THE EPIDEMIOLOGY OF TICK-BORNE RELAPSING FEVER IN THE UNITED STATES

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Abstract. Each year, many residents of and visitors to endemic regions of the western United States are exposed to the vector of tick-borne relapsing fever (TBRF), an underrecognized and underreported disease. Through review of report forms and literature review, we identified 450 cases of TBRF acquired in the United States in 11 western states (and in British Columbia by a U.S. resident) from January 1977 to January 2000. Exposure sites were in forested areas, at varying elevations, in mountainous regions (Cascade, Rocky Mountain, San Bernardino, and Sierra Nevada ranges) of the United States and Canada and in limestone caves in central Texas. Only 13 counties accounted for approximately 50% of all cases. Forty percent of the cases were not residents of the state where TBRF exposure occurred, including 7% from 11 states where TBRF is not endemic. TBRF is endemic in the United States and is a disease affecting travelers, who may return home with the disease to areas where physicians are not familiar with it.

INTRODUCTION

Eight tick-borne illnesses are endemic in the United States. Lyme disease, Rocky Mountain spotted fever, and tularemia are nationally notifiable; babesiosis, Colorado tick fever, ehrlichiosis, tick-borne relapsing fever (TBRF), and tick paralysis are not.1 Each year, many residents of and visitors to endemic regions of the western United States are exposed to the tick vector of TBRF, Ornithodoros hermsi. TBRF is underrecognized and underreported and may be falsely identified as Lyme disease.2 Reporting to health departments has been passive and incomplete.2

TBRF is characterized by recurring episodes of fever and nonspecific symptoms (e.g., headache, myalgia, arthralgia, and abdominal complaints). The illness is caused by infection with Borrelia species that vary their surface antigens, leading to repeated stimulation of the immune system by each new antigen and a febrile response by the patient.34 These Borrelia (spirochetes) are transmitted to humans by exposure to the bite of an infected Ornithodoros tick. The infection usually responds to treatment with antibiotics such as penicillin, tetracycline, or erythromycin.4

Acquisition of human TBRF is generally restricted to the geographical range of the tick vectors. Ornithodoros species of ticks are argasid (soft) ticks that have nocturnal feeding habits and painless bites (Figure 1). The primary reservoirs of Borrelia are rodents such as deer mice, chipmunks, squirrels, and rats.5 Unlike the body louse that transmits louse-borne relapsing fever and lives only several weeks, Ornithodoros ticks may live many years between blood meals and harbor spirochetes for prolonged periods.5 In Texas, cases have been associated with entering caves where the tick, O. turicata, harbors B. turicatae.6 In most western states and southern British Columbia, B. hermsi is transmitted by O. hermsi in forested areas at elevations ranging from < 2,000 feet to > 7,000 feet. In these locations, patients often report exposure in rustic cabins, summer vacation homes, and permanent residences where rodent nests may harbor these ticks.5 Although uncommon, TBRF may also be caused by transmission of B. parkeri by the bite of O. parkeri whose geographic distribution is similar to B. hermsi.7

TBRF was considered an emerging pathogen in the United States in the 1940s, worthy of heightened attention by public health officers, practicing physicians, and specialists.8 However, in recent decades, attention to the epidemiology of TBRF has been limited compared with that devoted to Lyme disease, another tick-borne borrelia. Most published studies have been outbreak investigations and state-specific case series,2,6,7,9–13 We describe the geographic distribution of reported cases of TBRF in the United States and briefly review the recommendations for preventing this illness.

MATERIALS AND METHODS

TBRF is reportable in Arizona, California, Colorado, Idaho, New Mexico, Nevada, Texas, Utah, and Washington. It is not reportable in Oklahoma and Wyoming and has not been reportable in Montana since 1987 or Oregon since 1989. It was not reportable in Texas during 1988 through 1992.

Demographic, clinical, and geographic information from disease report forms and records of TBRF cases were requested from the health departments of states where TBRF had been previously reported and nearby states, including Wyoming, North and South Dakota, and Kansas. We reviewed published reports of TBRF for cases occurring during or after 1980; we requested supplemental information (e.g., demographics, county of exposure and county of residence) for cases with TBRF when such information was not published. A few additional unpublished unreported cases were identified by one physician (New Mexico) and through contact with physicians in an endemic region where cases had probably been reported but such reports were unavailable (Idaho).2

A confirmed patient was defined as a person who had both febrile illness and detection of spirochetes by Wright-Giemsa or dark-field microscopy in a peripheral blood smear. A probable patient was defined as a person who had a relapsing febrile illness and an exposure associated with a confirmed case, a positive serology (immunofluorescent assay or enzyme-linked immunosorbent assay confirmed by Western blot), or an epidemiologically appropriate exposure (e.g., slept in a rustic cabin, camped or hiked, or explored a cave in an endemic area). Probable cases also included cases reported...
to states where information on Wright-Giemsa or dark-field microscopy was missing from available records. A Jarisch-Herxheimer reaction (JHR) was defined as an acute exacerbation of the patient’s symptoms within several hours after treatment with an antibiotic or the report of this diagnosis on a state’s case report form or in a published report.

RESULTS


We identified 450 cases of TBRF (300 confirmed and 150 probable cases), including 206 cases that have been reported in the medical literature.2,10,11,13–19 The median patient age was 35 years (range, birth–81 years); 108 (24%) patients were younger than 18 years. The cases included 235 males (52%) and 178 females (40%); information regarding sex was missing for 37 (8%).

Onset date was available for 425 (94%) cases. Cases occurred during all months of the year: 320 (71%) cases were reported from June through September; most cases occurred in July (108 cases, 24%) and August (104 cases, 23%) (Figure 2). Because the organism and habitat for the vector of TBRF are different in Texas (B. turicatae acquired in caves) compared with other regions endemic for TBRF, we also examined the seasonality of this disease for patients exposed in Texas. In this state, the peak did not occur during the summer; the majority of cases were diagnosed during the late fall and early winter months (approximately 50% with onset in November, December, and January).

Information on the exposure circumstances was available for 388 (86%) cases. The most commonly reported exposures were visiting or living in a cabin or rural dwelling (57%), exposure in their own home (16%), and engaging in a recent outdoor activity (such as hiking or cave exploring) (17%). Among 209 reports with rodent information, 156 (75%) patients noted that rodents were present at the exposure site.

Information on county of exposure was known for 418 patients. Thirty-two patients had been exposed in more than one county. The geographic distribution of exposure sites by county demonstrated that persons are most commonly exposed in or near mountains such as along the Cascade, Sierra Nevada, San Bernardino, and Rocky Mountain ranges (Figure 3). The state with the greatest number of cases was California (n = 95), followed by Colorado (n = 89), Washington (n = 72), Idaho (n = 53), Oregon (n = 47), Texas (n = 26), Arizona (n = 23), Nevada (n = 17), Utah (n = 11), New Mexico (n = 6), Wyoming (n = 2), and Montana (n = 1). For four cases, the state of exposure was not determined because patients had traveled in more than one endemic state during the exposure period. Six cases occurred in British Columbia residents who had traveled to Idaho and one case in a United States resident who had traveled to British Columbia. Fifty-one percent of patients were exposed in 13 counties; Larimer County, Colorado (n = 37), Kootenai County, Idaho (n = 34), Coconino County, Arizona (n = 20), Spokane County, Washington (n = 19), San Bernardino County, California and Jefferson County, Oregon (n = 16 each), Stevens County, Washington (n = 15), Placer County, California, Okanogan County, Washington, and Jefferson County, Colorado (n = 14 each), Mono County, California (n = 12), and Washoe County, Nevada, and Fresno County, California (n = 9 each).

TBRF in persons traveling outside their state of residence was common; 178 (40%) patients were residents of states other than the state of TBRF exposure, including 30 (7%) patients from 11 states where TBRF is not endemic (Alabama, Florida, Hawaii, Iowa, Kansas, Minnesota, Nebraska, New York State, Ohio, Virginia, and Wisconsin) (Figure 4). Although data collection was inadequate to describe the frequency of multiple cases occurring at a single site, our data included both relatively large contemporaneous outbreaks from the same source (an outbreak at the north rim of the Grand Canyon National Park)10 and cases that shared the same site but occurred in different months (an outbreak at Big Bear Lake, California)19 or years (a family in eastern Washington State whose residence had a rodent infestation).
Many patients experienced several relapses before their illness was diagnosed. Among the 222 patients with information on the number of relapses, the median number of relapses was two; 49 (22%) patients experienced four or more relapses (range, 0–15 relapses). Information on the JHR was recorded for 129 patients; of these, 50 (39%) patients experienced Jarisch-Herxheimer symptoms. Only one patient died, a neonate born to a mother who was also infected (mortality 1/450 = 0.22%).

**Illustrative case report.** During the late summer of 1995, a 28-year-old man experienced abrupt onset of fever (39.4°C), frontal headaches, anorexia, diffuse myalgia, low back pain, drenching sweats, rigors, and occasional nausea and vomiting. The following day, he developed a diffuse erythematous macular rash without petechiae or exudate. On the third day, he was admitted to a hospital in Casper, Wyoming. He appeared acutely ill with an oral temperature of 39.2°C, pulse of 100, respiratory rate of 16, and normal blood pressure. The patient had mild posterior pharyngeal erythema but no skin lesions. He had a tender, palpable liver, and mild splenomegaly. Laboratory evaluation revealed a total white blood cell count of 7.5 × 10^9/L (16% bands) and platelet count of 72 × 10^9/L. A laboratory technologist noted multiple spirochetes on the Wright-Giemsa stained peripheral blood smear. Intravenous doxycycline (200 mg) was administered initially followed by 100 mg every 12 h. A JHR occurred 30 minutes after the initial dose with rapid development of hypotension, rigors, fever (39.4°C), and appearance of acute illness. Within 18 hours, he showed marked clinical improvement and was discharged after 3 days. He completed a 7-day course of oral doxycycline (100 mg every 12 hours) with complete clinical recovery.

During the week before his illness, the patient worked for 1 week as a landscaper along the Platte River near Glenrock, Wyoming (elevation, 5,025 feet). This region has high brush and few trees (many are Cottonwood) and is not heavily forested; therefore it was dissimilar to regions of the western United States that harbor *B. hermsii*. He had no travel history outside Wyoming in the months before his illness. The blood smear did not test positively with a *B. hermsii*-specific fluorescent antibody technique at the Rocky Mountain Labora-
Borrelia species.

**DISCUSSION**

Our investigation updates the epidemiology of TBRF in the United States by examining passive surveillance reports in addition to reviewing published and unpublished reports of this disease. Among the findings of our study, we demonstrate that TBRF can be acquired in most of the United States west of the Mississippi River and in all the states in or west of the Rocky Mountains. Many of the persons with illnesses diagnosed with TBRF were travelers from other states to endemic states. The frequent association with outdoor recreational activities and the peak in number of cases occurring during common vacation months (summer) provide evidence that TBRF is a traveler’s disease. Additional evidence includes reports of TBRF after a car trip through four endemic states and diagnosed in Boston, after camping in the Rocky Mountains and vacationing in northern Arizona and diagnosed in Detroit, and after travel to the U.S. Virgin Islands and Saudi Arabia and diagnosed in the United States. Also, there has been one report of TBRF in Cincinnati, Ohio involving a child without a history of travel. Ornithodoros species recognized as vectors of TBRF in the United States have not been identified in Ohio.

TBRF is endemic in the western United States, southern British Columbia, the plateau regions of Mexico, Central and South America, the Mediterranean, central Asia, and throughout most of Africa, with the exception of the Sahara Desert and the rain forest belt. In the United States, the first report of TBRF occurred in 1905 in New York State involving a traveler to Texas. TBRF has been recognized in the western United States since it was reported in Jefferson County, Colorado in 1915. Because this early report of four campers became infected while asleep, ticks are stimulated by warmth and carbon dioxide to seek out and feed on the occupants usually during the night. This report includes one death from TBRF in a neonate. The rapid diagnosis of TBRF because of its severe symptoms, which may include very high temperature and hypotension (especially during the JHR), reports of death from TBRF are much less common than from louse-borne relapsing fever, which caused millions of deaths during the 20th century. Mortality rates of TBRF vary by geographical region (range, 0–8%). These rates are consistent with our report. The report of the death in our case series is important because some physicians may believe that TBRF is not a cause of death in the United States. 

In our investigation, half of the cases were exposed in only 13 counties in six states. Although we are not certain why the cases were mainly concentrated in so few counties, it may be due to better awareness and reporting of TBRF in those counties, greater popularity of those sites for human visits, a greater density of the tick vector population in those areas, or a combination of these factors. This information is important for prevention of TBRF. Also, the epidemiology of TBRF is not uniform and, therefore, is deserving of further investigation. For example, the vector and species of Borrelia are different in some regions (e.g., Texas where the exposure activity [cave exploration] is a common exposure mode) unlike the northwest, where rustic-cabin dwelling and sometimes hiking are common. The acquisition of TBRF after contact with limestone caves led to an association between TBRF and the lost mines of San Saba and the mythical gold of the Spaniards, which was allegedly hidden in the central region of Texas, where these caves are found along with the majority of TBRF exposures in the state. In Texas the pathogen is typically transmitted by the bite of O. turicata, whereas in the northwest O. hermsii transmits B. hermsii. O. turicata is found in caves, in rodent, owl and snake burrows, and under houses, whereas O. hermsii is found where chipmunks, tree squirrels, and pine squirrels reside. Less information is available about B. parkeri and O. parkeri, and most cases of TBRF in the west have been attributed to B. hermsii and O. hermsii even though the distribution of these ticks overlap. Several decades ago, a few cases of TBRF were associated with O. parkeri in low-elevation areas of Stanislaus County, California.

From this study, seasonality of the disease also appeared to be different for the southwest compared with the northwest, evidenced by Texas having more of a late-fall early-winter peak compared with the summer peak in all other states combined. Cases of TBRF do occur in winter months in the northwest and southwest albeit less frequently than the summer. Winter cases are typically associated with human activity that alters behavior of the tick vector. After entering a cold cabin and lighting a fire, ticks are stimulated by warmth and carbon dioxide to seek out and feed on the occupants usually while asleep.

Our investigation includes the first report of cases of TBRF in Wyoming and the first report of TBRF in Montana in several decades. Although we could find no cases of TBRF in Kansas or Oklahoma, we found a report of two Oklahoma cases of TBRF diagnosed in 1978 associated with Ornithodoros ticks not recognized as O. hermsii or O. turicata. During 1934–1941, TBRF had occurred in four Oklahoma counties (Harper, Alfalfa, Washita, and Grant Counties). Eleven cases of TBRF were reported in Clarke County, Kansas, during 1931–1934, and O. turicata has been recovered in Clarke County. We are aware of no other reports from these states, suggesting that, although the vector and pathogen may still reside in these states (and perhaps Ohio), either the risk for acquiring the disease there is very low or TBRF is unlikely to be recognized. O. talaje has been reported in several western states and in Minnesota, Wisconsin, and New York State but is not a known vector of TBRF.

This report includes one death from TBRF in a neonate. Only one other U.S. neonatal TBRF death has been reported. Neonatal infection with Borrelia may be very severe; spirochetes have been demonstrated in the cerebrospinal fluid. Although there is a theoretical risk of death from TBRF because of its severe symptoms, which may include very high temperature and hypotension (especially during the JHR), reports of death from TBRF are much less common than from louse-borne relapsing fever, which caused millions of deaths during the 20th century. Mortality rates of TBRF vary by geographical region (range, 0–8%). These rates are reported to be higher in small children and pregnant women, consistent with our report. The report of the death in our case series is important because some physicians may believe that TBRF is not a cause of death in the United States.
This series includes six pregnant women and two infants infected in utero.\textsuperscript{2,3} Infec-
tion in pregnant women may be more severe than in other persons, and miscarriages are com-
mon.\textsuperscript{2,28} Transmission may be transplacental or possibly sec-
tary to traversing the birth canal.\textsuperscript{41–43} In several reports, cesarean delivery produced uninfected infants; however, for
only one of those reports was the delivery concurrent with
TBFR illness in an untreated mother.\textsuperscript{19} In louse-borne relaps-
ing fever, a high density of spirochetemia and gestational age
have been associated with poor outcome.\textsuperscript{44,45}

This analysis has several limitations. Because reporting of
TBFR is passive in the few states where it is a notifiable
disease, and TBFR is generally considered a low-priority pub-
lic health condition, information available to produce our
maps was limited, possibly resulting in an underestimation of
the distribution and magnitude of TBFR in the United States.
For many states, case reports are available for only a few
years. To limit the overlap of our study with previous reports
of TBFR, we included only cases after 1976. Therefore, our
maps do not include two cases reported from 1976 in Rio
Arriba County, New Mexico,\textsuperscript{46} and several other earlier case
reports. In Idaho, where a high number of cases were ex-
posed, records of TBFR were either discarded or lost. This
led us to search for cases in Idaho through physician and
laboratory contacts (active surveillance) and state public
health bulletin review. Also states where TBFR is not report-
able are unlikely to maintain records of TBFR when it is
incidentally reported.

TBFR has not gained the recognition of some of the other
endemic western United States tick-borne diseases and
zoonoses (e.g., Hantavirus, Rocky Mountain spotted fever,
and plague) probably because of an incorrect perception that
the mortality rate was zero.\textsuperscript{17} One could argue that TBFR is
another emerging infectious disease. In the 1940s, Texas and
California had the highest incidence. Our maps demonstrate
that this remains true of California, but other locations now
have more reports of TBFR than Texas.\textsuperscript{25} Without good sur-
veillance, the mortality and morbidity are likely underesti-
mented. Often when one case is identified, other cases are
found among family members or fellow travelers. These cases
usually go undetected with passive surveillance.

Surveillance is information for action. In the case of TBFR,
that action may include prevention and education of the pub-
lic and physicians about the epidemiology and clinical pre-
sentation of the disease. No patient who has traveled to an
endemic state should have to relapse more than once without
TBFR being considered and a blood sample being examined
for spirochetes during a febrile episode. Another diagnosis to
consider in travelers and residents of the western United
States is Colorado tick fever, which may also relapse. Other
diagnoses should also be considered depending on clinical
presentation and travel history.

Prevention of TBFR includes avoiding rodent and tick-
infested dwellings and infested natural sites such as animal
burrows or caves. Rodent proofing of homes and vacation
cabins and assessing and limiting rodent-friendly environ-
ments around homes may be performed with the consultation
of local health department environmental health specialists
and pest removal services. Chemical treatment of rodent-
infested areas is available and should be administered by pest
control specialists. Contact with ticks and potential animal
vectors should only occur while wearing gloves: one person
from California contracted TBFR after contaminating his
hands with the blood of an infected squirrel.\textsuperscript{24} Finally, wear-
ing clothing that protects skin from access by the tick (such as
long pants, long sleeved shirts, or hats for cave explorers) and
wearing insect repellents on exposed skin and clothing (e.g.,
permethrin) may help prevent this disease. However, protec-
tion by clothing is probably limited during sleeping in poten-
tially infested dwellings.

We provide the largest U.S. series of TBFR and the most
complete maps of its distribution in recent decades. We en-
courage physicians to report cases of TBFR to their health
departments. We also encourage endemic states without re-
porting to reconsider making TBFR a reportable disease,
especially with the popularity of wilderness travel, the migra-
tion of many persons to the endemic states for work and
retirement living, and the potential for neonatal death.

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