



# Spotted Fever Rickettsiosis

(Including Rocky Mountain Spotted Fever)

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## Disease Plan

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Last updated: August 2, 2019 Dallin Peterson.

Questions about this disease plan?

Contact the Utah Department of Health Bureau of Epidemiology: 801-538-6191.

✓ **CRITICAL CLINICIAN INFORMATION**

<b>Clinical Evidence</b>
<p>Signs/Symptoms</p> <ul style="list-style-type: none"> <li>• Fever</li> <li>• Headache</li> <li>• Rash (it often does not appear early in illness but most patient develop a rash)</li> <li>• Nausea</li> <li>• Vomiting</li> <li>• Stomach Pain</li> <li>• Muscle Pain</li> <li>• Lack of appetite</li> </ul>
<p>Period of Communicability</p> <ul style="list-style-type: none"> <li>• Rocky Mountain Spotted Fever (RMSF) is not transmitted from person to person.</li> </ul>
<p>Incubation Period</p> <ul style="list-style-type: none"> <li>• The mean incubation period ranges from 3-14 days; most occur 5-7 days after exposure.</li> </ul>
<p>Mode of Transmission</p> <ul style="list-style-type: none"> <li>• Transmission is through the bite of an infected tick, <i>Dermacentor andersoni</i> or <i>Amblyomma aurelatum</i> (dog tick).</li> </ul>
<b>Laboratory Testing</b>
<p>Type of Lab Test/Timing of Specimen Collection</p> <ul style="list-style-type: none"> <li>• Polymerase chain reaction (PCR) testing is most effective early in the course of disease.</li> <li>• Pared serologic testing is most effective using IFA assay for IgG antibodies collecting acute and convalescent specimens.</li> </ul>
<p>Type of Specimens</p> <ul style="list-style-type: none"> <li>• Whole blood (purple, yellow, or blue top tube) is preferred for PCR testing. Serum can also be used if only sample available. Minimum sample volume of 4 mL and shipped frozen on dry ice in a plastic tube.</li> <li>• Serum (red top tub or serum separator) or whole blood (purple, green, or blue top tube) is most effective for serologic testing. Minimum sample volume 4 mL and shipped refrigerated or on ice packs.</li> <li>• Convalescent serology specimens should be collected 2-4 weeks later.</li> </ul>
<b>Treatment Recommendations</b>
<p>Type of Treatment</p> <ul style="list-style-type: none"> <li>• Recognition of early and empiric treatment with doxycycline can prevent severe morbidity or death.</li> </ul>
<b>Contact Management</b>
<p>Isolation of Case</p> <ul style="list-style-type: none"> <li>• None</li> </ul>
<p>Quarantine of Contacts</p> <ul style="list-style-type: none"> <li>• None</li> </ul>
<b>Infection Control Procedures</b>
<ul style="list-style-type: none"> <li>• None</li> </ul>

## ✓ WHY IS SPOTTED FEVER IMPORTANT TO PUBLIC HEALTH?

Tickborne rickettsial diseases (TBRD) continue to cause severe illness and death in otherwise healthy adults and children, despite the availability of low cost, effective antimicrobial therapy. In the United States, *R. rickettsii* is transmitted to humans by several tick species, the American dog tick (*Dermacentor variabilis*), Rocky Mountain wood tick (*Dermacentor andersoni*) and the brown dog tick (*Rhipicephalus sanguineus*), which is found on dogs and around people's homes.

In eastern Arizona, between 2003 and 2010, roughly 140 cases of Rocky Mountain Spotted Fever (RMSF) were reported, and approximately 10% of the people diagnosed with the disease died. Almost all of the cases occurred within communities with a large number of free-roaming dogs. The incidence of RMSF in the United States has increased during the last decade, from less than two cases per million persons/year in 2000 to over six cases per million persons/year in 2010. Left untreated, RMSF has a death rate of nearly 20-80%.

Utah is a family-oriented state with a young population base, and is highly recreational (e.g., hiking, camping), making exposure to ticks likely. Families may be frequently exposed to wooded or grassy areas and family pets such as dogs. Conducting surveillance for diseases such as RMSF allows public health to determine when new diseases are emerging in our area so we can provide information to providers that may result in earlier diagnosis and prevent severe morbidity and mortality due to these diseases.

## ✓ DISEASE AND EPIDEMIOLOGY

### Clinical Description

The onset of RMSF is sudden. Cases usually present with a moderate to high fever, significant malaise, muscle pain, headache, chills, and eye inflammation. Over half of cases develop a rash or small bruises on the arms and legs, which typically begins 2–6 days after the onset of illness. The rash spreads to much of the body, including the palms and soles. Among untreated individuals, these signs and symptoms typically persist for 2–3 weeks, and the case-fatality rate ranges from 20-80%. More advanced manifestations include loss of red blood cells (anemia) and platelets (thrombocytopenia), severe clotting disorders, damage to the major organ systems, and shock. If the disease is promptly recognized and treated, death is uncommon. However, overall in the U.S., the reported case fatality rate for RMSF has been 3–5% in recent years.

### Causative Agent

Rocky Mountain spotted fever is caused by the bacterium *Rickettsia rickettsii*.

## Differential Diagnosis

Differential diagnosis for RMSF includes ehrlichiosis, meningococemia, and enteroviral infection.

## Laboratory Identification

Serologic assays are the most widely available and frequently used methods for confirming cases of RMSF. Blood samples taken early (acute) and late (convalescent) in the disease are the preferred specimens for evaluation. Most patients demonstrate increased IgM titers by the end of the first week of illness. Diagnostic levels of IgG antibody generally do not appear until 7-10 days after the onset of illness. There may be considerable variability for these tests among laboratories as no standards exist. *Testing two sequential serum or plasma samples together in the same laboratory to demonstrate rise in IgG or IgM antibody levels is essential to confirm an acute infection.* Commercial laboratories do have capabilities for serologic IgM and IgG testing.

The most rapid and specific diagnostic assays for RMSF rely on molecular methods like PCR, which can detect DNA present at levels of 5-10 rickettsiae in a sample. While organisms can be detected in whole blood samples obtained at the acute onset of illness in a few hours, rickettsial DNA is most readily detected in fresh skin biopsies like those used in immunostaining procedures. PCR availability is extremely limited in Utah and will most likely have to be sent to CDC – Fort Collins Arboviral Branch for testing.

**Utah Public Health Laboratory (UPHL):** UPHL can assist with RMSF diagnosis by facilitating isolation of *R. rickettsii* from clinical samples like whole blood and biopsies. These materials will be shipped unfrozen, or frozen and on dry ice, to ensure optimal chances of isolation at the CDC. Isolation may require several weeks, but isolates are very important for investigating differences in the pathogenic properties and antimicrobial resistance of rickettsiae which cause disease in different parts of the United States. The CDC also has the capability of performing immunostaining on biopsied tissues. UPHL can also facilitate sending paired acute and convalescent serum or plasma samples to CDC for IgG and IgM testing.

## Treatment

Treatment decisions should be based on epidemiologic and clinical clues, and should never be delayed while waiting for confirmation by laboratory results. Doxycycline, tetracycline, and chloramphenicol are the preferred antibiotics for treatment.

## Case Fatality

If the disease is promptly recognized and treated, death is uncommon. Overall, in the U.S., the reported case fatality rate for RMSF has been 3–5% in recent years.

## Reservoir

The primary vector for RMSF is the dog tick (*Dermacentor variabilis*), which also serves as a reservoir. Among ticks, *R. rickettsii* is spread trans-ovarially (adult tick to egg) and trans-stadially (between life stages). While several small wild animals, as well as dogs, may have antibodies to *R. rickettsii*, their role as possible reservoirs in the maintenance of RMSF is uncertain.

## **Transmission**

RMSF is acquired from the bite of an infected tick. Laboratory data suggest that the tick must remain attached for at least 4–6 hours before the transmission of *R. rickettsii* can occur.

## **Susceptibility**

Susceptibility is general. Infection is thought to confer lasting immunity.

## **Incubation Period**

Signs of RMSF typically develop one week after exposure (range 3–14 days). The length of the incubation period is associated with the magnitude of exposure to *R. rickettsii* (greater exposure typically results in a shorter incubation period).

## **Period of Communicability**

RMSF is not communicable from person to person.

## **Epidemiology**

RMSF is widespread in the U.S., with most cases reported from the southern and mid-western states. RMSF is relatively rare in Utah; cases occur most frequently in states south of Utah. RMSF incidence rises between April and October, when the risk of contact with ticks is greatest. The risk of mortality from RMSF is higher for men, people over the age of 40 years, those who are racially non-white, individuals who do not develop (or recognize) the typical rash, and individuals with no reported history of a tick bite. As children tend to have more contact with tick-infested areas, most reported cases are in people under the age of 15 years. While rare, accidental transmission in the laboratory setting has been reported.

Utah averages one case approximately every five years. The case definition requires the presence of both acute and convalescent serologies, and few clinicians order and/or patients provide convalescent sera. Therefore, it is likely that this disease is more prevalent in Utah than the data suggest.

## ✓ PUBLIC HEALTH CONTROL MEASURES

### Public Health Responsibility

- Identify the source of infection and prevent further transmission.
- Investigate all suspect cases of disease and fill out and submit appropriate disease investigation forms.
- Provide education to the general public, clinicians, and first responders regarding disease transmission and prevention.
- Identify clusters or outbreaks of this disease.

### Prevention

#### *Managing Special Situations: Response to a Tick Bite*

The longer a tick remains attached to someone, the higher the likelihood of disease transmission. Individuals should promptly remove any attached tick using fine-point tweezers. The tick should not be squeezed or twisted, but grasped close to the skin and pulled straight out using steady pressure. Whenever an attached tick is removed from the body, one should monitor one's health for the appearance of rash, fever, or flu-like symptoms, and should immediately seek the advice of a health care provider should any symptoms occur, especially if the tick was attached for more than 24 hours. It may be helpful to save the tick after removal for two reasons: 1) if the person who was bitten goes on to develop signs or symptoms such as fever, flu-like symptoms, or a rash, it may be helpful for the physician to know the type of tick; and 2) depending on the circumstances of the bite (e.g., when a person was bitten, the type of tick, how long it was attached), a physician may choose to treat the person who was bitten. The tick may be kept either securely sealed in a small plastic bag or attached, with clear tape, to a piece of paper. For individuals who do not wish to keep the tick, it can be either drowned in alcohol or flushed down the toilet.

If an individual chooses to have the tick tested, the following information should be taken into account:

- Tests performed on ticks are not perfect, and they do not test for all infections that ticks may carry. Therefore, even with a negative result, people should still monitor for the appearance of rash, fever, or other unusual symptoms, and should immediately seek the advice of a healthcare provider should any symptoms occur.
- If someone has been infected by a tick bite, symptoms may begin to occur even before the results of tick testing are available. People should not wait for tick testing results before seeking medical advice, should any symptoms develop.
- A positive test on a tick is not an automatic indication that treatment is needed. A positive test indicates that the tick was infected, but not that the tick was successful in spreading the infection to the person bitten. The longer a tick is attached, the greater the chance that it will spread infection. Positive test results should be discussed with a health care provider.

## **Preventive Measures**

### *Environmental Measures*

Prevention of RMSF, along with other diseases spread by ticks, involves making yards less attractive to ticks.

- Keep grass cut short.
- Remove leaf litter and brush from around the yard.
- Prune low lying bushes to let in more sunlight.
- Keep woodpiles and bird feeders off the ground and away from the home.
- Keep the plants around stone walls cut short.
- Use a three-foot wide woodchip, mulch, or gravel barrier where the lawn meets the woods, and remind children not to cross that barrier.
- Ask a landscaper or local nursery about plants to use in the yard that do not attract deer.
- Use deer fencing (for yards 15 acres or more).

If an individual chooses to use a pesticide to reduce the number of ticks on his/her property, he/she should be advised to hire a licensed applicator who is experienced with tick control. A local landscaper or arborist may be a licensed applicator. In general, good tick control can be achieved with no more than two pesticide applications in any year. Advise individuals to ask, when selecting an applicator, if they will provide:

- A written pest control plan that includes information on the pesticide to be used.
- Information about non-chemical pest control alternatives.
- Signs to be posted around the property after the application.

### *Personal Preventive Measures/Education*

There is no vaccine to protect against RMSF. If someone lives, works, or spends leisure time in an area likely to have dog ticks, they should be advised of the following:

- The single most important thing to prevent a tick-borne disease is to check for ticks once a day. Favorite places ticks like to go on the body include areas between the toes, back of the knees, groin, armpits, neck, along the hairline, and behind the ears. Remember to also check children and pets. Promptly remove any attached tick using fine-point tweezers. The tick should not be squeezed or twisted, but grasped close to the skin and pulled straight out using steady pressure.
- Stick to main pathways and the centers of trails when hiking.
- Wear long-sleeved, light colored shirts and long pants tucked into socks.
- Talk to a veterinarian about the best ways to protect pets and livestock from ticks.
- Use repellents containing DEET (N,N-diethyl-m-toluamide), and choose a product that will provide sufficient protection for the amount of time spent outdoors. Product labels often indicate the length of time that one can expect protection from a product. DEET is considered safe when used according to the manufacturer's directions. The efficacy of DEET levels off at a concentration of 30%, which is the highest concentration recommended for children and adults. DEET products should not be used on children less than two months of age. Mosquito netting may be used to cover infant carriers or to protect other areas for children less than two months of age.

- The following precautions should be observed when using DEET products:
  - Avoid using DEET products that combine the repellent with a sunscreen. Sunscreens may need to be reapplied too often, resulting in an over application of DEET.
  - Apply DEET on exposed skin, using only as much as needed.
  - Do not use DEET on the hands of young children, and avoid applying repellent to areas around the eyes and mouth.
  - Do not use DEET over cuts, wounds, or irritated skin.
  - Wash treated skin with soap and water after returning indoors, and wash treated clothing.
  - Avoid spraying DEET products in enclosed areas.

Permethrin-containing products will kill mosquitoes and ticks on contact. Permethrin products are not designed to be applied to the skin. Clothing should be treated and allowed to dry in a well-ventilated area prior to wearing. Because permethrin binds very tightly to fabrics, once the fabric is dry, very little of the permethrin gets onto the skin.

## **Chemoprophylaxis**

None.

## **Vaccine**

None.

## **Isolation and Quarantine Requirements**

**Isolation:** None.

**Hospital:** None.

**Quarantine:** None.



## ✓ CASE INVESTIGATION

### Reporting

All suspect and confirmed cases of RMSF are reportable to public health in Utah.

#### Laboratory Criteria for Reporting

Report any illness to public health authorities that meets any of the following laboratory criteria:

Any patient with laboratory evidence of SFR (including RMSF) including any of the following:

- Detection of SFGR nucleic acid in a clinical specimen via amplification of a *Rickettsia* genus- or species-specific target by polymerase chain reaction (PCR) assay, OR
- Elevated IgG antibody titer in one or more serology samples reactive with SFGR antigen by IFA, OR
- Isolation of SFGR from a clinical specimen in cell culture and molecular confirmation (e.g., PCR or sequence).

#### Vial Records Criteria for Reporting

Report any illness to public health authorities that meets any of the following vital records criteria: A person whose death certificate lists SFT (including RMSF) as a cause of death or a significant condition contributing to death.

#### Other Criteria for Reporting

Report any illness of person whose healthcare record contains a diagnosis of Spotted Fever Rickettsiosis (including Rocky Mountain spotted fever).

### Case Definition

#### Spotted Fever Rickettsiosis (including RMSF) (2019)

##### Clinical presentation

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).

Disease onset averages one week 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 20-80% 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), has 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 has been reported for some other spotted fever rickettsioses.

### **Clinical evidence**

Fever as reported by the patient or a healthcare provider, AND one or more of the following: rash, eschar, headache, myalgia, anemia, thrombocytopenia, or any hepatic transaminase elevation.

### **Epidemiologic evidence**

None required for case classification.

### **Laboratory evidence**

Confirmatory laboratory evidence:

- Detection of SFGR nucleic acid in a clinical specimen via amplification of a Rickettsia genus- or species-specific target by PCR assay, OR
- Serological evidence of a fourfold increase in IgG-specific antibody titer reactive with SFGR antigen by IFA between paired serum specimens (one taken in the first two 19-ID-07 6 weeks after illness onset and a second taken two to ten weeks after acute specimen collection)\*, OR
- Demonstration of SFGR antigen in a biopsy or autopsy specimen by IHC, OR
- Isolation of SFGR from a clinical specimen in cell culture and molecular confirmation (e.g., PCR or sequence).

Presumptive laboratory evidence:

- Has serologic evidence of elevated IgG antibody at a titer  $\geq 1:128$  reactive with SFGR antigen by IFA in a sample taken within 60 days of illness onset.\*\*

Supportive laboratory evidence:

- Has serologic evidence of elevated IgG antibody at a titer

\*A four-fold rise in titer should not be excluded (as confirmatory laboratory criteria) if the acute and convalescent specimens are collected within two weeks of one another.

\*\*This includes paired serum specimens without evidence of fourfold rise in titer, but with at least one single titer  $\geq 1:128$  in IgG-specific antibody titers reactive with SFGR antigen by IFA.

### **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 confirmatory or presumptive laboratory evidence of infection with no clinical information available, OR
- A clinically compatible case (meets clinical criteria) that has supportive laboratory evidence.

A person previously reported as a probable or confirmed case-patient may be counted as a new case-patient when there is an episode of new clinically compatible illness with confirmatory laboratory evidence.

### **Case Investigation Process**

- Fill out morbidity form.
- Verify case status.
- Fill out disease investigation form.
- Determine whether patient had travel/exposure history consistent with acquisition of disease in Utah or elsewhere.
- If patient acquired disease in Utah, attempt to identify the source of transmission and eliminate it.

### **Outbreaks**

More than one laboratory confirmed case of RMSF in Utah in a year would constitute an outbreak.

### **Identifying Case Contacts**

Not applicable.

### **Case Contact Management**

Not applicable.

## ✓ REFERENCES

Centers for Disease Control, Case Definitions for Infectious Conditions Under Public Health Surveillance. MMWR 46 (RR-10), 1997.I.

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## ✓ VERSION CONTROL

Update. August 2, 2019: Updated new case definition per CSTE.

Update. May 8, 2018: Update Critical Clinician Information and ELR white/grey list rules.

Update. December 8, 2016: Updated references.

Update. April 7, 2016: Updated CSTE guidance for reporting and added minimum data set.

## ✓ UT-NEDSS Minimum/Required Fields by Tab

### Demographic

- County
- State
- Date of Birth
- Birth Gender
- Ethnicity
- Race
- First Name
- Last Name
- Middle Name
- Area Code
- Email Address
- Extension
- Phone Number

### Clinical

- Date Diagnosed
- Date of Death
- Disease
- Clinicians
- Diagnostic Facilities
- Symptoms
- Onset Date

### Laboratory

- Lab Test Date
- Organism
- Specimen Source
- Test Result

### Epidemiological

- NA

### Investigation

- Did the patient travel outside the U.S. during the exposure period?

### Contacts

NA

### Reporting

- Date first reported to public health

### Administrative

- State Case Status

## ✓ SPOTTED FEVER RICKETTSIOSIS RULES FOR ENTERING LABORATORY TEST RESULTS

The following rules describe how laboratory results reported to public health should be added to new or existing events in UT-NEDSS. These rules have been developed for the automated processing of electronic laboratory reports, although they apply to manual data entry, as well.

### Test-Specific Rules

*Test specific rules describe what test type and test result combinations are allowed to create new morbidity events in UT-NEDSS, and what test type and test result combinations are allowed to update existing events (morbidity or contact) in UT-NEDSS.*

Test Type	Test Result	Create a New Event	Update an Existing Event
IgG Antibody	Positive	Yes	Yes
	Negative	No	Yes
	Equivocal	No	Yes
IgM Antibody	Positive	Yes	Yes
	Negative	No	Yes
	Equivocal	No	Yes
PCR/Amplification	Positive	Yes	Yes
	Negative	No	Yes
	Equivocal	No	Yes

### Whitelist Rules

*Whitelist rules describe how long an existing event can have new laboratory data appended to it. If a laboratory result falls outside the whitelist rules for an existing event, it should not be added to that event, and should be evaluated to determine if a new event (CMR) should be created.*

**Spotted Fever Rickettsiosis Morbidity Whitelist Rule:** If the specimen collection date of the laboratory result is two years or less after the event date, the laboratory result should be added to the morbidity event.

**Spotted Fever Rickettsiosis Contact Whitelist Rule:** Never added to contact.

### Graylist Rule

*We often receive laboratory results through ELR that cannot create cases, but can be useful if a case is created in the future. These laboratory results go to the graylist. The graylist rule describes how long an existing event can have an old laboratory result appended to it.*

**Spotted Fever Rickettsiosis Graylist Rule:** If the specimen collection date of the laboratory result is 30 days before to seven days after the event date of the morbidity event, the laboratory result should be added to the morbidity event.

**Other Electronic Laboratory Processing Rules**

If an existing event has a state case status of “not a case,” ELR will never add additional test results to that case. New labs will be evaluated to determine if a new CMR should be created.