WHO case definitions for suspected and probable SARS

SARS is suspected in patients with:

- High fever (> 38°C)
- One or more respiratory symptoms (such as cough, shortness of breath, or breathing difficulty), and
- Close contact with a person previously diagnosed with **SARS** (having cared for, lived with, or had direct contact with bodily secretions of a person with **SARS**).
- **SARS** is probable when a patient meets the criteria of a suspected case and there is radiological evidence of infiltrates consistent with pneumonia or respiratory distress syndrome

Avian influenza

Avian influenza is a disease of birds caused by influenza A viruses. Sometimes people exposed to infected birds may themselves be infected by avian influenza. The H5N1 subtype of avian influenza very rarely passes from poultry to man. In the rare events where H5N1 has jumped from poultry to humans it has caused severe illness with almost 50% mortality. According to the Health Protection Agency as of November 2005 there had been no cases of avian influenza in travellers and no efficient transmission of infection from person to person. The risk to travellers from avian influenza remains very low.

Treatment with oseltamivir has been found to be helpful but for the latest guidelines and affected countries see:

www.hpa.org.uk/infections/topics_az/influenza/avian/algorithm.htm

The **clinical assessment criteria of avian influenza** are:

- fever 38 °C or above **OR** history of fever
- AND**
- respiratory symptom (e.g. cough, dyspnoea or severe unexplained illness)
- AND**
- travel to a high-risk area for avian influenza H5N1 within seven days of onset of symptoms

PLUS

- close contact (less than one metre) with live or dead domestic fowl, wild birds or swine in any setting including bird markets
- OR**
- Close contact with other cases of severe respiratory distress or unexplained death from the high risk area
- OR**
- Part of Health Care Worker cluster of severe unexplained respiratory distress
- OR**
- Laboratory worker with potential exposure to influenza

Useful web addresses

Health protection agency

<http://www.hpa.org>

World Health Organisation

<http://www.who.int/en>

Hospital for Tropical Diseases

<http://thehtd.org>

National Centre for Infectious Diseases (USA)

<http://www.cdc.gov/travel/>

References:

1. Infections; LHPACf. Foreign travel-associated illness - England, Wales, and Northern Ireland - Annual Report 2005; 2005.
2. Habib-N-A B-R-H. Respiratory infections in the traveler. *Curr Opin Pulm Med*. 2000; **6**(3): 246-9.
3. MacLennan JM UR, Obaro S, Griffiths D, *et al*. Carriage of serogroup W-135, ET-37 meningococci in The Gambia: implications for immunisation policy? *Lancet*. 2000; **356**(9235): 1078.
4. Temime-L B-P-Y, Valleron-A-J, Guillemot-D. Penicillin-resistant pneumococcal meningitis: high antibiotic exposure impedes new vaccine protection. *Epidemiol-Infect*. 2005; **133**(3): 493-501.
5. Steffen R, DuPont H. Manual of travel medicine and health.: Hamilton, BC: Decker; 1999.
6. Al-Abri SS, Beeching NJ, Nye FJ. Traveller's diarrhoea. *Lancet Infect Dis*. 2005 Jun; **5**(6): 349-60.
7. Looke DFM, Robson JMB. *Infections in the returned traveller MJA* 2002; **177**(4): 212-9.
8. Matteelli A, Carosi G. *Sexually Transmitted Diseases in Travelers clin Infect Dis*. 2001; **32**: 1063-7.
9. Walker M, Kublin JG, Zunt JR. Parasitic central nervous system infections in immunocompromised hosts: malaria, microsporidiosis, leishmaniasis, and African trypanosomiasis. *Clin Infect Dis*. 2006; **42**(1): 115-25.
10. Thang HD, Elsas RM, Veenstra J. Airport malaria: report of a case and a brief review of the literature. *Neth J Med*. 2002 Dec; **60**(11): 441-3.
11. Jelinek T. Dengue fever in international travelers. *Clin Infect Dis*. 2000; **31**: 144-7.
12. Murray S, Weir E. *West Nile virus CMAJ*. 2005; **173**(5): 484.
13. Lima AA. Tropical diarrhoea: new developments in traveller's diarrhoea. *Curr Opin Infect Dis*. 2001 Oct; **14**(5): 547-52.
14. Ericsson CD. Travellers' diarrhoea. *Int J Antimicrob Agents*. 2003 Feb; **21**(2): 116-24.
15. Sabrià M, Pedro-Botet ML, Gómez J, *et al*. Fluoroquinolones vs Macrolides in the Treatment of Legionnaires Disease. *Chest*. 2005; **128**(3): 1401-6.
16. Spira AM. Preparing the traveller. *Lancet*. 2003; **361**(9366): 1368.
17. Salit I, Sano M, Boggild A, *et al*. Travel patterns and risk behaviour of HIV-positive people travelling internationally. *CMAJ*. 2005; **172**(7): 884-8.