

Fever and rash

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Abstract

The patient presenting with fever and a rash presents a diagnostic challenge. While this syndrome suggests an infectious aetiology, the differential diagnosis remains broad, and requires a thorough history and physical examination to distinguish potential non-infectious causes. Epidemiological evidence is important in the differential diagnoses. The commonest febrile illnesses presenting with rash in the returned traveller are arboviral infections (dengue and chikungunya), infectious mononucleosis caused by Epstein–Barr virus (EBV) or cytomegalovirus (CMV), and tick-borne diseases (rickettsioses).

Keywords chikungunya; dengue; fever; infectious mononucleosis; rash; rickettsiae; travel

Fever and rash is a relatively common presentation in travellers returning from the tropics, comprising around 4% of febrile ‘syndromes’ presenting to travel or tropical diseases clinics.¹ The presence of a rash as part of a febrile illness, although rarely pathognomonic, focuses the differential diagnosis. It is important to remember that rashes are common and may be caused by another medical condition unrelated to travel, or a drug reaction to medications taken at the time of travel. A systematic approach is important, as a rash can be either a manifestation of a mild illness or an indicator of a potentially fatal contagious disease.

Diagnosis

Initial assessment

A preliminary assessment should focus on two broad considerations:

- Does this patient show signs of severe sepsis or organ dysfunction requiring urgent cardiorespiratory support and antibiotic therapy?
- Does the travel history indicate potential exposure to pathogens causing serious illness with a risk of nosocomial transmission, requiring immediate isolation and barrier precautions (e.g. viral haemorrhagic fevers (VHF))?

History

Rash can be associated with tropical and cosmopolitan infections (Table 1). A detailed history is essential and should include:

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What's new?

- Chikungunya is an arbovirus infection that has circulated in a recent epidemic originating in Reunion Island in the Indian Ocean since early 2005 with ongoing reports of spread to Europe and Australasia
- Due to exponential increases in global travel during recent years, clinicians must be alert to the possibility of exotic infections in the returned traveller

- Pattern of the illness – timing of the onset of illness related to travel provides an estimate of the incubation period of potential tropical infections. Presence of associated symptoms and the distribution of rash may provide important clues.
- Detailed travel history – including departure and return dates, urban or rural exposure, accommodation used and activities undertaken, with clear timings in relation to onset of illness. The travel history should also include previous tropical exposure.
- Exposure to vector-borne and zoonotic infections – exposure to specific vectors such as ticks, fleas, or mites, should be sought. Often ticks and mites are not seen whilst attached, but a history of walking in rural or wilderness areas indicates potential exposure. Possible exposure to zoonoses should be sought by direct questioning about animal contact but also through determining indirect exposure, for example, to fresh water for leptospirosis.
- Detailed sexual history – HIV seroconversion, secondary syphilis and disseminated gonococcal infection all commonly cause rash.
- Past medical history – for example, endocarditis risk factors and immunosuppression.
- Immunization history – childhood and travel immunizations.
- Drug history – including malarial prophylaxis, recent antibiotics, known allergies.
- Exposure to infectious contacts.
- Sun exposure.

General examination

Preliminary assessment should determine oxygenation, cardiovascular status and presence of cerebral impairment or meningism. Particular attention should be paid to:

- eyes – conjunctivitis, conjunctival petechiae, jaundice
- oropharyngeal mucosa – erythema, exudate, ulceration, vesicles, petechiae, Koplik's spots, oral candida
- lymphadenopathy – localized, generalized
- hepatosplenomegaly
- genital examination – ulceration.

Examination of the skin

Full exposure is very important. Distinctive signs, such as an eschar following a tick bite (Figure 1), can be limited to skin folds. Involvement of the palms and soles is a feature of particular infections, such as hand, foot and mouth disease (Coxsackie A16) and secondary syphilis. Rashes can be macular, papular, nodular, vesicular, bullous or pustular, evolving in different

Causes of rash and fever – tropical and cosmopolitan infections

Organism/disease	Rash (% cases)	Distribution	Vector/exposure risk	Associated features
Dengue	M, MP, PP (50%)	Tropical, subtropical, worldwide	<i>Aedes</i> mosquito, urban and rural	Myalgia, haemorrhage, shock
Chikungunya	M, MP (50%)	Tropical, subtropical Africa and Asia	<i>Aedes</i> mosquito, urban and rural	Polyarthralgia
Rickettsia	M, MP, PP, V	Worldwide	Ticks	
African tick typhus	MP, PP, V (46%)	Sub-Saharan Africa	Ticks rural/wilderness	Eschar common, headache
Mediterranean spotted fever	MP, PP (90%)	Mediterranean and sub-Saharan Africa, India	Ticks, urban, suburban	Eschar common
Rocky Mountain spotted fever	MP, PP (90%)	USA, Central and South America	Ticks, rural/wilderness	Eschar rare
Scrub typhus – <i>Orientia tsutsugamushi</i>	M, MP (35–90%)	Asia, Pacific Islands	Larvae trombiculid mites (chiggers), rural	Eschar common
Typhoid fever – <i>Salmonella typhi/paratyphi</i>	M (rose spots) (20%)	Wherever risk of faecal contamination of water	Faecal–oral, poor sanitation	Prolonged fever, splenomegaly
Leptospirosis	M, MP, PP (20%)	Worldwide	Exposure to rat/rodent urine (fresh water)	Conjunctivitis, myalgia
Schistosomiasis	U (Katayama fever)	Africa, Asia, South America, Caribbean	Freshwater snails	Eosinophilia
Yellow fever	PP	Central and South America, Africa	Mosquito-borne urban/rural	Jaundice
Lassa fever	MP, PP	West Africa	Rodent urine, rural	Pharyngitis, retrosternal pain, encephalitis, haemorrhage
Ebola/Marburg	MP, PP	West/Central Africa	Unknown, ? monkeys/bats, rural/wilderness	Abdominal pain, D + V, haemorrhage
South American haemorrhagic fevers	PP	South America		
West Nile virus	MP	Africa, USA	<i>Culex</i> , <i>Aedes</i> mosquitoes, urban	Encephalitis
Measles	MP	Worldwide		Cough, conjunctivitis, Koplik's spots
Varicella–zoster virus	MP, V	Worldwide		Coryza, pneumonitis
Epstein–Barr virus	MP, PP	Worldwide		Pharyngitis, lymphadenopathy, splenomegaly
Cytomegalovirus	MP	Worldwide		Pharyngitis, lymphadenopathy, splenomegaly
Toxoplasmosis	MP	Worldwide	Cats	Lymphadenopathy
HIV	MP	Worldwide	Sexual, IVDU, vertical transmission	Pharyngitis, lymphadenopathy, splenomegaly
Rubella	MP	Worldwide	Human	Coryza, arthralgia
<i>Staphylococcus aureus</i>	PP, E	Worldwide	Human, IVDU	Shock, heart murmur
<i>Streptococcus pyogenes</i>	E	Worldwide	Human	Pharyngitis, cellulitis, shock
<i>Neisseria meningitidis</i>	PP	Worldwide	Human	Shock, meningitis
<i>Neisseria gonorrhoeae</i>	PP	Worldwide	Sexual	Septic arthritis
Syphilis, <i>Treponema pallidum</i>	MP, PP, PU, V	Worldwide	Sexual	Genital ulceration

D + V, diarrhoea and vomiting; IVDU, intravenous drug use; M, macular; MP, maculopapular; PP, petechial/purpuric; E, erythrodermic; PU, pustular; U, urticarial; V, vesicular. The % values given for the frequency of rash in particular infections are derived from case series.

Table 1

stages of the illness. Generalized erythema is associated with bacteria producing erythrogenic toxins (*Streptococcus pyogenes*, *Staphylococcus aureus*) and drug reactions, and urticarial rashes are associated with parasitic infections. Combinations of the rash forms can occur, and a single infection, such as dengue, may cause various morphologies.

Fever and rash in the returning traveller

The commonest febrile illnesses presenting with rash in the returned traveller are arboviral infections (dengue and chikungunya), infectious mononucleosis caused by Epstein–Barr virus (EBV) or cytomegalovirus (CMV), and tick-borne diseases (rickettsioses).^{2,3}

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