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# Tick-Borne Relapsing Fever Outbreak among a High School Football Team at an Outdoor Education Camping Trip, Arizona, 2014

Jefferson M. Jones,[1,2]* Carter R. Hranac,[3] Mare Schumacher,[4] Kim Horn,[5] Darlene M. Lee,[5] Joel Terriquez,[5] David M. Engelthaler,[6] Marie Peoples,[4] Jennifer Corrigan,[4] Adam Replogle,[7] Nina Souders,[5] Kenneth K. Komatsu,[1] and Nathan C. Nieto[3]

[1]*Arizona Department of Health Services, Phoenix, Arizona;* [2]*Epidemic Intelligence Service, Atlanta, Georgia;* [3]*Northern Arizona University, Flagstaff, Arizona;* [4]*Coconino County Public Health Services District, Flagstaff, Arizona;* [5]*Flagstaff Medical Center, Flagstaff, Arizona;* [6]*Translational Genomics Research Institute, Flagstaff, Arizona;* [7]*Centers for Disease Control Division of Vector-Borne Disease, Fort Collins, Colorado*

*Abstract.* During August 2014, five high school students who had attended an outdoor education camp were hospitalized with a febrile illness, prompting further investigation. Ten total cases of tick-borne relapsing fever (TBRF) were identified—six cases confirmed by culture or visualization of spirochetes on blood smear and four probable cases with compatible symptoms (attack rate: 23%). All patients had slept in the campsite's only cabin. Before the camp, a professional pest control company had rodent proofed the cabin, but no acaricides had been applied. Cabin inspection after the camp found rodents and *Ornithodoros* ticks, the vector of TBRF. Blood samples from a chipmunk trapped near the cabin and from patients contained *Borrelia hermsii* with identical gene sequences (100% over 630 base pairs). Health departments in TBRF endemic areas should consider educating cabin owners and pest control companies to apply acaricides during or following rodent proofing, because ticks that lack rodents for a blood meal might feed on humans.

## INTRODUCTION

Tick-borne relapsing fever (TBRF) in North America is caused by infection with one or more species of the genus *Borrelia* (*Borrelia hermsii*, *Borrelia parkeri*, and *Borrelia turicatae*). The pathogen is transmitted to humans through the bite of an infected *Ornithodoros* soft tick (*Ornithodoros hermsi*, *Ornithodoros parkeri*, and *Ornithodoros turicatae*, respectively).[1] Common symptoms include fever, headache, myalgia, arthralgia, and gastrointestinal complaints.[2] TBRF is endemic in the western United States, typically occurring in forested areas at elevations > 1,500 m (associated with *B. hermsii*).[3] *Ornithodoros* species are nidicolous soft ticks (Argasidae) that feed on rodents.[4] In North America, TBRF is ecologically maintained in wild rodent hosts, including chipmunks (*Tamias* spp.) and tree squirrels (*Tamiasciurus* spp.).[5] Humans are at the greatest risk for TBRF when sleeping in infested buildings, often after extended periods of innocupancy.[6] TBRF is a reportable disease in 12 western states, including Arizona. During 1982–2013, a total of 22 autochthonous TBRF cases among Arizona residents (annually 0–3 cases) were reported. The two largest outbreaks in Arizona occurred along the north rim of Grand Canyon National Park, including 62 cases in 1973[4] and 17 cases in 1990.[7] Both of these outbreaks occurred in Coconino County, which contains mountainous forest, and *O. hermsi* is endemic to this region.[2]

On August 10, 2014, Coconino County Public Health Services District was notified by the local hospital that five high school students who attended the same camp were hospitalized with fever, headache, and myalgia. All five patients attended a 3-day camp on August 1–3 located in a ponderosa pine (*Pinus ponderosa*) forest 7,000 feet in elevation ~15 miles north of Flagstaff, AZ. Public health officials instructed campsite operators to close the campsite immediately and began an investigation. The investigation goals were to identify exact locations of patient exposure, identify additional cases, prevent further disease, and determine the species of *Borrelia* responsible for TBRF infection in the outbreak.

## MATERIALS AND METHODS

**Epidemiologic and clinical investigation.** A probable case was defined as the presence of greater than or equal to three of four symptoms of fever, chills, myalgia, and headache in a person who slept in the campsite's cabin or tents during August 1–3, 2014. Persons who were only present during the daytime ($N = 26$) or slept in a trailer brought to the campsite ($N = 2$) were excluded since the primary risk for disease is sleeping in infested buildings.[6] A confirmed case had laboratory confirmation by either visualization of spirochetes in an attendee's blood smear or isolation of *B. hermsii* by blood culture.

Risk factors were estimated using a case–control study design. Confirmed and probable cases were compared with controls, defined as camp attendees who slept in the campsite's cabin or tents and did not meet the case definition. Telephone surveys were conducted to collect data regarding demographics, symptoms since attending the camp, healthcare sought and treatment given, and risk factors, including activities and sleeping location. Odds ratios and 95% confidence intervals were calculated using SAS® version 9.3 (SAS Institute Inc., Cary, NC). Incubation period was calculated as the number of days between the first day of camp, August 1, and the date of symptom onset. We also reviewed available medical records for patients with confirmed disease from the local hospital and tertiary hospital.

Available blood samples were sent to the Centers for Disease Control and Prevention (CDC) for confirmatory testing by isolation of *B. hermsii* from blood culture. For culture, 50 μL of ethylenediaminetetraacetic acid (EDTA) blood from each patient sample were placed in a 5-mL polypropylene tube containing 4.5 mL Barbour-Stoenner-Kelly-II (Centers for Disease Control, Division of Vector-Borne Diseases, Bacterial Diseases Branch, Fort Collins, CO) medium supplemented with 12% young rabbit serum and incubated

*Address correspondence to Jefferson M. Jones, Office of Infectious Disease, Arizona Department of Health Services, 150 North 18th Avenue, Phoenix, AZ 85007. E-mail: jjones10@cdc.gov

at 34°C. All cultures were visually confirmed as positive for motile spirochetes during days 4–6.

**Environmental investigation.** During early August 2014, we interviewed campsite managers and pest control company employees who worked on campsite cleaning activities, including rodent proofing. On August 12–13, a public health team consisting of members of Coconino County Public Health Services District, Northern Arizona University (NAU), Translational Genomics Research Institute, and the Arizona Department of Health Services inspected the campsite to identify specific TBRF exposure routes. The investigation included the systematic search for *Ornithodoros* spp. ticks, evidence of reservoir host presence, and collection of rodent nesting material. Public health investigators visually inspected the cabin where the majority of patients had slept during August 1–3 and where presumed exposure had occurred.[3] Visual inspection included detailed examination of all bedding, walls, floors, bookshelves, and subfloor crawlspace using a flashlight. All wall hangings were removed and visually inspected. To sample potential rodent reservoir hosts, 138 XL live-traps (H. B. Sherman Traps, Inc., Tallahassee, FL) were placed throughout the camp, including inside the cabin and surrounding structures. Traps were set during the evening and checked the following morning. Captured animals were identified to species and bled through abrasion of the retro-orbital sinus. Whole blood was placed in tubes containing EDTA and stored on ice until further processing. All rodent sampling was approved by the NAU institutional animal care and use committee (NAU protocol No. 12-009). Investigators placed dry ice ($CO_2$) traps in the areas of potential exposure to attract and collect nearby ambulatory soft ticks. Because of the nidicolous nature of *Ornithodoros* spp. ticks, investigators collected all rodent nesting material and attempted to collect soft ticks using a Berlese funnel (enclosed funnel using a heat lamp to extract ticks from the nesting material into a container with alcohol). Nesting material was placed in the funnel for 72 hours, and then vials containing 70% ethanol were inspected by using a dissection microscope. Before reopening the campsite, a public health team returned on August 27 for reinspection.

Six rodent whole blood samples, two soft ticks, and three whole blood samples from patients were subjected to DNA extraction using the DNeasy® Kit (QIAGEN, Valencia, CA). DNA was analyzed for the presence of *B. hermsii* 16S ribosomal RNA by using quantitative polymerase chain reaction (qPCR) that utilizes previously developed primers and a hybridization probe.[8] Positive samples were further identified using a nested-PCR protocol to detect the 16S-23S intergenic spacer (IGS) region (*rrs-rrlA*, IGS) of *Borrelia* spp.[9] The nested-PCR product was gel extracted by using a QIAquick® kit (QIAGEN) and sequenced by using an ABI 3730 (NAU Environmental Genetics and Genomics Laboratory). Forward and reverse products were aligned by using Clustal X (Dublin, Ireland), phylogenetic reconstruction was conducted by using MrBayes (http://mrbayes.csit.fsu.edu/), and visualized by using FigTree (A. Rambaut, http://tree.bio.ed.ac.uk/software/Þgtree/).

## RESULTS

**Epidemiologic and clinical investigation.** Telephone surveys and interviews of campsite staff revealed 42 persons (38 high school–aged football players and four adult coaches) had slept in a cabin and one adult coach had slept in a tent at the campsite; 23 of 43 (53%) attendees completed interviews. All were male. Six cases were confirmed by spirochetemia detection on blood smear (Figure 1); four (67%) blood samples were sent to CDC and all had *B. hermsii* isolated by culture. Four probable cases were reported, for a total of 10 cases. Patients were between ages 15–17 and 33 years. All patients slept in the campsite's only cabin. Median incubation time was 7 days (range 2–10 days) (Figure 2). Interviews were not conducted for four patients with confirmed illness, and medical records were used as a proxy. Comparing cases to controls, no associations were found to be significant.

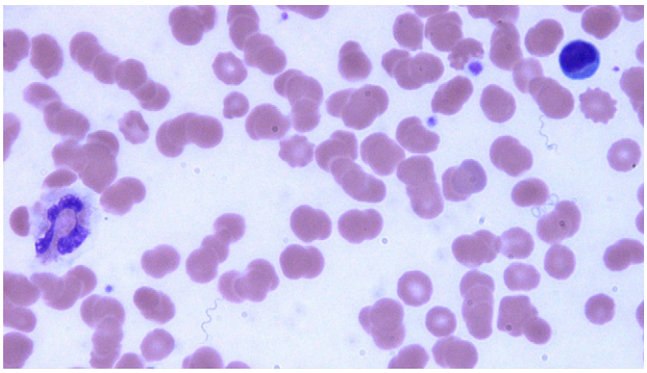

FIGURE 1. Spirochetes identified on peripheral blood smear of patient with tick-borne relapsing fever, Arizona, 2014.

Among patients with confirmed disease, 5/6 (83%) presented with thrombocytopenia (platelets < 150/μL [median 77/μL, range 30–178/μL]). Four of six (67%) were hospitalized with length of stay from 1 to 2 days (Table 1). Among 10 patients with a case, 10 (100%) experienced fever, headache, and myalgia; nine (90%) experienced arthraglia (Table 2). Eight (80%), including all six patients with a confirmed case, were treated with doxycycline 100 mg twice/day for 7–10 days. No patients had any known major complications (e.g., Jarisch–Herxheimer reactions). No patients with a confirmed case had any relapsing fever episodes, and two of four (50%) patients with a probable case reported a single relapsing episode.

**Environmental investigation.** The campsite consists of a cabin, a men's restroom building, a women's restroom building, several tents, and several sport and recreational areas. Interviews with campsite management and review of pest control company records revealed that during July 17–24, 2014, rodent nests and feces were removed from the campsite's only cabin, the men's restroom building, and women's restroom building by a professional pest control company, and the buildings were disinfected. Lumber and steel wool had been placed to prevent rodent entry. No acaricide had been applied because cabin infestation by soft ticks had not been considered at the time. During the investigation on August 12–13, the public health team found multiple gaps in the walls, windows, and floors of the cabin. Rodent droppings were found throughout the cabin, and two dead wood rats (*Neotoma* spp.) were also found. Nesting material was collected from areas used as storage space underneath the first floor. No ticks were obtained by using the $CO_2$ traps or the Berlese funnel traps. Six of 138 (4%) traps contained rodents, including one vole (*Microtus* species), one deer mouse (*Peromyscus maniculatus*), and four chipmunks (*Tamias dorsalis*). All trapped rodents were caught in traps located

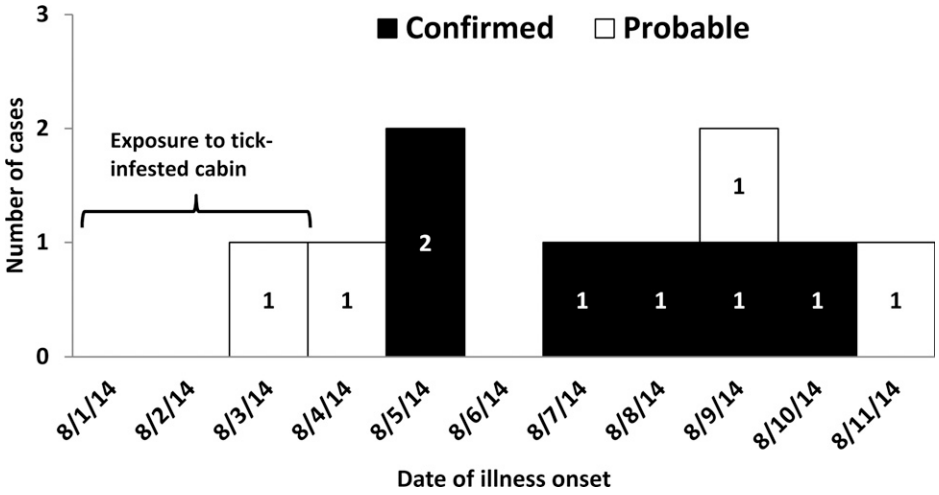


FIGURE 2. Epidemiologic curve by date of illness onset for confirmed and probable cases of tick-borne relapsing fever outbreak in Coconino County, Arizona, August 2014.

outside. Two of six rodents (33%), both of which were chipmunks, tested positive for *B. hermsii* by qPCR. *Borrelia hermsii* IGS sequencing of three patients and one chipmunk samples revealed identical sequences (100% over 630 base pairs) both belonging to genomic group I (GGI). The second chipmunk sample had a single nucleotide base difference at base-pair position 514 (GenBank accession nos. KU955330 and KU955331; Figure 3).

Recommendations were sent to campsite management to clean the campsite and disinfect the areas with rodent droppings, remove all items stored between the first floor of the cabin and ground, store food in rodent-proof containers, and use a licensed pest control company to apply acaricides to eliminate soft ticks and seal openings for improved rodent proofing before reopening the campsite facilities. Reinspection by the public health team on August 27 collected one desiccated larval tick and one live nymphal *O. hermsi* tick (Figure 4), both located near areas where camp attendees slept. Neither of the ticks collected at the campsite tested positive for *B. hermsii* by qPCR. A pest control company returned after the environmental investigation to apply acaricides to cracks and crevices in the main cabin site.

## DISCUSSION

This is the largest reported TBRF outbreak among Arizona residents since 1990. We hypothesize that rodent-proofing efforts without acaricide application during 2 weeks before patient infections led to infected tick questing and patient exposure; argasid ticks, which are long-lived, will search for alternate blood-meal hosts (e.g., sleeping campers) when their typical hosts are excluded.[10] Although rodents were found in the cabin after the outbreak, the rodent removal and rodent proofing before the camp likely reduced the amount of rodent ingress.

Clinical symptoms were similar to those published in a substantial case series of 182 patients,[2] although significant differences including relapsing episodes (20% versus 79%) and chills (60% versus 89%) were less commonly noted during this outbreak. This outbreak likely had fewer relapsing episodes because of rapid diagnosis and treatment of patients (treatment < 4 days of symptom onset for patients with a confirmed illness), compared with participants from retrospective studies. In addition, no Jarisch–Herxheimer reactions were observed, although this complication was reported among 54% of 61 patients with TBRF in a case series.[2] We hypothesize that early diagnosis might have resulted in lower bacterial burdens and a reduced probability of adverse reactions to antimicrobial treatment. No specific sleeping location in the cabin was associated with disease, in contrast to a different cabin-associated outbreak that reported the floor and a specific bunk were associated with TBRF infection.[11] In this investigation, ticks and evidence of rodent ingress were found in multiple locations throughout the cabin, indicative of widespread infestation.

TABLE 1
Clinical characteristics of patients with confirmed tick-borne relapsing fever, Arizona, 2014

| Patient identifier | 1 | 2 | 3 | 4 | 5 | 6 |
|---|---|---|---|---|---|---|
| Age (years) | 17 | 17 | 17 | 15 | 16 | 33 |
| Incubation period (days) | 7 | 8 | 4 | 7 | 6 | 9 |
| Length of hospital stay (days) | 1 | 1 | 2 | 1 | 2 | 0 |
| White blood cell count ($10^3$/mL; ref: 4.0–10.5) | 6.7 | 5 | 7.3 | 3.4 | 8 | 10.2 |
| Hemoglobin (g/d; ref: 12.0–16.0) | 14.2 | 13.7 | 12.2 | 11.1 | 15 | 17.2 |
| Platelet count (/μL; ref: 150–450) | 58 | 88 | 35 | 30 | 94 | 83 |
| C-reactive protein (mg/dL; ref: < 0.9) | 17.1 | 22.2 | 3.2 | Unknown | 144.6 | Unknown |
| Blood urea nitrogen (mg/dL; ref: 5–25) | Unknown | 16 | 11 | 19 | 16 | 17 |
| Creatinine (mg/dL; ref: 0.1–1.3) | Unknown | 0.99 | 1.1 | 1.19 | 1 | 1.1 |
| Peripheral blood smear | Spirochetes | Spirochetes | Spirochetes | Spirochetes | Spirochetes | Spirochetes |
| Culture | Positive | Positive | Positive | Positive | Not done | Not done |

ref = reference range. Positive culture = organisms morphologically consistent with *Borrelia* species that were recovered from culture in Barbour-Stoenner-Kelly-II media.

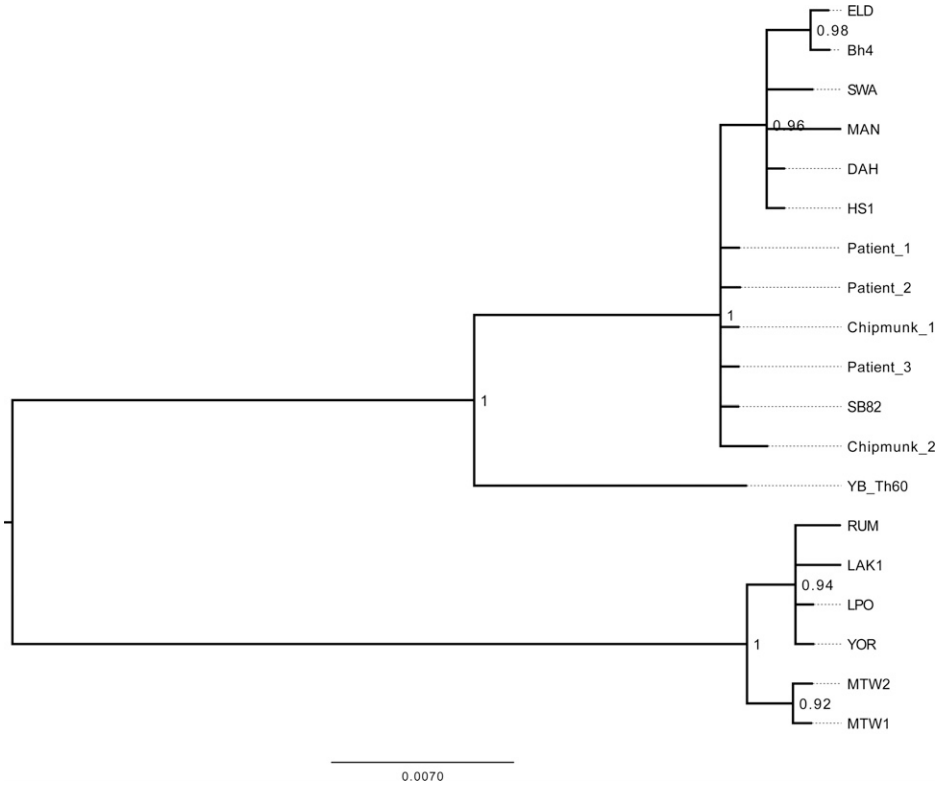


FIGURE 3. Phylogenetic analyses of *Borrelia hermsii* intergenic spacer (IGS) sequences from infected wild caught chipmunks (*Tamias dorsalis*) and infected patients from northern Arizona (accession numbers KU955330 and KU955331). The tree was constructed by using MrBayes, and the numbers at the nodes correspond to the posterior probabilities after 1,000,000 iterations. Representative *B. hermsii* IGS sequences and accession numbers are as follows: *B. hermsii* GGI strains BH4 (AY515267), ELD (DQ845745), MAN (DQ845748), HS1 (AY515265), DAH (DQ845746), SWA (DQ845749), SB82 (AY515266), YBTh60 (GQ175068), *B. hermsii* GGII strains MTW1 (EU203147), MTW2 (EU203148), YOR (DQ845744), LPO (AY515270), LAK1 (DQ845742), and RUM (DQ845743).

Although the collected ticks tested negative for *B. hermsii*, identical *B. hermsii* IGS sequences from the human and chipmunk whole blood samples indicate the patients likely contracted TBRF from ticks that had fed on rodents in the cabin area (Figure 3). Although Arizona has a history of TBRF infection, this is the first report of IGS sequence variants from the region.[12,13] The *B. hermsii* IGS sequences from this study were most similar to *B. hermsii* IGS GGI and within that group, closest to strain SB82 (GGI, Type 2) that was isolated from a human patient in Colorado.[12] In other western states, chipmunks (*Tamias* spp.) are considered among the primary vertebrate reservoir hosts; tree squirrels (*Tamiasciurus* spp.), wood rats (*Neotoma* spp.), and a northern spotted owl (*Strix occidentalis*) have had evidence of active infections and most likely contribute to the ecological maintenance.[12,14,15]

Hantavirus and *B. hermsii* are both endemic in numerous areas in the western United States, and exposure to rodent-infested buildings is a risk factor for both pathogens.[3,16] Health-care providers should consider both diseases depending

FIGURE 4. Nymphal *Ornithodoros hermsi* found in site of likely tick-borne relapsing fever transmission, Arizona, 2014.

TABLE 2

Symptoms of patients with confirmed or probable tick-borne relapsing fever outbreak—Arizona, August 2014

| | Total ($N$ = 10) | Confirmed ($N$ = 6) | Probable ($N$ = 4) |
|---|---|---|---|
| Symptom | $n$ (%) | $n$ (%) | $n$ (%) |
| Fever | 10 (100) | 6 (100) | 4 (100) |
| Headache | 10 (100) | 6 (100) | 4 (100) |
| Myalgia | 10 (100) | 6 (100) | 4 (100) |
| Arthralgia | 9 (90) | 6 (100) | 3 (75) |
| Abdominal pain | 7 (70) | 5 (83) | 2 (50) |
| Chills | 6 (60) | 4 (67) | 2 (50) |
| Fatigue | 6 (60) | 2 (33) | 4 (100) |
| Vomiting | 5 (50) | 4 (67) | 1 (25) |
| Cough | 3 (30) | 2 (33) | 1 (25) |
| Dizziness | 3 (30) | 3 (50) | 0 |
| Syncope | 2 (20) | 2 (33) | 0 |
| Rash | 2 (20) | 2 (33) | 0 |

on exposure risks and overall clinical scenario; 83% of our patients had thrombocytopenia, and TBRF should be considered in the differential diagnosis when febrile thrombocytopenia is detected.[6] Increased awareness by health-care providers might lead to earlier diagnosis, decreasing repeat visits to health-care facilities and associated costs.[3] After TBRF was confirmed in this outbreak, a rapid response and communication among the hospital clinicians, laboratory, health department, and campsite management led to successful efforts to diagnose and treat infected patients with doxycycline and to prevent further infections. Because patients were likely exposed to infectious ticks because of a lack of acaricide application at the time of rodent proofing, health departments in endemic areas should consider educating pest control companies and cabin owners regarding the importance of acaricide application immediately after rodent proofing or after other local causes of rapid rodent population declines (e.g., plague epizootics).[7]

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Authors' addresses: Jefferson M. Jones, Arizona Department of Health Services, Phoenix, AZ, and Epidemic Intelligence Service, Centers for Disease Control and Prevention, Atlanta, GA, E-mail: jjones10@cdc.gov. Carter R. Hranac and Nathan C. Nieto, Northern Arizona University, Flagstaff, AZ, E-mails: crh244@gmail.com and nathan.nieto@nau.edu. Mare Schumacher, Marie Peoples, and Jennifer Corrigan, Coconino County Public Health Services District, Flagstaff, AZ, E-mails: mschumacher@coconino.az.gov, mpeoples@coconino.az.gov, and jcorrigan@coconino.az.gov. Kim Horn, Darlene M. Lee, Joel Terriquez, and Nina Souders, Flagstaff Medical Center, Flagstaff, AZ, E-mails: hornkimatflag@gmail.com, darlene.lee@nahealth.com, joel.terriquez2@nahealth.com, and nina.souders@nahealth.com. David M. Engelthaler, Translational Genomics Research Institute, Flagstaff, AZ, E-mail: dengelthaler@tgen.org. Adam Replogle, Centers for Disease Control and Prevention Division of Vector-Borne Disease, Fort Collins, CO, E-mail: xhk9@cdc.gov. Kenneth K. Komatsu, Arizona Department of Health Services, Phoenix, AZ, E-mail: ken.komatsu@azdhs.gov.

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