

Murine Typhus

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Murine typhus, also called endemic typhus, is an acute febrile illness caused by the bacteria *Rickettsia typhi* or *Rickettsia felis*. Rickettsial infections are caused by obligate intracellular Gram-negative bacteria of the genus *Rickettsia*. The bacteria grow in the hindgut of the flea and are shed in its feces. The bacteria is spread to humans when the feces are inoculated into the bite, frequently through scratching.

Murine typhus used to be common in the United States, but was almost entirely eradicated due to a campaign begun in 1945 that focused on vector and environmental control measures. In 1943, Louisiana had 423 cases. Since 1940s, however, nationwide incidence has dropped to less than 100 cases per year. Louisiana saw two cases in the 1960s, two cases in the 1970s, none in the 1980s, and one in the 1990s. However since 2010, Louisiana has begun receiving electronic lab reports with results that may be indicative of murine typhus. It is difficult to tell if this is because there is an actual increase in murine typhus, or whether it is an artifact caused by laboratory testing which was previously unavailable. Murine typhus also remains common worldwide, mainly in coastal and port cities, especially those with large rodent populations. Sporadic outbreaks do occur in the United States, typically in California and Texas.

Epidemiology

Unlike epidemic typhus, which is transmitted through lice, the vector for murine typhus is fleas. *R. typhi* is spread through the oriental flea, *Xenopsylla cheopis*, and *R. felis* is typically spread through the cat flea, *Ctenocephalides felis*. The common reservoirs for *X. cheopis* are the black rat or roof rat (*Rattus rattus*), and Norway or wharf rat (*Rattus norvegicus*), although it has been found in many other rodent species. Common reservoirs for *C. felis* are domestic and feral cats, opossums, and domestic dogs. There have been reports of *R. felis* in a variety of other mammal species, including rodents and livestock, however. Literature supports the opossum as a primary host, with one study finding large overlap between areas of endemic murine typhus transmission and seropositive opossum ranges.

There is also potential for travelers to contract murine typhus in other countries where the disease is endemic, especially in coastal cities of tropical and semitropical areas.

Most cases of murine typhus have been documented in the late summer and early fall, although regional variations are seen. California transmission occurs more frequently in summer and fall, whereas Texas cases are more often seen in late spring and early summer. Hawaii sees cases throughout the year.

Transmission seems to be more correlated with flea vector activity than reservoir activity – flea propagation requires hot, dry environments.

Clinical Description

After an incubation period of six to 14 days (average time: 12 days) an acute, nonspecific febrile illness develops. The fever may last between three to seven days. Most cases also report headache, chills, arthralgia, and myalgia, and some report rash. The rash normally erupts on the upper trunk and spreads outward, usually excluding the face, soles of the feet, and palms, which can help differentiate it from Rocky Mountain Spotted Fever, where the rash does typically extend to the palms and soles of the feet. Laboratory abnormalities that have been reported include anemia, leukopenia, thrombocytopenia, or elevation of hepatic transaminases.

Due to its general symptoms, murine typhus frequently goes unrecognized or is confused with other diseases.

The mortality rate for murine typhus with appropriate antibiotic use is less than 1%. Without treatment, however, the disease becomes more severe, and potential for complications increase. Because it may take up to 10 days for antibodies to become present, antibiotic therapy should be administered upon suspicion of a rickettsial infection. The disease is normally less severe in children. Risk factors include advanced age and immunocompromised status.

Surveillance

Murine typhus is not currently a reportable condition in Louisiana.

Laboratory Tests

Serologic assays are the most widely available and frequently used methods for confirming cases of murine typhus. The indirect immunofluorescence assay (IFA) is generally considered the current standard procedure. IFA can be used to detect either IgG or IgM antibodies. Blood samples taken during acute and convalescent phases, separated by two to three weeks, are the preferred specimens for evaluation.

Diagnostic levels of IgG antibody generally do not appear until seven to 10 days after the onset of illness. It is important to consider the amount of time it takes for antibodies to appear when ordering laboratory tests, especially because most patients visit their physician relatively early in the course of the illness, before diagnostic antibody levels may be present. The value of testing two sequential serum or plasma samples together to show a rising antibody level is considerably more important in confirming acute infection with rickettsial agents because antibody titers may persist in some patients for years after the original exposure.

Collect one red-topped tube of blood within seven (7) to ten (10) days after the onset of illness and a second specimen 14 to 21 days later. Submit blood as spun down sera or as refrigerated whole blood.

Serologies for rickettsial diseases can be cross-reactive, so specimens should be tested against a panel of Rickettsia antigens to differentiate between disease due to Spotted Fever and Typhus groups.

A reliable option is polymerase chain reaction testing, which isolates small segments of DNA from the

organism's genome. This is the most useful test early in the course of the illness, before an antibody response is detected.

Another approach to murine typhus diagnostics is immunostaining. This method is used by taking a skin biopsy of a rash from an infected patient prior to therapy or within the first 48 hours after antibiotic therapy has been started. There are concerns, however, about the sensitivity of this test. This assay may also be used to test tissues obtained at autopsy.

The Weil-Felix test is not appropriate for determination of murine typhus.

Treatment

The treatment of choice is doxycycline or another tetracycline antibiotic. Chloramphenicol is also an appropriate treatment, if doxycycline is contraindicated.

Delayed treatment increases the length of the illness and the risk for complications.

Case Definition

Clinical Presentation

Murine typhus is characterized by any of the following symptoms: fever ($\geq 100.4^{\circ}\text{F}$), headache, malaise, anorexia, chills, myalgia, rash, leukopenia, thrombocytopenia, or elevation of hepatic transaminases, in the absence of any other known cause. Rash usually starts on the trunk and spreads to the entire body, usually excluding the face, palms, and soles of the feet. Symptoms tend to mimic epidemic typhus, but are generally milder.

Confirmed

Clinically compatible case that is confirmed by one of the following laboratory tests:

Laboratory confirmation tests:

- Serological evidence in paired acute and convalescent serum specimens of a four-fold or greater change in antibody titer reactive with *R. typhi* or *R. felis* by indirect immunofluorescence assay (IFA), complement fixation (CF), latex agglutination (LA), microagglutination (MA), or indirect hemagglutination antibody (IHA) test, ideally taken at least three weeks apart OR
- Detection of *R. typhi* or *R. felis* by PCR assay OR
- Demonstration of positive *R. typhi* or *R. felis* antigen in tissue or skin lesion (biopsy) or organ tissue (autopsy) OR
- Isolation of *R. typhi* or *R. felis* from clinical specimen in cell culture

Probable

Clinically compatible case with supportive lab results

Supportive laboratory results:

- Serologic evidence in a single serum specimen of elevated IgM and/or IgG antibody reactive to *R. typhi* or *R. felis* antigen by IFA with a titer of $\geq 1:128$.

- A single CF of ≥ 16 OR
- Other supportive serology (single titer $> 1:64$ by an LA, IHA, or MA test)

Suspected

- 1) A clinically compatible case with an epidemiological link to a confirmed case (ie, shares household or exposure with confirmed case), but does not have laboratory testing, or
- 2) a case with laboratory evidence of past or present infection but no clinical or epidemiological information is available (ie, a laboratory report).

Exposure

Any patient who had opportunity to come into contact with opossums, domestic animals, or their fleas, including outdoor exposure at home and/or at work. Travel to tropical or semitropical coastal cities, or those with large rat populations, is also considered a potential exposure. The patient does not need to report flea bites to be considered exposed.

Prevention

Eliminate habitat of opossums, stray cats, and rodents by trimming foliage, eliminating heavy undergrowth, clearing woodpiles, and covering holes, crawlspaces, and passageways. Holes, burrows, and rat runs may be treated with insecticide. Flea populations should be reduced before rodent control measures are taken, or else fleas will leave and seek new hosts, which may increase chances of infection among humans and domestic animals.

Do not feed wild or feral animals. Keep trash cans covered, and cover pet food that is kept outside. Eliminate any food or water sources that may attract wild or feral animals.

Flea prevention should be used on domestic pets, and they should not be allowed to roam freely, where they can come into contact with infected fleas.

Insect repellent containing DEET, gloves, and goggles should be worn before cleaning any of these areas. Spraying thoroughly with disinfectant can also help eliminate transmission through feces. Do not attempt to relocate feral or wild animals – contact local animal control agencies.

Hospital Precaution and isolation: Standard precautions should be taken.