

Public Veterinary Medicine: Public Health

An outbreak of tick-bite-associated illness among military personnel subsequent to a field training exercise

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- Many tick-borne human diseases mimic other illnesses.
- Diagnoses are rarely based on comparison of acute and convalescent titers.

In late August 1993, several US Air Force security police personnel at a base in Arizona developed similar vague signs and symptoms of systemic illness. Forty-four members of their unit had recently returned from a 2-week (August 11 to 23) training exercise at Little Rock Air Force Base (AFB), Arkansas that had involved personnel from 4 other AFB (in Alabama, New Mexico, Texas, and Washington). During the first 8 days of the exercise (August 11 to 18), individuals from Arizona lived and attended classes in wooden barracks in an area surrounded by tall grass, weeds, and perennial bushes. The last 5 days of the exercise (August 19 to 23), they lived and trained in the field, in an ecologic transition area consisting of a mosaic of grass and tall (40 to 55 cm) brush known to support large populations of ticks.¹

Index patients (a 21-year-old Caucasian female and a 25-year-old Caucasian male) complained of substantial fatigue, severe headaches, myalgia, and mild gastrointestinal upsets of 2 to 3 days' duration. When examined on August 31 and September 1, both had mild lymphadenopathy and a fever (oral temperature, 37.8 and 38.3 C). The female patient reported that she had been bitten by ticks during the field training portion of the exercise and had a skin rash that a nurse practitioner described as a "bull's-eye" lesion. Physical

findings and history led to a clinical suspicion of Lyme disease, and doxycycline was prescribed for both patients. Blood samples from both patients were submitted for CBC. A sample of the female patient's serum was submitted to the Epidemiologic Research Division's laboratory at Brooks AFB, Texas, for determination, by use of an ELISA, of *Borrelia burgdorferi* total antibody titer.²

Both patients had a mild leukocytosis, with a high percentage of segmented neutrophils (79 to 88%) and a low percentage of lymphocytes (6 to 11%). The female patient was considered by the nurse practitioner to be seropositive for *B burgdorferi* on the basis of the ELISA titer (predicted index value [PIV], 0.41), and medical authorities at the Arizona AFB began to contact their counterparts at the 4 other AFB to alert them to the possibility of a Lyme disease outbreak. However, because the titer was low, the need for such a widespread alert was questioned, and it was decided to conduct an investigation to determine the most likely cause of illness in these 2 patients.

Physicians at the 5 AFB were asked to identify all individuals who became ill after participating in the Arkansas training exercise. All Arizona personnel who had participated in the exercise, and 29 others from the same unit who had not, were questioned on September 17 and 18. Information obtained included: where they had lived during the previous month, whether they had been bitten by ticks or insects during that period, whether they had been exposed to any vertebrate animals during that period, whether they had been treated for any illness in the previous 6 weeks, and if so, what signs or symptoms had developed by date of onset. Those who participated in the training exercise also were asked what measures they had used to prevent tick and insect bites.

From the completed questionnaires and subsequent review of medical records, 13 individuals from the Arizona AFB were found to have become ill following participation in the exercise. Only the 2 index patients voluntarily sought medical attention prior to the outbreak investigation. Onset of illnesses ranged from August 20 to September 15. No such illnesses were reported from personnel at the other 4 AFB. Of the 13 individuals who became ill, 11 reported severe

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fatigue, 9 complained of headaches, and 8 had a skin rash. The rash was maculopapular and had appeared on the extremities first and then spread to the trunk. A few individuals reported rare petechiae or subcutaneous hemorrhages. Six had myalgia and some degree of lymphadenopathy; 5 reported a fever (oral temperature, 37.8 to 38.6 C). A few individuals had nausea, diarrhea, loss of appetite, and vomiting. The case definition was established as any 2 of the most frequent findings (severe fatigue, headache, skin rash) or 1 of these findings plus myalgia, lymphadenopathy, or fever,^{3,4} with illness onset between August 20 and September 1. Eleven individuals met the case definition. Median date of onset was August 28. All affected personnel were treated with doxycycline, and all recovered uneventfully. None of the individuals who had not participated in the training met the case definition.

Case patients were between 21 and 34 years old (median, 27 years old). There were 2 Caucasian females, 1 African-American male, 1 Hispanic male, and 7 Caucasian males. Demographics of the individuals who participated in the exercise but did not meet the case definition (internal control subjects) and of the individuals from the same unit who had not participated (external control subjects) were similar to the case patients, except that the external control subjects tended to be older (median age, 31.5 years) than the case patients. Approximately 40 (90%) of the Arizona personnel who had participated in the field training received briefings, before the exercise, concerning protection against ticks and insects; 38 (86%) had tucked their uniform pants into their combat boots, 33 (76%) had used N,N-diethyl meta-toluamide insect repellent when in the field, 15 (33%) had treated their uniforms with permethrin, and all had used self-aid or "buddy-care" checks daily to remove ticks. Most had shaken their uniforms frequently.

Nine of the 11 case patients and approximately 70% of the internal control subjects reported that they had been bitten by ticks while in Arkansas. During the field training portion of the exercise (August 19 to 23), personnel lived in tents, slept in sleeping bags, crawled through brush and tall grass, and performed other activities that brought them in close contact with the ground and vegetation. Most tick bites occurred in this environment. None of the external control subjects, who remained in Arizona, reported being bitten by ticks.

Initial (early convalescent) and follow-up (late convalescent) blood samples were obtained from all case patients, 10 internal control subjects (who had gone to Arkansas), and 10 external control subjects (who had remained in Arizona). Internal and external control subjects volunteered blood samples and were a nonrandom convenience sample, commonly used in outbreak investigations.⁴ Initial samples were collected on September 22; follow-up samples were collected on October 21. Follow-up samples were not obtained from 2 case patients and 2 internal control subjects.

On the basis of clinical signs and symptoms and discussions with Arkansas public health officials, samples were submitted for a standard panel of differential

titers to tick-borne agents^{3,4,a}: IgM titer to *Rickettsia rickettsii* (samples with titer \geq 1:64 were considered seropositive); IgM titer to *R typhi* (samples with titer \geq 1:64 were considered seropositive); total immunoglobulin titer to *Francisella tularensis* (samples with titer $>$ 1:80 were considered seropositive); total immunoglobulin titer to *B burgdorferi* (samples with PIV $>$ 1.00 were considered seropositive); IgM titer to *Coxiella burnetii* (samples with titer \geq 1:16 were considered seropositive); and IgM titer to *Ehrlichia chaffeensis* (samples with titer \geq 1:16 were considered seropositive).^{2,5,6} All tests were performed by the Epidemiologic Research Division at Brooks AFB, Texas, except for the assays of antibody to *E chaffeensis*, which were performed by the Centers for Disease Control and Prevention, Atlanta, Ga. Initial and follow-up samples were assayed concurrently, and laboratory personnel did not know whether samples were from case patients or from control subjects.

Five of the 11 case patients were initially seropositive for, or seroconverted to, *R rickettsii*; 6 of 10 internal control subjects were either initially seropositive or seroconverted.^b Because sera were not diluted to determine end-point titer, the highest titers were reported only as $>$ 1:128. None of the external control subjects were seropositive for, or seroconverted to, this antigen. One case patient who was not seropositive for *R rickettsii* had an equivocal titer (0.87 PIV) for antibody to *B burgdorferi*, and 1 other case patient who was not seropositive for *R rickettsii* was seropositive for *E chaffeensis*. One internal control subject who was seropositive for *R rickettsii* was also seropositive for *R typhi*. One external control subject was seropositive for *C burnetii*. Results of all other serologic tests were negative.

Data from this investigation were entered into a computer-based system for analyzing epidemiologic data.^c The "rows \times columns" contingency tables for χ^2 and Fisher's exact tests, odds ratios (OR), and confidence limits (CL) were analyzed and calculated. All statistical tests were two-tailed, and significance levels were set at $P < 0.05$. Yates' corrected χ^2 analysis of the data revealed that participation in the Arkansas training exercise (August 11 to 23) was significantly associated with subsequent development of illness ($P < 0.02$; OR, 10.84; exact 95% CL of the OR, 1.44 and 457.32). Subsequent illness was significantly associated with a history of tick bites ($P = 0.033$; OR, 8.36; exact 95% CL, 1.15 and 77.44). Also, participation in the training exercise was significantly associated with a history of tick bites (Fisher's exact test, $P < 0.0001$) and with subsequent seropositivity to *R rickettsii* (Fisher's exact test, $P < 0.005$). Among those for whom follow-up titers were available, a history of tick bites was weakly associated with subsequent seropositivity to *R rickettsii* (Yates' corrected χ^2 test, $P = 0.063$; OR, 6.40; exact 95% CL, 0.93 and 50.46). However, meeting the case definition was not significantly associated ($P = 0.273$) with seropositivity to *R rickettsii*.

Findings from this outbreak investigation suggested that approximately 75% of the Arizona personnel who participated in the Arkansas exercise were bitten by ticks during the field training, and approxi-

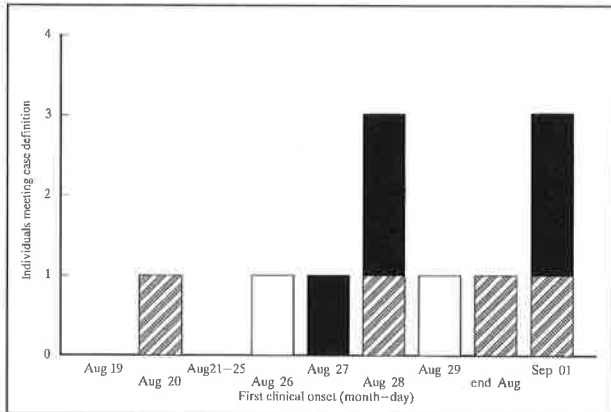


Figure 1—Epidemic curve constructed after an outbreak of Rocky Mountain spotted fever among personnel who participated in a military training exercise at Little Rock Air Force Base, Arkansas, in 1993. □ = Individuals who did not report having been bitten by ticks and had negative serologic test results; ▨ = individuals who reported having been bitten by ticks and had negative serologic test results; and ■ = individuals who reported having been bitten by ticks and had positive serologic test results.

mately 50% of those were consequently infected with *R. rickettsii*. Eleven subsequently developed clinical Rocky Mountain spotted fever (RMSF). Subtracting 5 to 7 days (the incubation period for RMSF) from the median onset date (August 28) coincides with the field training portion of the exercise, when individuals were at greatest risk of exposure to tick bites (Fig 1).

We believe that positive test results for organisms other than *R. rickettsii* were coincidental.^{4,7} However, the 1 case patient who was seropositive for *E. chaffeensis* did not report a skin rash. One internal control subject who was seropositive both for *R. rickettsii* and for *R. typhi* did not report any signs or symptoms or flea bites. Arkansas has several areas, especially its military bases, known to be endemic for RMSF and human ehrlichiosis, but not murine typhus.^{3,4,7,8} The Arkansas Department of Health reported that the most common tick-borne diseases in human residents between 1989 and 1994, in descending order, were tularemia (some cases not tick-borne), RMSF, Lyme disease, and ehrlichiosis. Murine typhus was not reported.⁸ Ticks were not collected from or by the individuals who participated in the Arkansas training exercise. *Dermacentor variabilis* was the most likely vector in this outbreak,⁴ but some believe *Amblyomma americanum* may be a vector of RMSF in the south-central United States.^{3,9,10}

Personnel from Arizona remained together during the field training portion of the exercise, at a considerable distance from the others. This may explain why no individuals from the other 4 AFB were reported to have similar illnesses. Rocky Mountain spotted fever is a classic microecologic niche zoonotic disease, for which ticks act both as the reservoir (transovarial and transtadial transmission) and as the vector.⁹ Usually, only small percentages (1 to 5%) of ticks from RMSF-endemic niches have been found to be infected with virulent *R. rickettsii* at any particular time.^{9,11,d}

The Arizona personnel who participated in the training exercise were knowledgeable about tick-bite prevention. Although not everyone used all available preventive techniques, the incidence of RMSF was only 25% (11/44) following 5 days of intense exposure in an environment known to have large tick populations and high prevalences of tick-borne illnesses.^{1,12} However, the low percentage (33%) of individuals who reported using permethrin-impregnated uniforms may have led to more tick bites and more infections.⁷ In a report of a similar outbreak,⁴ it was stated that use of available preventive measures “always” or “most of the time” did not reduce the risks of tick bites or *R. rickettsii* infections.

Finding a gradient in the natural history of a disease (more individuals exposed than infected; more infected than clinically ill; and more with mild than with serious disease) is expected in outbreak investigations.⁴ From the serologic portion of this investigation, we can infer that only 43 to 56% of those infested with or bitten by enough ticks to recall the exposure became seropositive to *R. rickettsii*. Six internal control subjects became seropositive to *R. rickettsii* but did not develop the defined illness. Of 11 case patients, only 2 voluntarily sought medical treatment prior to the investigation.

Not all case patients in this outbreak recalled having been bitten by ticks, and not all were seropositive for *R. rickettsii* (Fig 1). Case patients had a slightly lower, but similar, rate of seropositivity to *R. rickettsii* than did internal control subjects. This reflects similar risks of exposure and is consistent with the finding that many *R. rickettsii* infections in human beings are subclinical.^{7,11,13} In addition, people with RMSF who are treated promptly and appropriately tend to have diminished IgM titers to *R. rickettsii*.^{9,14,15} All the ill individuals in this outbreak were treated appropriately and relatively early in the course of disease. Immunoglobulin M titers to *R. rickettsii* are usually undetectable 2 months after the illness.⁹ In this investigation, follow-up sera were not collected until 60 days after the earliest clinical onset.

Public health veterinarians should remember that although most human cases of RMSF are reported from the south atlantic and west/southcentral regions of the United States, RMSF has been reported from nearly all of the 48 contiguous states.^{9,14,16} Endemic foci have been recognized in urban areas of large northeastern and midwestern metroplexes, and RMSF may be acquired during travel in an endemic area.^{8,9,14} Patients with clinical RMSF are motivated to seek medical care, but only 20 to 50% report having been bitten by ticks. Often, exposure to ticks (removing them from pets, or camping) is not elicited in the medical history.^{3,9,14} Clinical signs and symptoms of RMSF may mimic many other illnesses of the central nervous, gastrointestinal, and respiratory systems, and the hallmark rash may not be evident in all patients.^{3,9,14,15}

Ticks are excellent vectors of disease agents because of their firm attachment to hosts, wide host range, slow feeding, relative longevity, and need for blood meals at each stage of development. They are also reservoirs for many infectious agents.¹⁷ During the

past 10 years, more vector-borne human diseases have been transmitted in the United States by ticks than by any other order of arthropods.¹⁶ Each of these zoonoses in human beings tends to be both regional and seasonal. Most public health departments use fact sheets to educate the public about ticks, tick-borne illnesses, and other zoonoses. Private veterinary practitioners should also take every opportunity to explain zoonotic disease prevention to their clients. Rocky Mountain spotted fever remains an important tick-borne zoonosis in the United States because of its multifaceted ecology, its endemicity and prevalence, and its severity when misdiagnosed or inadequately treated.^{9,14,15}

^aBerry DA, McChesney TC, Arkansas Department of Health, Little Rock, Ark: Personal communication, 1993.

^bContact authors for demographic, exposure, and serologic data (11 cases and 20 comparisons) without identifiers.

^cEpi-Info, version 6, Centers for Disease Control and Prevention, Atlanta, Ga.

^dGoddard J, Mississippi State Department of Health, Jackson, Miss: Personal communication, 1994.

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