

PUBLIC HEALTH REFERENCE SHEET

Typhus Fever



Name	Epidemic (louse-borne) typhus caused by <i>Rickettsia prowazekii</i> Murine (endemic) typhus caused by <i>Rickettsia typhi</i> Scrub typhus caused by <i>Orientia tsutsugamushi</i> EXCLUDES: All other Rickettsia species; see spotted fever rickettsiosis
Reservoir & Transmission	Epidemic typhus – humans and flying squirrels, vector human body louse, flying squirrel ectoparasites Murine typhus – rodents, vector fleas Scrub typhus – rodents, vector trombiculid mites, and chiggers Transmitted directly to humans by infected arthropod vectors during feeding, when a person inadvertently inoculates the arthropod bite wound (or other breaks in the skin) with rickettsial pathogens or inhaling bacteria or inoculating conjunctiva with infectious material
Incubation Period	Epidemic typhus and murine 1–2 weeks, commonly 12 days. Scrub typhus 6–12 days
Common Symptoms	Common symptoms that typically develop within 1 week of infection include fever, headache, malaise, nausea, or vomiting Can be accompanied by a maculopapular, petechial, or vesicular rash, or sometimes an eschar (a dark necrotic scab) at the site of the mite bite
Gold Standard Diagnostic Test	Serologic testing provides retrospective confirmation and is most accurate when acute and convalescent phase serum samples are compared; a \geq fourfold rise in antibody titer between paired specimens is diagnostic in indirect immunofluorescence antibody assays.
Risk Groups	All age groups are at risk during visits to endemic areas and that are exposed to vector fleas, lice, mites, chiggers.
Geographic Significance	Epidemic typhus - Central Africa; North, Central and South America; Asia Murine typhus - temperate, tropical, and subtropical areas worldwide Scrub typhus - Asia-Pacific region (north Australia, China, Indonesia, maritime Russia); Middle East (Afghanistan); possibly several countries in sub-Saharan Africa

What is typhus fever?

Typhus fevers are a group of diseases caused by bacteria that are spread to humans by fleas, lice, and chiggers. Typhus fevers include epidemic (louse-borne) typhus, murine (endemic) typhus, and scrub typhus. This reference sheet will individually break down all three diseases.

What is epidemic typhus fever?

Epidemic typhus, also called louse-borne typhus, is an uncommon disease caused by a bacteria called *Rickettsia prowazekii* (*R. prowazekii*).

What is the occurrence of epidemic typhus fever?

Most commonly it occurs among people living in crowded conditions where body lice are prevalent (e.g., refugees housed in camps, incarcerated populations). Outbreaks often happen during the colder months. Travelers at greatest risk for epidemic typhus include people who provide medical or humanitarian aid to people living in refugee camps and those who visit

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impoverished areas affected by war, famine, or natural disasters. Active foci of epidemic typhus are in the Andes region of South America and some parts of Africa, including but not limited to Burundi, Ethiopia, and Rwanda. Epidemic typhus has not occurred in the United States for approximately the past century; however, a zoonotic reservoir exists in the southern flying squirrel, and sporadic sylvatic epidemic typhus cases are reported when these animals invade people's homes or cabins.

How is epidemic typhus fever transmitted?

The primary vector of epidemic typhus is the pediculus humanus corporis (human body louse). People become infected with *R. prowazekii* when they come into contact with the feces or crushed bodies of infected lice via cut or injured skin. Inhalational exposure of dried louse feces may also occur. *R. prowazekii* can remain infective in louse feces for up to 100 days. Body lice can proliferate to large numbers and rapidly transmit disease among crowded human populations by hiding out in clothes, blankets, or bedding.

In the United States, cases of epidemic typhus have been associated with exposure to flying squirrels or their nests. Fleas and lice carried by the squirrels become naturally infected with *R. prowazekii*; however, the exact mechanism of transmission remains unknown.

Who is at risk of epidemic typhus fever?

All age groups are at risk for typhus fever infections during visits to endemic areas. Transmission risk increases with time spent participating in outdoor activities, particularly during seasons of peak feeding and lifecycle activity for the vector. However, typhus fever infections occur year-round in many parts of the world.

What are the signs and symptoms of epidemic typhus fever?

The signs and symptoms vary, often with sudden onset of headache, chills, malaise, fever, or general pains. A macular eruption appears on the fifth or sixth day, initially on the upper trunk, followed by spreading to the entire body, but usually not to the face, palms, or soles. The eruption is often difficult to observe in patients with darkly pigmented skin and/or absent in up to 40% of patients. Cough and tachypnea may be present and neurological signs are common, including confusion, drowsiness, coma, seizures, or hearing loss.

What are the potential complications of epidemic typhus fever?

Patients with epidemic typhus can develop organ failure or other severe sequelae requiring hospital-based management. Death can occur if antimicrobial drug treatment is delayed or if not treated.

How is epidemic typhus fever diagnosed?

Diagnosis is based on clinical findings and epidemiologic factors as reliable, early diagnostic tests are not available. Epidemic typhus should be considered in patients with persistent fever, a history of body louse exposure in crowded or unhygienic areas, or persons who may have come in contact with flying squirrels or their nests. When treated early, patients may experience a less severe illness and shorter recovery time.

R. prowazekii can be detected via indirect immunofluorescence antibody (IFA) assay, immunohistochemistry (IHC), polymerase chain reaction (PCR) assay of blood, plasma, tissue samples, or culture isolation. Serologic tests are the most common means of confirmation and can be used to detect either IgG or IgM antibodies. Acute specimens are taken during the first week of illness and convalescent samples are taken 2–4 weeks later. Detectable levels of IgG or IgM antibodies generally do not appear until 7–10 days after the onset of illness.

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How is epidemic typhus fever treated?

Because epidemic typhus can progress rapidly to severe illness, clinicians should initiate therapy as soon as infection is suspected and not wait to receive confirmatory test results. Epidemic typhus has the potential to spread rapidly among persons living in close quarters, so precautions should be taken to rapidly identify and treat patients and to eliminate body louse infestations.

Doxycycline is the treatment of choice for suspected cases of acute epidemic typhus and Brill-Zinsser disease in adults and children of all ages. Recommended dosages of doxycycline include:

- Adults: 100 mg twice per day
- Children under 45 kg (100 lb.): 2.2 mg/kg body weight given twice a day

Patients should be treated for at least 3 days after the fever subsides and until there is evidence of clinical improvement (usually 7–10 days).

How can epidemic typhus fever be prevented?

No vaccine is available for preventing typhus fever infections. Antibiotic prophylaxis is not recommended, and antimicrobial agents should not be given to asymptomatic people.

Instruct travelers going to typhus-endemic areas to minimize their exposure to infectious arthropods and avoid animal reservoirs. Improve living conditions with provisions for bathing and washing clothes. Treat prophylactically those who are subject to risk by application of residual insecticide to clothing and uniforms (dusting or impregnation), and in the case of an epidemic, directly to the skin as well.

What are some Public Health considerations?

- Isolation is not required after proper delousing of patient, clothing, living quarters, and household contacts.
- All immediate contacts should be kept under surveillance for 2 weeks.
- Every effort should be made to trace the infection to the immediate source.
- The best epidemic measure for rapid control of typhus is application of an insecticide with residual effect to all contacts. Where louse infestation is known to be widespread, systematic application of residual insecticide to all people in the community is indicated. Treatment of cases in an epidemic may also decrease the spread of disease. In epidemics, individuals may protect themselves by wearing silk or plastic clothing tightly fastened around wrists, ankles, and neck, and by impregnating clothes and uniforms with repellents or permethrin.
- *R. prowazekii* has been produced as a possible bioweapon and was used before World War II. It is infectious by aerosol, with a high case-fatality rate. The initial reference treatment of any suspected case is a single dose of 200 mg of doxycycline in situations where doxycycline is limited in supply.

What is murine typhus?

Murine typhus is a flea-borne illness caused by the bacterium *Rickettsia typhi*.

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What is the occurrence of murine typhus?

This illness is distributed worldwide, particularly in and around port cities and coastal regions with large rodent population. Murine typhus has been reported among travelers returning from Africa, Asia, and the Mediterranean Basin. Most cases acquired in the United States are reported from California, Hawaii, and Texas.

How is murine typhus transmitted?

People become infected with *R. typhi* when they come into contact with infected flea feces via scratched or abraded skin. Exposure can also occur when mucous membranes are exposed to infected feces or when a patient inhales the feces.

Several flea species have been identified as potential vectors for murine typhus, including the rat flea (*Xenopsylla cheopis*), cat flea (*Ctenocephalides felis*), and mouse flea (*Leptopsyllia segnis*). Opossums, dogs, and cats living in urban or suburban areas have also been implicated as host species for fleas carrying *R. typhi* in recent cases in the United States and Spain.

Who is at risk for murine typhus?

People are at risk for fleaborne rickettsioses when traveling in endemic regions; when they are exposed to flea-infested cats, dogs, and peridomestic animals; or when they enter or sleep in areas infested with rodents.

What are the signs and symptoms of murine typhus?

Symptoms of the disease manifest 7–14 days post-exposure, with patients usually displaying fever combined with either headache or rash. Other possible symptoms include muscle pain, loss of appetite, nausea, vomiting, abdominal discomfort, cough, or cognitive changes. A rash is common during the first week, lasting between 1 to 4 days. This rash usually begins on the trunk and spreads outwards, avoiding the palms of hands and soles of feet. However, its appearance can differ among patients or might be entirely absent, making it an unreliable diagnostic indicator. Routine lab tests often reveal anemia, low platelet and white blood cell counts, low sodium levels, and increased liver enzyme levels.

What are the potential complications of murine typhus?

Patients with murine typhus can develop organ failure or other severe sequelae, requiring hospital-based management. Death can occur.

How is murine typhus diagnosed?

For lab confirmation, *Rickettsia typhi* can be detected using various methods such as IFA, IHC, PCR, and culture isolation. PCR is best when used within the first week of illness, before administering doxycycline. Serologic tests, especially using IFA, are common for murine typhus confirmation, focusing on detecting IgG or IgM antibodies. Diagnosis often comes from a notable increase in antibody titer from initial to later stages of illness. IgG, appearing 7–10 days post-onset, is more reliable than IgM. Persistent antibody titers from past exposures can confuse diagnosis. Thus, only recent titer changes reliably confirm acute infections. Since *Rtyphi* antigens can cross-react with other species like *R. prowazekii* and *R. felis*, it's crucial to run parallel tests for specificity. IHC detects typhus group Rickettsia in fixed tissue samples.

How is murine typhus treated?

Due to the vague symptoms of murine typhus and early test unreliability, treatment should hinge on clinical signs, exposure history, and travel to tropical areas. Early treatment leads to milder

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illness and quicker recovery. Waiting for diagnostic tests before treatment isn't advised. Clusters of murine typhus are found in the U.S., so suspected cases must be reported to curb its spread.

Doxycycline is the treatment of choice for suspected cases of murine typhus in adults and children of all ages. Recommended dosages of doxycycline include:

- Adults: 100 mg twice per day
- Children under 45 kg (100 lbs.): 2.2 mg/kg body weight given twice a day

Patients should be treated for at least 3 days after the fever subsides and until there is evidence of clinical improvement (usually 7–10 days).

How can murine typhus be prevented?

Instruct travelers and Service members going to murine endemic areas to minimize their exposure to infectious arthropods and avoid animal reservoirs. Apply insecticide powders with residual action to rat runs, burrows, and harborages. Control rodents or opossums (North America) around premises or home of patient. To avoid increased exposure of humans, wait until flea populations have first been reduced by insecticides before instituting rodent control measures.

What are some Public Health considerations?

- Case report to local health authority obligatory in most states.
- In endemic areas with numerous cases, use of a residual insecticide effective against rat or cat fleas will reduce the flea index and the incidence of infection in humans.
- Disaster implications are that cases can be expected when people, rats, and fleas are forced to coexist in close proximity, but murine typhus has not been a major contributor to elevated disease rates in such situations.

What is scrub typhus?

Scrub typhus, also known as bush typhus, is a disease caused by a bacteria called *Orientia tsutsugamushi*.

What is the occurrence of scrub typhus?

Scrub typhus is endemic to regions of east Asia (China, northern Japan), Southeast Asia (India, Indonesia, Sri Lanka), the Pacific (eastern Australia), and several parts of south-central Russia. Cases of disease also have been described from several unexpected regions, including the United Arab Emirates and southern Chile, and the cases appear to be caused by newly recognized species of *Orientia*.

How is scrub typhus transmitted?

Scrub typhus is transmitted to humans through bites from infected larval trombiculid mites, commonly known as chiggers. The following species are known vectors of scrub typhus: *Leptotrombidium pallidum*, *L. fuji*, *L. scutellare*, and *L. akamushi*. Seasonality of the disease is determined by the appearance of larvae. In temperate zones, scrub typhus season is observed mainly in the fall, but also occurs in the spring. If a person is bitten by an infected mite, disease occurs within 7–10 days and typically lasts 14–21 days without appropriate treatment.

Who is at risk of scrub typhus?

More people worldwide are at risk for scrub typhus than for any other rickettsial disease; >1 million cases occur annually, mostly in farmers or people with occupational exposure. Travel-

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acquired cases of scrub typhus occasionally are reported among people who visit rural regions of countries where *O. tsutsugamushi* is endemic, and exposure is often associated with participating in recreational activities (e.g., camping, hiking, rafting). Rare urban cases have been described. Occupational infection is restricted mainly to adult workers (males more than females) who frequent overgrown terrain or other mite-infested areas, such as forest clearings, reforested areas, new settlements, or newly irrigated desert regions. Service members deploying to or training in endemic areas are also at risk.

What are the signs and symptoms of scrub typhus?

Symptoms of scrub typhus begin abruptly, 7 or more days after exposure. Typical signs and symptoms include:

- Fever and chills
- Headache
- Myalgia
- Eschar: the area around the bite may develop a necrotic skin lesion known as an eschar. The eschar may appear before the individual begins to develop systemic symptoms. Common sites of an eschar are axilla, under the breast, and groin, but less often on the abdomen, back, and extremities. Multiple eschars have been reported.
- Altered mental status, ranging from confusion to coma or delirium
- Lymphadenopathy
- Rash: about 25–50% of scrub typhus patients develop a rash. The rash is usually macular or maculopapular. Typically, it will begin on the abdomen of an infected individual and then spread to the extremities. Petechiae are uncommon.

What are the potential complications of scrub typhus?

Severe manifestations usually develop after the first week of untreated illness and may include multiple organ dysfunction syndrome with hemorrhaging, acute respiratory distress syndrome, encephalitis, pneumonia, renal or liver failure, and death.

During pregnancy, scrub typhus frequently leads to spontaneous abortion. Relapses may occur following apparent recovery in cases where inadequate treatment has occurred. Relapse is usually less severe than the initial presentation.

How is scrub typhus diagnosed?

The most rapid and specific diagnostic assays for scrub typhus rely on molecular methods like PCR, which can detect DNA in a whole blood, eschar, or tissue sample. Immunostaining procedures can also be performed on formalin-fixed tissue samples. Since scrub typhus is not common in the United States, confirmatory tests are not typically available at state and local health departments; nonetheless, indirect IFA, culture, and PCR assays can all be performed at the CDC through submission from state health departments. Diagnosis is typically confirmed by documenting a fourfold rise in antibody titer between acute and convalescent samples. Acute specimens are taken during the first week of illness, and convalescent samples are taken 2–4 weeks later. IgG antibodies are considered more accurate than IgM, but detectable levels of IgG antibody generally do not appear until 7–10 days after the onset of illness.

Because antibody titers may persist in some individuals for years after the original exposure, only demonstration of recent changes in titers between paired specimens can be considered reliable confirmation of an acute scrub typhus infection.

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How is scrub typhus treated?

Doxycycline is the treatment of choice for suspected scrub typhus in persons of all ages.

Recommended dosages of doxycycline include:

- Adults: 100 mg twice per day
- Children under 45 kg (100 lbs): 2.2 mg/kg body weight twice per day

Treatment alternatives primarily for patients with severe doxycycline allergy or women who are pregnant include azithromycin, chloramphenicol, or rifampin. Patients should be treated for at least 3 days after the fever subsides and until there is evidence of clinical improvement. Single-dose or short courses of doxycycline may lead to a relapse in illness.

Rigorous reevaluation of earlier reports of doxycycline-resistant scrub typhus has revealed those reports to be incorrect.

How can scrub typhus be prevented?

Prevention focuses on avoiding chigger bites and understanding the environments where chiggers are found.

- Prevent contact with infected mites through personal prophylaxis by impregnating clothes, uniforms, and blankets with miticidal chemicals (permethrin and benzyl benzoate) and application of mite repellents (diethyltoluamide) to exposed skin surfaces.
- Eliminate mites from the specific sites through application of chlorinated hydrocarbons, such as lindane, dieldrin, or chlordane, to ground and vegetation in environs of camps, mine buildings, and other populated zones in endemic areas.

What are some Public Health considerations?

Use surveillance to include:

- Implementing and maintaining robust surveillance systems can help detect outbreaks early and guide response measures.
- Persons with similar exposures should be monitored for fever and treatment initiated quickly when needed.
- Tourists visiting and Service members deploying to endemic areas should be informed about the risks of scrub typhus and the preventive measures they can adopt.
- Currently, scrub typhus, flea-borne (murine) typhus, and epidemic typhus are not nationally notifiable conditions; however, your state may require notification. Please check with your state and local health departments about reportable diseases. Further information for public health professionals can be found at <https://www.cdc.gov/typhus/info/index.html>.
- When reporting cases of typhus fever in the Disease Reporting System internet (DRSi)—
 - Specify the clinical form of the disease.
 - Document relevant travel and deployment history occurring within the incubation period (epidemic or murine typhus: 1–2 weeks; scrub typhus: 6–12 days).
 - Document the circumstances under which case patient was exposed, including duty exposure, occupational activities, environmental exposures, or other high-risk activities.
 - There can be antibody cross-reactivity between spotted fever and typhus group antigens. In cases where IgM or IgG titers are positive for both diseases, report the case under the disease most consistent with the case's clinical presentation, exposure history, and travel history.

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