Surveillance of Flea-Borne Typhus in California, 2011–2019

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Abstract. Flea-borne typhus (FBT), also referred to as murine typhus, is an acute febrile disease in humans caused by the bacteria Rickettsia typhi. Currently, cases of FBT are reported for public health surveillance purposes (i.e., to detect incidence and outbreaks) in a few U.S. states. In California, healthcare providers and testing laboratories are mandated to report to their respective local public health jurisdictions whenever R. typhi or antibodies reactive to R. typhi are detected in a patient, who then report cases to state health department. In this study, we characterize the epidemiology of flea-borne typhus cases in California from 2011 to 2019. A total of 881 cases were reported during this period, with most cases reported among residents of Los Angeles and Orange Counties (97%). Demographics, animal exposures, and clinical courses for case patients were summarized. Additionally, spatiotemporal cluster analyses pointed to five areas in southern California with persistent FBT transmission.

INTRODUCTION

Flea-borne typhus (FBT), also known as endemic typhus or murine typhus, is a febrile disease caused by Rickettsia typhi. The Gram-negative, intracellular bacterium is a member of the typhus group rickettsiae and is closely related to Rickettsia prowazekii, the causative agent of epidemic typhus. Like other Rickettsia species, R. typhi relies on arthropods and mammalian hosts to maintain its life cycle. Rickettsia felis, a species in the transitional Rickettsia group, has also been suggested as an agent of FBT. However, R. felis has not been identified in human infections in California.

The FBT transmission cycle revolves around the primary mammalian host (Rattus spp.) and arthropod vector, the rat flea (Xenopsylla cheopis). This cycle is often referred to as the urban cycle. In Texas and California, an additional cycle of transmission involves opossums (Didelphis virginiana) as a potential reservoir to R. typhi and the cat flea (Ctenocephalides felis) as the principal arthropod vector.2,3 This cycle is often referred to as the suburban cycle due to the ecological overlap between opossums, cats, and humans outside major city centers. Fleas may acquire the bacteria while feeding on rickettsia-infected hosts. The bacteria reside in the midgut epithelium of the flea, where they can be transmitted to humans or other hosts by introducing infected feces onto flea bite wounds or mucous membranes.4

Human infections are often characterized by nonspecific symptoms, including fever, headache, myalgia, and rash. Most infections are considered self-limiting and mild but may require inpatient care. A review of typhus group rickettsiases surveillance in Texas noted that 59.6% of case patients were hospitalized from 2003 to 2013.5 Although the mortality rate of FBT is relatively low (0.4%), it may progress to severe disease in 10% to 25% of cases.1,6,7 Clinical severity of FBT is associated with older age, delayed diagnosis, use of sulfonamide antibiotics, glucose-6-phosphate dehydrogenase deficiency, and alcoholism.8 Severe manifestations have been reported to occur in 28% of cases.9 Manifestations of severe illness include hepatic injury and conditions compromising renal, pulmonary, central nervous system function, shock, bronchiolitis, pneumonia, encephalitis, renal failure, and sepsis.9,10–11

Flea-borne typhus occurs worldwide, particularly in tropical or subtropical coastal regions. Cases of FBT in the United States peaked in 1944 when more than 5,000 cases were reported nationally. The implementation of vector control programs decreased the number of cases in the United States through host removal (rodent trapping) and dichlorodiphenyltrichloroethane use for household pest control as well as targeted control of rat harborage.12,13 In the 1950s, fewer than 100 cases were reported in the United States annually.14,15 Currently, most human cases in the United States are reported from Hawaii, southern Texas, and southern California.15

Flea-borne typhus is not nationally notifiable, although FBT cases in California have been reportable since 1916. Mandatory electronic laboratory reporting of typhus group Rickettsia-positive samples began in 2011.16,17 Reported cases in California have increased in recent years, particularly in southern California, where an endemic focus has emerged in a region within Los Angeles and Orange Counties. For this study, data for FBT cases were captured using a single case definition from 2011 to 2019, facilitating a standardized collection of demographics, clinical, and laboratory information. This article aims to summarize FBT surveillance data from this period to characterize the current epidemiology of the disease in California. Furthermore, this report outlines spatiotemporal clusters of FBT detected in Los Angeles County. Assessing these data may improve local public health response and highlight areas for improvement in FBT surveillance.

MATERIALS AND METHODS

Data sources. The California Department of Public Health (CDPH) receives reports of notifiable disease incidence case report forms (CRFs) electronically through the California Reportable Disease Information Exchange (CalREDIE) or directly from local health jurisdictions (LHJ; i.e., county or
city health departments). Most typhus cases are identified after case-patients seek medical care for their symptoms. Serologic assays detect immunoglobulin antibodies (i.e., IgG or IgM) in serum samples or R. typhi DNA in whole blood samples. Local health jurisdictions receive notifications from providers or laboratories of positive FBT case-patients. The LHJs collect case-patient information using an FBT-specific case report form. Reports include basic demographic information such as residence, place of work, race/ethnicity, age, and gender, as well as more detailed data describing the clinical course, diagnostic test results, possible exposures, and illness resolution. The CRF data are submitted electronically to CDPH directly or via CalREDIE.

This report summarized surveillance data following the California surveillance case definition used between 2011 and 2019 to describe the epidemiology of reported cases. This surveillance case definition classified reports as confirmed, probable, or suspect and do not necessarily reflect clinical definitions for flea-borne typhus. Briefly, confirmed cases under the surveillance case definition must be clinically compatible (e.g., experienced fever, headache, myalgia, or rash) with laboratory confirmed evidence. Laboratory-confirmed evidence included a 4-fold increase in titer between acute and convalescent samples, a positive IgG and IgM serologic response ($>1:128$) in a single sample, or detection of DNA for R. typhi or other Rickettsia species by quantitative polymerase chain reaction (qPCR), excluding R. rickettsii, in blood or tissue. Probable cases have clinically compatible symptoms and supportive laboratory evidence (i.e., either IgM or IgG positive for R. typhi antigen by immunofluorescence assay $>1:128$ without convalescent titer or positive qPCR). Suspect cases lack clinical evidence of disease or are without documentation of disease course (e.g., clinical assessments not performed, or no medical records are available) and have supportive laboratory evidence. Some probable cases that are epidemiologically linked to a confirmed case (e.g., family member) may be reclassified as confirmed cases. Only confirmed and probable reports were considered cases of FBT and analyzed in this study (Supplemental Table 1).

Race and ethnicity were combined to form a new variable, race/ethnicity, to evaluate the demographics of reported cases. Hispanic or Latino ethnicity was collapsed into the race category. For example, if a person identified ethnicity as Hispanic or Latino and White race on their CRF, their race/ethnicity record was reflected as Hispanic or Latino. A person without indication of Hispanic or Latino ethnicity on their CRF was recorded as their race alone (e.g., non-Hispanic Asian was recorded as Asian).

Animal exposures (e.g., fleas, opossums, rats, cats, dogs) were collected from fields on the CRF and supplemental forms. Frequency of exposures were tabulated if the infected person reported the animal in or near their home residence or place of work.

Some CRFs included supplemental hematology results. Thrombocytopenia was classified as a platelet count less than normal human platelet count range lower limit (<150,000 platelets per microliter of blood), leukopenia as a reduction in white blood cell count <3.5/$\mu$L. Elevated liver enzymes were classified if either aspartate transaminase (AST) levels exceeded 40 IU/L or alanine transaminase (ALT) levels were above conventionally accepted upper normal limits for adults, 40 IU/L.18-21

County population and demographic data were retrieved from corresponding 1-year American Community Survey (ACS) estimates. Racial/ethnic and gender composition of typhus cases in Los Angeles County and Orange County were compared with their respective proportion of the county population using ACS population demographic estimates. County race and ethnicity estimates followed the same combination criteria as used in the FBT race/ethnicity variable combination. Cumulative incidence rates (i.e., reported cases per population) were calculated per 100,000 population at risk from 2011 through 2019 using the average estimated population for Los Angeles and Orange Counties.

Household addresses were mapped for cases reported from each jurisdiction, assuming these served as the primary exposure location. Records of FBT cases among persons experiencing homelessness (PEH) were reviewed to identify the location of their encampment by address or general location. Coordinates corresponding to the centroid of a given neighborhood were assigned to PEH if the individual acknowledged living in that area at the likely time of exposure (e.g., a PEH without an address acknowledging they lived in Central City East (“Skid Row”) would be assigned the coordinates corresponding to the centroid of Central City East, Los Angeles). Household addresses were included in the spatiotemporal cluster analysis if 1) location was obtainable, including latitude and longitude; 2) location could be geocoded to a census tract upon case record review if household addresses were not available; 3) location was within a census tract with a population greater than zero; and 4) date of episode was available in the case record.

During the surveillance period, the population did not fluctuate greatly for Los Angeles and Orange counties. The total population in these counties increased by approximately 2.9% from 2010 to 2020, with an estimated average increase of 1% year-to-year from 2011 to 2019.22,23 Therefore, the 2017 ACS 5-year census tract population estimates were used to represent all years under study. Population data were downloaded from the 2017 ACS 5-year estimates for each census tract in Los Angeles and Orange Counties. County and census tract shapefiles for 2017 were accessed using California Open Data Portal. California city shapefiles for 2017 originate from the U.S. Census Bureau’s TIGER/Line database and are publicly available from the U.S. Open Data portal.

**Spatiotemporal cluster analysis.** Case addresses were aggregated by census tracts to retrieve the number of cases per tract per month for the surveillance period. Census tracts were chosen as the unit of analysis due to 1) the availability of underlying population data for each census tract to standardize the raw count data; 2) the ability to create zero-count data, observations with zero cases, otherwise unavailable while using case-only FBT typhus data; and 3) maintenance of privacy for patients by not directly disclosing their location. To model count data at the census tract level correctly, a discrete Poisson model was used for the spatiotemporal cluster analysis. A maximum cluster radius of 2.3 kilometers was specified to provide practical value (i.e., development of prevention and intervention efforts in smaller localities) to identified clusters and determined by calculating the median area of cities in Los Angeles and Orange Counties in square meters (Supplemental Table 2). Cluster centers were restricted from geographically overlapping. With case counts temporally aggregated to monthly case counts per census
tract, the minimum temporal cluster size was set to 1 month and the default maximum temporal cluster size (50% of period under study) was used in SatScan. Relative risks for retrospective spatiotemporal clusters were calculated by estimating the risk within the cluster divided by the estimated risk outside the cluster conditioned on the cumulative number of cases observed in the specified time and space. Spatiotemporal cluster analyses were conducted using SatScan v9.7. Maps and plots were created using ArcGIS Pro 2.7.0.

This study was considered exempt for human subjects review by the California Health and Human Services Agency’s Federal wide assurance #00000681; approval was obtained from the Office of Human Research Protections, Committee for the Protection of Human Subjects (Project: 2020-117).

RESULTS

Flea-borne typhus surveillance. From 2011 to 2019, 881 cases of FBT were reported to CDPH; 529 (54.9%) met the case definition for confirmed and 352 (36.6%) were probable. The number of cases reported each year within the timeframe ranged from 47 in 2011 to a peak of 164 cases in 2018 (Figure 1). Cases were reported from 16 local health jurisdictions. Most cases were reported from Los Angeles County (n = 685, 77.8%) and Orange County (n = 169, 19.2%). The cumulative incidence rate was 6.82 cases per 100,000 in Los Angeles County and 5.38 cases per 100,000 in Orange County during the 9-year surveillance period. Sporadic cases were reported in other southern California counties, including San Diego (n = 5), San Bernardino (n = 4), and Riverside (n = 1). Cases occur throughout the year, but approximately half (n = 439, 49.8%) occur during the summer months June through September (Figure 2).

The distribution of clinical and laboratory findings was similar for both classifications and thus were combined in Table 1 (demographics) and Table 2 (clinical and laboratory findings). Most cases were reported among males (n = 504, 57.2%). The median age among reported cases was 43 (0–93; Table 1). White (n = 374, 42.5%) and Hispanic or Latino (n = 291, 33.0%) race and ethnicity were most frequently reported. Forty-nine (5.6%) case patients identified as Asian, 30 (3.4%)
as Black or African American, 5 (0.6%) as Native Hawaiian or Pacific Islander, and 4 (0.5%) as American Indian or Alaskan Native. Interestingly, when considering only Los Angeles and Orange County cases, non-Hispanic White case-patients were underrepresented when compared with the population distribution in Los Angeles and Orange counties (Figure 3). Race and ethnicity data were unknown for 128 (14.5%) case-patients.

A total of 733 (83.2%) case-patients reported receiving inpatient care. Among those with hospitalization admission and discharge dates available (n = 659, 74.8%), the median length of initial stay was 4 (range 0–84) days. Twenty-nine (3.29%) case-patients were readmitted for a median period of 3 (range 0–8) days after their initial hospitalization. The average time between the onset of symptoms and collection of positive antibody test was 12.6 (SD = 23.4) days. Reported clinically compatible signs and symptoms were fever (n = 865, 98.2%), headache (n = 651, 73.9%), myalgia (n = 494, 56.1%), and rash (n = 379, 43.0%). Other commonly reported symptoms included nausea or vomiting (n = 453, 51.4%) and cough (n = 314, 35.6%). Thrombocytopenia was reported in 194 (22.0%) case-patients, leukopenia in 227 (25.8%) case-patients, and elevated liver enzymes (AST or ALT) in 169 (19.2%) case-patients (Table 2).

Of the self-reported animal exposures to cats, dogs, opossums, rodents, and fleas around the case-patients’ household or at the employment location, cat exposures were most frequently reported by case-patients (n = 466, 52.9%) throughout the surveillance period (Table 3). Exposures to dogs (n = 436, 49.5%), opossums (n = 333, 37.8%), rodents (n = 230, 26.1%), and fleas (n = 188, 21.3%) were also noted by cases. History of bug bites during the incubation period (within 14 days before the onset of symptoms) was recalled in 199 (22.6%) case-patients.

**Spatiotemporal clusters.** Out of all reported FBT cases reported in Los Angeles and Orange Counties between 2011 and 2019 (N = 854), 830 were included in the spatiotemporal clustering analysis. Twenty-four cases were excluded from further analysis because of missing or unobtainable location data. There were 8,057 census tracts analyzed from Los Angeles and Orange Counties with a mean (SD) tract area of 50.08 km$^2$ (416.99 km$^2$) and a mean (SD) population of 4,858.97 (2,234.59). Eight spatiotemporal clusters were detected (Figure 4). Most of these clusters were in communities in the city of Los Angeles (Table 4). Two geographically and temporally limited clusters with high relative risks were identified in Willowbrook (RR = 102.9; n = 11), a community in south central Los Angeles County, and San Gabriel Valley (RR = 232.37; n = 5). The combination of smaller temporal window and high RR in these clusters provide evidence of past outbreaks. On the other hand, the most cases reported in a single cluster were identified in Long Beach (RR = 7.54; n = 29) in a temporal window over 4 years long.

**DISCUSSION**

Flea-borne typhus cases in California have reached the highest levels measured in decades. Los Angeles County reported 75 cases of FBT between 1984 and 1994. Between 2002 and 2010, 185 cases of FBT were reported in California. The present study totaled 881 cases reported, 4.8 times more than that of the previous 9-year period, with an average of 97.8 cases per year. Reported cases show the specificity of FBT to the Los Angeles Basin in California, with a greater frequency of cases occurring during summer months. Considering that flea reproduction, feeding, and maturation are all increased during warm weather, it is reasonable to infer that the seasonality of FBT transmission is related to flea biology.

Most demographic findings were similar to those of prior studies. More case-patients were male, which is consistent with prior FBT case series in Colombia (58%), Spain (55%), Greece (57–61%), and Texas (55%). This contradicts race and ethnicity among typhus group rickettsiosis (TGR) cases in Texas, in which 64% of TGR cases were Hispanic or Latino. In an ideal disease surveillance
system, the demographics of disease reports (including non-cases) would reflect those of the population at risk. Discrepancies between observed and expected demographics among cases could then be tested to indicate high-risk groups. Unfortunately, we cannot make this comparison without comprehensive demographic data for suspect and non-cases. In the context of passive disease surveillance for FBT, it is difficult to describe disease risk due to unmeasured confounding in the surveillance system. For example, the under-representation of Hispanic or Latino persons among FBT cases may not necessarily point to a lower risk for this population but a lower likelihood of being tested and diagnosed with FBT. This inconsistency signals a potential gap in FBT surveillance that requires further investigation.

The percentage of cases reporting fever, myalgia, and rash in our study was similar to that of prior studies.5 Also, upper normal limits may also depend on various factors including age, sex, race or ethnicity, preexisting conditions, and location of testing laboratory.37–39 A higher proportion of case-patients in our study reported nausea or vomiting (51.4%), diarrhea (29.4%), and abdominal pain (31.6%) than in prior studies (26.7%, 18.6%, and 18.8%, respectively).7 Thrombocytopenia (22.0%) was also less common than in a systematic review of FBT cases (42.2%).7 Complete blood tests (e.g., platelet counts, white blood cell counts) were unavailable for a high proportion of case records (22%) in the current study. Hospitalization was reported for 83.2% of case-patients in the present study. The proportion hospitalized (83.2%) is higher than that reported for typhus group rickettsioses in Texas from 2003 to 2013 (59.6%) and in a case series of 29 patients in Germany (64%).5,40

At least one animal exposure was recorded for most cases (99.1%). The reported exposures were consistent with animal exposures reported in Texas, except for a lower proportion of reported exposure to fleas in the present study.5 Animal exposure data collected via case-patient recall are problematic for elucidating the role of urban animals in FBT transmission cycles. These data are predicated on what the person sees, thus potentially underreporting animals that are more active at night, such as rodents and opossums. Domestic animals such as dogs and cats may also be overrepresented due to pet ownership. A limitation of the exposure data presented is that they differentiate free-roaming animals, pets owned by the case household, or pets belonging to others in the community. The surveillance data also do not account for flea control medication use, meaning that animal exposure may not indicate R. typhi exposure. Although the findings may direct general hypotheses on reservoirs and vectors, better characterization would be gained from on-the-ground ecological studies or standardized improvements in exposure data collection.

Geographically and temporally smaller clusters with larger relative risks detected in SatScan are highly indicative of potential health hazards. Two resulting spatiotemporal clusters relate to outbreaks (e.g., five or more cases within 1 month to 1 year in a defined area) of flea-borne typhus determined by local health jurisdictions. The Willowbrook (cluster 1) and downtown Los Angeles (cluster 8) clusters each included a time frame that fits with previously reported outbreaks in Los Angeles County.41 The extremely high RR estimates in the resulting spatiotemporal clusters are because these outbreaks were geographically confined and occurred over a relatively short time frame. Similarly, the San Gabriel Valley cluster (cluster 4) corresponds with a brief but well-documented outbreak in a mobile home park.42

Long periods, such as periods extending multiple years, observed in most of the clusters (clusters 2, 3, and 5–7; Table 4) may reflect populations or areas with persistent FBT

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**TABLE 3**

Self-reported animal exposures around household or employment location among FBT case-patients, California, 2011–2019

<table>
<thead>
<tr>
<th>Reported exposure</th>
<th>Total reported (N = 881)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cats</td>
<td>466 (52.9%)</td>
</tr>
<tr>
<td>Dogs</td>
<td>436 (49.5%)</td>
</tr>
<tr>
<td>Opossums</td>
<td>333 (37.8%)</td>
</tr>
<tr>
<td>Rodents</td>
<td>230 (26.1%)</td>
</tr>
<tr>
<td>Fleas</td>
<td>188 (21.3%)</td>
</tr>
</tbody>
</table>

FBT = flea-borne typhus.
transmission rather than emerging health hazards. The Pasadena Public Health Department reports localized hotspots year-to-year and reported epidemic levels of FBT reported in 2018. The resulting high RR and long temporal period in Cluster 3 is likely due to combining effects of FBT persistence in independent hotspots annually and outbreaks in 2018. Cluster 2 (i.e., Long Beach) had relatively low relative risk and higher number of cases in a period over 4 years long and may be attributed to FBT endemicity in the city of Long Beach. The remaining clusters (5–7) in communities within the city of Los Angeles have lower RRs, fewer cases, and long temporal intervals. These may point to areas where cases are periodically reported or where risk is higher than expected. In other words, FBT cases arise from these areas frequently enough to suggest association with some underlying process, but elucidating specific reasons will require further research.

The combination of significant high transmission areas in Pasadena and Long Beach and the absence of spatiotemporal clusters in Orange County despite a significant disease burden warrant further attention. Long Beach and Pasadena are two of three state-recognized city-level health jurisdictions in California. All other local health jurisdictions operate at the county level. It is worth considering whether these findings are driven by differential public health activities improving knowledge and awareness of FBT in high-risk locations, resulting in differences in FBT surveillance ascertainment between each of the four jurisdictions included in the region.

These data present potential biases and limitations. Because most cases are identified after seeking health care, the data captured here likely represent relatively severe infections of R. typhi. The discrepancy between lower rates of severe cases historically (10–25%) and the relatively high proportion of cases receiving inpatient care in the present data (83.2%) point to potential selection bias. The surveillance system’s reliance on a person to seek out medical attention to receive adequate testing and subsequently being identified as a case may cause an underestimation in FBT cases, especially in the context of typically moderate clinical signs and symptoms of FBT. Furthermore, social and economic pressures such as income, healthcare access, and health insurance play a significant role in an individual’s cost–benefit perception when considering seeking a healthcare provider. This is further supported by the overrepresentation of non-Hispanic White individuals and underrepresentation of Hispanic or Latino individuals in the present data, as health disparities in Hispanic or Latino communities may act as a barrier to being identified as a case. As such, evaluation of socioeconomic variables in future reported

**Table 4**

<table>
<thead>
<tr>
<th>Cluster</th>
<th>Community/City</th>
<th>RR (cases)</th>
<th>P value</th>
<th>Period</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Willowbrook</td>
<td>102.9 (n = 11)</td>
<td>&lt; 0.0001</td>
<td>9/1/2018–11/30/2019</td>
</tr>
<tr>
<td>2</td>
<td>Long Beach</td>
<td>7.54 (n = 29)</td>
<td>&lt; 0.0001</td>
<td>7/1/2015–10/31/2019</td>
</tr>
<tr>
<td>3</td>
<td>Pasadena</td>
<td>21.76 (n = 16)</td>
<td>&lt; 0.0001</td>
<td>6/1/2016–2/28/2019</td>
</tr>
<tr>
<td>4</td>
<td>San Gabriel Valley</td>
<td>232.37 (n = 5)</td>
<td>0.0009</td>
<td>3/1/2015–8/31/2015</td>
</tr>
<tr>
<td>5</td>
<td>Silver Lake</td>
<td>8.76 (n = 16)</td>
<td>0.0042</td>
<td>7/1/2016–11/30/2019</td>
</tr>
<tr>
<td>6</td>
<td>Cypress Park</td>
<td>10.71 (n = 14)</td>
<td>0.0042</td>
<td>12/1/2016–11/30/2019</td>
</tr>
<tr>
<td>7</td>
<td>Alhambra</td>
<td>14.42 (n = 11)</td>
<td>0.015</td>
<td>9/1/2014–12/31/2018</td>
</tr>
<tr>
<td>8</td>
<td>Downtown Los Angeles</td>
<td>14.94 (n = 10)</td>
<td>0.039</td>
<td>7/1/2017–11/30/2019</td>
</tr>
</tbody>
</table>

FBT = flea-borne typhus.

* Cluster locations are generalized to major cities or prominent neighborhoods and may also include neighboring areas. Clusters are ordered by increasing P value. For this study, exact P values were not indicated if < 0.0001.

**Figure 4.** Spatiotemporal clusters of reported flea-borne typhus cases, Los Angeles and Orange Counties, 2011–2019.
FBT cases is warranted. Although the association with summer months may indicate a change in animal or vector activity, it could be confounded by increased outdoor activity among people in the summer relative to the winter. In the spatiotemporal cluster analysis, using static population estimates for all census tracts in the study period corresponding to the 2017 5-year ACS estimates may not accurately measure the underlying population at risk. However, this issue may be nominal considering that the estimated population change from 2010 to 2019 is estimated to be only 2.0% in the area where clusters were detected.22 Using FBT case count data by census tract may introduce aggregation bias by assuming all persons within a tract are at equal risk and may not reflect reality when evaluated with more granularity or at the individual-level. Similarly, PEH are at considerably higher risk for exposure to FBT due to increased time spent outdoors, living conditions that attract rodents and free-roaming animals, and less access to flea-control for pets but may not be captured in census tract population estimates. This parallels findings for other vector-borne diseases such as bartonella.46,47 Therefore, it is likely that the cluster including the downtown Los Angeles outbreak underestimates the relative risk of FBT among PEH and overestimates that of the general public in the area.

Lastly, classification of cases may exist in the surveillance data. The ability to detect rickettsial disease immune response fluctuates during the time course of infection. Serological testing for antibody response (i.e., IgM and IgG) may not appear in detectable levels until 5 to 10 days after an individual presents symptoms.48 Therefore, a sample collected early in disease course (i.e., < 14 days post-inoculation) from a truly infected individual may result in low antibody titers (i.e., IgM or IgG ≤ 1:64) that do not meet the case definition. The use of a single serological result to classify a case may lack specificity due to a relatively low cutoff titer (> 1:64), and use of IgM for laboratory criteria as both a low titer and IgM-only positive may represent cross-reactivity with other agents.49,50 However, since adoption of a more specific case definition in 2020 (eliminating IgM as laboratory support, increasing cutoff titer to ≥ 1:128, and allowing single positive titer as probable, not confirmed, laboratory support), FBT cases continue to increase in these areas. Because we combined confirmed and probable cases for this analysis, our conclusions would be similar using the more conservative 2020 case definition.

During this surveillance period, data show a substantial and concerning increase in reported FBT cases even when underestimating the true burden of disease. Flea-borne typhus is a significant vector-borne disease endemic to Los Angeles and Orange Counties in California with sporadic outbreak potential. Additionally, a high percentage of severe cases observed warrant targeted health education and improvements in pest control, particularly in areas identified as having persistent localized risk. This information adds to the modern metadata about FBT as research continues to show FBT is a potentially serious disease. Flea-borne typhus public health surveillance would greatly benefit from further research in host and vector ecology in this region of California.

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