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Rocky Mountain Spotted Fever Characterization and Comparison to Similar Illnesses in a Highly Endemic Area—Arizona, 2002–2011

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Abstract

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Author contributions. J. J. R. had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

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Background—Rocky Mountain spotted fever (RMSF) has emerged as a significant cause of morbidity and mortality since 2002 on tribal lands in Arizona. The explosive nature of this outbreak and the recognition of an unexpected tick vector, *Rhipicephalus sanguineus*, prompted an investigation to characterize RMSF in this unique setting and compare RMSF cases to similar illnesses.

Methods—We compared medical records of 205 patients with RMSF and 175 with non-RMSF illnesses that prompted RMSF testing during 2002–2011 from 2 Indian reservations in Arizona.

Results—RMSF cases in Arizona occurred year-round and peaked later (July–September) than RMSF cases reported from other US regions. Cases were younger (median age, 11 years) and reported fever and rash less frequently, compared to cases from other US regions. Fever was present in 81% of cases but not significantly different from that in patients with non-RMSF illnesses. Classic laboratory abnormalities such as low sodium and platelet counts had small and subtle differences between cases and patients with non-RMSF illnesses. Imaging studies reflected the variability and complexity of the illness but proved unhelpful in clarifying the early diagnosis.

Conclusions—RMSF epidemiology in this region appears different than RMSF elsewhere in the United States. No specific pattern of signs, symptoms, or laboratory findings occurred with enough frequency to consistently differentiate RMSF from other illnesses. Due to the nonspecific and variable nature of RMSF presentations, clinicians in this region should aggressively treat febrile illnesses and sepsis with doxycycline for suspected RMSF.

Keywords

Rocky Mountain spotted fever; American Indians; AIAN; tick-borne; *Rhipicephalus sanguineus*

Rocky Mountain spotted fever (RMSF), caused by the tick-borne pathogen *Rickettsia rickettsii*, was sporadically reported in Arizona prior to confirmation of a fatal case on an American Indian reservation in 2003, linked to an unexpected vector, *Rhipicephalus sanguineus* (the brown dog tick) [1, 2]. Through 2011, 219 human RMSF cases and 16 fatalities (case fatality rate, 7.3%) were reported from 4 Arizona reservations, and 2 additional reservations reported RMSF exposure in humans and/or dogs during 2012 [3, 4]. Affected tribes reported *R. sanguineus* infestation and large populations of free-roaming dogs [1, 2]. During the last decade, RMSF outbreaks caused by *R. sanguineus* have been documented in Mexico and South America [5, 6]. However, *R. sanguineus* ticks and the *R. rickettsii* organism found in Arizona are genetically distinct from those in Mexico, and the origin of the Arizona outbreak and reasons for its recent emergence remain unclear [5, 7, 8].

RMSF is easily treated with tetracyclines early in the illness, but other broad-spectrum antibiotics are not effective and doxycycline is the treatment of choice in patients of all ages [9–11]. The nonspecific clinical presentation of RMSF, lack of a sensitive early diagnostic test, and necessity of choosing an antibiotic not typically used for other common illnesses or sepsis make identification and management of cases challenging. Physicians need key information to guide early clinical decisions. Geographic patterns of infection and epidemiologic risk factors are important variables in these decisions.

The Arizona RMSF outbreak is unusual because it occurred in association with a previously unrecognized tick vector in the United States, and emerged rapidly in a region where RMSF was not previously recognized. Its recent detection in tribal communities where multiple documented underlying health disparities exist [12, 13] lends importance and urgency to characterizing the epidemiology of this outbreak. The unique combination of host, vector, pathogen, and environmental variables within this outbreak suggest that important differences in the clinical manifestations and RMSF epidemiology may exist compared to the broader US experience [9, 14–17]. This study describes RMSF in this emerging setting to aid in differentiation of this potentially deadly disease from similar illnesses.

METHODS

Data, Definitions, and Analysis

We performed a retrospective medical record review of patients prompting *R. rickettsii* testing from 1 June 2002 through 30 September 2011 in community A, and 1 January 2005 through 30 September 2011 in community B at community Indian Health Service health facilities and 11 referral hospitals. At least 1 illness symptom prompted RMSF testing; individuals tested without symptoms following a tick bite or exposures were excluded. This broad definition was intended to capture a complete spectrum of illness in patients tested for RMSF, considering that RMSF illnesses may be atypical or nonspecific.

A confirmed RMSF case was defined as a person reporting illness and a 4-fold change in immunoglobulin G (IgG)– or immunoglobulin M (IgM)–specific antibody titer reactive with *R. rickettsii* antigen by indirect immunofluorescence assay (IFA) between paired serum specimens taken after the onset of symptoms with at least 1 titer of ≥1:128 dilution, or detection of *R. rickettsii* DNA in a clinical specimen via amplification of a specific target by polymerase chain reaction (PCR) assay, or demonstration of spotted fever group antigen in a biopsy or autopsy specimen by immunohistochemical staining.

A probable RMSF case was defined as a person reporting illness and who did not meet criteria for a confirmed case, and had serologic evidence of elevated IgG or IgM antibody reactive with *R. rickettsii* antigen by IFA with at least 1 titer of ≥1:128 dilution.

A non-RMSF illness was defined as a person reporting illness and had at least 2 negative serologic *R. rickettsii* antigen titers (<1:64) and the second titer drawn no earlier than day 14 after symptom onset.

All patients who met 1 of these definitions were included in this review. A subset of case samples underwent sequencing and restriction fragment length polymorphism analysis targeting rickettsial DNA, to confirm *R. rickettsii* as the pathogen. The nucleic acid sequence of this outbreak strain was published previously [5, 7]. Patients with titers of 1:64 that did not increase were excluded from the review, because this low-level reactivity was considered insufficient evidence to confidently confirm or rule out recent infection.

Demographic information, medical history, illness history, and clinical information were anonymously recorded. Symptoms or exposures were excluded from analysis if there was no

documentation of their presence or absence. Data were analyzed using EpiInfo [18]. Statistical differences in categorical variables were evaluated using a χ^2 test, and when the expected value of a cell was <5, Fisher exact test was used. Statistical differences in continuous variables were evaluated using an analysis of variance test or the Mann–Whitney/Wilcoxon 2-sample test when a nonparametric test was more appropriate. Statistical significance was set at $\alpha = .05$.

Health Facilities and Service Populations

Community A and B health facilities are, respectively, rural 40-bed and 8-bed Indian Health Service hospital and outpatient facilities on tribal reservations in Arizona, with user populations of >16 100 and >11 900 persons. Neither facility has an intensive care unit, resulting in patient transfers for specialized care to referral facilities.

Definitions of Terms

A case is a confirmed or probable RMSF case; dog contact is any documentation of dog interaction, including dog ownership or feeding strays; fever is a temperature ≥38°C (100.4°F) or reported fever by the patient or caretaker. Tick exposure includes tick bites and ticks observed on pets or in frequented environments. Abnormal laboratory values are those outside standard range; liver tests were based on age-adjusted standards.

Ethics Review

The project was intended to prevent disease in response to an immediate public health threat and was therefore judged exempt by the Centers for Disease Control and Prevention's institutional review board on a nonresearch basis. The study was approved by the community A and B tribal councils through resolutions 11-2010-302 and AU-11-223, respectively.

RESULTS

Demographics

We identified 205 patients with RMSF (cases) and 175 with non-RMSF illnesses (Table 1). Among all subjects, 52% were male and all were American Indians except 1 person who worked on tribal lands. The median age among cases was 11 years, significantly higher than that of patients with non-RMSF illnesses (median, 2 years; Figure 1). Among cases, 85 had confirmed RMSF and 120 had probable RMSF. Cases occurred in each month, with seasonal differences in different peak months in communities A and B (September and July, respectively; Figure 2).

Exposures and Historical Medical Conditions

Dog contact and tick exposure were significantly more frequent among cases than among patients with non-RMSF illnesses (86% vs 69% and 55% vs 41%, respectively; Table 1). Sick contacts and travel frequency differed significantly between cases and patients with non-RMSF illnesses, but tick exposure was infrequently reported in both. The only medical history significantly more frequent among RMSF cases than patients with non-RMSF

illnesses was asthma, occurring in 8% of cases. Alcoholism and diabetes among adults were the most common underlying health conditions among cases; the frequency did not differ significantly from non-RMSF illnesses (27% vs 23% and 22% vs 20%, respectively).

Medical Care and Treatment

Cases and patients with non-RMSF illnesses both presented to health facilities a median of 2 times during illness (cases: range, 0–9 and mean = 1.87; non-RMSF illness: range, 0–7 and mean = 1.94). Both first presented for care on median day 2 (cases: range, 1–11; non-RMSF illness: range, 1–12). Cases were significantly more likely to be treated with doxycycline than were patients with non-RMSF illnesses (87% vs 78%, respectively; risk ratio [RR], 1.69; 95% confidence interval [CI], 1.09–2.62), and children more often than adults (91% vs 81%, respectively; RR, 2.14; 95% CI, 1.05–4.37).

Fifteen fatalities (7.3%) and 86 (42.0%) hospitalizations (including 29 ICU admissions [14.1%]) occurred among cases. There were no deaths and 29 (16.6%) hospitalizations (7 ICU admissions [4.0%]) among patients with non-RMSF illnesses. Cases were significantly more likely to result in fatality (RR undefined; $P = .0007$), hospitalization (RR, 2.53; 95% CI, 1.75–3.66; $P < .0001$), and ICU admission (RR, 3.53; 95% CI, 1.59–7.87; $P < .0001$) compared with patients with non-RMSF illnesses.

Signs and Symptoms

Fever was frequent but not universal among cases (81%; Table 2). Temperature maximum and range did not differ significantly between cases and patients with non-RMSF illnesses (38.8°C [range, 35.8°C–41.3°C] vs 38.4°C [range, 35.4°C–41.3°C]; Table 2). Although fever was present in all fatalities [11], no fever was documented in 8 of 85 (9%) confirmed cases (3 of whom were hospitalized) and 30 of 117 (26%) probable cases (4 of whom were hospitalized). Twenty cases without documented fever had a rash, and 14 reported a tick bite and other symptoms. One afebrile patient presented 5 days after symptom onset, required intensive care, suffered digit necrosis, and had a maximum temperature of 37.7°C. Patients without documented fever averaged 1.4 outpatient visits (range, 1–4). Rash occurred in 130 of 192 (68%) cases and 92 of 166 (55%) non-RMSF illnesses. Twenty of 119 cases with rash descriptions reported pruritic rash (17%); another 4% were vesicular and 2% were urticarial, descriptions not usually associated with RMSF.

The triad of fever, rash, and tick exposure was significantly more frequent among cases than patients with non-RMSF illnesses (32% vs 16%, respectively; RR, 1.46; 95% CI, 1.16–1.84), but represented a minority of cases.

Headache occurred in a majority of cases, but was not statistically more frequent than among patients with non-RMSF illnesses (58% vs 48%). Nausea (47%), red or draining eyes (15%), mental status change (17%), peripheral edema (12%), hepatomegaly (5%), and neck pain (11%) were all significantly more frequent among cases than patients with non-RMSF illnesses, but occurred in a minority of patients.

Initial Laboratory Findings

The initial mean serum sodium level was significantly lower among cases than among patients with non-RMSF illnesses (Table 3), but only by 2 mEq/L (136 vs 138, respectively); chloride and potassium were similar (101 vs 103 and 3.9 vs 4.2, respectively). Initial platelet count mean was significantly lower among cases than among patients with non-RMSF illnesses, although not abnormally low for either group (269×10^3 platelets/μL vs 350×10^3 platelets/μL, respectively). However, initial platelet counts were low ($<130 \times 10^3$ platelets/μL) in 17 of 141 (12%) cases, compared to only 2 of 144 (1.4%) among patients with non-RMSF illnesses. White blood cell counts were similar, but neutrophil count was significantly higher (67% vs 56%) and lymphocyte and monocyte counts significantly lower (20% vs 32% and 7% vs 8%, respectively) among cases vs patients with non-RMSF illnesses.

Initial liver test means were often elevated among both adults and children, but only alanine aminotransferase and aspartate aminotransferase among adult cases were significantly higher among cases than among patients with non-RMSF illnesses. Among children, no liver tests were significantly more elevated among cases than among patients with non-RMSF illnesses. Tests evaluating inflammatory and coagulation status (C-reactive protein, D-dimer, prothrombin time, partial thromboplastin time, international normalized ratio [INR], fibrinogen levels) were infrequently performed and usually conducted late in the illness course. When performed, prothrombin time, INR, and D-dimer differed significantly between cases and patients with non-RMSF illnesses.

Imaging Studies

Eighty-five (41.5%) confirmed or probable cases underwent at least 1 chest radiograph. Of these, 50 (59%) were interpreted as abnormal, and 19 (22%) specifically suggested pneumonia as a diagnosis. Head computed tomography (CT) scans were performed in 28 (13.6%) patients, and 9 chest (4.4%), 11 abdominal (5.4%), and 4 pelvic CTs (2.0%) were documented. Magnetic resonance imaging studies were performed in 6 cases (5 head and 1 extremity image). Ultrasound studies were performed in 21 (10.2%) cases including 17 abdominal, 4 chest or cardiac, and 2 extremity studies. Nine of 17 (52.9%) abdominal ultrasounds were abnormal, including abnormal gallbladders, pericholecystic fluid, gallstone pancreatitis, cholelithiasis, hepatosplenomegaly, and hepatic steatosis.

Non-RMSF Illnesses

Non-RMSF illnesses were not always ascribed to a specific pathogen, as is true for many nonspecific febrile illnesses that are diagnosed and treated routinely in primary care settings. In this cohort, illness cause was occasionally confirmed as another bacteria or virus through diagnostic testing (bacterial cultures, rapid viral tests).

DISCUSSION

This review characterizes RMSF clinical characteristics and epidemiology since its 2002 emergence in Arizona American Indian communities. In this series, RMSF disease patterns differed from US aggregate reports [19]. Although RMSF in most US regions peaks in June

and July, consistent with seasonal activity of *Dermacentor variabilis* and *Dermacentor andersoni* ticks, in Arizona human cases peaked in July and September in community B and community A, respectively (Figure 2). Both communities exhibited a bimodal pattern of disease onset, with declines during June, the driest month in both communities. Aggregate cases peaked during July–October (54.6%), corresponding with seasonal monsoons and indicating that climatic factors such as moisture may contribute to the ecology of tick populations and RMSF transmission in this region. Seasonal analysis also indicates that human RMSF infection exists year-round.

Although fever was frequent among both cases and patients with non-RMSF illnesses (81% and 84%, respectively), it was not universally detected in all RMSF cases, and fever among cases was less frequent than reported in other studies, ranging from 94% to 100% [20–26]. While this finding contrasts with much of the reported literature, it should be noted that presence of fever is a required symptom for national RMSF reporting [27], likely resulting in an inclusion bias for fever frequency among US reported cases and also likely causing physicians to discount RMSF consideration for patients without fever. Thirty-eight cases (19%) in our series lacked documented fever during the course of illness, including 8 of 85 (9.4%) confirmed cases and 30 of 117 (25.6%) probable cases, suggesting that non-febrile RMSF illness occurs in this patient population, or that fever may not always be detected at the time a patient presents for care. For example, patients with sepsis or multiorgan system failure may exhibit hypothermia rather than fever, as occurred in late-presenting patients in this review. Probable cases only require 1 titer ≥1:128, allowing that an elevated titer may represent prior undetected RMSF illness with persistently elevated titer. However, a serosurvey conducted among children in the same communities during 2003–2004 revealed that only 10 of 215 (4.7%) children had *R. rickettsii* titers ≥1:128 [8]. The non-febrile probable cases, therefore, represent an RMSF infection that was either atypical because no fever was present or reported during patient evaluation, or a prior RMSF illness that was likely atypical or mild as it did not get tested for RMSF or come to medical attention at that time. Therefore, lack of fever should not exclude suspicion of RMSF in highly endemic areas such as this.

Strikingly, almost 50% of the cases in this review occurred in patients aged ≤10 years. The mean and median age among these cases (19.8 and 11 years, respectively) is lower than those of RMSF among the general US population (46 and 42 years, respectively) [28] and is lower than the mean age of 33 years reported among American Indians nationwide [29]. The younger age observed among these cases may reflect the unique vector and environmental factors in this region. The dog plays a central role in the RMSF transmission cycle in Arizona by harboring infected ticks [3, 8, 30]. Children may interact with dogs and their habitats more frequently than adults, resulting in greater exposure. In this series, the median age of those with non-RMSF illnesses was significantly lower than that of cases (2 vs 11 years, respectively), likely because fever was considered an important indicator for RMSF testing, and fever occurs commonly in young children.

The variability of symptom frequency in this population makes a presumptive diagnosis of RMSF difficult for the clinician. Fever, present in 81% of patients and 100% of fatalities, was the most reliable indicator to guide timely, effective, and optimal treatment, although

fever was a late symptom in some fatalities [11]. No other signs or symptoms, either alone or in combination, were frequent enough to consistently identify at least two-thirds of RMSF cases. Rash was significantly more frequent among cases than among patients non-RMSF illnesses (68% vs 55%) but less common than that reported in numerous other studies [19–22, 24–26]. Although rash is often considered a hallmark of RMSF, 60% of RMSF cases in this review lacked a demonstrable rash initially and 32% failed to develop any rash while ill. Fever and rash together occurred in significantly more cases (57%) than in patients with non-RMSF illnesses (41%), but this combination is too infrequent to exclude RMSF from consideration if both are not present. Cough, nasal congestion, ear pain, and irritability occurred significantly more frequently among patients with non-RMSF illnesses than cases, but could not be used reliably to rule out RMSF as they also often occurred in cases. This series also demonstrates that presence or absence of abnormal laboratory values is not reliable for early treatment decisions, since in many cases values were only slightly abnormal or did not turn abnormal until disease was advanced.

In this study, imaging procedures reflect widespread vasculitis and organ involvement that accompanies most RMSF cases. Abnormal findings indicating nonspecific inflammation may unfortunately lead the clinician away from an underlying diagnosis of RMSF. Because 22% of chest radiographs in this series suggested pneumonia and 59% were abnormal, RMSF should be viewed as a potential etiology of community-acquired pneumonia (CAP) in this region. National guidelines for CAP treatment include doxycycline alone or paired with a β-lactam antibiotic [31], and clinicians should consider using doxycycline as part of standard treatment for CAP in patients from Arizona Indian reservations.

This review is subject to several limitations. Patients with titers <1:128 or with enzyme-linked immunosorbent assay testing alone are included in the national case definition for reporting, but were excluded from this analysis to minimize false positives due to cross-reactivity from non-rickettsial antigens. Because RMSF serology cross-reacts with other species of *Rickettsia* (including *Rickettsia massiliae*, which was detected in at least 1 tick from the region and has been reported to cause human illness in international settings [32, 33]), patients diagnosed by serology alone could in theory be infected with other spotted fever group rickettsiae; however, *R. massiliae* patients typically have eschars [33, 34], which were lacking among these patients. Furthermore, PCR and nucleic acid testing of human specimens demonstrate *R. rickettsii* as the only detectable circulating *Rickettsia* species causing patient illness in this region.

In conclusion, this review characterizes RMSF during the first decade of emergence on tribal lands in Arizona. We found significant differences in the clinical presentation and epidemiology of disease compared to other parts of the United States, highlighting the need for region-specific medical education in this area. Providers in this region must remain vigilant for RMSF year-round and among younger ages than previously reported. The central role the dog plays in human exposure to rickettsial-containing *R. sanguineus* ticks emphasizes the importance of community-wide animal control and pet health programs, including tick prevention. The lack of a timely diagnostic RMSF test and the high fatality rate that occurs when RMSF treatment is delayed advocates that doxycycline be used aggressively among patients in this region presenting with a febrile illness and/or sepsis.

Additional analysis investigating the high fatality rate in this population is published elsewhere [11].

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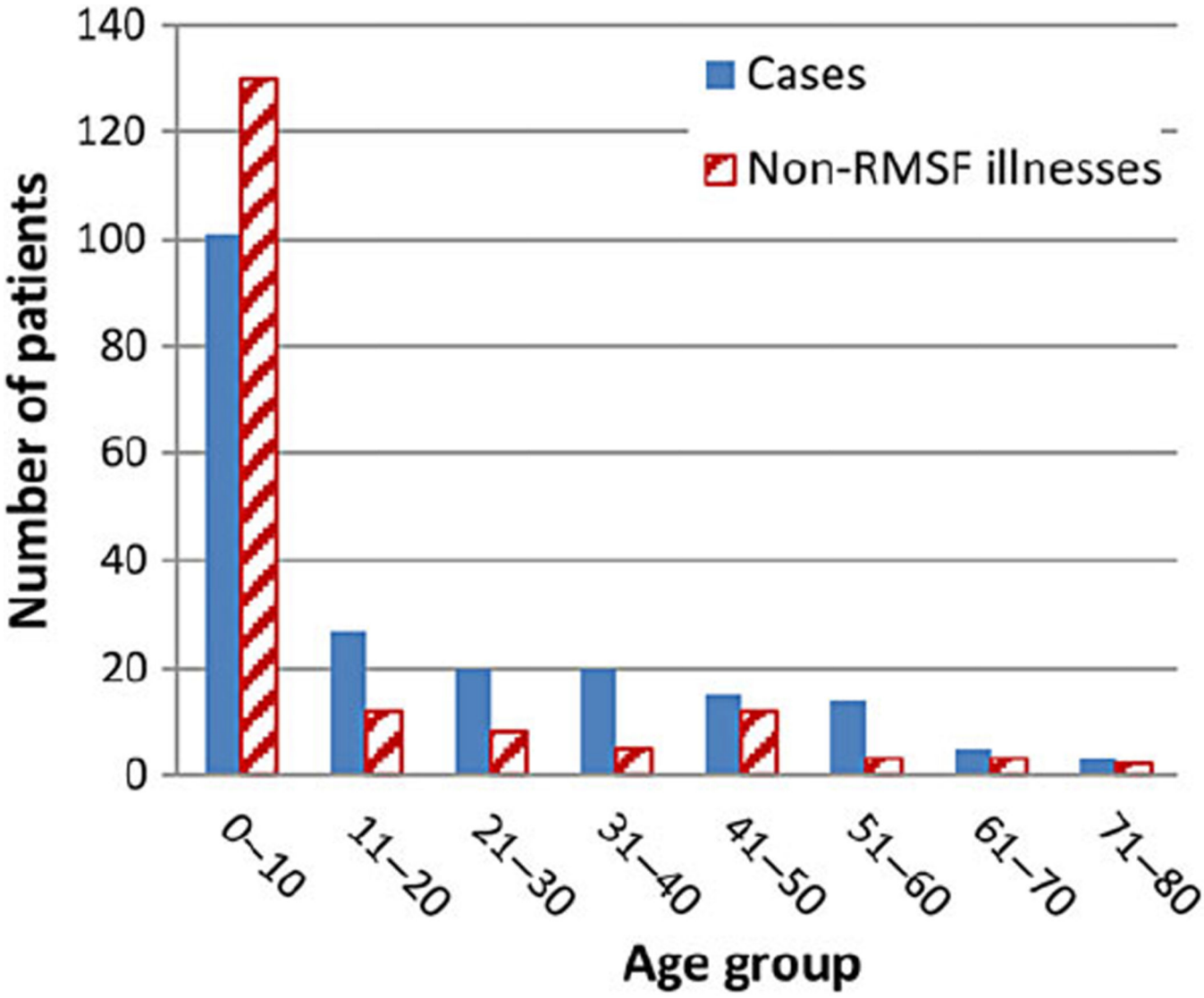

Figure 1.
Number of Rocky Mountain spotted fever (RMSF) cases and non-RMSF illnesses by age group in 2 tribal communities in Arizona.

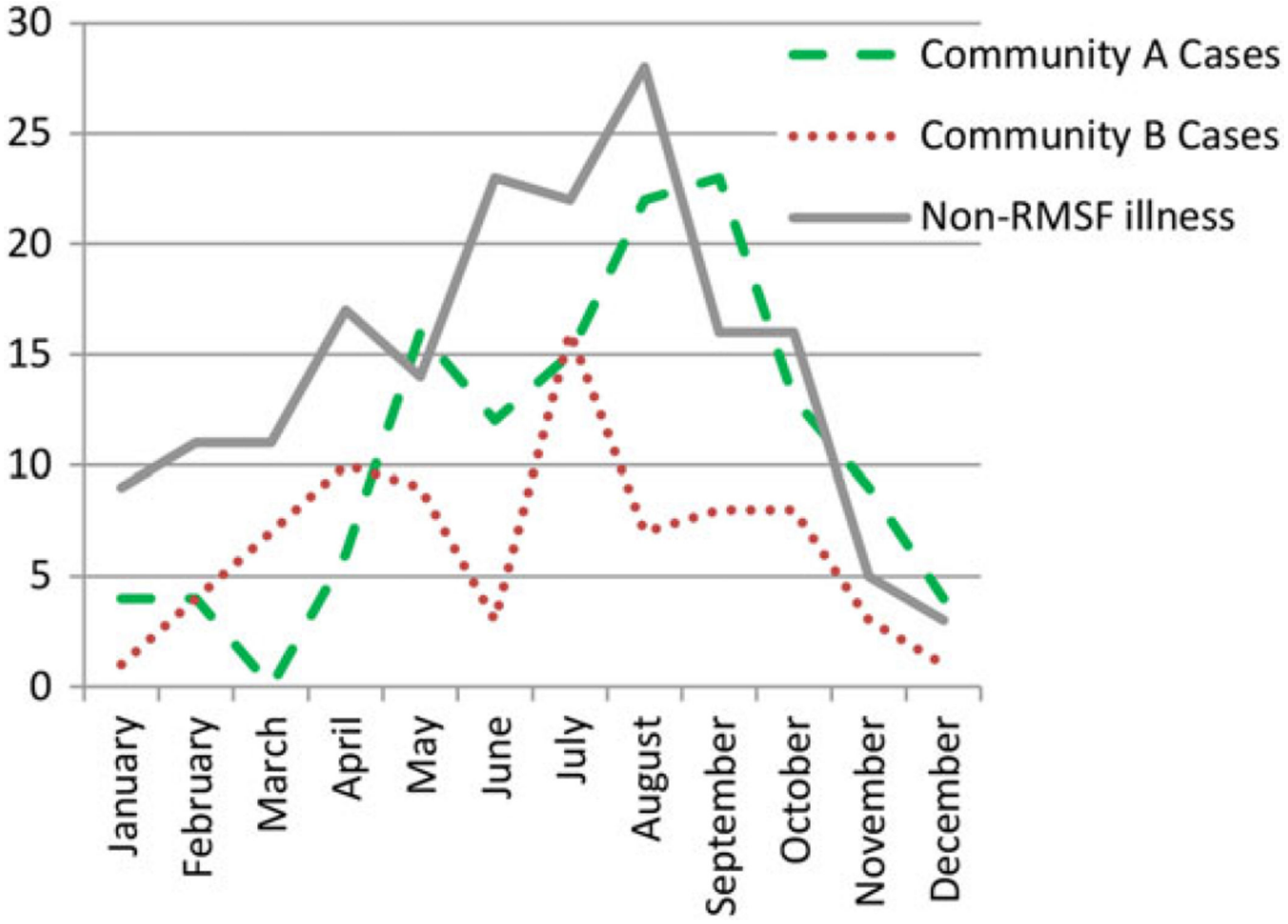

Figure 2.
Month of symptom onset of Rocky Mountain spotted fever (RMSF) cases and non-RMSF illnesses in 2 tribal communities in Arizona.

Table 1

Demographics, Exposures, and Past Medical History Among Rocky Mountain Spotted Fever (RMSF) Cases and Patients With Non-RMSF Illness From 2 Tribal Communities in Arizona

Demographic	Cases, No. (%)	Non-RMSF Illness, No. (%)	Risk Ratio	95% CI
No. of patients	205	175		
Age, y, median/mean (range)*	11/19.8 (7 mo–78 y)	2/11.0 (2 mo–79 y)	*P* = .000	
Race	204 American Indian, 1 white	175 American Indian	NA	NA
Male sex	106/205 (52)	92/174 (53)	0.97	.80–1.18
Exposures				
Dog contact*	77/90 (86)	60/87 (69)	1.73	1.08–2.77
Tick exposure*	73/132 (55)	48/118 (41)	1.32	1.04–1.67
Sick contacts*	17/43 (40)	8/39 (21)	1.50	1.01–2.20
Travel*	6/37 (16)	1/35 (3)	1.80	1.21–2.67
Past medical history				
Alcoholism (age >17 y)	22/81 (27)	8/35 (23)	1.07	.83–1.38
Asthma*	17/205 (8)	2/174 (1)	1.71	1.43–2.06
Autoimmune disorder	2/205 (1)	3/174 (2)	0.74	.25–2.16
Diabetes (age >17 y)	18/82 (22)	7/35 (20)	1.04	.78–1.37
Heart disease	4/205 (13)	3/174 (2)	1.05	.55–2.02
Hepatitis	3/204 (2)	3/173 (2)	0.92	.41–2.10
Hypertension	26/205 (13)	13/174 (8)	1.27	.99–1.62
Lung disease, chronic	4/205 (2)	5/174 (3)	0.82	.39–1.71
Renal insufficiency/failure	0/204 (0)	3/174 (2)	0	0–1.65
Thyroid disease	6/205 (3)	4/174 (2)	1.11	.66–1.86
Tuberculosis	2/204 (1)	2/174 (1)	0.93	.35–2.48

The following conditions were not present in any subjects included in this study: AIDS/human immunodeficiency virus, transplant recipients, asplenia, glucose-6-phosphate dehydrogenase deficiency.

The following conditions were present in 1 case and 1 patient with non-RMSF illness: cancer, cerebrovascular accident/stroke, deep vein thrombosis, and sickle cell disease.

Abbreviations: CI, confidence interval; NA, not applicable; RMSF, Rocky Mountain spotted fever.

*Statistically significant difference.

Table 2

Symptoms Among Rocky Mountain Spotted Fever (RMSF) Cases and Non-RMSF Illnesses From 2 Tribal Communities in Arizona

Symptom	Cases, No. (%)	Non-RMSF Illness, No. (%)	Risk Ratio	95% CI
General and skin				
Fever	164/202 (81)	142/169 (84)	0.92	.73–1.15
T_{max}, median (range)	38.2°C (35.8–41.3)	38.3°C (35.4–41.3)	*P* = .896	
Rash*	130/192 (68)	92/166 (55)	1.28	1.04–1.59
Fever and rash*	108/190 (57)	71/164 (43)	1.29	1.06–1.57
Fever and tick exposure	58/131 (44)	40/117 (34)	1.22	.96–1.53
Rash and tick exposure*	48/128 (38)	23/114 (20)	1.44	1.15–1.81
Triad (fever/rash/tick exposure)*	41/127 (32)	18/113 (16)	1.46	1.16–1.84
Headache	78/135 (58)	37/77 (48)	1.15	.94–1.42
Fatigue	60/130 (46)	23/65 (35)	1.16	.95–1.41
Myalgia	53/129 (41)	28/61 (46)	0.94	.77–1.15
Chills	47/133 (35)	24/69 (35)	1.01	.82–1.24
Lethargy	24/121 (20)	12/57 (21)	0.98	.75–1.26
Irritability	20/123 (16)	38/87 (44)*	0.51	.35–.74
Lymphadenopathy	5/129 (4)	7/92 (8)	0.70	.36–1.38
Head/eyes/ears/nose/throat				
Nasal congestion*	43/155 (28)	66/136 (49)	0.64	.49–.83
Sore throat	27/134 (20)	12/76 (16)	1.11	.87–1.41
Red or draining eyes*	22/148 (15)	9/111 (8)	1.28	1.01–1.65
Ear pain	13/126 (10)	15/69 (22)	0.69	.45–1.04
Periorbital edema	7/147 (5)	3/105 (3)	1.21	.80–1.84
Pulmonary/cardiovascular				
Cough*	68/169 (40)	73/138 (53)	0.79	.64–.98
Peripheral edema*	18/147 (12)	3/120 (3)	1.63	1.32–2.02
Chest pain	12/129 (9)	4/65 (6)	1.17	.86–1.58
Wheezing	9/164 (6)	14/147 (10)	0.73	.43–1.22
Gastrointestinal				
Nausea*	74/156 (47)	38/109 (35)	1.23	1.01–1.50
Emesis	77/169 (46)	58/144 (40)	1.10	.90–1.35
Anorexia	51/125 (41)	51/106 (48)	0.87	.68–1.11
Diarrhea	52/163 (32)	45/137 (33)	0.98	.78–1.23
Abdominal pain	48/154 (31)	25/115 (22)	1.22	.99–1.50
Hepatomegaly*	7/145 (5)	1/124 (1)	1.65	1.24–2.20
Jaundice	6/149 (4)	3/113 (3)	1.18	.73–1.90

Symptom	Cases, No. (%)	Non-RMSF Illness, No. (%)	Risk Ratio	95% CI
Dysphagia	3/120 (3)	1/51 (2)	1.07	.60–1.90
Splenomegaly	2/143 (1)	4/125 (3)	0.62	.20–1.93
Neurologic				
Dizziness	21/110 (19)	5/48 (10)	1.20	.96–1.50
Mental status change*	29/169 (17)	5/137 (4)	1.66	1.38–1.99
Neck pain*	16/141 (11)	2/74 (3)	1.40	1.15–1.70
Seizure	7/142 (5)	3/78 (4)	1.09	.72–1.65
Photophobia	5/117 (4)	1/45 (2)	1.16	.80–1.68

Abbreviations: CI, confidence interval; RMSF, Rocky Mountain spotted fever; T_{max}, maximum documented temperature.

*Statistically significant difference.

Table 3

Initial Laboratory Findings for Rocky Mountain Spotted Fever (RMSF) Cases and Non-RMSF Illnesses From 2 Tribal Communities in Arizona

Laboratory Test	Mean Laboratory Values for Cases[a]	No.	Mean Laboratory Values for Patients With Non-RMSF Illness[a]	No.	*P* Value
WBC count, $\times 10^3$ cells/μL	11[H]	183	11[H]	144	.587
WBC differential					
Neutrophils, %*	67	181	56	143	.000
Bands, %	10	83	6	43	.975
Lymphocytes, %**	20[L]	179	32	139	.000
Monocytes, %**	7	179	8	140	.003
Eosinophils, %	1.2	179	1.4	139	.45
Hemoglobin, g/dL*	13.9	140	12.8	134	.000
Hematocrit, %*	40.4	141	38.4	134	.002
Platelet count, $\times 10^3$ platelets/μL**	269	141	350	144	.000
Sodium, mEq/L**	136[L]	173	138	135	.043
Potassium, mEq/L**	3.9	134	4.2	126	.001
Chloride, mEq/L**	101	128	103	125	.030
Bicarbonate, mEq/L	22	135	22	125	.371
Creatinine, mEq/L	1.0	134	0.7	126	.084
BUN, mEq/L	14	134	11	125	.174
Glucose, mEq/L	114[H]	147	108[H]	120	.786
Adult SGPT/ALT, IU/L*	57.1[H]	70	29.7	27	.017
Child SGPT/ALT, IU/L	38.5[H]	92	27.1	90	.590
Adult SGOT/AST, IU/L*	140.1[H]	70	58.0[H]	27	.052
Child SGOT/AST, IU/L	91.0[H]	93	56.4[H]	91	.441
Adult ALP, IU/L	130.2[H]	69	132.2[H]	26	.862
Child ALP, IU/L	223.9	92	225.6	90	.876

Laboratory Test	Mean Laboratory Values for Cases[a]	No.	Mean Laboratory Values for Patients With Non-RMSF Illness[a]	No.	*P* Value
Adult GGT	147.1[H]	13	223.0[H]	11	.415
Child GGT	35.8[H]	16	25.7	24	.478
Adult total bilirubin, mg/dL	1.1	57	0.7	27	.083
Child total bilirubin, mg/dL	0.8	86	0.5	82	.068
LDH, IU/L	849[H]	5	401[H]	4	.364
C-reactive protein, IU/L	50.0[H]	11	50.0[H]	16	.983
Albumin, g/dL**	3.9	117	4.7	98	.010
PT, sec**	15.8[H]	27	42.3[H]	15	.022
PTT, sec	41.8[H]	28	37.3[H]	24	.869
INR**	1.4	32	5.2[H]	25	.001
Fibrinogen, g/L	199[H]	9	102[H]	1	.602
D-dimer, ng/mL*	1701[H]	8	98.3	5	.019

Abbreviations: ALP, alkaline phosphatase; BUN, blood urea nitrogen; GGT, gamma-glutamyl transferase; INR, international normalized ratio; LDH, lactate dehydrogenase; PT, prothrombin time; PTT, partial thromboplastin time; RMSF, Rocky Mountain spotted fever; SGOT/AST, serum glutamic oxalacetic transaminase/aspartate aminotransferase; SGPT/ALT, serum glutamic pyruvic transaminase/alanine aminotransferase; WBC, white blood cell.

[a]The superscript H indicates above normal limits; superscript L indicates below normal limits.

*Significantly higher in cases than in patients with non-RMSF illness.

**Significantly lower in cases than in patients with non-RMSF illness.