Assessment of returning travellers with fever

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Abstract

Millions of people travel to the tropics each year and a significant minority of them become ill, either during their stay or shortly after their return. Most have mild, self-limiting illnesses, but a few have a life-threatening condition. This article outlines how to evaluate fever in the returning traveller and discusses important infection control and public health measures. A detailed travel history, which takes into account travel destinations, specific activities and risk factors in relation to the onset of symptoms, is essential for constructing a comprehensive list of differential diagnoses and guiding appropriate investigations. Importantly, all travellers returning from the tropics with a fever should be investigated for malaria.

Keywords Fever aetiology; fever assessment; fever diagnosis; imported fever; MRCP; travel; traveller

Key points

- Always remember to take a travel history in any patient presenting with a fever or history of fever
- Think why this *person*, from this *place*, is developing these *symptoms* at this *time*
- A malaria rapid diagnostic test and malaria film should be requested in all patients returning from the tropics with a history of fever. A positive malaria result should be acted upon on the same day
- Assess the risk of a transmissible infection and isolate the patient where appropriate (fever + diarrhoea or respiratory symptoms or rash)
- Patients with a febrile illness within 21 days of travel to a country where viral haemorrhagic fever (VHF) is endemic should be isolated and have a VHF risk assessment performed
- Antimicrobial resistance is an emerging global problem. Travel outside northern Europe and Australasia and hospitalization is associated with an increased risk of antimicrobial resistance. If bacterial infection is suspected, discuss antibiotic choices with your local microbiologist

Why is this topic important?

In 2015, UK residents made 10.1 million visits to countries other than Europe and North America.[1] In addition in 2015, there were 36.1 million visits to the UK from overseas residents.[1] Up to 70% of travellers to developing countries report health problems, and 8–15% are unwell enough to seek medical attention, with fever a common complaint.[2]

Although many of these patients have self-limiting illnesses, for example influenza, an important minority have a more serious tropical infection that, if missed, could become life-threatening (as with malaria – Case 1) or have significant public health implications (as with enteric fever – Case 2). The difficulty is in identifying these low-frequency events. This paper provides a pragmatic approach to the assessment of fever in the returned traveller. Additional telephone advice is available, 24 hours a day, to support with further evaluation of these patients (see Sources of help box).

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How to take a travel history

Table 1 outlines the key themes that should be covered when taking a comprehensive travel history.

Travel destination: the risk of acquiring an infection while travelling varies according to the country visited (Table 2), the local environs (urban or rural) and the activities or exposures encountered (Table 3). Knowledge of the geographical distribution and relative incidence of infectious diseases is important in assessing these patients and can aid clinicians in constructing their differential diagnosis. For example, among travellers returning from South-East Asia or the Caribbean with a fever, dengue is an important differential diagnosis, whereas enteric fever is more likely in travellers from South Asia.[2] In contrast, malaria remains the most important single cause of fever in travellers returning from sub-Saharan Africa.[2]

As seen with the recent Ebola outbreak in West Africa or the Middle East respiratory syndrome coronavirus (MERS-CoV) outbreak, travellers can rarely present with life-threatening infections that if missed have significant public health consequences. Travellers whose symptoms started within 21 days of travel to sub-Saharan Africa, in particular West and Central Africa, should have a more detailed risk assessment for viral haemorrhagic fevers (VHFs) (see Case 1). It should be noted, however, that some VHFs, in particular Crimean–Congo haemorrhagic fever, have a more global distribution. It is often worth asking the patient whether they are aware of any local outbreaks (e.g. Ebola, *Legionella*) while they were travelling, or local areas of particularly high endemic risk (e.g. for

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Case 1. Malaria

A 41-year-old man presented to a district hospital with a 48-hour history of fever, headache and myalgia. Three days earlier, he had returned from Nigeria, where he had been visiting friends and relatives. At triage, he was febrile (39°C) and tachycardic (122 beats per minute), with a normal blood pressure. His Glasgow Coma Scale score was 15/15 and his respiratory rate 24 breaths per minute, and he had normal oxygen saturation on room air.

Given his recent travel to West Africa, he was identified as being at risk of a viral haemorrhagic fever (VHF) and isolated in a side room. Because of concerns about infection risk, no initial investigations were sent. The patient was discussed with the National Imported Fever Service and, after a further risk assessment, personal protection measures were implemented. The patient had stayed in basic accommodation in an area endemic for Lassa fever. He denied contact with funerals, hospitals or unwell individuals, and reported no exposure to caves, mines, bats, primates or ticks. Given his geographical exposure, he was classified as a high possibility for VHF, the laboratory was informed, and an urgent test for malaria was performed.

His blood film revealed *Plasmodium falciparum* (parasitaemia 14%), and subsequent investigations revealed acute kidney injury (serum creatinine 312 micromol/litre). He was treated with intravenous artesunate and transferred to intensive care in a regional infectious diseases unit. Initial concerns about VHF led to unnecessary delays in making the diagnosis of malaria; fortunately, he made a full recovery.

Learning points

- The initial presenting symptoms and signs of many tropically acquired infections are often non-specific
- VHF is very rare in travellers. Travellers are far more likely to have malaria or another infection. All returning travellers with fever or history of fever should be tested for malaria
- A VHF risk assessment should be performed in travellers with a fever >37.5°C whose symptoms started within 21 days of travel to a VHF-endemic area (see Sources of help box). Specifically, ask about the following: (1) contact with individuals with known or strongly suspected disease; (2) travel to area with a known outbreak; (3) living or working in basic rural conditions in a Lassa-endemic region; (4) visits to caves or mines, or contact with bats, primates or antelopes (Ebola, Marburg); and (5) tick bites, crushed ticks or attendance at animal slaughter (Crimean–Congo haemorrhagic fever)
- Screening for VHF should prompt the use of appropriate personal protective equipment (see Sources of help box) but should not delay investigations. Any delay in the diagnosis of falciparum malaria can lead to serious and sometimes fatal consequences
- Any patient thought to be at risk of VHF should be discussed with the National Imported Fever Service (see Sources of help box).

Case 2. *Salmonella typhi.*

A 34-year-old man returned to the UK after spending 4 weeks visiting his family in Bangladesh. He was up to date with travel vaccinations, including typhoid and hepatitis A. One week before his return, he had developed a febrile illness and had been treated for malaria, with no improvement. After further blood tests, was told he had typhoid and was treated with ciprofloxacin.

On arrival home, he presented to hospital with fever, headache and a dry cough. He had a temperature of 39.0°C and a respiratory rate of 28 breaths per minute. Although tachycardic, he had an adequate blood pressure. His chest was clear and he had 2 cm hepatomegaly. Investigations revealed a normal differential white count, normal renal function, mildly raised transaminases and a clear chest radiograph. A provisional diagnosis of enteric fever was made, and his antibiotic was changed to intravenous ceftriaxone. He gradually improved.

Two sets of blood cultures taken before changing the antibiotic were sterile, so a bone marrow aspirate was performed. Bone marrow cultures confirmed the presence of *Salmonella typhi*, resistant to ciprofloxacin. Following 3 days of intravenous ceftriaxone, treatment was changed to oral azithromycin. He completed 14 days of effective therapy.

Learning points

- Enteric fever is an uncommon but important cause of fever, particularly in travellers returning from Asia
- Vaccination provides incomplete protection against *Salmonella Typhi* and none against *Salmonella paratyphi*
- Many resource-limited settings lack facilities for blood culture, so use serology (Widal's test) instead. In most settings, this lacks sensitivity and specificity, and it is often positive in individuals who have previously been vaccinated. It is not recommended
- Blood cultures have a sensitivity of >80%, with their highest yield within the first week of symptoms. Stool and urine cultures become positive after the first week of illness. Although invasive, a bone marrow aspirate has a higher sensitivity than blood culture and should be considered in patients who have already taken antibiotics and in whom there is diagnostic uncertainty[2]
- Antimicrobial resistance is an emerging global issue and should be considered in all returning travellers as it can influence antibiotic choices
- More than 80% of *Salmonella typhi* and *S. paratyphi* isolates imported into the UK from Asia are resistant to fluoroquinolones but remain sensitive to ceftriaxone.[5] This is therefore the recommended first-line agent, particularly for severe disease. Oral azithromycin can be used for uncomplicated infection; however, if the isolate is proven to be sensitive, ciprofloxacin remains the most effective treatment option. Regardless of which antibiotic is used, the fever takes several days to respond. If the isolate is known to be sensitive, failure to defervesce is not a reason to change antibiotics

schistosomiasis). Up-to-date information on disease outbreaks is available online (see Sources of help box).

Purpose and duration of travel: travellers visiting friends and relatives (VFR), expatriates, overseas healthcare workers and backpackers often stay for longer periods than tourists and can have closer contact with local populations. This can put them at greater risk of acquiring certain infections, for example malaria, enteric fever, tuberculosis, hepatitis A and sexually transmitted

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