

# A woman with persistent fever and a skin lesion

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## CASE

A previously well Malaysian woman aged 52 years was referred for fever, headache, myalgia, anorexia and malaise of one week duration. She had participated in a cross-country hike in Selangor, Malaysia, about two weeks before the onset of her illness. This included trekking across an oil palm plantation. On examination, she had a temperature of 38.1°C, and a lesion was found near the left popliteal fossa (Figure 1). There was tender lymphadenopathy in the left inguinal area.

## Question 1

What are the differential diagnoses for this lesion?

## Question 2

What investigations are indicated?

## Answer 1

Figure 1 shows a raised erythematous lesion with a dark central necrotic area. The differential diagnoses include:

- an eschar that may be due to a rickettsial infection
- cutaneous anthrax
- tularemia
- ecthyma due to various bacterial infections, fungal infections, trauma or spider bites.

## Answer 2

In addition to screening for the infections listed above, blood cultures and investigations for dengue fever and

other viral infections, typhoid fever and leptospirosis may be considered, given the patient's travel history.

## CASE CONTINUED

Investigation results were:

- haemoglobin: 12.8 g/dL, white cell count: 3700 (N70% L25%), platelets:  $145 \times 10^9/L$
- aspartate aminotransferase (AST) 75 IU/L, alanine aminotransferase (ALT) 98 IU/L
- positive immunoperoxidase testing of immunoglobulin M (IgM) for *Orientia tsutsugamushi* (1:400).

The patient was diagnosed with scrub typhus and treated with oral doxycycline 100 mg twice daily for a week. Fever and symptoms resolved, and recovery was uncomplicated.

## Question 3

What is scrub typhus? How is it transmitted?

## Question 4

What are the clinical features of scrub typhus?

## Question 5

In what other conditions may eschars be found?

## Question 6

What investigations are used to diagnose scrub typhus?

## Question 7

What are the treatment options?

## Answer 3

Scrub typhus is one of the rickettsioses and is caused by the Gram-negative organism *Orientia tsutsugamushi*.<sup>1</sup> It occurs in Central and Southeast Asia, the Pacific and Indian Ocean Islands, and northern Australia, where it is recognised to occur in rainforests.<sup>2,3</sup> Travellers are at risk of acquiring this infection.

The mode of transmission is through the bite of larval-stage trombiculid mites (*Leptotrombidium* spp.; also referred to as 'chiggers') infected with *O. tsutsugamushi*. An eschar develops at the bite site.<sup>4</sup>

Trombiculid mites are found in areas of dense scrub and vegetation. Their life cycle consists of egg, larval, nymphal and adult stages. Adults and nymphs live in the soil and feed on plants, but larval forms may bite animals such as rodents or mice; humans may be incidental victims. Mites are small (0.2–0.4 mm) and are usually only visible under magnification.<sup>4</sup>

## Answer 4

The incubation period is approximately 10 days but may vary from six to 21 days and presents with fever, chills, headache, nausea, vomiting, conjunctivitis and

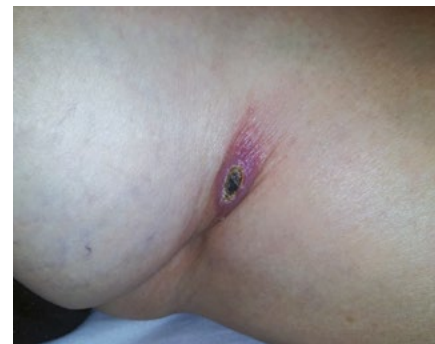


Figure 1. Skin lesion near left popliteal fossa

myalgia.<sup>5,6</sup> A macular rash involving the trunk and limbs may develop towards the end of the first week. Lymphadenopathy and splenomegaly may occur.

Patients with more severe disease may develop delirium, jaundice, pneumonitis, meningoencephalitis, myocarditis, multi-organ failure and disseminated intravascular coagulation.

Eschars appear as raised erythematous papules with dark central necrotic areas. They often occur in warm, damp and covered areas of the body such as the chest and inframammary area, abdomen, axilla, groin and genitalia and may be missed on clinical examination.<sup>4</sup> The eschar is painless, and the patient may be unaware of it, although it can sometimes be pruritic. Eschars heal in 3–4 weeks, sometimes with scarring and pigmentation.

Common laboratory findings in cases of scrub typhus include leukopenia, thrombocytopenia and elevated liver transaminases.<sup>2</sup>

Untreated scrub typhus has significant morbidity and mortality rates. A meta-analysis of untreated scrub typhus found a median duration of fever of 14.4 days and a median mortality of 6%.<sup>7</sup>

**Answer 5**

Eschars may be found in other acute infections, and some differentiating clinical features of these conditions are summarised in Table 1.

**Answer 6**

Scrub typhus may be diagnosed with serological investigations such as indirect immunofluorescence antibody

and indirect immunoperoxidase assays showing rising titres of IgM antibodies against *O. tsutsugamushi*.<sup>8,9</sup> Polymerase chain reaction can be performed on blood and tissue specimens.

**Answer 7**

Doxycycline orally, or intravenously for those with more severe disease, is the drug of choice in scrub typhus.<sup>2,6,10</sup> Treatment should be continued for a week to prevent relapse. Alternative drugs are azithromycin, telithromycin and rifampicin. Azithromycin is considered safe in pregnancy.

There is currently no vaccine available.

**Key points**

- Scrub typhus should be considered in patients with persistent fever and a history of travel to an endemic area.
- In the presence of an eschar, appropriate antibiotics for scrub typhus may be commenced while awaiting investigative results.
- Travellers at risk should be advised on preventive measures against tick bites, such as wearing protective clothing and using insect repellents, and should avoid walking barefoot and sitting or lying on bare ground.

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**Table 1. Differential diagnoses for eschars**

Disease	Organism	Background	Features of eschar
Cutaneous anthrax <sup>11</sup>	<i>Bacillus anthracis</i>	Contact with animals or animal products contaminated with spores of <i>B. anthracis</i> Population at risk includes those in the agricultural industry	Often found in exposed areas such as hands, wrists, arms, face and neck May have surrounding blistering, haemorrhage and oedema
Tularemia <sup>12</sup>	<i>Francisella tularensis</i>	Found in the northern parts of North America, Europe and Asia Spread by ticks or deerfly bites or direct contact with infected animals or meat	Often found on hands, upper and lower limbs. Associated with regional lymphadenopathy