Rickettsial (Spotted and Typhus Fevers) and Related Infectious Agent

Rickettsial infections are caused by a variety of obligate intracellular, gram-negative bacteria from the genera *Rickettsia*, *Orientia*, *Ehrlichia*, *Neorickettsia*, and *Anaplasma*. Rickettsia are further classified into the typhus group and spotted fever group (SFG), and *Orientia* comprises the classic scrub-typhus group.

Mode of Transmission

Most rickettsial pathogens are transmitted by ectoparasites such as fleas, lice, mites, and ticks during bloodfeeding or from scarification of infectious feces from these vectors that may be deposited on the skin. Many rickettsiae of concern to travelers, including *Ehrlichia* sp., *Anaplasma* sp., and most SFG rickettsiae, are transmitted by ticks. Mites transmit the SFG rickettsia *R. akari*, which causes rickettsialpox. Chiggers, the immature stage of *Leptotrombidium* mites, transmit *Orientia tsutsugamushi*, the etiologic agent of scrub typhus. Fleas serve as vectors for *R. typhi* and *R. felis*, which cause endemic or murine typhus and cat flea rickettsiosis, respectively. Human body lice and the ectoparasites of flying squirrels can transmit *R. prowazekii*, the causative agent of epidemic or louse-borne typhus. *Neorickettsia sennetsu* causes sennetsu fever and is likely transmitted by the ingestion of infected trematodes in raw fish. Transmission of rickettsiae following blood transfusion is rare but has been reported during the asymptomatic incubation period of those diseases.

Occurrence

SFG and typhus group rickettsiae have been reported worldwide. SFG rickettsial infections among travelers include African tick-bite fever (ATBF) from Africa and the Caribbean islands; Mediterranean (or Boutonneuse) spotted fever from southern Europe and Africa; Indian tick typhus from India; Astrakhan fever from southeastern Europe and Central Africa; Israeli tick typhus from Mediterranean basin; Thai tick typhus from Asia and Australia; Queensland tick typhus and Australian spotted fever from eastern Australia; tick-borne lymphadenopathy from European countries; North Asian tick typhus from China and Russia; and Rocky Mountain spotted fever (RMSF) and *R. parkeri* from North, Central, and South America.

Rickettsialpox, transmitted by house-mouse mites, circulates in urban centers in Ukraine, South Africa, Korea, Balkan states, and the United States. The agent may spill over and occasionally be found within some wild rodent populations.

Scrub typhus is endemic in northern Japan, Southeast Asia, the western Pacific islands, eastern Australia, China, maritime and several parts of south-central Russia, India and Sri Lanka. More than one million cases occur annually. Unusual travel-associated cases of scrub typhus have been diagnosed in individuals returning from Ghana to Japan and from Dubai to Australia. Flea-borne rickettsioses caused by *R. typhi* and *R. felis* are widely distributed, especially throughout the tropics and subtropics and in port cities and coastal regions with rodents. Murine typhus has been reported among travelers returning from Asia, Africa, and southern Europe and has also been reported from Hawaii, California, and Texas in the United States.

Epidemic typhus occurs in communities and populations where body lice are prevalent. Outbreaks have often been tied to periods of war, poverty, and natural disasters, especially during the colder months when infested clothing is not laundered. Active foci of endemic typhus are known in the Andes regions of South America and in Burundi and Ethiopia. Sylvatic epidemic
Typhus is also endemic among flying squirrels in the eastern United States. Tick-associated reservoirs of *R. prowazekii* have been described in Ethiopia, Mexico, and Brazil.

Ehrlichiosis is most commonly reported in the southeastern and south-central United States where the lonestar tick, *Amblyomma americanum*, and white-tailed deer are commonplace. It is also found in Brazil and Panama. In Europe and Asia, transmission of monocytic ehrlichiosis may be due to *E. chaffeensis* or related organisms such as *E. muris* that are associated with ticks of the *Ixodes persulcatus* complex, found on small rodents and passerine birds. Anaplasmosis occurs worldwide, corresponding with the ranges of *Ixodes persulcatus* group ticks. Known endemic regions include the United States, Europe, China, Siberia, Russia, and Korea.

Sennetsu fever occurs in Japan, Malaysia, and possibly other parts of Asia.

**Risk for Travelers**

All ages are at risk for rickettsial infections with travel to endemic areas, especially when participating in outdoor activities during spring and summer months when ticks and fleas are most active, but infection can occur throughout the year.

Game hunting, traveling to southern Africa, and traveling during November through April represent specific risk factors for ATBF in travelers. One study estimated that the risk of a traveler contracting a rickettsiosis in southern Africa is four to five times higher than that of acquiring malaria.

Contact with tick-infested dogs in areas endemic for certain SFG rickettsiae increases risk of acquiring disease. Outbreaks of rickettsialpox most often occur following contact with infected rodents and their mites, especially during natural die-offs or extermination of infected rodents that cause the mites to seek out new hosts, such as humans.

Most travel-acquired cases of scrub typhus occur during visits to rural areas in endemic countries for activities such as camping, hiking, or rafting.

Humans exposed to flea-infested cats, dogs, and peridomestic animals while traveling in endemic regions are at greatest risk for flea-borne rickettsioses.

Travelers at greatest risk for epidemic typhus include those who may work with and/or visit areas with large homeless populations, impoverished areas or refugee camps, and regions that have recently experienced war or natural disasters, especially during the colder months. Sylvatic epidemic typhus cases occur only from direct contact with flying squirrels or their nesting materials.

Sennetsu fever can be contracted from consuming raw infected fish.

**Clinical Presentation**

Although the clinical presentation varies by pathogen, some common symptoms that typically develop within 1–2 weeks of exposure include fever, headache, malaise, and sometimes nausea and vomiting. Most tick-transmitted rickettsioses are accompanied by a macupapular, vesicular or petechial rash, and/or an eschar at the site of the tick bite.

While many rickettsial diseases cause mild or moderate illness, epidemic typhus and RMSF can be quite severe and may be fatal in 20%–60% of untreated cases.

Most symptoms associated with rickettsial infections are very nonspecific and require further tests to make an accurate diagnosis.
Diagnosis
If clinical symptoms and the epidemiologic history are compatible with rickettsial infections, the following diagnostic tests should be utilized:

- PCR test
- Specific immunohistologic detection of rickettsiae

Isolation of a rickettsial agent by culture during the acute stage of illness and before antibiotic treatment. The diagnosis can be confirmed at a later time by obtaining acute- and convalescent-phase serum from the patient. In patients suspicious for rickettsial disease, an acute-phase serum should be drawn and held in case serology becomes necessary at a later time. Most serum specimens collected during the acute stage of rickettsial diseases do not contain antirickettsial antibodies, although immune responses to scrub typhus rickettsiae can be very rapid.

Treatment
Diagnosing a rickettsial infection can be difficult, but rapid treatment with appropriate antibiotic therapy is critical for rapid recovery. Treatment must be based on clinical suspicion and not be delayed pending results of laboratory tests. Antibiotics of the tetracycline class (doxycycline in particular) have a high degree of efficacy and low toxicity in treating rickettsial infections, even in children. Depending on the specific pathogen, chloramphenicol, azithromycin, fluoroquinolones, and rifampin may also be considered, but these are not universally effective for all rickettsial agents, nor have they been evaluated by controlled clinical trials.

The standard treatment regimen consists of 200 mg of doxycycline daily for 3–14 days or 2.2 mg/kg body weight per dose administered twice daily (orally or intravenously) for children weighing <100 lbs. (45 kg). However, the specific type and duration of antibiotic administered may vary, depending on the disease and kinetics of defervescence. Physicians can consult with CDC to obtain further information and access diagnostic services.

Preventive Measures for Travelers
No vaccines or drugs are available for preventing infection. The best prevention is to minimize exposure to fleas, ticks, and animal reservoirs when traveling in endemic areas. The proper use of insect repellents, avoiding vector-infested areas, and wearing protective clothing are important ways to reduce risk.

These precautions are especially important for persons with underlying conditions that may compromise their immune systems, as these individuals may be more susceptible to severe disease.

Source: U.S. CDC (Centers for Disease Control), Atlanta, Georgia, USA. World Trade Press is not in the health care business and accepts no liability for statements on this page.