



A SUBURBAN NEIGHBORHOOD OUTBREAK OF MURINE TYPHUS SOUTH PASADENA, MAY 2005

BACKGROUND

Murine typhus is an acute febrile illness resulting from infection with *Rickettsia typhi*—a small Gram-negative, obligate intracellular bacterium. It is transmitted to humans by flea bites and contamination of the bite site or skin abrasions with *Rickettsia typhi*-containing flea feces. Murine typhus is known to be endemic in southern California and Texas—most cases in these two regions have occurred in the absence of the classical transmission cycle; i.e., the flea vector (*Xenopsylla cheopis*, and the oriental rat flea) and the rodent host (*Rattus norvegicus*, the brown rat). However, peridomestic opossums and their fleas have shown to play an important role in murine typhus transmission—especially in urban and suburban areas of Los Angeles County (LAC). Annually, approximately 8 to 17 murine typhus cases are reported in LAC. Most cases are residents of central LAC foothills. Transmission of infection is most likely due to reservoir animals such as opossums and rats that live in these areas with heavy foliage.

In mid-May 2005, ACDC investigated an outbreak of murine typhus involving residents a single street block in South Pasadena. The index case was hospitalized on May 14 at a medical center in the San Gabriel Valley with a febrile-rash syndrome and was initially suspected of having West Nile virus (WNV) infection. Subsequent serologic laboratory studies supported the diagnosis of murine typhus. Further investigation was prompted when ACDC subsequently received telephone calls from the index case's neighbors experiencing similar compatible symptoms. Ultimately, two confirmed, two probable and two possible cases were documented (see case definition below).

METHODS

Case Finding: Murine typhus is on the list of reportable communicable diseases within LAC. The index case was diagnosed and reported from a large medical center in the San Gabriel Valley on May 14, 2005. Following this report, the LAC Department of Health Services (DHS) Communication Office drafted and disseminated a press release that: 1) described the ongoing investigation of murine typhus, 2) advised clinicians to report suspect cases to Public Health, and 3) recommended that individuals with signs and symptoms consistent with murine typhus seek medical care. The press release was circulated to local newspapers in known typhus endemic areas and posted on the LAC DHS website. In addition, a health alert network (HAN) communication summarized the press release and was disseminated to emergency rooms and clinicians. Residents of households within three blocks were notified of the ongoing investigation, provided with health information, and were requested to seek medical attention should they develop compatible symptoms. Finally, since an elementary school was located across the street from the investigation site, a letter was sent to all parents and students of this school that advised them of the outbreak investigation and recommended that they seek medical attention should they develop consistent symptoms of infection.

Investigation: An ACDC public health nurse interviewed each suspected case, completed a standardized case history report and reviewed hospital or clinic medical records if available. The Alhambra district public health nursing unit assisted with obtaining specimens for confirmation of these suspected cases.

Laboratory Testing: Free serological testing by immunofluorescent antibody (IFA) was provided through the LAC Public Health Laboratory (PHL) for diagnosis and confirmation of cases. In addition, serum already tested at commercial laboratories were also sent to LAC PHL for additional confirmatory IFA testing.

Environmental Investigation: On May 25, LAC DHS sent an environmental health specialist, an epidemiologist, and a public health nurse to conducted interviews and inspect the homes and yards of three of the four suspect households. The environmental health specialist inspected the properties for



overgrown foliage, rats, and opossums. Educational materials on murine typhus was distributed to the households within three surrounding blocks of the suspected households and to the local elementary school located across the street of the index case.

Case Definitions:

- **Confirmed:** Laboratory confirmation of murine typhus infection plus consistent clinical signs and symptoms including at least two of the following: fever, headache, myalgias, rash or fatigue with supporting. Confirmation was defined as paired serological specimens showing at least a four-fold rise in IgG antibodies between acute and convalescent sera.
- **Probable:** At least two clinical signs and symptoms consistent with murine typhus infection without a supporting alternative diagnosis, but only a single supportive positive serological test suggesting recent infection (IgM > 4 times and/or IgG > 4 times normal).
- **Possible:** At least two clinical signs and symptoms consistent with murine typhus infection without supporting alternative diagnosis, but no laboratory results to support the diagnosis.

RESULTS

Surveillance for cases revealed a total of six cases (Table 1), two female (including the index case) and four male. The average age of the cases was 46.7 years (median 49 years). Of the six cases, illness was confirmed in two cases (the index case and her son), probable in two cases and possible in two cases. Onset of symptoms occurred within roughly 2 weeks of each other during March 2005.

Index Case (Case 1): The index case was a previously healthy 49 year-old female who reported symptom onset on May 6, 2004. She reported a history of fevers up to 104° F, nausea vomiting, fatigue, muscle pain and a faint macular-papular rash on her chest and abdomen. She sought medical care and was diagnosed with a viral syndrome by her primary care physician. After eight days of persistent symptoms, she was admitted to a local medical center with a diagnosis of fever and dehydration. Her treatment revealed elevated transaminases five times normal values; however, a viral hepatitis panel was negative. Her blood and urine cultures were negative and radiological studies were normal. During her hospitalization, an infectious disease consultation was completed where animal, mosquito, travel, and flea exposures were queried. She reported she had recently found three dead possums on her property and has two indoor/outdoor cats with recent histories of flea bites. Both murine typhus and WNV serologies were subsequently ordered. Acute murine typhus serology revealed borderline positive IgM and negative IgG. Convalescent serology drawn two weeks later was strongly positive—both IgM and IgG had increased 16-fold since her acute serology (Table 1). Her WNV serology was IgG positive but IgM negative. The case was treated with a short course of doxycycline and improved quickly.

Case 2: Approximately 10 days after her symptom onset, her 10 year-old son also reported experiencing fevers, fatigue, and muscle weakness without rash. He was seen by his pediatrician and was diagnosed with a “viral syndrome.” Upon request, murine typhus serologies were obtained, but did not support the diagnosis of acute infection. Convalescent titers, obtained two weeks later, were strongly positive (1:1024 IgM and IgM), thus supporting the diagnosis of murine typhus. The son’s symptoms resolved on without treatment.

Cases 3 through 6: Four additional suspected cases were investigated—all residing in households on the same street as the index case. Two of the four cases (Case 3 and Case 6) were classified as *probable* since both had clinical signs and symptoms consistent with infection and a single supportive serological specimen; these cases were not hospitalized, but treated with doxycycline and improved rapidly. Both had convalescent serologic evaluation taken 10 and 18 days after symptom onset. Case 3 had IgG and IgM titers 16 times the normal value and Case 6 had IgM two times normal and IgG eight times above the cut off.

Two additional cases (Cases 4 and 5) had symptoms suggestive of murine typhus without any other explanation. In both cases, serologic testing either did not support the diagnosis or was not obtained. As such, both were classified as *possible* cases. Because of his age (81 years), Case 4 was hospitalized to



rule out sepsis and was found to be hypotensive. His onset date was 17 days after the index case. An acute murine typhus serology was obtained during his hospitalization, but being within the normal cut off values this did not support the diagnosis of murine typhus infection. Unfortunately, Case 4 would not consent to convalescent serologic laboratory testing. Case 4 was presumptively treated with doxycycline and recovered. Case 5 was the nephew of Case 4 and also resided in the same household. He reported fever and chills for seven days—nine days after index case's onset. Case 5 refused any offers to have serologic testing. He recovered without treatment.

Environmental Investigation: A site investigation conducted May 24 did not reveal any opossums (live or dead) on the four properties of the six cases; however, the cases of three of the households (representing Cases 1, 2, 3, and 6) self-reported the presence opossums. Most notably, the index case reported that three dead opossums had been removed by animal control a few weeks earlier—this is significant considering the index case and her son (Case 2) were the only cases with confirmed infection in this investigation.

In addition, during the environmental investigation tree rats were noted on the property of the index case and her son (Case 1 and Case 2) and on one of the neighboring households (Case 3). In addition, significant overgrown vegetation was noted on all four properties. No additional trapping for opossums or rats, cat serological testing, or flea collection was completed during this investigation.

DISCUSSION

Murine typhus is an established endemic vector-borne disease in LAC. Surveillance has demonstrated it is localized to hillsides and adjoining communities of Pasadena, Alhambra, South Pasadena, and Los Feliz. Fortunately many clinicians, especially infectious disease clinicians, in these endemic areas are aware of the risks and order appropriate diagnostic testing.

Despite extensive outreach to find additional murine typhus cases, only two definite, two probable, and two possible cases were found on one street block of adjacent houses—no additional cases were found on adjoining streets. Although small clusters of murine typhus cases have been documented in past years, this is the largest outbreak of cases that ACDC has documented. It is interesting that the outbreak involved four households within one city block in South Pasadena. Cases occurred within a 17-day period in May after a large opossum die-off was noted by the index case. Three of the four households (representing four of the six cases) reported seeing opossums in their yards and also had indoor/outdoor cats. It is possible that cat fleas (*Ctenocephalides felis*) were infected with *R. typhi*. Since, none of the domestic cats or neighborhood cats was tested for evidence murine typhus infection, it is unknown whether cat fleas were the source of the human infection.

Murine typhus is generally benign but may cause severe disease including hepatitis, pneumonia, meningitis, and rarely death. Two of the cases in this investigation (Case 1 and 4) required hospitalization. The index case, Case 1, appeared to have the most severe disease with evidence of hepatitis. And Case 4, the elderly neighbor, had a septic picture with mental status changes. A thorough infectious disease work-up could not pinpoint an etiology; acute serological specimens were in normal range, but the patient refused convalescent blood testing.

For both Cases 1 and 2, convalescent titers were available to confirm the diagnosis of murine typhus. Most infectious disease and public health specialists recommend convalescent titers when the diagnosis is suspected. Currently, there is no established national or state case definition for murine typhus; however, in many serologically diagnosed viral diseases, both acute and convalescent serologies are required to make the diagnosis. In our index case, Case 1, although she experienced compatible symptoms for at least 10 days, she had normal IgG with a strongly positive IgM acutely, and her convalescent test demonstrated a four-fold rise in IgG with a four-fold decline in IgM. Interestingly, her son (Case 2) had normal IgG and IgM acutely, but his convalescent tests were both strongly positive (> 4 fold rise). It is possible that many cases in LAC are missed because clinicians obtain only an acute serology, which can be negative early in infection.



Murine typhus infection can be prevented through flea control measures on pets and in the yard. Foliage in the yard should be kept trim so that it does not provide harborage for small mammals. Screens can be placed on windows and crawl spaces to prevent entry of animals into the house. It is possible that heavy seasonal rainfall in 2005 contributed to overgrowth of plantings and increased populations of opossums.

REFERENCES

- Dumler, JS, Walker DH. *Rickettsi typhi* (Murine Typhus). In: Mandell, Douglas, and Bennett's Principles and Practices of Infectious Disease 6th edition. 2005; Vol 2: 2306-09.
- Azad AF, Radulovic S, Higgins JA, Noden BH and Troyer JM. Flea-borne Rickettsioses: Ecologic Considerations. *Emerg Infect Dis* 1997;3:319–27.
- Sorvillo FJ, Gondo B, Emmons R, Ryan P, Waterman SH, Tilzer A, Andersen EM, Murray RA, and Barr AR. A Suburban Focus of Endemic typhus in LAC: an association with seropositive domestic cats and opossums. *Am J Trop Med Hyg* 1993;48:269–73.
- Williams SG, Sacci JB Jr, Schriefer ME, et al. Typhus and typhuslike rickettsiae associated with opossums and their fleas in Los Angeles County, California. *J Clin Microbiol* 1992; 30:1758–62.
- General information about murine typhus is available from the ACDC website at www.lapublichealth.org/acd/vectormurine.htm

Table 1. Murine Typhus Investigation, South Pasadena, California, May 2005

Patient Suspect	Household	Case Status	Age (yrs.)	Sex	Date Symptom Onset	Symptoms	Hospitalization	Acute Serology*	Convalescent Serology*	Other Tests	Animal Exposures
Index Case 1	1	Confirmed	49	F	5/6/05	Fever, rash, headache, myalgia, nausea/vomiting	3 days 5/14/05 to 5/17/05	5/16/05 IgM 1:256 IgG <1:64	6/2/05 IgM 1:512 IgG 1:512	WNV+ IgG Elevated tranaminases	3 outdoor cats; 1 dog; 3 dead opossums noted in backyard.
Case 2	1 (Son of Index Case)	Confirmed	10	M	5/16/05	Fever, headache, chills, myalgia	None	5/20/05 IgM <1:64 IgG <1:64	6/7/05 IgM 1:1024 IgG 1:1024	None	Same as index. (above)
Case 3	2	Probable	59	M	5/13/05	Fever, headache, chills, myalgia	None	5/27/05 IgM >1:1024 IgG >1:1024	Not completed	None	No cats. Rodents and opossums noted nearby and under home within 2 weeks of onset.
Case 4	3	Possible	81	M	5/23/05	Fever, headache, chills, myalgia	None	5/24/05 IgG <1:64 IgM <1:64	Not completed	None	Unknown**
Case 5	3	Possible	26	M	5/15/05	Fever, headache	None	Refused testing	Not completed	None	Unknown**
Case 6	4	Probable	49	F	5/14/05	Fever, headache, chills, myalgia	None	6/17/05 IgG 1:128 IgM 1:512	Not completed	None	1 outdoor/indoor cat; 2 dogs. Rodents observed in house, garage and neighborhood. Opossums seen outside home.

* All listed results completed by the Los Angeles County Public Health Laboratory.

** While animal exposures are unknown, this household is nearby the households of the other cases and substantial overgrowth was noted during environmental investigation.