Spotted Fever Rickettsiosis, Including Rocky Mountain Spotted Fever (RMSF) Investigation Guideline

CONTENT:	**VERSION DATE:**
Investigation Protocol:	
• **Investigation Guideline**	**01/2010**
• **Tick-borne Rickettsial Disease Form**	**01/2010**
Supporting Materials found in attachments:	
• **Fact Sheet**	**02/2009**

Revision History:

Date	Replaced	Comments
02/2012	-	Removed references to KS-EDSS.

Released 1/2010
Current Version: 1/2010

Spotted Fever Rickettsiosis, Including Rocky Mountain Spotted Fever (RMSF)
Disease Management and Investigation Guidelines

CASE DEFINITION (CDC 2010)

Clinical Evidence:
Any reported fever and one or more of the following: rash, eschar, headache, myalgia, anemia, thrombocytopenia, or any hepatic transaminase elevation.

Laboratory Criteria for Case Classification:
For the purposes of surveillance,

- Laboratory confirmed:
  - Serological evidence of a fourfold change in immunoglobulin G (IgG)-specific antibody titer reactive with Rickettsia rickettsii or other spotted fever group 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 spotted fever group DNA in a clinical specimen via amplification of a specific target by PCR assay, or
  - Demonstration of spotted fever group antigen in a biopsy or autopsy specimen by IHC, or
  - Isolation of R. rickettsii or other spotted fever group rickettsia from a clinical specimen in cell culture.
- Laboratory supportive:
  - Has serologic evidence of elevated IgG or IgM antibody reactive with R. rickettsii or other spotted fever group antigen by IFA, enzyme-linked immunosorbent assay (ELISA), dot-ELISA, or latex agglutination.

Note: 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.

Exposure:
Exposure is defined as having been in potential tick habitats within the past 14 days before onset of symptoms. Occupation should be recorded if relevant to exposure. A history of a tick bite is not required.

Case Classification:

- Confirmed: A clinically compatible case (meets clinical evidence criteria) that is laboratory confirmed.
- Probable: A clinically compatible case (meets clinical evidence criteria) that has supportive laboratory results.
- Suspect: A case with laboratory evidence of past or present infection but no clinical information available (e.g. a laboratory report).

LABORATORY ANALYSIS

The organism in the acute phase of illness is best detected by polymerase chain reaction (PCR) and immunohistochemical methods (IHC) 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.

- The State Public Health Laboratory does not provide testing but testing may be arranged through other private and public laboratories.
- For additional information and/or questions concerning laboratory testing refer to online guidance at www.kdheks.gov/labs/lab_ref_guide.htm

EPIDEMIOLOGY

Spotted fever rickettsioses are a group of tickborne 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 *Rhiphicephalus sanguineus* (the brown dog tick). Age-specific illness is highest for children and older adults. In the United States, RMSF is a seasonal tick-borne disease that usually occurs between April and September when the risk of contact with ticks is greatest. Most cases occur to children <15 years of age as they spend more time in tick-infested areas. Accidental transmission in laboratory settings has occurred.

In addition to *Rickettsia rickettsii*, there are other similar agents transmitted by ticks that have been shown to cause human infections. In the United States, these include *Rickettsia parkeri*, which is transmitted by *Amblyomma maculatum* and causes a maculatum infection (a relatively mild, eschar-associated illness). There are also other genetically similar *Rickettsia* that are thought to cause occasional human illness, including one called 364D (*Rickettsia phillipi*, proposed). Because these agents appear to exhibit serologic cross-reactivity with available tests for *R. rickettsii*, it is likely that some human illnesses currently being attributed to RMSF are actually caused by these distinct rickettsial species, and more research is needed to determine their prevalence and geographic distribution.

DISEASE OVERVIEW

A. Agent:
Rickettsia species of the Spotted Fever group (obligate intracellular coccobacillus): *R. rickettsii*, *R. parkeri* and proposed *R. phillipi* (proposed).

B. Clinical Description:
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. The presence of an eschar at the site of tick attachment has been reported for some other spotted fever rickettsioses which usually present with clinical presentation that appears similar to, but may be milder than, RMSF.

C. Reservoirs:
The *Dermacentor* species of ticks (i.e., the American dog tick and the Rocky Mt. wood tick), *Rhiphicephalus sanguineus* (the brown dog tick) and *Amblyomma maculatum* (the Gulf Coast Tick) It is maintained in environment through a complex cycle involving both ticks and mammals and sometimes birds (i.e., *A. maculatum)*. Humans are considered accidental hosts.

D. Mode(s) of Transmission:
Transmission occurs from the bite of an infected tick or by the contamination of broken skin with the crushed tissue or feces of a tick. Laboratory data suggest that the tick must remain attached for 4 - 6 hours before transmission occurs. Person-to-person transmission does not occur, but there have been rare instances of transfusion associated transmissions.

E. Incubation Period:
Range 2-14 days; average 1 week.

F. Period of Communicability:
Not communicable person-to-person; ticks remains infective for life.

G. Susceptibility and Resistance:
Susceptibility is universal. After infection, immunity is believed to be lifelong.

H. Treatment:
Doxycycline is the treatment of choice. Chloramphenicol is an alternative when contraindications to tetracyclines exist (e.g., child < 8 years of age, pregnancy).

INVESTIGATOR RESPONSIBILITIES

1) Use current case definition, to confirm diagnosis with the medical provider.
2) Conduct a case investigation to identify potential source of infection.
3) Conduct contact investigation to identify additional cases.
4) Identify whether the source of infection is major public health concern.
5) Initiate control and prevention measures to prevent spread of disease.
- Not transmitted person to person; education will be the most effective prevention tool

6) Complete and report all information requested in the Kansas electronic surveillance system.
7) As appropriate, use the disease fact sheet to educate individuals or groups.

STANDARD CASE INVESTIGATION AND CONTROL METHODS

Case Investigation

1) Contact the medical provider who ordered testing of the case and obtain the following information. (This includes medical records for hospitalized patients.)
   - Use the Tick-borne Rickettsial Disease Form to identify any symptoms:
     - Record onset date.
     - Symptoms of fever, headache, myalgia, anemia, thrombocytopenia, leukopenia, elevated hepatic transaminases or others.
     - Underlying immunosuppressive condition.
     - Life threatening complications.
   - Examine the laboratory testing that was done to ensure all testing that could confirm the case has been reported in KS-EDSS.
   - Collect case's demographic data and contact information (birth date, county, sex, race/ethnicity, occupation, address, phone number(s))
   - Record hospitalizations: location, admission and discharge dates
   - Record outcomes: recovered or date of death
2) Interview the case or proxy to determine source and risk factors; focus on athe 2 week incubation period prior to illness onset.
   - Recent travel to endemic areas or history of possible exposure to ticks. List geographic location(s) and date(s). Consider:
     - Exposure to animals or pets with ticks.
     - Outdoor activities.
     - Occupational risks (e.g., laboratory worker, landscape worker, etc.).
   - History of tick bites, include geographic location of bite and date.

Contact Investigation

Contacts are those with possible exposure to the source of infection. Contacts are not persons in close proximity to a case; the disease is not transmitted person-to-person. Consideration should be given to any higher than normal incidence in reports of spotted fever symptoms in individuals that were in the same geographic location as the case's suspected exposure. For suspected outbreaks, refer to the Managing Special Situations section.

Isolation, Work and Daycare Restrictions

None required.

Case Management

None required.

Contact Management

1) Instruct those companions of the case who had similar exposures, i.e., tick, o monitor themselves for symptoms. Preventive treatment is not warranted. Treatment is necessary only if symptoms develop.
2) Those who exhibit any signs or symptoms compatible with tick-borne illness should be referred to their medical provider for evaluation.

Environmental Measures

Community-based integrated tick management strategies may reduce the incidence of tick-borne infections, but limiting exposure to ticks is presently the most effective method of prevention.

- Strategies to reduce vector tick densities through area-wide application of an acaricide (i.e., chemicals that kill ticks and mites) and control of tick habitats (e.g., leaf litter and brush) have been effective in small-scale trials.
- New methods under development include applying acaricide to rodents and deer by using baited tubes, boxes and deer feeding stations in areas where these pathogens are endemic.
- Biological control with fungi, parasitic nematodes, and parasitic wasps may play important roles in integrated tick control efforts.

Education

As opportunities allow, the following general messages should be distributed:

- In tick-infested areas, the highest risk of bites is occurs from March-July.
- The use of protective clothing, including light-colored garments, long pants tucked into socks, long-sleeved shirts, hats, as well as tick repellents, may reduce risk.
- Outdoor activities in tick-infested areas present many opportunities for exposure.
- Keep yards clear of excessive leaves, brush, and tall grasses. Walk in the center of trails to avoid contact with tall grasses and brush.
- When camping, sleep in screened tents. Hunters should be aware of tick infestations on mammals, especially deer and check for tick attachments after handling carcasses.
- Keep pets free of ticks.
- Transmission requires a long attachment. Check for ticks after spending time outdoors in tick infested areas.
- Remove attached ticks intact, do not leave embedded head parts. Use gentle, direct traction with tweezers or hemostat. Other methods, such as application of a hot match or petroleum products to the tick, are less reliable. Do not crush ticks as this may result in direct inoculation of spirochetes.
- Refer to Managing Special Situation – Tick Removal Procedure for more instructions.

MANAGING SPECIAL SITUATIONS

A. Outbreak Investigation:

- There are no formal outbreak definitions; however, the investigator may consider the possibility of an outbreak when there is an unusual clustering of cases in time and/or space.
- Notify KDHE immediately, 1-877-427-7317.
- Active case finding will be an important part of any investigation.

B. Tick Removal Procedure:

- Do not handle the tick with bare hands because infectious agents may enter through mucous membranes or breaks in the skin. This precaution is particularly directed to individuals who remove ticks from domestic animals with unprotected fingers. Children, the elderly and immunocompromised persons may be at greater risk of infection and should avoid this procedure.
- Use fine-tipped tweezers or shield fingers with a tissue, paper towel, or rubber gloves.
- Grasp the tick as close to the skin surface as possible and pull upward with steady, even pressure. Do not twist or jerk the tick; this may cause the mouthparts to break off and remain in the skin. If this happens, remove mouthparts with tweezers.
- Do not squeeze, crush, or puncture the body of the tick because its fluids (e.g., saliva, hemolymph and gut contents) may contain infectious organisms.
- After removing the tick, thoroughly disinfect the bite site and wash hands with soap and water.

DATA MANAGEMENT AND REPORTING TO THE KDHE

A. Organize and collect data.

- The Tick-borne Rickettsial Disease Form can be used for the collection of data.

B. Report data via the state electronic surveillance system.

- Especially data that collected during the investigation that helps to confirm or classify a case.

ADDITIONAL INFORMATION / REFERENCES

A. Treatment / Differential Diagnosis: American Academy of Pediatrics. 2009 Red Book: Report of the Committee on Infectious Disease, 28th Edition. Illinois, Academy of Pediatrics, 2009.

B. Epidemiology, Investigation and Control: Heymann. D., ed., Control of Communicable Diseases Manual, 19th Edition. Washington, DC, American Public Health Association, 2009.

C. Case Definitions: CDC Division of Public Health Surveillance and Informatics, Available at: www.cdc.gov/osels/ph_surveillance/nndss/casedef/case_definitions.htm

D. Animals in Public Places Compendium: www.kdheks.gov/epi/human_animal_health.htm

E. Diagnosis and Management of Tickborne Rickettsial Diseases: Rocky Mountain Spotted Fever, Ehrlichioses, and Anaplasmosis --- United States (MMWR 2006): www.cdc.gov/mmwr/preview/mmwrhtml/rr5504a1.htm

F. Additional Information (CDC): www.cdc.gov/rmsf/index.html

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DEPARTMENT OF HEALTH & HUMAN SERVICES
Centers for Disease Control and Prevention (CDC)
Atlanta, Georgia 30333

Tick-Borne Rickettsial Disease Case Report

Use for: Spotted fever rickettsiosis (SFR) including Rocky Mountain spotted fever (RMSF), Ehrlichiosis (*E. chaffeensis*, *E. ewingii*, & undet.), and Anaplasmosis (*A. phagocytophilum* & undet.).
Visit http://www.cdc.gov and use "Search" for complete Case Definition(s) or visit the disease web site(s) for a fillable/downloadable PDF version of this Case Report.

CDC# ☐☐☐☐ (1-4)

CDC CENTERS FOR DISEASE CONTROL AND PREVENTION

Form Approved
OMB 0920-0009

Patient's name: ______________________

Address: ______________________
(number, street)

City: ______________________

Date submitted: 01/11/2010 (mm/dd/yyyy) (5-6) (7-8) (9-12)

Physician's name: ______________________ Phone no.: ______________________

NETSS ID No.: (if reported) ☐☐☐☐☐☐ — ☐☐☐ — ☐☐
Case ID (13-18) Site (19-21) State (22-23)

1. State of residence: Postal abrv: ☐☐ (24-25)

2. County of residence: (26-50) ______________________
History of travel outside county of residence within 30 days of onset of symptoms?: 1 ☐ YES 2 ☐ NO 9 ☐ Unk

3. Zip code: (51-59) _____-_____

4. Sex: (60) 1 ☐ Male 9 ☐ Unk 2 ☐ Female

5. Date of birth: __ __ __ __ __ __ __ __ (mm/dd/yyyy) (61-62) (63-64) (65-68)

6. Race: (69) 1 ☐ White 2 ☐ Black 3 ☐ American Indian Alaskan Native 4 ☐ Asian 5 ☐ Pacific Islander 9 ☐ Not specified

7. Hispanic ethnicity: (70) 1 ☐ Yes 2 ☐ No 9 ☐ Unk

8. Indicate Disease (Presumed) To Be Reported: (71) 1 ☐ SFR (including RMSF) 2 ☐ Ehrlichiosis - *E. chaffeensis* 3 ☐ Anaplasmosis - *A. phagocytophilum* 4 ☐ Ehrlichiosis - *E. ewingii* 5 ☐ Ehrlichiosis/Anaplasmosis - Undetermined

9. Was a clinically compatible illness present? If there is no presence of clinical illness, then this is not a case. (72)
Clinical evidence - fever and one or more of the following: rash (primarily SFR), headache, myalgia, anemia, leukopenia (Ehrlch. & Anaplas.), thrombocytopenia, or elevated hepatic transaminases. 1 ☐ YES 2 ☐ NO 9 ☐ Unk
Eschar (aka tache noire) or black, necrotic area around site of known/possible tick bite present? 1 ☐ YES 2 ☐ NO 9 ☐ Unk

10. Date of Onset of Symptoms: __ __ __ __ __ __ __ __ (mm/dd/yyyy) (73-80)

11. Was an underlying immunosuppressive condition present? (81)
1 ☐ YES 2 ☐ NO 9 ☐ Unk
Specify condition(s): ______________________

12. Specify any life-threatening complications in the clinical course of illness: (82)
1 ☐ Adult respiratory distress syndrome (ARDS) 3 ☐ Meningitis/encephalitis
2 ☐ Disseminated intravascular coagulopathy (DIC) 4 ☐ Renal failure 9 ☐ None
8 ☐ Other: ______________________

13. Was the patient hospitalized because of this illness? (83) (If yes, date)
1 ☐ YES 2 ☐ NO 9 ☐ Unk __ __ __ __ __ __ __ __ (mm/dd/yyyy) (84-85) (86-87) (88-91)

14. Did the patient die because of this illness? (92) (If yes, date)
1 ☐ YES 2 ☐ NO 9 ☐ Unk __ __ __ __ __ __ __ __ (mm/dd/yyyy) (93-94) (95-96) (97-100)

15. Name of laboratory: ______________________ City: ______________________ State: __ __ Zip: __ __ __ __ __ - __ __ __ __

Below, indicate Y (Yes) or N (No), **ONLY** if the test or procedure was performed. **Lack of selection** indicates that the test or procedure was not performed.

16. Serologic Tests	Serology 1 COLLECTION DATE (mm/dd/yyyy) __ __ __ __ __ __ __ __ (101-2) (103-4) (105-8)		Serology 2* COLLECTION DATE (mm/dd/yyyy) __ __ __ __ __ __ __ __ (109-10) (111-12) (113-16)	
	Titer	Positive?	Titer	Positive?
IFA - IgG	(_____)	1 ☐ YES 2 ☐ NO (117)	(_____)	1 ☐ YES 2 ☐ NO (118)
IFA - IgM	(_____)	1 ☐ YES 2 ☐ NO (119)	(_____)	1 ☐ YES 2 ☐ NO (120)
Other test: ________ (121-130)	(_____)	1 ☐ YES 2 ☐ NO (131)	(_____)	1 ☐ YES 2 ☐ NO (132)

* Was there a fourfold change in antibody titer between the two serum specimens? 1 ☐ YES 2 ☐ NO (137)

17. Other Diagnostic Test? (Use # 16, S1 for collection date)	Positive?
PCR	1 ☐ YES 2 ☐ NO (133)
Morulae visualization*	1 ☐ YES 2 ☐ NO (134)
Immunostain	1 ☐ YES 2 ☐ NO (135)
Culture	1 ☐ YES 2 ☐ NO (136)

* Visualization of morulae not applicable for SFR.

18. Classify case **BASED ON** the CDC case definition (see criteria below): (138)
1 ☐ SFR (including RMSF) 2 ☐ Ehrlichiosis -*E. chaffeensis*
3 ☐ Anaplasmosis -*A. phagocytophilum* 4 ☐ Ehrlichiosis - *E.ewingii*
5 ☐ Ehrlichiosis/Anaplasmosis - Undetermined
______________________ (139-148)

(149) 1 ☐ **CONFIRMED** 2 ☐ **PROBABLE**

State Health Department Official who reviewed this report:
Name: ______________________
Title: ______________________ Date: __ __ __ __ __ __ __ __ (mm/dd/yyyy)

COMMENTS:

Confirmed SFR (including RMSF): A clinically compatible case with evidence of a fourfold change in IgG antibody titer reactive with *Rickettsia rickettsii* or other SFR antigens by IFA between paired serum specimens, one taken during the first week of illness and a second 2-4 weeks later, **OR** detection of *R. rickettsial* or other SFR DNA in a clinical specimen via amplification of a specific target by PCR assay, **OR** demonstration of SFR antigen in a biopsy/autopsy specimen by IHC, **OR** isolation of *R. rickettsia* or other SFR species from a clinical specimen in cell culture.

Probable SFR (including RMSF): A clinically compatible case with evidence of elevated IgG or IgM antibody reactive with *R. rickettsii* or other SFR antigens by IFA, enzyme-linked immunosorbent assay (ELISA), dot-ELISA, or latex agglutination (CDC uses an IFA IgG cutoff of ≥1:64 and does not use IgM test results as independent diagnostic support criteria.).

Note: Current commercially available ELISA tests cannot evaluate changes in antibody titer. IgM tests may be unreliable because they lack specificity. IgM antibody may persist for lengthy periods of time. When sera demonstrate elevated antibody responses to multiple infectious agents among rickettsial species, and between ehrlichial and anaplasmal species, the greater antibody response is generally directed at the actual agent involved.

Confirmed Ehrlichiosis/Anaplasmosis: A clinically compatible case with evidence of a fourfold change in IgG antibody titer reactive with *Ehrlichia chaffeensis or Anaplasma phagocytophilum* antigen by IFA between paired serum specimens (one taken during the first week of illness and a second 2-4 weeks later) **OR** detection of *E. chaffeensis* or *A. phagocytophilum* DNA in a clinical specimen via amplification of a specific target by PCR assay, **OR** demonstration of ehrlichial or anaplasmal antigen in a biospy/autopsy specimen by IHC, **OR** isolation of *E. chaffeensis* or *A. phagocytophilum* from a clinical specimen in cell culture.

Probable Ehrlichiosis/Anaplasmosis: A clinically compatible case with evidence of elevated IgG or IgM antibody reactive with *E. chaffeensis* or *A. phagocytophilum* by IFA, enzyme-linked immunosorbent assay (ELISA), dot-ELISA, or assays in other formats (CDC uses an IFA IgG cutoff of ≥1:64 and does not use IgM test results as independent diagnostic support criteria.), **OR** identification of morulae in the cytoplasm of monocytes or macrophages (Ehrlichiosis) or in the cytoplasm of neutrophils or eosinophils (Anaplasmosis) by microscopic examination.

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Supporting Materials

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