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Increasing Incidence of Rocky Mountain Spotted Fever among the American Indian Population in the United States

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Abstract. To examine trends of Rocky Mountain spotted fever (RMSF) incidence among American Indians compared with other race groups, a retrospective analysis of national RMSF surveillance data reported to the National Electronic Telecommunications System for Surveillance and the Tickborne Rickettsial Disease Case Report Forms system were used. The RMSF incidence for American Indians, which was comparable to those for other race groups during 1990–2000, increased at a disproportionate rate during 2001–2005. The average annual incidence of RMSF reported among American Indians for 2001–2005 was 16.8 per 1,000,000 persons compared with 4.2, 2.6, and 0.5 for white, black, and Asian/Pacific Islander persons, respectively. Most cases in American Indians were reported from Oklahoma (113.1 cases per 1,000,000), North Carolina (60.0), and Arizona (17.2). The incidence of RMSF increased dramatically among American Indians disproportionately to trends for other race groups. Education about tick-borne disease and prevention measures should be addressed for high-risk American Indian populations.

INTRODUCTION

Rocky Mountain spotted fever (RMSF) is a tick-borne zoonotic disease caused by infection with *Rickettsia rickettsii*.[1–3] Ticks, primarily the American dog tick (*Dermacentor variabilis*) and the Rocky Mountain wood tick (*Dermacentor andersoni*), serve as the reservoir and the vector for RMSF in the United States. The common brown dog tick (*Rhipicephalus sanguineus*), has also been recently identified as a vector for human disease in parts of eastern Arizona.[4] Rocky Mountain spotted fever is reported throughout most of the contiguous United States, and the annual incidence rate has increased from 2.0 cases per 1,000,000 persons in 1992 to 3.8 cases in 2002 per 1,000,000 persons annually.[1,2,5] However, because RMSF is difficult to diagnose, the number of actual RMSF cases is probably much higher than the studies of national reporting data suggest.

Symptoms of RMSF typically include acute onset of fever, headache, and myalgia within 14 days of a bite from an infected tick.[5] Severe cases may include acute respiratory distress syndrome, disseminated intravascular coagulopathy, and multi-organ failure. Tetracycline antibiotics are efficacious in the treatment of RMSF, and doxycycline is recommended for patients.[6,7] The case-fatality rate has been reported to be 1.2–5.8%,[8] but approached 60% in the pre-antibiotic era.[9] A mean of 37 deaths (range = 16–64) was estimated to occur annually during 1983–1998.[10]

The importance of infectious diseases, including RMSF, as a health issue among American Indians has been suggested through other studies.[11–14] In one study examining hospitalization data among American Indian populations, the RMSF hospitalization rate for American Indians living in Oklahoma during the 1980s and early 1990s was higher than the rate for the general population of Oklahoma.[13] An expanded study of hospitalization discharge data for American Indians during 1980–2003 indicated a high hospitalization rate among American Indians (12 per 1,000,000 persons), particularly among the Southern Plains region, which includes Oklahoma.[14] In 2003, an emerging focus of RMSF among American Indians was identified in eastern Arizona and associated with the brown dog tick.[4] Cases have continued to be reported among American Indians from this region (Levy C, unpublished data). These factors suggest that the epidemiology of RMSF among American Indians may be changing and deserves closer assessment.

The Centers for Disease Control and Prevention (CDC) monitors annual national trends in RMSF disease reporting through two surveillance systems: The National Electronic Telecommunications System for Surveillance (NETSS) and the Tick-Borne Rickettsial Disease Case Report Form (CRF) System. The NETSS collects information on diseases considered reportable through the National Notifiable Disease System, and state health departments submit official case counts electronically to CDC by this system.[15,16] Because NETSS data are considered to be official cases counts, these RMSF data are used to calculate incidence rates and monitor trends over time. The CRF system is a paper-based reporting system where states may voluntarily submit detailed information to CDC on tick-borne rickettsial disease cases, including RMSF.

Although data from the CRF system are not as complete as the RMSF data through NETSS in terms of overall case numbers and therefore are not useful for calculating incidence rates, CRF data enable assessment of clinical information on cases and monitoring of trends in RSMF-related hospitalizations and fatalities. Because RMSF data are reported to both systems without patient identifying information, the two systems cannot be reliably combined. In the present study, national RMSF case data reported during 2001–2005 through the NETSS and CRF system were analyzed to examine and describe the epidemiology and trends of RMSF for American Indians.

METHODS

Cases of RMSF reported to CDC by state health departments and private physicians through NETSS and through the Tick-Borne Rickettsial Disease CRF system for 1990–2005 were selected for the present study.[1,15,16] Cases reported

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by states to NETSS that met either confirmed or probable RMSF definition were considered to be RMSF cases in this study. The RMSF case definition during the study period included designations for confirmed RMSF (positive culture, demonstration of *Rickettsia* spp. in a clinical specimen by polymerase chain reaction or immunohistochemical test, or at least a four-fold change in serologic titers from acute-phase and convalescent-phase specimens) and probable RMSF (those cases with at least a single positive titer).[17,18] However, NETSS data were not specifically examined according to case status (i.e., probable versus confirmed cases) because the system does not permit assessment of the accuracy of stated case status. Some characteristics in the present study had missing or unknown information, which was excluded from the analysis; race was missing for 15% of cases reported through NETSS.

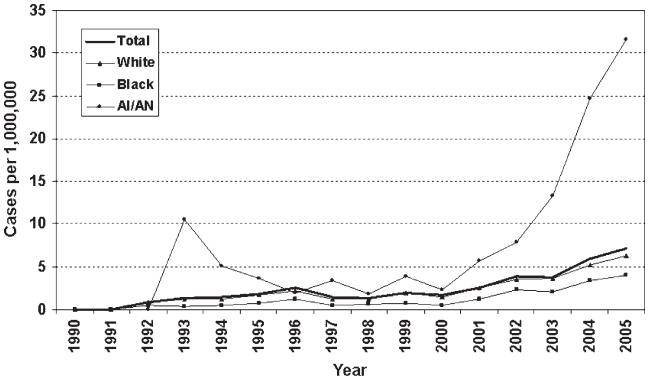
Incidence rates for RMSF were calculated using cases reported through NETSS and the corresponding census population for 1990 through 2005.[15,19] Incidence rates were expressed as the number of RMSF cases per 1,000,000 persons of the corresponding population. Annual incidence rates were calculated overall and by race group. Average annual incidence for the study period of 2001–2005 was examined by sex, age, race, and state of residence. Incidence for American Indians was compared with the other racial groups (white, black, and Asian/Pacific Islander). Rates for characteristics were compared using Poisson regression analysis to determine the risk ratios (RRs) and 95% confidence intervals (CIs).[20] Age was compared between groups using the Wilcoxon rank-sum test.[21]

Because NETSS does not collect detailed clinical information on cases, RMSF cases for 2001–2005 were further examined by CRFs submitted to CDC by state health departments. The CRFs were examined to identify risk factors for severe illness, including hospitalization and outcome. Because CRFs included information on laboratory test results, reports were reviewed by CDC staff for accuracy of case status assignment and, in some cases, adjusted as to confirmed or probable RMSF case designations. The case-fatality rate was calculated from CRFs and defined the proportion of persons for whom outcome was reported as death caused by RMSF. Comparisons of clinical characteristics were analyzed using the chi-square test or Fisher's exact test (two-sided).

RESULTS

Trends and incidence (NETSS data). During 1990–2000, the NETSS-reported annual incidence of RMSF among American Indians appeared slightly higher but comparable to that of other race groups (Figure 1). However, from 2001 through 2005, the annual incidence for American Indians increased dramatically; other race groups demonstrated more modest increases.

For 2001–2005, a total of 5,801 RMSF cases with a race group designation were reported to NETSS, including 259 (4.5%) RMSF cases reported as American Indians. During this period, the average annual incidence among American Indians was 16.8 per 1,000,000 persons, whereas the average annual incidence for white, black, and Asian/Pacific Islander persons was 4.2, 2.6, and 0.5 per 1,000,000, respectively. The rate for American Indians was significantly higher than that for each of the other race groups (white: RR = 4.0, 95% CI = 3.5–4.5; black: RR = 6.5, 95% CI = 5.6–7.5; Asian/Pacific Islander: RR = 37.1, 95% CI = 25.4–54.1). Increased incidence among American Indians compared with the other race groups was observed for males (19.9, 4.8, 3.0, and 0.5, respectively) and females (13.7, 3.7, 2.2, and 0.4, respectively).



* Annual rates for Asian/Pacific Islanders are not included since rates are less than 1 per million cases.

FIGURE 1. Annual incidence rates of Rocky Mountain spotted fever by race, 1990–2005, United States, National Electronic Telecommunications System for Surveillance.

During 2001–2005, the rate of RMSF among American Indians was significantly higher for males than females (19.9 and 13.7, respectively, RR = 1.4, 95% CI = 1.1–1.9). The rate difference between males and females was also seen among white (4.8 and 3.7, respectively, RR = 1.3, 95% CI = 1.2–1.4) and black persons (3.0 and 2.2, respectively, RR = 1.3, 95% CI = 1.1–1.6); no rate difference was seen between males and females among Asian/Pacific Islander persons (0.5 and 0.4, respectively).

The median age of an American Indian with RMSF (33.5 years) was significantly lower than that of white persons (median = 42 years; $P < 0.0001$) and black persons (median = 39 years; $P = 0.02$). Although not statistically significant, this rate was also lower than that of Asian/Pacific Islander persons (median = 38 years; $P = 0.1$). Cases of RMSF occurred among American Indians in all age groups (Figure 2) and the increase in incidence was observed across the age groups. The increased rate difference between American Indians and each of the other race groups was seen for all age groups.

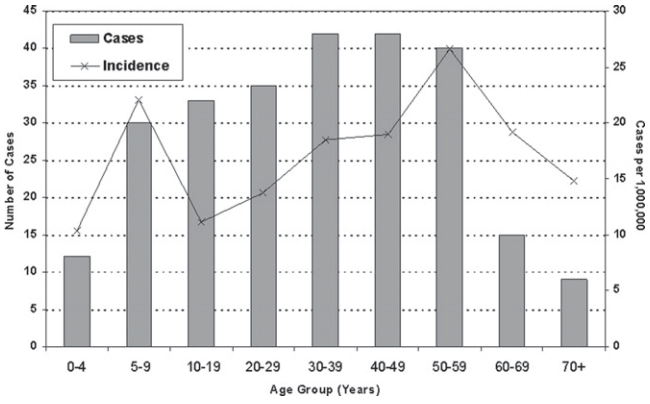


FIGURE 2. Number and incidence of Rocky Mountain spotted fever cases among American Indians by age group, 2001–2005, United States, National Electronic Telecommunications System for Surveillance.

FIGURE 3. Incidence of Rocky Mountain spotted fever cases in the United States for **A**, American Indians and **B**, all other persons, 2001–2005, United States, National Electronic Telecommunications System for Surveillance.

During the 2001–2005 study period, RMSF cases among American Indians were reported from 13 states; most cases occurred in Oklahoma (179, 69.1%), North Carolina (33, 12.7%), and Arizona (25, 9.7%) (Figures 3 and 4). The highest average annual rate was in Oklahoma (mean 113.1, peak 244.0 in 2005), and North Carolina (mean 60.0, peak 72.7 in 2003). The rate for Arizona was 17.2 (peak 40.8 in 2004).

Cases among American Indians reported during 2001–2005 occurred seasonally with most (87.3%) occurring in April through September, with June through August representing a peak in case onset. However, cases in American Indians reported in Arizona appeared to have an extended seasonality, with 32.0% occurring in October through December.

Hospitalization and outcome (CRF data). For 2001–2005, a total of 4,224 RMSF cases with a race group designation were submitted to CDC by CRFs; 227 RMSF cases (5.3%) were reported for American Indians. The CRF RMSF submissions appeared to parallel the NETSS RMSF submissions, and showed an increase comparable to the observed increase in RMSF cases via NETSS among all races.

Hospitalization was reported for 62 (27%) of 227 RMSF cases in American Indians; this proportion was similar to that of reported hospitalizations among persons of other races (Table 1). The proportion of reported hospitalized patients decreased among most race groups during 2001–2005, but was most dramatic among American Indians, from a high of 40.0% to a low of 16.7% in 2005. In contrast, the proportion of hospitalized patients decreased from 29.9% to 18.0% for white persons and from 45.3% to a low of 26.2% for black persons; few Asian/Pacific Islander persons were hospitalized. Among all American Indians with RMSF during 2001–2005, the age groups hospitalized most often included children less than five years of age (15%) and children 5–9 years of age (15%). In contrast, the age groups hospitalized most often were older adults, including those 50–59 years of age (17%) and 40–49 years of age (14%) among white persons and those 40–49 years of age (19%) and 20–29 years of age (17%) among black persons. There was no significant difference in hospitalization among for American Indian males and females (29% and 25%, respectively).

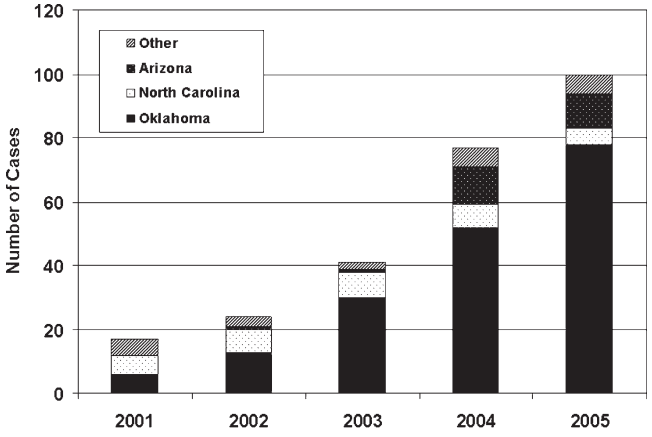


FIGURE 4. Number of Rocky Mountain spotted fever cases among American Indians by year for Oklahoma, North Carolina, and Arizona, 2001–2005, National Electronic Telecommunications System for Surveillance.

Among the RMSF cases reported by CRFs, 4 deaths of American Indians were reported. The case-fatality rate for American Indians (1.8%) was significantly higher than the rate for white persons (0.4%; $P < 0.02$). The case-fatality rate was also higher among American Indians than black persons (0.6%), although the difference was not significant ($P = 0.2$). No deaths were reported for Asian/Pacific Islander persons. For reported deaths in persons in which age was also reported, 3 cases occurred among American Indian children 5–9 years of age, and the case-fatality rate for this age group (11.5%) was significantly higher than the rate for white children 5–9 years of age (n = 3, 1.7%; $P < 0.03$); no deaths were reported for black children 5–9 years of age.

DISCUSSION

Although the incidence of RMSF has recently increased in the United States, the proportional rate of increase has been significantly greater among American Indians than in other race groups during 2001–2005. This difference is in sharp contrast to historical trends suggesting that American Indians have shown RMSF incidence rates that appear only slightly higher than other racial groups within the United States. The recent dramatic increase suggests that RMSF may be emerging as a more serious cause of disease among American Indians than has been previously understood.

American Indians may be at overall higher risk for infectious diseases than other populations, and some American Indians may also receive healthcare differently than other U.S. residents. Eligible American Indians may receive pre-paid healthcare through medical facilities funded by the Indian Health Service (IHS); some of these American Indians may also seek healthcare through private physicians by using more routine mechanisms. However, availability of such healthcare does not necessarily decrease disease risks. Studies have indicated that the American Indian population that uses the IHS healthcare system has a higher rate of infectious disease hospitalizations than that for the general U.S. population.[11,12]

During 2001–2005, the most dramatic increases of RMSF among American Indians were reported from Oklahoma and Arizona. The recent identification of the brown dog tick as a cause of RMSF in Arizona likely accounts for some of the observed increase in cases reported from that state.[4] The role of *Rhipicephalus sanguineus* as a possible factor in RMSF transmission for other American Indian populations, especially those residing in Oklahoma, has not been assessed but deserves serious exploration.

American Indians have been previously shown to have a higher incidence of RMSF than the U.S. general population in

TABLE 1
Selected characteristics of Rocky Mountain spotted fever cases by race, Tick-Borne Rickettsial Disease Case Report Forms, United States, 2001–2005

Characteristics*	American Indians No. (%)	All other races No. (%)	Whites No. (%)	Blacks No. (%)	Asian/Pacific Islanders No. (%)
Total	227 (100)	3,997 (100)	3,615 (100)	358 (100)	24 (100)
Case status					
Confirmed	29 (12.8)	275 (6.9)	261 (7.2)	12 (3.4)	2 (8.3)
Probable	198 (87.2)	3,722 (93.1)	3,354 (92.8)	346 (96.7)	22 (91.7)
Hospitalization					
Yes	62 (27.3)	979 (25.0)	858 (24.2)	113 (32.6)	–
No	165 (72.7)	2,934 (75.0)	2,684 (75.8)	234 (67.4)	–
Outcome					
Recovered	217 (98.2)	3,893 (99.5)	3,528 (99.6)	341 (99.4)	–
Died	4 (1.8)	19 (0.5)	14 (0.4)	2 (0.6)	

*Information is not completely reported for all available characteristics.

other studies.[13] Explanations for the differences in incidence for American Indians compared with other races may relate to social or anthropogenic factors resulting in increased rates of infection. For example, American Indians may typically live in more rural areas than other race groups, or may engage in recreational, social, or community activities that more frequently expose them to ticks, putting them at a high risk for RMSF.[13] Although increased rate of exposures offers a plausible explanation for increased incidence, it is unclear why those factors would have changed so dramatically beginning in 2001.

Another plausible explanation for the dramatic increase in incidence of RMSF among American Indians compared with other race groups may be related to changes in how cases are recognized and subsequently reported for this group. In this study, American Indians with RMSF were more likely to be classified as confirmed cases than other race groups. One possible explanation is that because some American Indians are able to obtain pre-paid healthcare, these persons may be more likely to undergo specific laboratory tests to aid an official diagnosis. Recognition and reporting of less severe RMSF appears to have improved more substantially among American Indians than for other race groups during the study period because the proportion of hospitalized cases decreased more substantially among this population. Recent publications and media attention highlighting RMSF risks and emergence among American Indian populations may have improved physician knowledge of RMSF in this population and thus influenced detection and reporting of some cases.[4,13,14]

This study suggests that particularly among children with RMSF, American Indian children experience a disproportionately higher case-fatality rate than was seen for children among other racial groups. The health disparities impacting care for American Indian children with RMSF are not well understood. Rocky Mountain spotted fever presents a clinical dilemma for physicians because it typically is manifested as a non-specific febrile illness that resembles other common childhood illnesses.[22] Rash may not develop for several days after onset, and the rash may be initially difficult to see in persons with darker skin tones, possibly causing a delay in clinical suspicion for RMSF. Even in more severe manifestations, diseases such as meningococcemia are usually considered higher on a list of diseases ruled out by physicians.[22] The early initiation of empiric therapy with doxycycline is imperative to reduce the likelihood of severe or fatal outcome for RMSF, but physicians may be reluctant to provide empiric tetracycline therapy for children because of unfounded concerns regarding dental staining.[22] More studies to understand the clinical issues related to higher case-fatality rates among American Indian children with RMSF are clearly needed.

The national surveillance systems used in this study have limitations. In general, RMSF is believed to be under-recognized and under-reported to NETSS because of the non-specific nature of clinical manifestations and the need to procure appropriate laboratory tests for diagnosis. However, NETSS is a passive data collection system, and there is no way to verify the accuracy of each RMSF case report submitted to CDC, which is an inherent problem of using NETSS data to determine national incidence rates. Any RMSF surveillance system designed to maximize case capture should include the possibility of a diagnosis based on serologic test results alone because these are the most widely available and commonly applied diagnostic tools. However, with this requirement comes the possibility of overestimating case counts because of difficulty in interpreting serologic laboratory findings, especially for cases in which presence of antibody from previous exposures or the presence of cross-reactive antibodies may result in an incorrect designation of probable RMSF infection. Interpretation is further hampered by the number of commercially available diagnostic tests and the wide variation in serologic cutoff values viewed as representing a positive RMSF case.

The Tickborne Rickettsial Disease CRF system provides a slightly more stringent assessment of the accuracy of confirmed and probable RMSF reports because laboratory data are supplied at the time of report and reviewed by CDC staff members. The CRFs also collect more detailed RMSF-related information than NETSS, enabling assessment of important clinical parameters such as hospitalization and case-fatality rates. However, states are not mandated to report cases by this system, making it an inappropriate choice for determining national incidence. Only by examining both surveillance systems can the national RMSF picture be ascertained.

The disproportionate increase in the incidence of RMSF among American Indians compared with each of the other race groups during 2001–2005 is striking. Regardless of whether the observed findings represent a true increase in case occurrence or merely improved recognition and reporting, there appears to be no question that American Indians experience rates of RMSF that are much higher than those observed for other racial groups. The high morbidity rate and occurrence of serious illness and death associated with RMSF, especially among children, necessitates further consideration of RMSF as an important public health issue among American

Indians. Prevention efforts are clearly needed specifically for American Indian populations, and a detailed understanding of the social and cultural factors influencing disease transmission are needed to appropriately target those messages. Tick-borne disease education and awareness should be provided to IHS and tribal physicians on the diagnosis, treatment, and risk factors of RMSF and other tick-borne diseases. Prompt appropriate antibiotic treatment is important, especially for children within high-risk areas. These prevention strategies are important to improve the awareness and treatment of RMSF and to reduce the burden of tick-borne disease among American Indians.

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