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### Acknowledgements

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## CASE REPORT

# Is Rocky Mountain Spotted Fever Transmitted in Maine?

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<b>Introduction:</b>	Tick-borne disease occurs worldwide, and, recently, its distribution has been changing. Rocky Mountain spotted fever (RMSF) is widespread across the United States and is being monitored for introduction to non-endemic areas.
<b>Clinical findings:</b>	A 65-year-old male presented to the emergency department with fevers, myalgias, arthralgias, and a maculopapular rash of unclear etiology. He had a history of psoriatic arthritis under treatment with adalimumab, as well as exposure to local ticks, but no known recent bites. Initial testing showed transaminitis, worsened chronic thrombocytopenia, and slight neutropenia with an absolute neutrophil count of 2330 cells/ $\mu$ L (reference value: 2400-7600 cells/ $\mu$ L). His tick panel was negative for Lyme, anaplasma, babesia, and ehrlichia. The patient was stable and discharged.
<b>Diagnoses, Interventions, and Outcomes:</b>	The patient was evaluated in the clinic and found to have improving symptoms but worsening transaminitis. He was empirically given doxycycline, and his repeat tick panel was also negative for Lyme, anaplasma, babesia, and ehrlichia. Abdominal ultrasound was unremarkable, and viral serologies were negative for hepatitis B and C, HIV, cytomegalovirus, and Epstein-Barr virus. His subsequent testing was positive for Spotted Fever Group IgG. He completed empiric treatment, and his symptoms and lab abnormalities resolved. The case was reported to the state of Maine Center of Disease Control and Prevention.
<b>Conclusions:</b>	This case does not meet requirements for diagnostic confirmation of RMSF, but it illustrates the diagnostic considerations for tick-borne febrile illness in Maine.
<b>Keywords:</b>	Rocky Mountain Spotted Fever, tickborne illness, rickettsia rickettsii, Spotted Fever Rickettsioses

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## CASE PRESENTATION

A 65-year-old male presented to the emergency department in late August. He reported 10 days of fevers, myalgias, fatigue, night sweats, and arthralgias. He also noticed a rash on his torso, back, and extremities over the previous five days. He was being treated with adalimumab for psoriatic arthritis and had contracted Lyme disease and ehrlichiosis 12 years earlier. He had a mild transaminitis and worsening of chronic thrombocytopenia (approximately 100 000 to 72 000/ $\mu$ L). Lyme antibodies were undetectable. Polymerase chain reaction (PCR) tests were negative for anaplasmosis, babesiosis, and ehrlichiosis. The patient was clinically stable for discharge.

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In a clinic visit 5 days later, the patient's fevers and rash had improved. He admitted frequent tick exposure in wooded areas but denied recent bites or travel. He had a faint maculopapular rash with satellite lesions of the upper extremities. Repeat labs showed worsening alanine transaminase 83 to 261 (0-40 U/L) and aspartate transaminase 73 to 174 (0-37 U/L). He was given empiric doxycycline pending further workup 16 days after the onset of his symptoms.

Abdominal ultrasound, creatinine kinase, and viral serologies were unremarkable. His repeat tick panels remained negative. At a follow-up clinic visit after 9 days of doxycycline treatment, he only had mild residual fatigue. The next day, testing for the Spotted Fever Group Antibody IgG resulted as 1:256 (reference value <1:64) with negative IgM, concerning for recent or current infection. Repeat labs showed resolution of all prior abnormalities.

## DISCUSSION

While the American dog tick (*Dermacentor variabilis*) exists in Maine, it is not known to carry the *Rickettsia rickettsii* (*R. rickettsii*) bacterium that causes Rocky Mountain spotted fever (RMSF).<sup>1</sup> There are no confirmed cases of RMSF within the state. RMSF is rarely seen and typically associated with travel exposure.<sup>1</sup> In New England, the known endemic tick illnesses are Lyme, babesia, anaplasma, *Borrelia miyamotoi* (*B. miyamotoi*), and the increasingly recognized Powassan virus. These illnesses are transmitted by the blacklegged deer tick *Ixodes scapularis*.

RMSF is a reportable disease classified with the Spotted Fever Rickettsioses (SFR), which includes illnesses by *R. parkeri*, *R. species 364D*, and *R. akari*.<sup>2,3,4</sup> These illnesses share cross-reactive antibodies, manifest with similar constitutional symptoms, and usually have an associated rash or eschar (most cases of *R. parkeri*).<sup>2</sup> *R. rickettsii* is transmitted by the American dog tick east of the Rocky Mountains and on the Pacific Coast. It is the only SFR-linked tick in New England (Figure 1).<sup>2,5</sup> RMSF was first described in the Rocky Mountains, but 60% of cases occur in North Carolina, Oklahoma, Arkansas, Tennessee, and Missouri (Figure 2).<sup>2,6</sup> Some tick species continue to expand their range due to climate change, resurgence of the white-tailed deer population, reforestation, and dispersal by birds. This expansion is evidenced by the northward movement of the lone star tick that transmits ehrlichiosis.<sup>7,8</sup> Since 2000, the annual incidence of SFR has increased from 495 to 6248. However, in 2017, fewer than 10 cases were reported in Maine compared with 1439 cases of Lyme, 663 of anaplasmosis, and 118 of babesiosis.<sup>2,7</sup>

*R. rickettsii* has an incubation period of 3-12 days before manifestation of early symptoms (<5 days), including fever, headache, malaise, and gastrointestinal distress. A maculopapular rash, which can involve palms and soles, starts 2-4 days after the fever. In untreated patients, late symptoms usually present after 5 days and include a petechial rash from vasculitis, organ failure, paralysis, and encephalopathy. These late, severe manifestations designate RMSF as the deadliest tick-borne illness worldwide. With the introduction of tetracyclines, the mortality rates associated with RMSF have declined significantly to 5-10%.<sup>2,3,9</sup>

The standard cross-reactive serological test for all SFR-group diseases is the indirect immunofluorescence antibody (IFA) for IgG against the *R. rickettsii* antigen.<sup>2</sup> Antibodies are detectable 7-10 days after infection. However, to diagnose a recent infection, acute and convalescent serologies obtained 2-4 weeks apart must reveal a fourfold increase, often to  $\geq 1:256$ .<sup>2,10</sup> Titers usually wane to <1:256 within a few months and are undetectable at one year. In some cases, they may be elevated for up to 4 years.<sup>10</sup> The CDC (Centers for Disease Control and Prevention) deems cases as “confirmed” if both acute and convalescent titers reveal the fourfold increase that indicates seroconversion.<sup>11</sup> For more specific diagnosis of each SFR-group disease, there is upcoming expanded access to pan-*Rickettsia* PCR assays.<sup>9,11</sup>

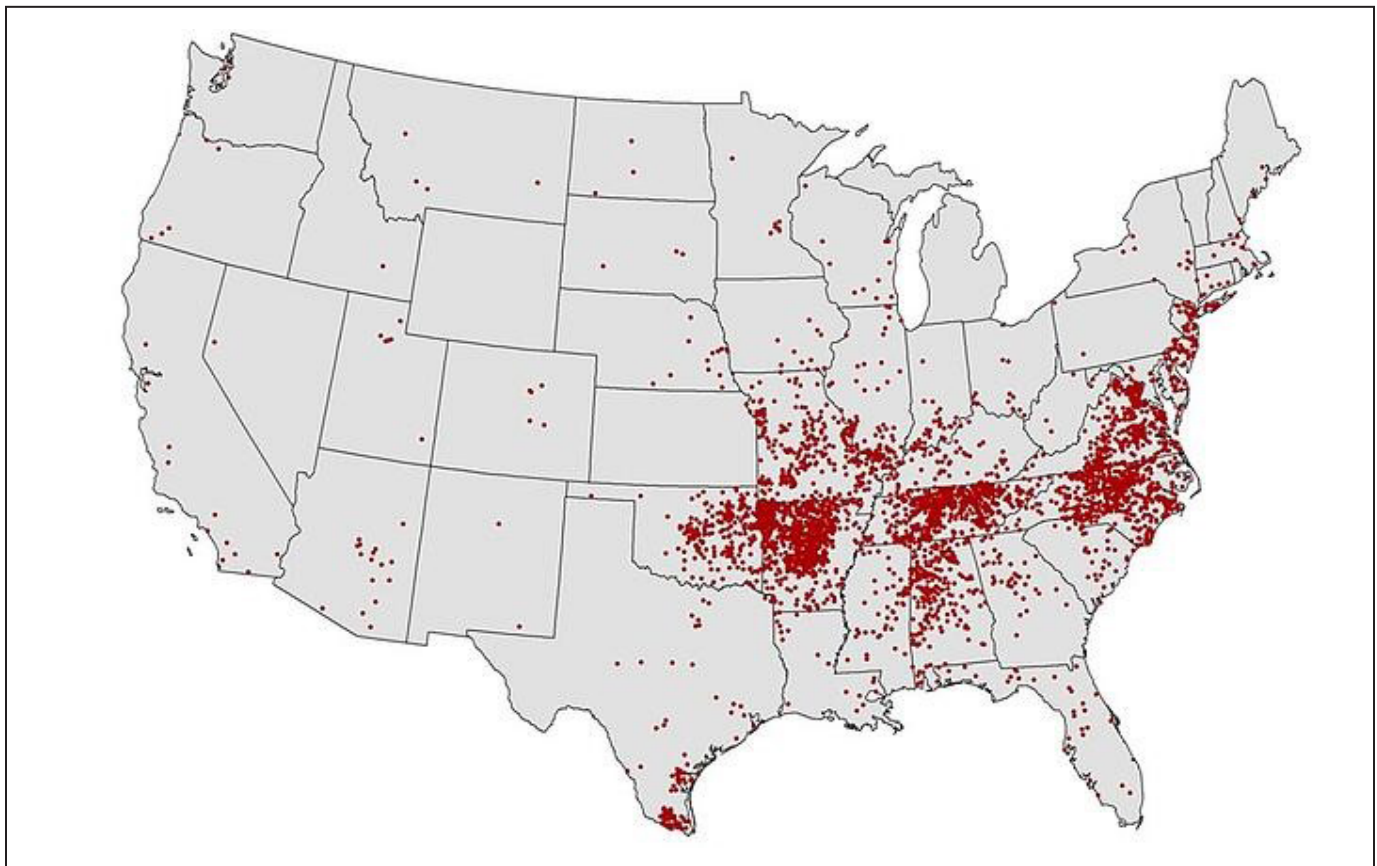
In this patient, lab testing excluded anaplasma, babesia, Lyme, and ehrlichiosis. He did not have neurological manifestations of Powassan virus. He was not tested for the remaining *Ixodes scapularis* disease *B. miyamotoi*; however, with a rash that occurs in <10% of *B. miyamotoi* cases and the absence of sepsis, this finding is unlikely.<sup>12,13</sup> While the single-elevated SFR IgG titer raises some concern for RMSF, the mild clinical course in an untreated patient, lack of typical rash progression from wrists/ankles to trunk, and late-summer timing of the illness broaden the differential diagnosis.<sup>2,14</sup> Additionally, other less-severe SFR diseases with cross-reactive antibodies are possible culprits, as are a variety of viral syndromes that may be represented by the transaminitis and reactive lymphocytosis (11%; 690/ $\mu$ L absolute count) in this patient.

While we do not propose a new endemic area of RMSF, the lack of widespread access to specific diagnostic testing obscures the distribution of each rickettsial disease. There is increasing recognition of the changing distributions in tick-borne disease in the Northeastern United States, including the northward movement of the lone star tick. Given the similar presentations of these illnesses, a careful approach to the differential diagnosis and confirmation of the diagnosis is essential, and it may help highlight changes in areas where the disease occurs.<sup>15</sup>



**Figure 1:** *Dermacentor variabilis* (American Dog Tick)<sup>5</sup>

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**Figure 2:** Cases of Rocky Mountain Spotted Fever Reported to the CDC in 2014<sup>6</sup>



## Conflicts of Interest: None

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