OUTBREAK OF TICK-BORNE RELAPSING FEVER AT THE NORTH Rim OF THE GRAND CANYON: EVIDENCE FOR EFFECTIVENESS OF PREVENTIVE MEASURES

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Abstract. An outbreak of tick-borne relapsing fever (TBRF) originating at the North Rim of Grand Canyon National Park was investigated in 1990. To determine risk factors for the disease, almost 7,000 parties of visitors were surveyed; over half responded, representing > 10,000 people. Fifteen cases of confirmed or probable TBRF were identified in visitors and 2 in employees. All patients except one experienced symptoms after overnight stays in a group of cabins that had not been rodent-proofed after a TBRF outbreak in 1973 (relative risk for visitors [RR] 8.2, 95% confidence interval [CI] 1.1–62). Seven cases of TBRF were associated with a single cabin (RR 98, 95% CI 30–219). Structural flaws and rodent nests were common in the implicated cabins and rare in unaffected cabins. This investigation suggests that measures to rodent-proof cabins at sites where TBRF is endemic prevent reinfection of cabins by infected rodents and tick vectors, thereby preventing the spread of disease in humans.

INTRODUCTION

Tick-borne relapsing fever (TBRF) caused by infection with Borrelia hermsii is an acute disease that is endemic in forested mountainous areas of western North America.1-3 Sporadic cases4-6 and common-source outbreaks5-7 of TBRF in these areas are usually associated with overnight stays in cabins in which rodents have nested. Ornithodoros hermsi, the tick vector of B. hermsii, is often recovered from rodent nests in the attics, below the floors, or behind the walls of cabins in which ill people have slept.

In 1973, 62 cases of TBRF were identified in people who had stayed overnight in rustic cabins at the North Rim of Grand Canyon National Park, representing the largest North American outbreak of the disease to date.8 After that outbreak, ~3,000 kg of rodent-nesting material was removed from the cabins, and it was recommended that all of the visitor cabins at the site undergo structural alterations that would prevent entry and nesting of rodents in the spaces above the ceilings, behind the walls, and below the floors. However, such “rodent-proofing” measures were completed for only a portion of these historic cabins.

In July 1990, 2 cases of TBRF, confirmed by observation of spirochetes on peripheral blood smears, were reported in visitors who had stayed overnight in cabins at the North Rim of Grand Canyon National Park. An investigation was conducted by the Centers for Disease Control and Prevention and the Arizona Department of Health Services in cooperation with the National Park Service.9 The recognition of cases at this site in 1990 allowed us to compare the occurrence of TBRF among tourists who stayed in rodent-proofed cabins and non–rodent-proofed cabins and thereby to assess the effect of these preventive measures on the risk of TBRF among visitors 17 years after their implementation.

BACKGROUND AND METHODS

Situated 2,400 m above sea level, the North Rim of Grand Canyon National Park is 345 km by road from the canyon’s South Rim. The North Rim is inaccessible because of snow during the winter and opens each year from mid-May through mid-October. In 1990, ~300,000 people from throughout the United States and many foreign countries visited the North Rim. Nearly 75,000 visitors stayed overnight at the park in 40 motel rooms or in historic log cabins of the Grand Canyon Lodge, which are owned by the Park Service and managed by a private concessions company. The cabins are divided into 2 groups, which are separated by a road leading to the Grand Canyon Lodge: 23 cabins housing 56 rental units compose the southeast group; 79 cabins containing 105 rental units (as well as sleeping quarters for 47 employees) are included in the northwest group. Cabins in the southeast group were rodent-proofed after the 1973 outbreak of TBRF.

Outbreak investigation. A confirmed case of TBRF was defined as an illness occurring with onset 2–21 days after an overnight stay at the North Rim in which spirochetes were observed on a peripheral blood smear. A probable case of TBRF was defined as a febrile illness in which fever and at least 3 of 4 characteristic symptoms (chills, sweats, myalgia, and headache) were present, and in which a clear history of remission of symptoms followed by relapse was reported. If there was no relapse, a similar illness (fever plus at least 3 symptoms) in which antibody to B. hermsii was demonstrated in a serum specimen by enzyme-linked immunosorbent assay (ELISA) was also counted as a probable case. Febrile illnesses in which sore throat, cough, diarrhea, or dysuria was the chief complaint were excluded even if they otherwise met the case definition.

North Rim clinic records were reviewed at the dispensary, and all employees were questioned regarding occurrence of symptoms compatible with TBRF. Serum was obtained from consenting symptomatic and asymptomatic employees for serological testing.

Names and addresses were obtained for registered guests of the lodge cabins from May 15 to August 2, 1990. A letter and a one-page screening questionnaire with responses for 5 people were mailed to each party for whom an address was available; visitors were asked to fill in responses for each member of the party. People reporting febrile illness with 3–4 characteristic symptoms (chills, sweats, myalgia, and headache) that began within 30 days of their visit to the North Rim were contacted by telephone and administered a more detailed questionnaire on the nature and timing of their symptoms. Whenever possible, serum specimens for antibody testing were obtained from these symptomatic people.
Park visitors after August 2 were given a notice explaining the symptoms of TBRF and instructing them to contact their physician and the Arizona Department of Health Services if they developed an illness with these symptoms.

This outbreak investigation was not considered research, but rather a public health response, and thus did not require human subjects clearance by an institutional review board. The information collected was specific to the public health problem being addressed and was not intended to be considered generalizable.

**Laboratory testing.** Antibody to *B. hermsii* was measured in serum specimens obtained from symptomatic visitors by ELISA by use of a whole-cell sonicate preparation of *B. hermsii* and methods previously described for *Borrelia burgdorferi* (Quan T, unpublished data). When possible, paired acute- and convalescent-phase serum specimens from symptomatic people were tested, but any single specimen demonstrating an optical density ratio (ODR) of \( \geq 4.0 \) compared with a pooled negative control was considered positive.

Results of serological testing of available specimens for confirmed cases, symptomatic people not meeting the clinical case definition, and asymptomatic people were compared.

**Environmental survey.** During August 1990, cabins were inspected for evidence of structural deficiencies and rodent access to the foundations, wall spaces, and attics. Accessible rodent nests and midden debris were collected and examined for soft ticks with Berlese-Tullgren funnels. At the time of this initial environmental investigation, TBRF source cabins were not yet identified. Acaricidal treatment of inner wall surfaces and attic, wall, and floor spaces of the cabins was performed as an interim measure. In May 1991, after TBRF source cabins were identified and before opening of the North Rim facilities for public use, all northwest cabins were inspected for rodent infestations; rodent nests and midden debris were removed and inner wall surfaces and attic, wall, and floor spaces were again treated with appropriate acaricides. Cabins requiring rodent-proofing measures were identified, and recommendations were made for structural improvements. A survey for *O. hermsii* ticks among natural rodent harborage sites (e.g., fallen trees, stumps, and hollow logs) was also conducted.

**RESULTS**

A total of 17 confirmed or probable cases were identified, 15 among visitors and 2 among employees. Demographic information, symptoms, and laboratory findings for visitor and employee cases are summarized in Table 1.

**Visitors.** Questionnaires were sent to 6,993 people representing registered groups of visitors who had stayed in cabins at the Grand Canyon Lodge. A total of 3,731 (53.3%) people from all 50 states and 12 foreign countries responded. These responses represented registered groups of visitors who had stayed in cabins at the Grand Canyon Lodge. A total of 3,731 (53.3%) people from all 50 states and 12 foreign countries responded. By use of the screening questionnaire, we found that 93 (0.92%) visitors reported febrile illnesses accompanied by 3–4 characteristic symptoms within 30 days of the park visit. Interviews were completed with 84 (90%) of these symptomatic people, and in total, 2 confirmed and 13 probable cases of relapsing fever were identified, resulting in an attack rate for visitors of 1 per 1,000 person-nights of exposure (Table 1). Two visitors had documented spirochetemia; however, only one had a serum specimen available for ELISA testing. The specimen, obtained 4 weeks after onset of illness, was negative according to our ODR criteria. Eleven illnesses in visitors were counted as cases on the basis of relapsing febrile illness. Three of these patients had serum specimens obtained several months after illness, but none had ODR \( > 4.0 \). Two visitors had illnesses counted as “probable cases” on the basis of febrile illness and positive serology without a recurrence or documented spirochetemia.

**Employees.** Questionnaires were completed by 184 (75.4%) of 244 employees of the concessions company and the National Park Service. Two employees reported relaps-
ing febrile illnesses that were counted as probable cases of relapsing fever (Table 1); both had positive serum assays. The ages of the 17 visitor and employee case-patients ranged from 19 to 61 years; 8 (47%) were men. They were residents of 8 states, Canada, and Germany. Only 5 patients (3 visitors and 2 employees) were suspected at the time of their illnesses to have TBRF. The reported incubation periods for visitor cases ranged 2–21 days (median, 8 days). Patients reported a median of 3 episodes (range, 1–8 episodes) of febrile illness (Table 1). Nine patients were hospitalized; one employee also presented with evidence of meningitis.

No child aged < 18 years was identified with illness meeting the case definition, and the difference in attack rates between children and adults was statistically significant (Table 2). However, 4 children were identified with acute febrile illness that was promptly treated with empiric antibiotics and resolved (data not shown).

Of the 15 visitors with confirmed or probable TBRF, 14 had stayed in cabins in the northwest cabin group (relative risk [RR] for northwest vs southeast cabins, 8.2, 95% confidence interval [CI] 1.1 to 62) (Table 2). No significant differences between the northwest and southeast cabin groups were detected with regard to rates of completion of the mailed screening questionnaire or the telephone interview, duration of stay, or proportion of visitors reporting febrile illnesses that did not meet the case definition.

Cases in 7 visitors were associated with a single cabin in the northwest cabin group, cabin 81–86 (RR versus other cabins 98, 95% CI, 30–219). The attack rate among visitors staying in this cabin structure was 40.2 per 1,000 person-nights. Two additional visitors staying in cabin 81–86 reported illness with high fever 7 and 9 days after their visit. Both were treated early with antibiotics and did not relapse; serum was available from one of these visitors and was negative for antibodies to *B. hermsii*, and the illnesses did not meet the case definition for this investigation. Both employee case-patients lived in lodge cabins in the northwest cabin group. (Table 1).

**Serological testing.** Serum specimens were obtained from 88 asymptomatic employees residing at the North Rim and from 17 employees and 34 visitors with a history of illness. Table 3 presents the distribution of ELISA results according to illness category. Convalescent serum specimens from 6 case-patients with relapsing febrile illness or spirochetemia demonstrated a mean ODR of 3.6 (Standard deviation [SD], 3.9; range, 0.75–10.4). Serum specimens from 15 people with fever and at least 3 characteristic symptoms without relapse demonstrated a mean ODR of 2.0 (SD, 2.5; range, 0.25–9.2). Two of these had ELISA ODR > 4 and were counted as cases.

Serum specimens obtained from 30 people with illnesses that were not compatible with the clinical case definition (i.e., without fever plus at least 3 symptoms) demonstrated a mean ODR of 1.20 (SD, 1.1; range, 0.13–4.1). Two employees with illness had convalescent-phase serum specimens demonstrating ELISA ODRs of 4.1. One reported an illness of 3 days duration characterized by subjective fever, myalgia, diarrhea, and abdominal pain, and the other reported an illness characterized by fatigue and anorexia, which lasted 10 days and improved during treatment with tetracycline. Neither of these illnesses met the case definition. Serum specimens obtained from 88 asymptomatic employees demonstrated a mean ODR of 1.08 (SD, 0.68; range, 0.001–2.89).

**Environmental survey.** At the time of the on-site 1990 investigation, only 2 cases were known to have occurred after the affected patients stayed overnight in specific cabins. It was evident that rodents had ample access to the foundations and attic spaces in many of the northwest cabins. For example, cabin 81–86 had a large hole through the exterior log wall, which was used for the passage of a gas pipe. This uncovered, oversized hole allowed ingress of rodents

### Table 2

<table>
<thead>
<tr>
<th>Variable</th>
<th>No. people exposed</th>
<th>Person-nights</th>
<th>Attack rate per 1,000 person-nights</th>
<th>Relative risk (95% confidence interval)</th>
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<td>Age (years)</td>
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<tr>
<td>&lt;15</td>
<td>0</td>
<td>2,477</td>
<td>3,903</td>
<td>0</td>
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<td>15–44</td>
<td>10</td>
<td>3,952</td>
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<td>&gt;45</td>
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<td>3,745</td>
<td>5,808</td>
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<td>Sex</td>
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<td>Male</td>
<td>8</td>
<td>4,790</td>
<td>7,669</td>
<td>1.0</td>
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<tr>
<td>Female</td>
<td>7</td>
<td>5,106</td>
<td>8,018</td>
<td>0.9</td>
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<tr>
<td>Cabin group</td>
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<tr>
<td>Northwest</td>
<td>14</td>
<td>6,336</td>
<td>10,078</td>
<td>1.5</td>
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<tr>
<td>Southeast</td>
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<td>5,899</td>
<td>0.2</td>
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<tr>
<td>Cabin</td>
<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Cabin 81–86</td>
<td>7</td>
<td>90</td>
<td>174</td>
<td>40.2</td>
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<tr>
<td>Other cabins</td>
<td>8</td>
<td>10,084</td>
<td>16,002</td>
<td>98 (30–219)</td>
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</table>

* Relative risk undefined, *P* < 0.05 by Fisher’s exact test for age < 15 years compared with all others.

### Table 3

<table>
<thead>
<tr>
<th>Symptoms</th>
<th>ELISA OD ratio*</th>
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<td>Case</td>
<td>≤4.0</td>
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<tr>
<td>III, with positive smear</td>
<td>1</td>
</tr>
<tr>
<td>III, fever plus 3 symptoms and relapse</td>
<td>3</td>
</tr>
<tr>
<td>III, fever plus 3 symptoms, no relapse</td>
<td>13</td>
</tr>
<tr>
<td>II, other</td>
<td>28</td>
</tr>
<tr>
<td>Not III</td>
<td>88</td>
</tr>
</tbody>
</table>

* ELISA = enzyme-linked immunosorbent assay; OD, optical density.
† Patients counted as probable cases based on serological results.
to hollow wall and attic spaces. In contrast, rodent-proofing measures conducted in 1974, such as metal flashing and mesh covering of openings to the exterior foundations, walls, eaves, and fireplace masonry, remained intact on the cabins in the southeast group, and evidence of recent or currently active rodent infestations was rare: in 3 of 56 units, mouse droppings and small rodent nests were found under the water heaters. A few small rodent nests were collected from attic spaces of northwest cabins associated with index cases. No *O. hermsi* ticks were present in these nests. On the basis of the initial field assessment, the walls and baseboards of cabins in the northwest cabin group were treated with acaricides in August 1990.

In May 1991, all North Rim structures were evaluated for infestations of rodents. Buildings that were rodent infested had accessible nests and accumulated debris removed. Each infested cabin was rodent-proofed by covering or filling holes on the exterior with appropriate materials. Each structure that required rodent-proofing measures was also treated with acaricides to eliminate ticks that may have remained after they dispersed from their nests. Chemical treatment consisted of applying a spray of chloropyrifos to interior walls and baseboards and insufflating a silica gel–based desiccant powder into floor, wall, and ceiling spaces. The southeast cabin group did not require acaricide treatment.

Special attention was given to the cabins associated with TBRF cases. Eleven rental units contained in 10 northwest cabins were identified as overnight accommodations for 16 of the 17 TBRF case-patients. Cabin 81–86 accounted for 7 cabins were identified as overnight accommodations for 16 TBRF cases. Eleven rental units contained in 10 northwest cabin group did not require acaricide treatment. The south-east cabin group did not receive acaricide treatment.

In 1990, there were anecdotal reports of reduced rodent populations, but there was no documented epizootic of plague.

We observed that rodent-proofing measures remained largely intact and were effective in preventing rodents from nesting within most of the structures of the southeast cabin group. We also observed that only one probable case occurred in a visitor staying in these rodent-proofed cabins, whereas 16 cases (14 visitors and 2 employees) occurred in the other group of cabins. This suggests that the measures taken to rodent-proof the southeast cabins were effective in preventing illness 17 years after they were implemented.

The occurrence of 7 patients plus 2 additional symptomatic people in a single cabin highlights the focal nature of this endemic infection. Cabin 81–86 had readily accessible pine squirrel nests in the attic space. Similarly, in the 1973 outbreak, cabin 88–93—located 2 doors away from cabin 81–86—was associated with 7 cases; that structure also had pine squirrel nests in the attic (Maupin G, unpublished data). *Tamiasciurus hudsonicus* was found to be highly susceptible to experimental infection with *B. hermsii* and is an important TBRF reservoir, along with chipmunks, at the North Rim of Grand Canyon National Park.

We undoubtedly underestimated the morbidity of *B. hermsii* infections originating at the North Rim in 1990 for several reasons. First, because only visitors who registered with a valid address could be contacted, not all visitors were represented in our study. Additionally, only 53% of those surveyed actually responded, and language barriers may have limited the ability of foreign visitors to respond to the survey. Further, because the case definition used in this study required remission and relapse of symptoms or a positive serological test, some people with illness caused by *B. hermsii* may not have been counted because their illness resolved.
after one episode—often with antibiotic therapy that was prescribed empirically for febrile illness. Our finding of no illnesses meeting the case definition in children could have been due to the use of empiric antibiotics for this age group early in a febrile illness. In the 1973 outbreak, only 7 of 16 confirmed cases and 12 of 46 clinical cases relapsed after a symptom-free interval.\textsuperscript{6}

Conversely, because laboratory confirmation is lacking for most of the cases presented here, and because the sensitivity and specificity of the case definitions we used are unknown, it is possible that some illnesses counted here as TBRF cases were in fact due to other causes. Such misclassification would be unlikely, however, to occur preferentially within visitors staying in a single cabin or group of cabins. Although misclassification is possible, the cases reported are clinically similar to those described in the 1973 TBRF outbreak at the North Rim of the Grand Canyon.\textsuperscript{6}

The small number of patients with available serum and the small number of patients diagnosed with spirochetemia make it impossible to evaluate the serological test used in this investigation in comparison with the diagnostic standard. However, the observation that one confirmed case-patient and 3 of 5 case-patients with classic relapsing fever illness tested had negative serological results suggests that the sensitivity of the serological test was low. However, the times of specimen collection ranged from a few weeks to several months after illness, and there were too few serological data to interpret the effect of the timing of specimen collection in relation to illness or of antibiotic treatment on serological response. Nonetheless, the low prevalence of ELISA results above the ODR cutoff of 4.0 among ill people without classic relapsing fever in this setting suggests that the test’s specificity may have been relatively high.

The people potentially exposed to TBRF during this 1990 outbreak visited the Grand Canyon from around the world. Because most case-patients resided in nonendemic areas, physicians treating them had a low index of suspicion for TBRF. These factors make it relatively easy for cases and outbreaks of TBRF that originate at heavily used tourist sites to go unrecognized. However, the results of this investigation support the recommendation that park officials and businesses maintaining cabins at sites where TBRF is endemic assure these cabins are adequately rodent-proofed.

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