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Rocky Mountain Spotted Fever in the United States, 2000–2007: Interpreting Contemporary Increases in Incidence

John J. Openshaw, David L. Swerdlow, John W. Krebs, Robert C. Holman, Eric Mandel, Alexis Harvey, Dana Haberling, Robert F. Massung, and Jennifer H. McQuiston*
Division of Viral and Rickettsial Diseases, National Center of Zoonotic, Vector-Borne, and Enteric Diseases, Centers for Disease Control and Prevention, Atlanta, Georgia

Abstract. Rocky Mountain spotted fever (RMSF), a potentially fatal tick-borne infection caused by *Rickettsia rickettsii*, is considered a notifiable condition in the United States. During 2000 to 2007, the annual reported incidence of RMSF increased from 1.7 to 7 cases per million persons from 2000 to 2007, the highest rate ever recorded. American Indians had a significantly higher incidence than other race groups. Children 5–9 years of age appeared at highest risk for fatal outcome. Enzyme-linked immunosorbent assays became more widely available beginning in 2004 and were used to diagnose 38% of cases during 2005–2007. The proportion of cases classified as confirmed RMSF decreased from 15% in 2000 to 4% in 2007. Concomitantly, case fatality decreased from 2.2% to 0.3%. The decreasing proportion of confirmed cases and cases with fatal outcome suggests that changes in diagnostic and surveillance practices may be influencing the observed increase in reported incidence rates.

INTRODUCTION

Rocky Mountain spotted fever (RMSF) is a tick-borne disease caused by the intracellular bacterium *Rickettsia rickettsii*.[1,2] Rocky Mountain spotted fever has long been considered one of the most severe tick-borne rickettsial infections, with pre-antibiotic case-fatality rates reported as high as 65–80% in some case series[1–4];contemporary estimates from 1981 to 1998 placed modern case-fatality rates at around 3% of reported cases.[5,6] The disease causes fever, headache, abdominal pain, and rash in a majority of patients, and may also lead to complications such as encephalitis, acute respiratory distress syndrome, and coagulopathies.[1,2] Although most antibiotics are characteristically ineffective against *R. rickettsii*, tetracyclines offer excellent clinical results. However, a delay in administration of doxycycline, the recommended drug of choice, has been shown to increase the likelihood of fatal outcome.[7,8]

Because of its potential for severe outcome, RMSF is considered a notifiable condition in the United States. Surveillance for RMSF is a passive system that has provided important information on epidemiologic trends of infection.[9] Assessment of historical reports of case counts indicated some fluidity in annual case counts, with the years 1981–1998 marking a period of overall decline in the incidence and number of reported RMSF cases.[5,6,10] In the most recently published national summary, an increase in RMSF incidence was observed, from an all-time low of 1.4 cases per million in 1998 to 3.8 cases per million in 2002.[10] To determine if RMSF reports and incidence have continued to increase and to characterize the epidemiology of cases, we examined RMSF cases reported during 2000 through 2007.

METHODS

National surveillance systems. Rocky Mountain spotted fever is a nationally notifiable disease within the National Notifiable Diseases Surveillance System.[11] The U.S. Centers for Disease Control and Prevention (CDC) receives electronic reports of RMSF cases from state health departments through the National Electronic Telecommunications System for Surveillance (NETSS); these data are used to calculate national incidence and basic demographics (such as gender, race, and age).[12] Because NETSS does not collect patient outcome or laboratory data, a second supplemental system based on manually submitted case reports forms (CRFs) is also used; CRF data are used to determine case fatality and hospitalization ratios, and to report diagnostic tests used. Both systems rely on physicians to appropriately recognize and report RMSF to state health departments. In addition, both systems rely on the appropriate application of a national case definition, specifically the classification of confirmed cases and probable cases.[13,14] Two different case definitions were in effect during the studied period; the case definition was changed in 2004 to permit use of enzyme-linked immunosorbent assays (ELISA) for diagnosis of probable cases, and to permit use of commercial laboratory cutoffs for determination of positive test results.[13,14]

Analytic and statistical methods. Confirmed and probable RMSF cases reported to NETSS from 2000 through 2007 were used to calculate incidence rates by region, state, county, sex, age, and race. Population estimates for years 2000–2007 were obtained from the U.S. Census Bureau,[15] and U.S. regions followed census classifications. Rocky Mountain spotted fever was not considered a notifiable disease during some years in Maine (2003–2007), Washington (2003–2004, 2006–2007), Alaska (2005–2007), and Hawaii (2006–2007); however, when collected, reports from those states were analyzed. The year of RMSF illness onset instead of reporting year was used for analyses; therefore, the number of cases presented here may differ from reports of the annual number of cases published in *MMWR* annual summaries. Incidence rates were expressed as the number of RSMF cases per million corresponding U.S. population. Confirmed and probable RMSF cases reported by CRFs were used to calculate the proportion of hospitalizations and case fatality rate, and to examine diagnostic test usage. Reports missing information were excluded from that segment of the analysis. Poisson regression analysis was used to compare groups. Winter onset cases were compared by region using the χ^2 test; EpiInfo was used for statistical calculations.[16]

*Address correspondence to Jennifer H. McQuiston, Division of Viral and Rickettsial Diseases, Centers for Disease Control and Prevention, 1600 Clifton Road, Mailstop G-44, Atlanta, GA 30333. E-mail: fzh7@cdc.gov

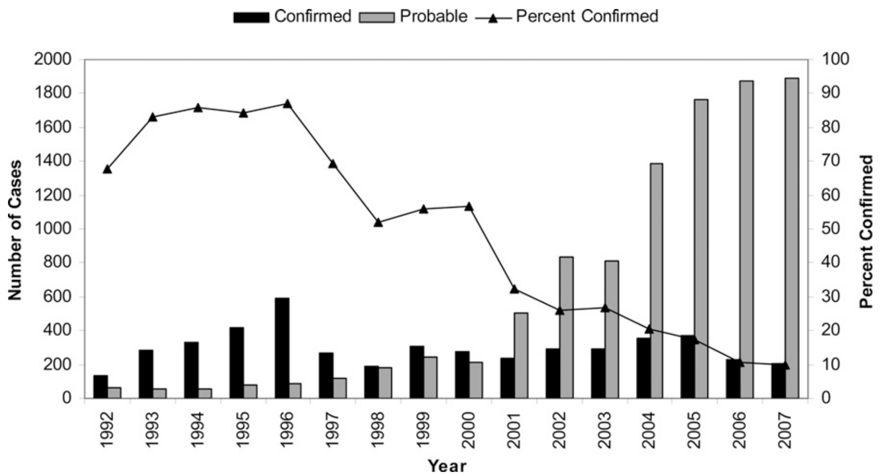

FIGURE 1. Rocky Mountain spotted fever cases by case classification status, 1992–2007, United States (determined by National Electronic Telecommunications System for Surveillance).

RESULTS

NETSS data. *Overall incidence*. Through NETSS, 11,531 RMSF cases were reported with an onset date January 1, 2000 through December 31, 2007. Among those with a recorded case status in NETSS, 19.6% were confirmed and 80.4% were probable cases. The percent of cases meeting a confirmed case definition decreased during the study period to 9.7% of cases in 2007 (Figure 1).

The lowest number of reported cases was 490 in 2000 and the highest was 2,133 in 2005. National incidence increased during 2000 through 2007, from 1.7 in 2000 to a peak of 7.2 cases per million persons in 2005 with 7.0 cases per million reported in both 2006 and 2007 (Figure 2). The average incidence for the first half of the reporting period (2000–2003) was 3.0 cases per million, whereas the average annual incidence for the latter half of the reporting period (2004–2007) was 6.8 cases per million.

Cases were reported from 46 states and the District of Columbia during the study period. Five states—North Carolina, Oklahoma, Arkansas, Tennessee, and Missouri—accounted for 64% of all RMSF cases (Figure 3). The West North Central, South Atlantic, East and West South Central census regions all had incidence rates above the national average incidence (Table 1). With the exception of the Pacific and Middle Atlantic regions, incidence in all regions increased more than 200% from the first half (2000–2003) to the second half (2004–2007) of the reporting period (Table 1).

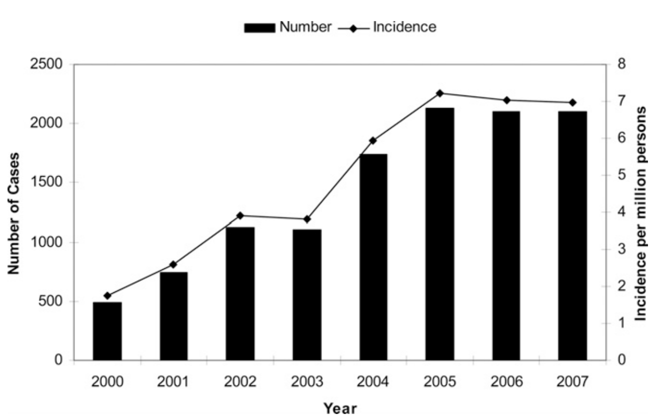

FIGURE 2. Rocky Mountain spotted fever cases and incidence (per millions persons), 2000–2007, United States (reported through the National Electronic Telecommunications System for Surveillance).

Demographics. Slightly more males (56.9%) than females were reported with RMSF through NETSS. Most cases during the study period occurred in whites (86.8%), followed by blacks (7.9%), and American Indians (3.9%); fewer cases involved Asian/Pacific Islanders (0.6%), or persons reporting a race category of "Other" (0.8%). Hispanic ethnicity was reported for 4.1% of cases. Race-specific incidence was higher among American Indians (16.8 cases per million population) than those for white (4.4), black (2.6), and Asian/Pacific Islander (0.5) race groups. The overall mean and median age of onset was 46 and 42 years of age, respectively. Incidence increased with age, peaking in the 50–59 and 60–69 age groups (6.9 and 7.0 cases per million, respectively) (Figure 4).

Seasonality. Among the NETSS cases that indicated an onset month, RMSF peaked in June and July ($N = 3429$, 38%). Fewer cases ($N = 351$, 4.1%) reported onset during the colder winter months of December, January, or February. Middle Atlantic states (New York, New Jersey, and Pennsylvania) reported a significantly higher proportion of cases with winter onset than other U.S. regions (9.3% and 3.9%, respectively; $P < 0.001$).

CRF data. A total of 7,796 RMSF reports were submitted by CRFs that stated an illness onset during 2000 through 2007. The cases reported through CRFs were similar to NETSS cases in terms of gender (57.4% male), age (mean age 40 years, median 41), and race distribution (86.6% white, 8.4% black, 4.4% American Indian, 0.6% Asian/Pacific Islanders) (Table 2). However, cases reported by CRF were less likely to be classified as confirmed (5.8%) than cases reported through NETSS (19.6%); CRF case classifications are considered more accurate because they are verified by CDC staff on the basis of provided laboratory data, and corrected when necessary.

Hospitalizations. The overall proportion of hospitalized CRF cases was 23.4%. Confirmed cases had a higher percent of patients hospitalized (37.4%) compared with that for probable cases (22.6%). The annual percent of patients hospitalized decreased during the study period, from a high of 36.4% reported in 2000 to a low of 18.1% reported in 2005 (Figure 5A). A higher proportion of males were hospitalized

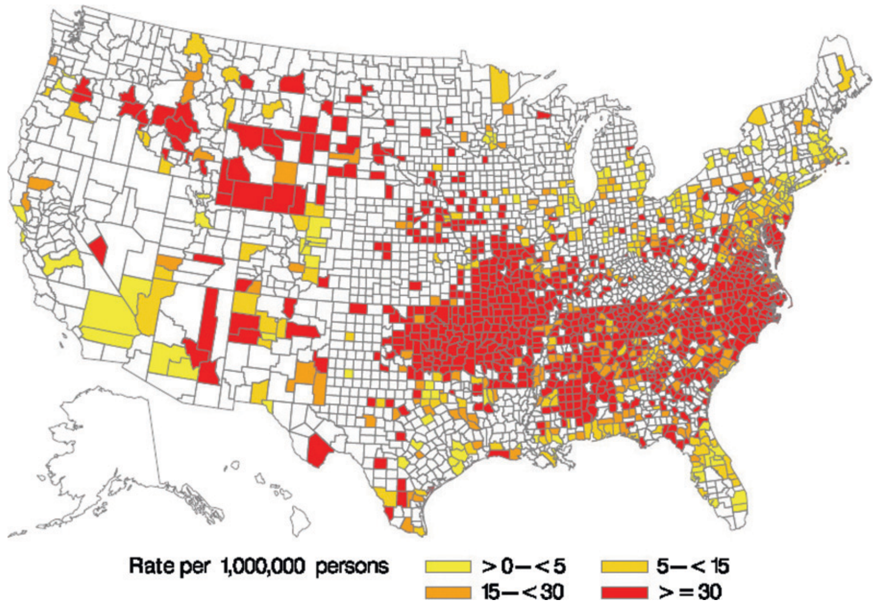

FIGURE 3. Rocky Mountain spotted fever incidence by county, 2000–2007, United States (reported through the National Electronic Telecommunications System for Surveillance).

than females (25.0% and 21.7%, respectively; $P < 0.001$). The percent of patients hospitalized was highest among 0–4 year olds (36.2%) and 70 + year olds (38.5%) (Figure 5B). By race, blacks were most frequently hospitalized (31.0%), followed by American Indians (24.5%), whites (23.0%), and Asian/Pacific Islanders (22.7%). Specific life-threatening complications, including meningitis/encephalitis ($N = 95$, 1.7%), renal failure ($N = 28$, 0.5%), adult respiratory distress syndrome ($N = 25$ cases, 0.4%), and coagulopathy ($N = 11$ cases, 0.2%), were reported for a minority of patients.

Fatal outcome. The overall proportion of CRF cases with fatal outcome was 0.5%. Confirmed cases had a higher percentage of patients with fatal outcome (3.0%) compared with probable cases (0.3%). The annual case fatality decreased during 2000 to 2007 (Figure 6A). American Indians experienced the highest reported case fatality (2.2%), followed by whites (0.5%) and African Americans (0.2%). Among cases stratified by age, the highest case fatality was reported among patients aged 5–9 years (2.6%), adults 70 + years (1.3%), and children aged 0–4 years (1.2%) (Figure 6B).

Laboratory testing. During the study period, the focus of RMSF testing shifted away from indirect immunofluorescent assay (IFA) immunoglobulin (Ig)G assays, concomitant with a 2004 change in the case definition that included qualitative assays (ELISA) for categorization of probable cases. While only 2.8% of cases reported in 2001 were based on ELISA testing, this percentage increased to a mean of 38.3% for 2005–2007 (Figure 7). Although the specific assay used was not always provided, at least 11% of cases reported using assays that detected IgM antibodies. Use of polymerase chain reaction (PCR), culture, or immunochemical stains for RMSF diagnosis was noted for less than 0.5% of reported cases.

DISCUSSION

The incidence of RMSF reported through national surveillance increased 4-fold during 2000–2007 to approximately 7 cases per million persons annually, the highest annual rate recorded since record-keeping was first established early in the 20th century (Figure 8).[5,6,9,10] Along with the unprecedented increase in incidence, a decrease in the percentage of patients with fatal outcome was also observed, to a record-breaking low.[5,6,9,10] The recent precipitous decline in reported case fatality is not easily explained by current medical advances, as the prescribed treatment of RMSF, mainly empiric administration of effective antibiotics and provision of supportive care, has not changed in the past 20 years.[8]

The causes of past historical fluctuations in RMSF incidence and case fatality have been widely speculated. A 1950s low in case reports has been suggested to have resulted from a void in surveillance activities after the death of a prominent RMSF researcher who had spurred disease surveillance efforts, and an increase in the 1970s was speculated to have been impacted by the evolution of new RMSF diagnostic tests.[9] The observed contemporary changes should also be subject to close scrutiny.

Since 2000, several important changes have occurred that may have influenced public health surveillance activities for RMSF. A new CRF data collection tool was introduced in 2001, and its availability was widely advertised to state health departments.[8] Two other less severe tick-borne rickettsial diseases, ehrlichiosis and anaplasmosis, became reportable around the same time, and states were encouraged to use the same CRF reporting system that was being used for RMSF.[8] These factors may have stimulated interest in tick-borne disease surveillance at the physician and state level and led to improved detection of tick-borne illnesses. The publication of a document in 2006 providing national guidelines for the diagnosis, treatment, and management of tick-borne rickettsial diseases, including RMSF, ehrlichiosis, and anaplasmosis, may have influenced physician recognition of these diseases and increased diagnosis and reporting practices.[8] An influx of federal monies to state programs to support public health preparedness (from $42 million in 2000, to an annual mean

TABLE 1

Rocky Mountain spotted fever case reports and incidence (per million persons) by state and geographic region, 2000–2007, United States (National Electronic Telecommunications System for Surveillance)

Region	2000–2007 n	2000–2007 Incidence	2000–2003 Incidence	2004–2007 Incidence	Percent change 2000–2003 vs. 2004–2007
New England	95	0.84	0.46	1.21	+ 260%
Connecticut	6	0.22	0.22	0.22	
Maine*	1	0.10	0.00	0.19	
Massachusetts	58	1.13	0.62	1.63	
New Hampshire	4	0.39	0.20	0.58	
Rhode Island	25	2.94	1.41	4.47	
Vermont	1	0.20	0.00	0.40	
Middle Atlantic	489	1.52	1.11	1.93	+ 174.4%
New Jersey	170	2.48	1.56	3.39	
New York	127	0.83	0.48	1.16	
Pennsylvania	192	1.95	1.77	2.12	
East North Central	298	0.81	0.53	1.10	+ 207.0%
Illinois	124	1.23	0.68	1.77	
Indiana	30	0.60	0.45	0.76	
Michigan	30	0.37	0.30	0.45	
Ohio	107	1.17	0.86	1.48	
Wisconsin	7	0.16	0.00	0.32	
West North	1,146	7.30	3.79	10.74	+ 283.7%
Central	40	1.70	0.77	2.62	
Iowa	22	1.01	0.37	1.64	
Kansas	21	0.52	0.20	0.83	
Minnesota	963	21.00	11.09	30.64	
Missouri	74	5.32	2.18	8.40	
Nebraska	2	0.39	0.39	0.39	
North Dakota	24	3.88	3.29	4.46	
South Dakota					
South Atlantic	5,704	13.01	8.05	17.67	+ 219.5%
Delaware	67	10.19	4.69	15.40	
Dist. Columbia	10	2.15	1.73	2.57	
Florida	130	0.95	0.80	1.08	
Georgia	389	5.49	3.30	7.52	
Maryland	514	11.69	9.57	13.74	
North Carolina	3,581	52.61	29.70	74.16	
South Carolina	445	13.28	12.49	14.03	
Virginia	529	8.93	4.29	13.35	
West Virginia	39	2.70	1.67	3.74	
East South Central	1525	10.94	6.81	14.95	+ 219.5%
Alabama	381	10.55	3.92	17.03	
Kentucky	28	0.85	0.86	0.84	
Mississippi	156	6.77	7.18	6.38	
Tennessee	960	20.33	13.07	27.29	
West South	2,063	7.81	4.92	10.56	+ 214.6%
Central	802	36.57	23.27	49.44	
Arkansas	25	0.70	0.28	1.14	
Louisiana	1,064	37.85	24.68	50.71	
Oklahoma	172	0.96	0.40	1.49	
Texas					
Mountain	190	1.20	0.62	1.74	+ 278.6%
Arizona	51	1.11	0.09	2.02	
Colorado	22	0.60	0.34	0.85	
Idaho	29	2.61	0.75	4.33	
Montana	14	1.89	1.93	1.86	
Nevada	7	0.38	0.82	0.00	
New Mexico	24	1.59	0.54	2.60	
Utah	6	0.31	0.54	0.10	
Wyoming	37	9.19	6.05	12.23	
Pacific	21	0.06	0.06	0.05	–
Alaska*	0	–	–	–	
California	7	0.02	0.04	0.01	
Hawaii*	0	–	–	–	
Oregon	14	0.49	0.43	0.55	
Washington*	0	–	–	–	
Total	11,531	4.94	3.02	6.79	224.6%

* RMSF not considered a notifiable disease for all study years.

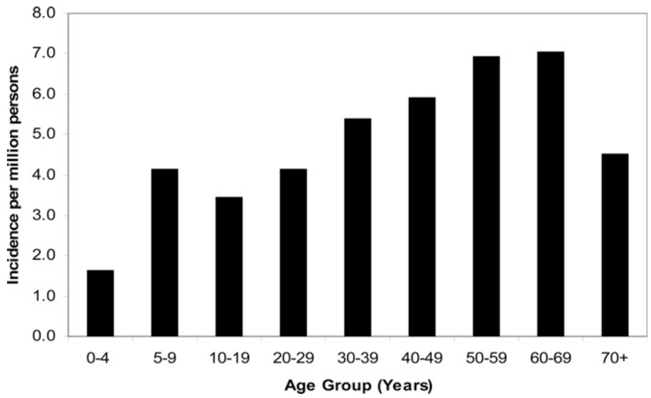

FIGURE 4. Rocky Mountain spotted fever incidence by age group, 2000–2007, United States (reported through the National Electronic Telecommunications System for Surveillance).

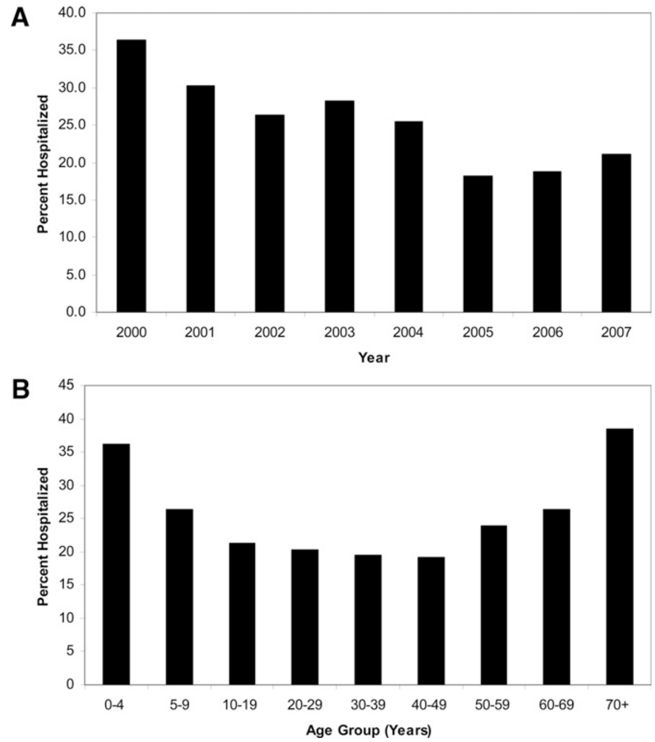

FIGURE 5. Rocky Mountain spotted fever hospitalizations (**A**) by year and (**B**) by age group, 2000–2007, United States (reported through Case Report Forms).

of $734 million from 2004–2007) may have further strengthened state capacities to conduct surveillance for previously neglected diseases, such as tick-borne illnesses [CDC, unpublished data]. Another factor that may have further contributed to the observed changes in incidence was the adoption of a new RMSF surveillance case definition 2004, to reflect an increasing trend among physicians to request ELISA tests for diagnosis of RMSF.[13,14] Although this case definition change was necessary to support changing clinical practices, this change resulted in the inclusion of probable cases with less supporting data than under past case definitions.

The number of reported cases meeting a confirmed case definition has remained stable during the last decade, but the overall percentage of confirmed cases has decreased (Figure 7). In our study, confirmed cases differed from probable cases in several important ways; case fatality among confirmed cases was 10 times that of probable cases and was also more likely to be hospitalized. Although the methods applied to confirmation of RMSF cases (i.e., testing of paired sera, culture, PCR, or immunohistochemistry (IHC) of biopsy and autopsy specimens) have remained consistent over time, the use of newer ELISA-based methods became more prominent during the study period, and most of the increase in RMSF reports can be

TABLE 2
Rocky Mountain spotted fever demographic profiles and outcome, 2000–2007, United States (National Electronic Telecommunications System for Surveillance [NETSS] and Case Report Forms [CRF])*

	NETSS		CRF	
	Number	Percent	Number	Percent
Number of cases	11,531	–	7,796	–
Confirmed	2,258	19.6	453	5.8
Probable	9,266	80.4	7,343	94.2
Male	6,511	56.9	4,413	57.4
Female	4,939	43.1	3,275	42.6
Race				
White	8,334	88.1	6,165	86.6
Black	762	8.1	596	8.4
American Indian	377	4.0	312	4.4
Asian/Pacific Islander	54	0.6	44	0.6
Other race	69	0.8	–	–
Hispanic ethnicity	338	4.1	239	3.7
Age (years)	46	–	40	–
Mean	42	–	41	–
Median				
Hospitalized	–	–	1,768	23.4
Not hospitalized	–	–	5,777	76.6
Confirmed cases hospitalized	–	–	162	37.4
Probable cases hospitalized			1,606	22.6
Died	–	–	35	0.5
Did not die	–	–	7,206	99.5
Confirmed cases died	–	–	13	3.0
Probable cases died			22	0.3

* Cases for which data not reported were excluded from that part of the analysis, so denominators may not be the same for all categories.

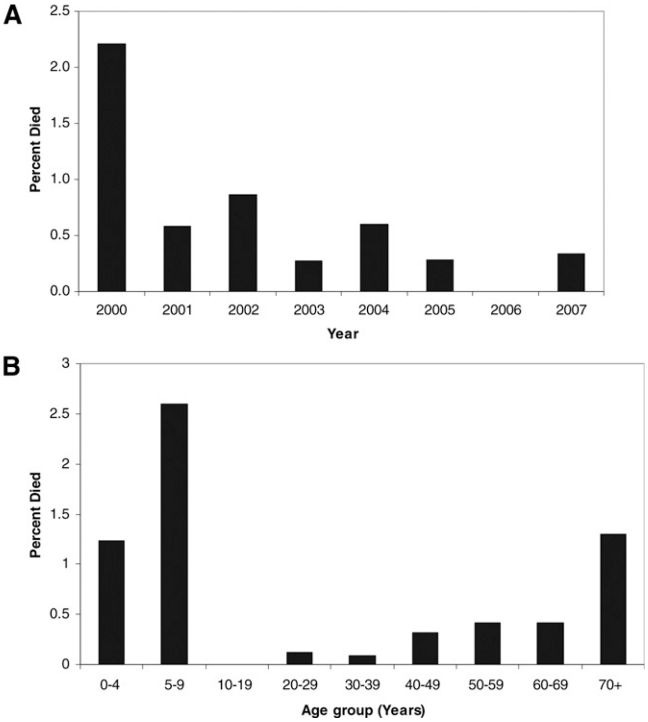

FIGURE 6. Rocky Mountain spotted fever case fatality (**A**) by year and (**B**) age group, 2000–2007, United States (reported through Case Report Forms).

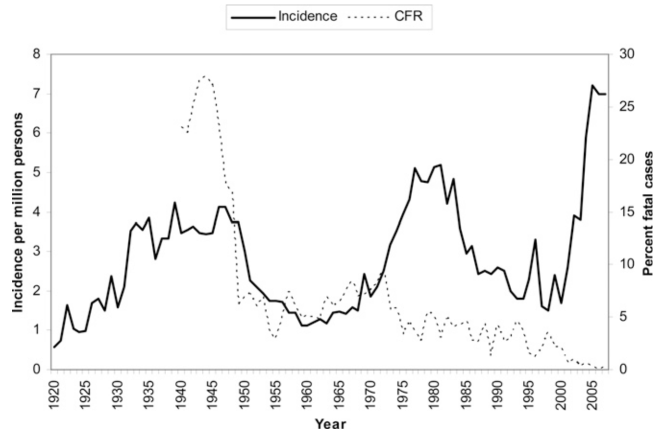

FIGURE 8. Historical surveillance for Rocky Mountain spotted fever, incidence and case fatality ratios (CFR) based on national surveillance data for the United States, 1920–2007. (From 1980 through 2007, incidence was derived from data reported through the National Electronic Telecommunications System for Surveillance, and percent fatal cases was derived from Case Report Forms).

attributed to an increase in the number of probable cases that were diagnosed with single serologic assays.

The use of single serologic tests for diagnosing acute rickettsial infections is questionable. Background seroprevalence for antibodies to *R. rickettsii* in the southeastern United States can be as high as 20% among healthy adults (CDC, unpublished data), and 10–12% in children.[17] Other studies examining background seroprevalence in northern states or among geographically widespread military personnel suggest a seroprevalence of 4% to 6%.[18,19] The diagnosis of RMSF based on a single serologic test, as predominantly occurred during the current study period, may result in the erroneous diagnosis in non-RMSF cases with historical titers from past exposures or with nonspecific cross-reactive IgM class antibodies. The reported sensitivity and specificity of single IgM tests have been reported as low as 23% and 77%, respectively, when compared with testing of IgG in paired sera, for the diagnosis of rickettsial infections in endemic areas.[20]

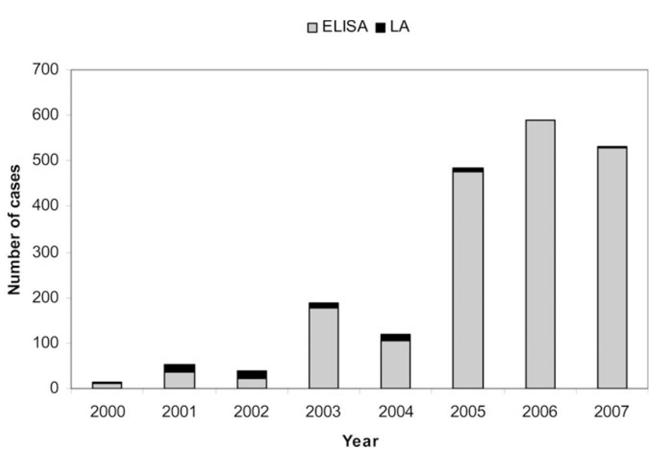

FIGURE 7. Rocky Mountain spotted fever cases diagnosed by enzyme-linked immunosorbent assays (ELISA) and latex agglutination (LA), 2000–2007, United States (reported through Case Report Forms).

The prevalence of anti-*R. rickettsii* antibodies appears to increase with age,[18,19] likely as a function of increased risk of exposure to either *R. rickettsii* or other rickettsial organisms over a lifetime, the effect of historical titers may be higher among adults. In the current study, children had a lower incidence rate compared with adults, but had the highest risk of fatal outcome, in contrast to prior studies that showed the highest incidence among children and placing older adults at greater risk for fatal outcome.[5,6] The incidence and risk for fatal outcome in children 0–9 years of age has actually remained fairly consistent over the past 15 years, ranging from 2 to 4 cases per million persons and 1–3% with a fatal outcome.[6,10] In contrast, incidence and case fatality among older age groups has changed dramatically. Given that background antibodies to RMSF increase with age,[18,19] this observation may suggest that single serologic tests have greater positive predictive value among children, and that single-titer data from this age group more accurately reflect true RMSF cases.

Another factor that may influence increased risk for fatal outcome among younger age groups is continued reluctance among healthcare providers to prescribe doxycycline to children. The performance of the recommended dose and duration of doxycycline is significantly superior when compared with alternative therapies,[7] and has been shown to have no appreciable impact on dental staining.[21] Reviews of healthcare providers in the southern United States have shown that 50–75% would prescribe an antibiotic other than doxycycline when presented with a child with suspect RMSF [CDC, unpublished data].[22] This continued practice may contribute to the continued higher proportion of RMSF cases with fatal outcome observed among children, and physicians should always prescribe doxycycline as the primary antibiotic of choice for the treatment of suspect RMSF in children.[23]

This study expanded a previously reported trend that American Indians experience disproportionate RMSF incidence and case fatality compared with other race groups.[24] During 2000–2007, American Indians experienced a burden of RMSF almost four times that of whites, and experienced a 4-fold greater risk of fatal outcome. An emerging focus of RMSF associated with *Rhipicephalus sanguineus* (the brown dog tick) was identified among American Indians in Arizona beginning in 2002 and continuing throughout the study period, and this outbreak has contributed to the increasing incidence within this race group.[25] It is clear that this group deserves renewed focus to identify reasons for this disparity and areas of appropriate intervention.[24–27]

We found that RMSF onset followed expected and previously reported seasonal trends,[5,6,10] with the majority of cases reporting illness onset during summer months when peak tick activity is expected. Only 4% of RMSF cases reported onset during winter months. A recent report had suggested that 15% of U.S. RMSF cases in 2006 occurred in December and January, and interpreted this as possible evidence of non-*Rickettsia rickettsii* infections being incorrectly reported as RMSF.[28] However, that report used date of publication in the *MMWR* as a surrogate for onset date. These dates do not correlate well because of lags in reporting times from state health departments.[29] In our study, only the Middle Atlantic region (New York, Pennsylvania, and New Jersey) reported a significantly higher rate of winter onset RMSF than other parts of the United States, despite having a low overall incidence of RMSF. This finding could reflect infection with and serologic cross-reactivity to other urban spotted fever group rickettsial infections known to be endemic in this region, such as *Rickettsia akari* (rickettsialpox) and for which confirmed cases are recognized year-round.[30]

In addition to *R. akari*, several other spotted fever group rickettsiae are known to cause human illness occurrence in the United States, including *Rickettsia parkeri*, *Rickettsia massiliae,* and *Rickettsia* spp. 364D.[31–38] There is also evidence that *Rickettsia amblyommii*, a tick-borne spotted fever group *Rickettsia* previously considered nonpathogenic, may cause mild illness and be misdiagnosed as RMSF on common serologic assays.[39] Geographic variations in severity have been noted, and a focus of unusually mild illness has been noted in North Carolina where *R. amblyommii* is prevalent.[40] A recent letter to *Lancet* suggested that up to one-third of U.S. cases diagnosed as RMSF might actually be caused by *R. parkeri* infection.[34] This supposition was based on testing of a relatively small set of specimens ($N = 15$) and may not be broadly representative of the U.S. situation[34]; however, it nonetheless highlights that current U.S. systems for RMSF surveillance are not necessarily specific for *R. rickettsii*. Extensive antigenic cross-reactivity occurs among organisms within the genus *Rickettsia*,[41–43] and the high percentage of cases reported in the United States that are diagnosed solely by antigenic detection methods means that case reports lack specificity. In fact, the disease historically thought of as "Rocky Mountain spotted fever" may be more correctly viewed as a constellation of infections caused by various species within the genus *Rickettsia,* with possible wide variations in clinical spectrum, disease severity, geographic distributions, and potential for fatal outcomes.[44–47] Beginning in 2010, the name of the reporting category will be changed to "Spotted Fever Rickettsioses (including RMSF)."[48] This description more accurately defines the spectrum of agents that may be causing disease, but will not change surveillance methods.

This period of increased reporting of RMSF has been accompanied by increases in other tick-borne diseases, including human ehrlichiosis, anaplasmosis, and Lyme disease.[29,49] Some researchers have speculated that increases in tick-borne diseases may be fueled by ecologic or climate changes,[50,51] and an increase in actual disease is clearly supported by some focal patterns of recent RMSF emergence.[25] However, the findings from our study suggest that the increase in reported RMSF incidence further involves a complex interplay of physician awareness, diagnostic practices, and reporting policies. In the future, development of active tick-borne disease surveillance programs in defined, geographic areas may help better assess the true burden of disease caused by *R. rickettsii* and other tick-borne diseases. In those studies, emphasis should be placed on acquiring appropriate specimens to ensure confirmation of a diagnosis. Until then, monitoring of national RMSF surveillance data will continue to provide the most valuable tool to track and monitor changing trends in RMSF epidemiology, despite its inherent limitations.

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Authors' addresses: John J. Openshaw, David L. Swerdlow, John W. Krebs, Robert C. Holman, Eric Mandel, Alexis Harvey, Dana Haberling, Robert F. Massung, and Jennifer H. McQuiston, Division of Viral and Rickettsial Diseases, Centers for Disease Control and Prevention, Atlanta, GA, E-mails: fzh7@cdc.gov.

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