

Rocky Mountain Spotted Fever

New World Spotted Fever, Spotted Fever, Tick Typhus, Tick-borne Typhus Fever, North American Tick Typhus, São Paulo Fever, Tobia Fever, Choix Fever, Macular Fever, Pinta Fever, Fiebre Maculosa, Fiebre Manchada

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Etiology

Rocky Mountain spotted fever results from infection by *Rickettsia rickettsii*, a pleomorphic, obligate intracellular, Gram negative coccobacillus in the family Rickettsiaceae.

Geographic Distribution

Rocky Mountain spotted fever is found throughout the continental United States, southern Canada, Mexico, Central America and parts of South America including Argentina, Brazil, Colombia and Costa Rica. Organisms related to *R. rickettsii* cause spotted fevers in other parts of the world. In the U.S., most human cases are seen in the Atlantic states from Delaware to Florida, as well as the South-central states (Arkansas, Louisiana, Oklahoma, and Texas) and the Pacific region (Oregon, California and Washington).

Transmission

Ticks serve as both reservoirs and vectors for Rocky Mountain spotted fever. In the U.S., the two major vectors are *Dermacentor variabilis* (the American dog tick) and *Dermacentor andersoni* (the Rocky Mountain wood tick). *D. variabilis* is found primarily in the midwestern and eastern U.S. and southern Canada. It also occurs in limited regions on the Pacific coast. *D. andersoni* is found in the western U.S. and parts of Canada. *Amblyomma americanum* (the Lone Star tick) has been suggested as a possible vector in the Southwest. *Amblyomma cajennense* is the major vector in South America. Other species of ticks can also carry or transmit Rocky Mountain spotted fever, but appear to be minor vectors.

Transmission usually occurs via the tick's saliva during feeding. The feeding process stimulates replication of *R. rickettsii*; several hours of attachment are usually needed before infection occurs. Late in the season, transmission can occur after 6 to 10 hours; early in the season, the organisms become activated more slowly. *R. rickettsii* can also be spread by exposure to a crushed tick's tissues, fluids or feces, which enter the body through breaks in the skin. This organism is stable in blood or tick tissues under ambient environmental conditions, and can remain viable for up to a year. It is rapidly destroyed in tick feces once it dries. Aerosol transmission has been reported only after laboratory accidents.

R. rickettsii is maintained primarily by transovarial and transstadial transmission in its tick vectors; approximately 1-5% of the susceptible tick population in any region carries this organism. Infected ticks carry *R. rickettsii* for life. Uninfected ticks are also infected, at a low rate, by feeding on infected rodent or small mammal reservoir hosts.

Disinfection

R. rickettsii is susceptible to 1% sodium hypochlorite, 70% ethanol, glutaraldehyde, formaldehyde and phenol. It can also be destroyed by moist heat of 121° C for a minimum of 15 min, or dry heat of 160-170° C for an hour, but is resistant to freezing. Ordinary household disinfectants including 70% isopropyl alcohol or 2% tincture of iodine can be used to disinfect a tick bite.

Infections in Humans

Incubation Period

The incubation period in humans is 2 to 14 days, with an average incubation period of approximately seven days.

Clinical Signs

In the early stages, Rocky Mountain spotted fever can be difficult to diagnose. A classic triad of fever, petechial rash and tick exposure is suggestive; however, the rash appears several days after the other symptoms, and the tick may not have been noticed.

The early signs are nonspecific and may include high fever, chills, malaise, severe headache, a slight cough, deep muscle pain and hypotension. Gastrointestinal signs including nausea, anorexia, vomiting, diarrhea and abdominal pain are frequently seen. Edema is also common. It may be either generalized or limited to the face, periorbital

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region or extremities. Ocular lesions may include conjunctivitis, photophobia, petechiae and, in severe cases, ocular hemorrhages, ocular palsy and vascular occlusion.

A nonpruritic macular rash, usually seen first on the wrists, forearms, ankles or scrotum, can appear from the 2nd to 14th day and spreads rapidly, often involving the palms or soles. The spots initially blanch when pressed, but later develop into the characteristic petechiae. In the later stages, the petechiae can coalesce to form ecchymoses and may be followed by necrotic or gangrenous changes. Up to 10-15% of patients never have a rash.

Rocky Mountain spotted fever can also involve the respiratory system, central nervous system or kidneys. Neurologic signs, which may include agitation, insomnia, aphasia, tremor, rigidity, ataxia, hemiplegia or paraplegia, delirium, hallucinations or coma, can be seen as early as the end of the first week. The neurologic signs can mimic encephalitis or meningitis. Hemorrhages are common, due to damage to the blood vessels; visible hemorrhages may be seen in up to 50% of patients. Gastrointestinal bleeding can also occur. Other complications may include pulmonary edema, acute respiratory distress syndrome, cardiac arrhythmias, coagulopathies and renal failure.

Although convalescence is usually rapid with early treatment, untreated patients may die in 8 to 15 days and more severe cases often require hospitalization. Untreated cases that are not fatal may be symptomatic for weeks or months. Sequelae, particularly after severe disease, can include gangrene of the extremities or neurologic signs including loss of bowel or bladder control, movement disorders, transient or permanent deafness, language difficulties or partial paralysis of the lower extremities.

Communicability

R. rickettsii is not transmitted directly from person to person; however, humans may be infected by the tick's feces, tissues or fluids during tick removal. One case was acquired in a blood transfusion.

Caution should also be used when handling blood and tissue specimens that may contain *R. rickettsii*. In laboratory workers, infections can occur by accidental parenteral inoculation or exposure to aerosols. Sources of the organism include naturally and experimentally infected mammals and their tissues, as well as ticks, their feces and tissues.

Diagnostic Tests

There is no widely available laboratory test that can rapidly diagnose Rocky Mountain spotted fever; therefore, testing is often used for confirmation rather than diagnosis. Treatment decisions are typically based on the symptoms, history and routine clinical laboratory findings.

Serology is most often used for confirmation; a fourfold rise in titer between the acute and convalescent samples is considered to be diagnostic. The most commonly used test is

the indirect immunofluorescence assay (IFA). An ELISA test has been recently introduced. Other serologic tests include indirect hemagglutination, latex agglutination, complement fixation and microagglutination. The Weil-Felix test, based on cross-reactive antigens of *Proteus vulgaris*, is nonspecific and insensitive and has generally been abandoned. Antibodies do not usually appear until 6 to 10 days after the first clinical signs.

Direct immunofluorescence or immunoperoxidase staining of a skin biopsy from the rash can sometimes detect *R. rickettsii*; however, the organisms are focally distributed and may not be found. Immunostaining can also be used on a variety of tissues at autopsy. PCR is also available.

Rickettsiae are fastidious and hazardous; therefore, isolation and identification is not widely available. *R. rickettsii* may be isolated from the blood during the first week of fever, in cell cultures or by animal inoculation into male guinea pigs or embryonated eggs.

Treatment

Treatment is most effective in the early stages of the disease, and is initiated without waiting for disease confirmation. Patients treated within the first 4-5 days often respond quickly to tetracycline antibiotics such as doxycycline; severely ill patients may take longer to respond and require long term treatment. Chloramphenicol may also be used in some situations.

Prevention

The risk of infection can be decreased by preventing tick bites. Protective footwear, clothing and insect repellents should be used in tick habitats. Ticks may be more visible on light-colored clothing. People who enter tick habitats should check frequently for ticks and remove them as soon as possible, using fine-tipped tweezers or gloved hands.

Bare hands should not be used to remove ticks, due to the risk of exposure to the tick's fluids or feces. If gloves are not available, the fingers should be shielded with a tissue or paper towel. The tick should not be squeezed, crushed or punctured. The CDC warns that tick removal techniques such as the use of hot matches or petroleum jelly may stimulate the tick to release additional saliva and could increase the risk of infection.

Tick bites should be thoroughly disinfected after removal of the tick, and the hands should be washed with soap and water. The CDC recommends freezing the tick in a plastic bag, for identification in case of illness.

Ticks should also be removed from pets, both to prevent dogs from becoming ill and to prevent ticks from entering the home. Acaricides, biological controls and control of tick habitats can decrease the populations of tick vectors in a community.

Although no licensed vaccine is currently available, experimental vaccines may at times be available.

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Preventative treatment with antibiotics, in patients with recent tick bites, is not recommended and may only delay the onset of clinical signs.

Morbidity and Mortality

Annually, approximately 700 cases of Rocky Mountain spotted fever are reported in the U.S. Most cases are seen in the southeast Atlantic coast states and the South-central region, and are mainly reported from April through September. Infections occur most often in children from 5 to 9 years old, and in adults older than 60 years.

The case fatality rate is 15-30% if the infection is untreated, and 3-5% if it is treated. Severe or fatal disease is more likely in older people and those with glucose-6-phosphate dehydrogenase deficiency, a sex-linked genetic condition that affects approximately 12% of African-American males in the U.S. Persons with this deficiency typically develop severe disease, which is often fatal within five days.

Infections in Animals

Species Affected

Rocky Mountain spotted fever affects dogs and humans. *R. rickettsii* has also been isolated from small mammals including opossums, rabbits, chipmunks, squirrels, rats and mice.

Incubation Period

Incubation periods from 2 to 14 days have been reported in naturally and experimentally infected dogs.

Clinical Signs

Rocky Mountain spotted fever is symptomatic only in dogs. In most wild animals, infection with *R. rickettsii* seems to be inapparent.

Subclinical and mild cases are common in dogs, but more severe infections can also be seen. The symptoms are highly variable; Fever, anorexia and depression are the most common signs. Other symptoms may include scleral injection, lymphadenopathy, coughing, mucopurulent oculonasal discharge, dyspnea, abdominal pain, diarrhea, vomiting, joint or muscle pain, and edema of the face or extremities. Ocular signs, including focal retinal hemorrhages, chorio-retinal exudate or retinal detachment, are often found.

Thrombocytopenia is common but typically mild. Epistaxis, petechial or ecchymotic hemorrhages, melena or hematuria are seen in less than a quarter of all cases, and are generally due to vasculitis rather than low platelet numbers. Petechiae and ecchymoses tend to be found mainly on the oral, ocular and genital mucous membranes. Increased permeability of the blood vessels can also cause hypotension and shock.

Neurologic disease is seen in approximately a third of cases, and may include vestibular dysfunction, altered mental states, generalized or localized hyperesthesia, intention tremors of the head, ataxia, paraparesis or tetraparesis. Seizures, cranial nerve deficits, myocardial inflammation, cardiovascular collapse, renal failure and coma can occur in the terminal stages. Clear vesicles, developing into pustules, have been noted on the oral mucous membranes in experimental infections. Necrosis of the extremities, necrotic skin lesions and disseminated intravascular coagulation have been reported in severe cases. Untreated survivors usually recover after two weeks or less. Chronic infections have not been reported.

Communicability

Direct transmission of Rocky Mountain spotted fever from dogs has not been reported; however, dogs can carry ticks that infect humans or other dogs, and humans may be infected by contact with the tick's feces, tissues or fluids during tick removal. Caution should also be used when handling blood and tissue specimens that may contain *R. rickettsii*. The ability of dogs to serve as a reservoir host is unresolved.

There have been several reports of concurrent infections in dogs and their owners, due to simultaneous exposure to infected ticks. Dogs can, therefore, serve as sentinels for human disease.

Diagnostic Tests

In dogs, Rocky Mountain spotted fever is often diagnosed retrospectively by serology. A fourfold rise in titer in acute and convalescent samples taken more than three weeks apart is diagnostic. A single high titer may also be suggestive. Cross-reactions are seen with other spotted fever group *Rickettsia*. The indirect fluorescent antibody test is the most commonly used serologic test.

Immunofluorescence can sometimes detect organisms in skin biopsies or at necropsy. A polymerase chain reaction (PCR) test may also be available.

Rickettsiae are fastidious and hazardous, and isolation is not widely available. In addition, the prolonged incubation period generally makes culture impractical for diagnosis. *R. rickettsii* can occasionally be isolated from the blood, liver, spleen or brain in cell cultures (Vero and other cells), or by animal inoculation into male guinea pigs or embryonated eggs.

Clinical pathology can support a diagnosis of Rocky Mountain spotted fever. Findings may include thrombocytopenia, which is often mild, leukopenia followed by moderate leukocytosis, hyperproteinemia and hypoalbuminemia. Coagulation abnormalities are sometimes found. Abnormalities in serum chemistry related to diseased organ systems may be seen.

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Treatment

Antibiotics (doxycycline or minocycline, and, less often, tetracycline or chloramphenicol) are used to treat Rocky Mountain spotted fever. The fluoroquinolones may also be effective. Antibiotics are most effective given early in the disease, before significant neurologic disease becomes apparent. The concurrent use of corticosteroids is controversial. These drugs are often used for ocular disease associated with Rocky Mountain spotted fever. They have been associated with gangrenous necrosis in some infected dogs treated with immunosuppressive doses; however, in one experimental study, there was no detrimental effect to their use, in conjunction with antibiotics, in dogs with mild to moderate disease.

Prevention

The risk of infection can be reduced by preventing tick bites with topical acaricides and prompt removal of ticks. The skin and hair coat should be checked frequently, and any ticks should be removed with fine-tipped tweezers or gloved hands. If ticks must be removed and gloves or tweezers are not available, the hands should be shielded with paper. The tick should not be squeezed, crushed or punctured, as its fluids may contain rickettsiae. Touching ticks, their fluids or feces with bare hands should also be avoided.

Tick bites should be thoroughly cleaned and disinfected after removal of the tick, and the hands should be washed with soap and water. The CDC warns against tick removal techniques such as the use of hot matches or petroleum jelly, which may stimulate the tick to release additional saliva and could increase the risk of infection.

No vaccines are available. Acaricides, biological controls and control of tick habitats can decrease the populations of tick vectors in a community.

Morbidity and Mortality

Rocky Mountain spotted fever is seen only from spring through early fall. In dogs, this disease usually occurs sporadically and is seen most often in animals less than three years old. Up to 63% of dogs in some areas are seropositive; some of these cases may be due to related rickettsiae in the spotted fever group.

In dogs, Rocky Mountain spotted fever may be subclinical, mild or severe. German shepherds may become ill more often than other breeds, and English Springer spaniels with phosphofructokinase deficiency are thought to develop more severe disease. Antibiotics usually result in prompt improvement in cases without neurologic signs or serious organ dysfunction; more severe infections may be slow to respond. Animals with CNS disease can have residual neurologic defects after treatment, and recovery may be slow in these cases. Dogs that have recovered have good immunity to reinfection.

Post-Mortem Lesions

Lesions reported in dogs include focal ischemic necrosis, thrombi and occlusions in blood vessels, and valvular endocarditis. Edema can be found on the face, extremities or male genital organs. Pulmonary edema may also be seen. Ecchymoses and petechiae have been found in various organs including the brain, heart, testes and lymph nodes. Microscopically, vasculitis and perivascular inflammatory cell infiltrates may be seen in most body tissues.

Internet Resources

- Centers for Disease Control and Prevention (CDC)
http://www.cdc.gov/ncidod/diseases/submenus/sub_rmsf.htm
- International Veterinary Information Service (IVIS)
<http://www.ivis.org>
- Material Safety Data Sheets – Canadian Laboratory Center for Disease Control
<http://www.hc-sc.gc.ca/pphb-dgsp/msds-ftss/index.html#menu>
- Medical Microbiology
<http://www.gsbs.utmb.edu/microbook>
- The Merck Manual
<http://www.merck.com/pubs/mmanual/>
- The Merck Veterinary Manual
<http://www.merckvetmanual.com/mvm/index.jsp>

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