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Fever in the returning traveller

Harriet Davidson
Angela Houston

Abstract

Global travel is increasingly a fact of modern life, and the rapid spread of severe acute respiratory syndrome coronavirus 2 leading to lockdown across the world has demonstrated the interconnectedness of the world's population. Illness in the returning traveller can range from trivial to life-threatening, and the concept of imported infection can be an intimidating diagnostic and management challenge. An important caveat is that even if your patient has returned from cuddling multimammate rats in Guinea 1 week ago, they could be febrile from a distinctly non-tropical urinary tract infection. That said, antimicrobial resistance is an established concern among returned travellers, which has further infection control implications. Infection control issues regarding isolation, personal protective equipment and notification to public health should always be considered for returning travellers on presentation often before diagnostic confirmation has been made. Always consider the risk of high-consequence infectious diseases.

Keywords Fever; imported fever; infection control; returning traveller; travel

Introduction

In 2019, UK residents made 93.1 million visits overseas, and overseas residents made 40.9 million visits to the UK.¹ Before severe acute respiratory syndrome coronavirus 2, we could reasonably have expected this to increase year on year. A recent review found that 43–79% of returning travellers from developing countries become ill on return and may seek medical attention.² Fever in these travellers is caused by tropical infections in 36% of cases (malaria being the most common at 22% of febrile presentations) and non-tropical in 36% (gastrointestinal infections, respiratory tract infections).³ This article aims to provide a framework to evaluate these patients. It is important to consider *when* the patient (*who*) has been doing *what*, *where*. The timing, exposures and location can often be usefully combined to prioritize testing. Working out the patient's clinical syndrome can also help guide a diagnosis.

Harriet Davidson MA MRCP DTM&H is a Registrar in Infectious Diseases and Microbiology at St George's Hospital NHS Foundation Trust, London, UK. Competing interests: none declared.

Angela Houston FRCP FRCPath DTM&H is a Consultant in Infectious Diseases and Microbiology at St George's Hospital NHS Foundation Trust, London, UK. Competing interests: none declared.

Key points

- A thorough history and examination guide investigation and management
- Malaria is the most common cause of febrile tropical infection – always send a blood smear
- Consider imported antimicrobial resistance
- If in doubt, isolate and talk to the infectious disease team

History

The history taken from a returning traveller establishes the solid backbone of any clinical assessment. Without adequate assessment of the patient's travel destinations, exposures and timeline, it would be easy to inappropriately rule out, or not even consider, the true diagnosis. This can be broken down into four main categories: Who? Where? What? When?

Personal factors: the 'Who?'

Consider the patient and their personal risk factors for disease acquisition abroad. A personal medical history and drug history are key. Consider any underlying immune suppression – for example, renal dialysis patients have an associated immune suppression and may have needed to access healthcare facilities while abroad for their chronic health condition. Has the patient been visiting friends and relatives? These travellers may have a different risk profile from tourists who have only frequented the 'beaten track'.

Destinations: the 'Where?'

The destination information should be as granular as possible. It can be easier to think of it as zooming in from national to particular: Country → city/rural → local geography (mountains/lakes/beach) → accommodation (family/hostel/hotel). This should be completed for any country travelled through, and for the last 12 months. Review the resources for outbreaks (Table 1) to ensure specifically asking about travel to areas with malaria transmission and continuing outbreaks.

Exposures: the 'What?'

What was the patient doing while abroad? Again, record as much detail as possible:

- work: what setting?
- leisure: what activities?
- sexual contact: what and with whom?
- hospital treatment or admission?
- insect bites?

Table 2 outlines some specific risks and disease associations.

Timeline: the 'When?'

Review the 12 months leading up to this presentation. Be sure to establish the onset and progress of the symptoms. You will then be able to allocate diagnoses as 'in' or 'out' based on incubation

Resources for outbreaks

- **Travel Health Pro (formerly the National Travel Health Network and Centre (NathNaC)):** Travel health information is produced by the NathNaC, a UK government organization. It is aimed at healthcare professionals advising travellers. Information is available by country, and as outbreak surveillance information. <https://travelhealthpro.org.uk/>
- **ProMED:** The Program for Monitoring Emergency Diseases (ProMED) is a programme of the International Society for Infectious Diseases. It is the largest publicly available system conducting global reporting of infectious disease outbreaks for up-to-the minute information on emerging and continuing outbreaks. <https://promedmail.org/>
- **Imported Fever Service (IFS):** This is a clinical advisory and specialist diagnostic service for medical professionals managing travellers who have returned to the UK with fever. After discussion with local microbiology, virology or infectious disease specialists, IFS can be consulted for advice and diagnostic panels to help secure a diagnosis. <https://www.gov.uk/guidance/imported-fever-service-ifs>

Table 1

periods It can be useful to think of events before, during and after each trip.

Before – are childhood vaccinations up to date? Has vaccination for country risk been completed before travel? For example, hepatitis A vaccination needs to be completed 14 days

before travel. Did the individual take malaria prophylaxis? Were there travel medicine appointments?

During – dates of travel and exposures are key. Also establish a timeline for the onset of symptoms and signs. If the person was

Activities and disease risks

Exposure	Common	Occasional	Rare but important
Bites			
Mosquito	Dengue, malaria	Chikungunya, West Nile fever, yellow fever, Japanese encephalitis, Zika virus	Filariasis
Tick	Lyme disease, tick typhus	Q fever	Other borreliosis (tick bite fever, relapsing fever), Crimean-Congo Haemorrhagic fever, ehrlichiosis, tick-borne encephalitis, tularaemia
Flea		Murine (endemic) typhus	Plague
Tsetse fly		Trypanosomiasis	
Animal	Cellulitis	Q fever, tularaemia	Anthrax, rabies, rat bite fever
Activity			
Cruise ships	Legionella, norovirus, hepatitis A/E		
Caving	Coccidiomycosis, histoplasmosis		Rabies
Farms	Brucella, Q fever		
Fresh-water exposure	Katayama fever (acute schistosomiasis), leptospirosis		<i>Acanthamoeba</i> , melioidosis
Game parks	Tick typhus		Anthrax, trypanosomiasis
Food/drink			
Faecally contaminated water	Amoebiasis, enteric fever, gastroenteritis, hepatitis A/E		Poliomyelitis
Unpasteurized milk	<i>Listeria</i> , <i>Salmonella</i> , <i>Shigella</i>	<i>Brucella</i>	
Undercooked food	Bacterial gastroenteritis, amoebiasis		Trichinosis
People			
Sexual contact	HIV, hepatitis A/B/C, pelvic inflammatory disease	Syphilis	
Funerals			Ebola

Adapted from Johnston *et al.* Fever in returned travellers presenting in the United Kingdom: recommendations for investigations and initial management. *Journal of Infection*. 2009, 59:1–18 [https://www.journalofinfection.com/article/S0163-4453\(0900154-6/fulltext](https://www.journalofinfection.com/article/S0163-4453(0900154-6/fulltext)

Table 2

Clinical syndromes and differential diagnoses

Fever and syndrome	Usual incubation period (range)	Key investigations
Incubation < 14 days		
<i>Undifferentiated fever</i>		
• Malaria (<i>Plasmodium</i> species)	6 days to years	Thick and thin blood films
• Dengue fever	4–8 days (3–14 days)	Flavirus serology
• Campylobacteriosis, salmonellosis, shigellosis	2–6 days (1–20 days)	MCS of faeces
• Typhoid fever (<i>Salmonella enterica</i> serotype Typhi)	7–18 days (3–60 days)	Blood culture, stool culture
• Acute human immunodeficiency virus infection	Acute illness, 10–28 days (10 days–6 weeks)	HIV test
<i>Fever with haemorrhage</i>		
• Viral haemorrhagic fever	3–14 days (usually <21 days)	
<i>Fever with respiratory findings</i>		
• Influenza	1–3 days	Respiratory viral swab
• Legionellosis (<i>Legionella pneumophila</i>)	5–6 days (2–10 days)	Urinary antigen
• Q fever (<i>Coxiella burnetii</i>)	14–21 days (2–29 days)	<i>Coxiella</i> serology
• SARS-1, MERS, SARS-CoV-2	2–10 days (WHO and PHE definition <10 days, SARS-CoV-2 up to 14 days)	Respiratory viral swab
Incubation 14 days to 6 weeks		
Malaria	6 days to years	As above
Typhoid fever	7–18 days (3–60 days)	As above
Hepatitis A	28–30 days (15–50 days)	HAV IgG/IgM
Hepatitis E	26–42 days (2–9 weeks)	HEV IgG/IgM
Acute schistosomiasis (Katayama fever)	Katayama fever 4–8 weeks	Stool/urine OCP, serology
Amoebic liver abscess (<i>Entamoeba histolytica</i>)	Weeks to months	Liver ultrasound, serology
Incubation > 6 weeks		
Tuberculosis	Primary, weeks; reactivation, years	Sputum/tissue sample for AFB microscopy and culture
Hepatitis B	60–90 days (45–180 days; rarely 9 months)	HBV serology
Visceral leishmaniasis (<i>L. donovani</i> , <i>L. chagasi</i> , others)	2–6 months (10 days to years)	Histopathology (bone marrow/spleen)

AFB, acid-fast bacillus; HAV/HBV/HEV, hepatitis A/B/E virus; MCS, microscopy, culture and sensitivity; MERS, Middle East respiratory syndrome; OCP, ova, cysts and parasites; PHE, Public Health England; SARS, severe acute respiratory syndrome; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2; WHO, World Health Organization.

Adapted from Incubation periods adapted from: Ryan *et al.* Illness after International Travel. NEJM 2002, 347 (7):505–516 <https://www.nejm.org/doi/10.1056/NEJMra020118>

Table 3

supposed to be taking malaria prophylaxis, check their compliance.

After – when did they return to their home country? How have they been?

Table 3 shows the incubation periods for important imported diseases,⁴ which narrows down the possible diseases the patient could have, based on their timeline.

Examination

Use an ‘A–E’ (Airway, Breathing, Circulation, Disability, Exposure) approach to assess the stability of the patient before progressing to a top-to-toe examination. In addition to the cardiopulmonary, abdominal and neurology examination, a

detailed skin examination is crucial. This may reveal rashes, bites, eschars, lymphadenopathy or even evidence of medical interventions. Remember to look under bra straps, in skin folds and on the feet.

Investigations

Having established a history and examined the patient, a basic investigation set should include a full blood count, renal function test, liver function tests, blood culture, blood smears and HIV test. The blood smear for malaria should be completed urgently – you should contact the duty biomedical scientist to inform them the sample is coming so they can ensure the result is available in a timely fashion, even if you are seeing the patient

out-of-hours. The smear should be repeated three times in the first 24–72 hours as sequestration of parasitized red cells means that malarial parasites are not always seen on a peripheral smear. Further investigations should be guided by the clinical syndrome, exposures and countries travelled to, but sending a respiratory viral swab, and urine for dipstick and microscopy, culture and sensitivity, also requesting a chest X-ray, is a good start. Table 3 lists the key investigations for important diseases.

Management

Early priorities of management are patient stabilization and infection control considerations. Could the patient have a syndrome compatible with a high-consequence infectious disease? If so, isolate them and have an early discussion with the local infectious disease service. There may be an urgent need to seek advice from the national public health service. Further treatment is determined by the most likely diagnosis. If the patient requires hospital admission, swabbing for resistant organisms is recommended, especially if there has been medical treatment abroad, as these travellers are at greater risk of being colonized by resistant bacteria.⁵

Case studies

Case 1

A 26-year-old man returned from Zanzibar with a fever and a rapidly deteriorating conscious state. He had sustained several mosquito bites while on holiday. A blood film demonstrated *Plasmodium falciparum* parasites with a parasitaemia of 6%. Computed tomography (CT) of his brain demonstrated diffuse cerebral swelling. Intravenous artesunate was started within 5 hours of his arrival in hospital. Despite treatment, a second CT scan demonstrated progression of swelling and evidence of critically elevated intracranial pressure, and he died 14 hours after admission. Before travelling he had visited a travel health clinic that had advised against malaria prophylaxis as it was the low season. The patient had a history of splenectomy, which had not been appreciated as a risk factor for severe malaria.

Learning point –patients’ personal risk factors affect their susceptibility to malaria, particularly its severe manifestations. In addition, always do a malaria film.

Case 2

A 54-year-old woman returned from Dubai with fever, cough and shortness of breath. She had been admitted to hospital in Dubai 2 days earlier with a respiratory infection and an oxygen requirement, but had self-discharged against medical advice and flown to the UK. A chest X-ray demonstrated left lower zone consolidation. C-reactive protein measured 513 mg/litre. She fulfilled the case definition for possible Middle Eastern respiratory syndrome virus and was therefore isolated in a negative-pressure side room. Public Health England was consulted. A urinary antigen test came back positive for *Legionella pneumophila*. She was commenced on treatment with levofloxacin and made a good recovery.

Learning point – isolation precautions can always be de-escalated, and not all imported infections turn out to be tropical. ◆

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