Rocky Mountain Spotted Fever and Spotted Fever Rickettsiosis

Merlin reporting code = 08309
Case report form (CRF): Tick-Borne Rickettsial Disease CRF
MERLIN EXTENDED DATA REQUIRED

Background
Spotted fever rickettsioses are a group of tick-borne infections caused by some members of the genus Rickettsia. Rocky Mountain spotted fever (RMSF) is an illness caused by Rickettsia rickettsii, a bacterial pathogen transmitted to humans through contact with ticks. Dermacentor species of ticks are most commonly associated with infection, including Dermacentor variabilis (the American dog tick), Dermacentor andersoni (the Rocky Mountain wood tick), and more recently Rhipicephalus sanguineus (the brown dog tick). Disease onset occurs 3-14 days following a tick bite. Age-specific illness is highest for children and older adults. Illness is characterized by acute onset of fever, and may be accompanied by headache, malaise, myalgia, nausea/vomiting, or neurologic signs; a macular or maculopapular rash appears 4-7 days following onset in many (~80%) patients, often present on the palms and soles. RMSF may be fatal in as many as 20% of untreated cases, and severe, fulminant disease can occur. In addition to RMSF, human illness associated with other spotted fever group Rickettsia species, including infection with Rickettsia parkeri (associated with Amblyomma maculatum ticks), Rickettsia amblyommii, and Rickettsia africae have also been reported. In these patients, clinical presentation appears similar to, but may be milder than, RMSF; the presence of an eschar at the site of tick attachment is useful for differentiating between R. parkeri or R. africae and most other spotted fever rickettsioses from R. rickettsii. Serologic tests for RMSF can cross-react with spotted fever Rickettsia (SFR) species.

Clinical criteria for case classification
Any reported fever or chills and one or more of the following: rash, eschar, headache, muscle aches, anemia, thrombocytopenia, or any hepatic transaminase elevation.

Laboratory criteria for case classification
Confirmatory:
• Serological evidence of a fourfold change in IgG-specific antibody titer reactive with Rickettsia rickettsii or other SFR antigen by indirect immunofluorescence assay (IFA) between paired serum specimens (one taken in the first week of illness and a second 2-4 weeks later), OR
• Detection of R. rickettsii or other SFR DNA in a clinical specimen via amplification of a specific target by polymerase chain reaction (PCR), OR
• Demonstration of SFR antigen in a biopsy or autopsy specimen by immunohistochemistry (IHC), OR
• Isolation of R. rickettsii or other SFR from a clinical specimen in cell culture.

Presumptive:
• Single elevated IgG antibody reactive with R. rickettsii or other SFR antigen by IFA, enzyme-linked immunosorbent assay (ELISA), dot-ELISA, or latex agglutination.

Epidemiological criteria for case classification
Exposure is defined as having been in potential tick habitats within the past 14 days before onset of symptoms. Occupation and travel history should be recorded if relevant to exposure. A history of a tick bite is not required.
Case classification
Confirmed:
A clinically compatible illness in a person with confirmatory laboratory evidence.

Probable:
A clinically compatible illness in a person with presumptive laboratory evidence.

Suspect:
A person with presumptive laboratory evidence but no clinical information available.

Comments
Acute illness is best detected by PCR and IHC methods in skin biopsy specimens, and occasionally by
PCR in appropriate whole blood specimens taken during the first week of illness, prior to antibiotic
treatment. Serology can also be employed for detection, however an antibody response may not be
detectable in initial samples, and paired acute and convalescent samples are essential for confirmation.

Current commercially available ELISA tests are not quantitative, cannot be used to evaluate changes in
antibody titer, and hence are not useful for serological confirmation. IgM tests are not strongly
supported for use in serodiagnosis of acute disease, as the response may not be specific for the agent
(resulting in false positives) and the IgM response may be persistent. Complement fixation (CF) tests
and other older test methods are neither readily available nor commonly used. CDC uses in-house IFA
IgG testing (cutoff of ≥1:64), preferring simultaneous testing of paired specimens, and does not use IgM
results for routine diagnostic testing.

Recently, a growing number of case reports have included commercial laboratory results as supportive
evidence. For example, the previous case definitions have used the word “antibody.” A review of testing
protocols and reagents distributed to the state laboratories reveal that these existing tests were specific
for IgG-class immunoglobulins. With the increased availability of IgM testing at commercial laboratories,
it becomes necessary to clarify the traditional meaning of the word “antibody” as used in all previous
definitions and routinely used by rickettsial laboratories. The use of IgM is less supported by scientific
evidence, and actually is complicated by false negatives when IgG is present and false positives when
rheumatoid factor or cross-reactive, non-rickettsial, antibodies are present. Thus, IgM testing cannot be
recommended for confirmation of cases at this time.

Acute and convalescent sera from reported cases must be sent to the Bureau of Public
Health Laboratories for confirmatory testing.