Rocky Mountain Spotted Fever
*Rickettsia rickettsii*

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**Introduction**

Rocky Mountain Spotted Fever (RMSF) is a bacterial disease carried and transmitted by ticks and is a potentially fatal human disease in Northern and Southern America. Transmission occurs via the bite of a tick infected with *Rickettsia rickettsii*. Symptoms vary widely from individual to individual and include fever, headache, abdominal pain, vomiting, and muscle pain. A rash may or may not be present throughout infection and is almost always absent in the first several days of infection. The resulting illness from RMSF is considered severe and can result in death if not properly and promptly treated. First line of treatment for all ages is tetracycline and chloramphenicol and is most effective when started before or on the first day of noticed symptoms. Diagnosis of the disease is made by analysis of clinical signs and symptoms, and a detailed medical history, and is in turn later confirmed by specialized laboratory tests. Precautions can limit contraction of RMSF and other tick-borne diseases.

**History**

The first known cases of RMSF began in the late 1800s when Edward E Maxey provided the first description of the disease now known as RMSF “of Idaho.” It was labeled as: “a febrile disease, characterized clinically by a continuous moderately high fever, and a profuse or purpuric eruption in the skin, appearing first on ankles, wrists, and forehead, but rapidly spreading to all parts of body.” This is also the first published acknowledgement of the disease to appear in medical literature.

Louis Wilson and William Chowning studied recorded cases of RMSF and were able to implicate ticks as the primary vector. From the 126 cases studied, wood ticks were identified as the carrier with confirmation by 1906. Howard T. Ricketts isolated the bacterial pathogen by 1910 and showed that it
was passed between mammals and ticks and back again. Ricketts also showed that the pathogen is transmitted transovarially to the ticks’ offspring and identified the mammalian tissues affected by *R. rickettsii* as the epithelial cells membranes and their nuclei. The name *Rickettsia rickettsii* was given to the bacterium in 1922. Tetracycline and chloramphenicol, the most effective drugs to combat RMSF, were introduced in the 1940s.

**The Pathogen**

*Rickettsia rickettsii* is a fastidious, small, Gram-negative coccobacillus with a lipopolysaccharide cell wall. Because of *R. rickettsii*’s size it is difficult to stain and see with traditional bacterial stains; instead it is best viewed after being stained with Giemsa or Gimenez stains. *R. rickettsii* resides and is maintained in nature by a normal life cycle of transition between ticks and wild mammals where it affects the epithelial tissues of the body and unlike others in the *Rickettsia* family it also affects the nucleus of the cell. The primary disease carrier are hard ticks, which serve as the reservoir and vector, including American dog tick (*Dermacentor variabilis*), Rocky Mountain wood tick (*Dermacentor andersoni*), and brown dog tick (*Rhipicephalus sanguineus*). The bacterial pathogen does not need to be transmitted to a host and can be maintained transovarially across several tick generations: bacteria are maintained from mother to offspring and through developmental stages. The role of animals in the lifecycle of *R. rickettsii* is not well understood and several hypotheses exist as to whether animals serve as secondary reservoirs or as an amplifying host.

**Signs and Symptoms**

RMSF patients present a wide range of symptoms that include many organ systems: including systemic, cutaneous, cardiac, pulmonary, gastrointestinal, renal, neurological, ocular, and skeletal muscle. RMSF is very serious and most patients are affected by a moderate to severe illness with a significant proportion requiring hospitalization. Elderly patients are the most at risk. Even though the CDC considers RMSF a survivable disease, the mortality rate is around 0.7% to 5%. When hospitalization is required, 15% of patients don’t survive. Left untreated, today’s death rates are about 20% compared to the 87% death rate pre-1940s. As a general rule however, patients who are going to die
usually do so during the second week even with treatment[^6.7] , an exception is seen in the African American community where a fulminant death by the fifth day results from a glucose-6-phosphate dehydrogenase deficiency, with hemolysis as a key symptom.[^4.7] The incubation period of RMSF is 7 days with a range of 2 to 14 days.[^4.6.7] Initial clinical symptoms are very similar to those of other tick borne illnesses and as a result make early definitive diagnosis difficult and thus delaying treatments during the time when treatments are most effective.[^2.3.4.7] While considering RMSF as the primary disease of concern it should be realized that a *R. rickettsii* infection appears to be like many other infections, so care must be taken to consider and rule out typhus, ehrlichiosis, other rickettsial diseases, immune complex vasculitis, meningococcemia, thrombotic thrombocytopenia purpura, enterovirus infection, typhoid fever, leptospirosis, dengue, infectious mononucleosis, bacterial sepsis, gastroenteritis or acute abdomen, bronchitis and pneumonia.[^1.4] The death rate from RMSF has decreased dramatically from a nearly fatal disease to one that has a death rate of less than one percent.[^6] Suspicions have been raised about today’s death rate and the suspected result is in misdiagnosis of RMSF vs. other *Rickettsia* strains or even other bacterial infections that were misdiagnosed.[^6] More problematic are situations where death from *R. rickettsii* was not credited to RMSF and diagnosed as being something different because diagnostic criteria are not specific relying on serologic and immunohistochemical tests that can not specifically identify *R. rickettsii* precisely.
Treatment

With a possible period of incubation lasting up to 14 days (mean 7 days) delayed diagnosis and treatment of RMSF can result in serious long term health impairments or even death and so the decision to treat should not be delayed by waiting for a laboratory confirmation.\textsuperscript{2,3,4,7} \textit{R. rickettsii} has the capability of infecting almost the entire body with epithelial tissue destruction as the primary target.\textsuperscript{2,3,4,7} Because of the threat of death or other serious impairments, patients who present with a rash and a fever should be suspected of having a \textit{R. rickettsii} infection and admitted to the hospital and treated with the tetracycline and chloramphenicol, the current drugs of choice; which are currently the only RMSF medications proven to be effective.\textsuperscript{4,7} Diagnosis confirmations from the laboratory should not allow treatment to be delayed, ideally treatment should be started by the 5\textsuperscript{th} day after infection; after which mortality rates triple.\textsuperscript{2} Treatment should be continued for at least 2 to 3 days after all signs and symptoms have disappeared.\textsuperscript{4} Twenty-three percent of physicians delay treatment until the rash presentation; justifiably so because the correct antibiotics are generally used only 28\% to 42\% of the time.\textsuperscript{4,7} However, for those who are prone to serious complications and die within the second week, waiting for a rash to develop puts approximately 10\% of the affected individuals at serious risk as rash is only present 85-92\% of the time.\textsuperscript{2,3,4} A rash is created by blood vessels leaking under the skin and presenting at the wrists and ankles first then moving toward the central body.\textsuperscript{4} Inappropriate treatments can also lead to a condition known as acute disseminated encephalomyelitis (ADEM); also known as post infectious or postvaccinal encephalomyelitis where 2/3 of RMSF sufferers lose neurologic functions that range from mental changes to limb paralysis.\textsuperscript{8} ADEM is believed to result from an immune response that activates myelin-reactive T-cells that in turn migrate to the central nervous system and attack the myelin sheath.\textsuperscript{8} It is suspected that a special immune environment is responsible for the resulting ADEM and may be as simple as an incomplete drug dosing regiment.\textsuperscript{8} Tetracycline and chloramphenicol have a convenient dose schedule and a broad therapeutic range across all age groups.\textsuperscript{4,7} However, the use of antibiotics in the complete absence of symptoms is not recommended as it does not make economic sense nor is it supported from a epidemiology standpoint.\textsuperscript{7}
The development of safe and effective antibiotics to treat RMSF has created a situation of low priority in the research and development of vaccines. The current drugs have reduced the urgency and perceived RMSF threat overall. Currently the FDA (Food and Drug Administration) has not approved any vaccinations for any of the *Rickettsia* species.

**Avoidance**

The best way to avoid an RMSF infection is to avoid contact with ticks and their habitats like heavily wooded areas. It is often impractical however for many to avoid these habitats as there livelihood depends on it. Preventative measures can be employed to limit direct skin contact with ticks such as insect repellent that contains diethyltoluamide (DEET) or permethrin that can be applied to clothing. Wearing long sleeves and pants with the loose edges tucked in when appropriate also helps limit skin contact. Other measures that reduce the chances of a tick exposure include not sitting on the ground and staying in the center of the trail. Ticks are difficult to avoid when entering their environments so the second line of defense should be the removal of any ticks from the body via the “tick check”. Tick checks should be done outdoors before entering the house by wearing light colored clothing to improve visibility of ticks; remove outdoor clothing promptly and wash and dry on high heat; check for ticks in the areas they like to attach to such as behind the ear, around the neck, under the arm pits, around the groin and behind the knees; shower to remove any unattached ticks that have escaped the visual check. When a tick is attached to the skin it is important to remove it promptly as *R. rickettsii* can be transmitted from the tick to the host in about 6 hours. Tick removal is accomplished by gripping the tick as close to the skin as possible and gently pulling in a smooth consistent non- jerking motion to avoid breaking off part of the tick in the skin, or crushing the tick before placing it into a container of disinfectant. *R. rickettsii* can also be transmitted from the body parts or fluids of the tick so care must be taken to properly handle the tick to limit the possibility of *R. rickettsii* exposure. Alcohol is the recommended disinfectant and the tick should be dropped into a container containing some alcohol and sealed tightly.
Conclusion

More than 100 years has passed since the first cases of RMSF have been clinically described.\textsuperscript{4} Out of the ten commonly seen tick borne diseases in the United States, RMSF remains one of the most severe tick borne diseases with the infection rate increasing in prevalence in just the past few years.\textsuperscript{6} Because symptoms vary widely from individual to individual and affect virtually every organ system and a rash is not always present (10\% of infected people), diligence needs to be practiced by those who enter the wilderness and by the medical staff that treats affected individuals.\textsuperscript{3} Development of better first line medical treatments beyond tetracycline and chloramphenicol have the potential for reducing the numbers of people that are affected each year and should be pursued.\textsuperscript{7} Diagnosis via clinical signs and symptoms have limited effectiveness in definitive diagnoses which further supports the need for the development of vaccines.\textsuperscript{4} The deployment of early serological methods should prove to be more effective at definitive diagnosis as they would target specific antibodies of \textit{R. rickettsii} in the early stages of infection. However, simple precautions may be all that is necessary to limit and possibly prevent the contraction of RMSF and other tick-borne diseases.\textsuperscript{6,2}
REFERENCES:


