Rocky Mountain Spotted Fever (RMSF)

By Haley Pollock

Etiologic Agent: *Rickettsia rickettsii* ¹

Transmission: Rocky Mountain Spotted Fever is transmitted via the bite of a biological vector - the tick, and is considered a metazoonosis as it requires both a vertebrate and invertebrate organism to complete its life cycle ¹,²,³,⁴. Transmission of *R. rickettsii* can only occur if the tick remains attached for at least 4-6 hours ⁸.

Reservoirs: Ticks serve as both vectors and reservoirs for this particular disease although some small animals such as rodents and dogs have been identified as possible reservoirs ³,⁸.

General Characteristics of Microorganism: *R. rickettsii* works by infecting endothelial cells within the lining of blood vessels, without actually circulating in the blood - unless the infection is extremely severe ¹. *R. rickettsii* is an obligate intracellular, aerobic, unicellular, gram-negative coccobacilli bacterium that act as parasites on the eukaryotic cells of blood vessels ⁶, ⁹. *R. rickettsii* lacks a distinct nucleus and membrane-bound organelles and does not have the ability to form a spore ¹⁰. It’s membrane is largely composed of lipopolysaccharides with no structures for motility ¹⁰.

Key Tests for Identification: Due to the lethal risk of RMSF, the CDC recommends treatment to begin based on clinical signs and symptoms, and to later confirm the disease using laboratory tests. Due to the fact that RMSF typically does not circulate in blood, blood specimens are not very useful for detecting the organism. A PCR or immunohistochemical staining can be performed if a rash has manifested on the skin ¹. Antibodies are not present within the first week of illness so, positive testing for antibodies may not appear until the disease has already progressed ¹. The best test is the indirect immunofluorescence assay that reacts to the *R. rickettsii* antigen and this is normally performed in two parts with the first test performed during early onset and the second two to four weeks later ¹. The assay looks for the presence of IgG and IgM, both of which begin to rise after the first seven days of illness and may stay at higher levels weeks or even months after exposure to RMSF, which is why two samples are taken to measure the change in antibodies instead of simply the presence. ¹

Signs and Symptoms: Fever, headache, abdominal pain, vomiting, nausea, lack of appetite, conjunctival injection, and muscle pain¹. The spotted part of the name comes from a red to purple, petechial rash that may develop as a result although it is often absent for the first few days after exposure, or may never appear at all ¹. Approximately 90% of RMSF patients develop the rash at some point during the course of the illness, with about 10% never developing it at all ¹. The bite of a tick is fairly painless and so, it is not until symptoms develop, approximately 2-14 days after infection, that patients seek medical treatment ¹. “The disease often frequently begins as a sudden onset of fever (CDC, 2013)”, as the name implies, a fairly non-specific symptom and without identification of the bite it may take several visits before RMSF is diagnosed. Rocky
Mountain Spotted Fever has a wide list of symptoms that most patients present in many different combinations 1.

**Historical Information:** The genus Rickettsia does not derive from Latin as most classifications do, but is instead named after Howard Taylor Ricketts who first characterized and researched the disease from 1906 to 1909, shortly before his untimely death of typhus - another Rickettsial disease, in 1910 3,10,11. In an ironic turn of events, after funding for Rickett’s RMSF research dried up he travelled to Mexico to investigate the typhus epidemic where he eventually contracted the disease that would kill him 12. According to Warner and Marsh, the disease was “first described among Native Americans, soldiers, and settlers in the Bitterroot River and Snake River valleys of Montana and Idaho during the late 1890s 3. S. Burt Wolbach is credited with being the first to describe the structure of the etiological agent, originally wanting to use the name *Dermacentroxenus rickettsii* 13. In 1922, Emile Brumpt proposed the name *Rickettsia rickettsii* for the specific strain that caused RMSF, feeling that it belonged in that genus despite Wolbach disputing it 10. That same year, more extensive research began to be conducted in western Montana as multiple deaths and outbreaks occurred among an influential town, including the untimely death of the Governor’s daughter and son-in-law. Much of this research was conducted by the Rocky Mountain Laboratories - the source of part of the disease name 1.

**Virulence Factors:** Damage done to the infected endothelial cells lining blood vessels of all major tissues and organs lead to systematic injury in a patient, which is responsible for the wide array of symptoms that an infected patient may experience 11. Adherence to the host cell occurs via adhesin proteins on the outer membrane, upon which they phagocytosed by the host cell where *R. rickettsii* is able to escape the phagosome and enter the cytoplasm 17. The escape is thought to be mastered by an enzyme, but is not well understood 17. The spotted fever strain of rickettsia do not accumulate in large numbers and lyse the cell like their typhus counterpart, instead leaving the cell by “stimulating polymerization of host cell-derived actin tails” allowing themselves to become momentarily motile and push through the membrane 17.

**Control/Treatment:** Doxycycline, tetracycline, and chloramphenicol are all broad-spectrum antibiotics that can be used to treat bacterial infections within the body and are often the first line of chosen treatment - although it is most effective if administered within the first five days 1, 5, 9. RMSF is not communicable from human to human therefore, control of the disease involves simply controlling the vector population within the area 8. Promptly and properly removing a tick attached to a human can help prevent transmission, since the microbe needs a certain amount of time to transmit 8. Rocky Mountain spotted fever is “the most lethal and most frequently reported rickettsial illness in the United States” according to Master, Olson, Weiner, and Paddock and has been reported in nearly every state from except for Maine and Vermont. 11

**Prevention/Vaccinations:** Although Rocky Mountain Spotted Fever is largely preventable, it can be fatal, even in healthy persons, if treatment is not begun upon early diagnosis. There is currently no vaccine available, which is why early treatment with doxycycline and other broad-spectrum antibiotics are the standard if RMSF is suspected 7. Preventative measures include creating an environment that is less friendly towards tick population - removing leaf litter, keep
short grass, preventing deer, who are often carriers of ticks, away from neighborhoods or living areas. Checking areas of the body, such as the groin, armpits, neck, hairline, ears, for ticks whenever there is the possibility of contact as well as wearing light colored, long sleeved clothes, pants, and hats for protection is also a good idea when entering a possible tick environment. DEET is an effective repellent for ticks, although application must be done carefully with caution as it is a powerful chemical.

Local Cases or Outbreaks: Rocky Mountain spotted fever “has been a reportable disease in the United States since the 1920's” according to the Center for Disease Control. Incidence in the states has increased to over 6 cases per million as of 2010, although the proportion of cases resulting in death has lowered. Although RMSF has been reported in nearly all 50 states, over 60% of the cases are received from five states: North Carolina, Oklahoma, Arkansas, Tennessee, and Missouri - with N. Carolina and Oklahoma being the highest. Within an endemic region of North Carolina there was “a suggested annual incidence rate of 42 cases per 100,00 children aged 5-9 years.” In two other endemic areas of North Carolina an overall incidence of 14.59 cases per 100,000 population were identified over the span of two years - from 1979 to 1981, with 84% of those cases presenting the typical rash.

Global Cases or Outbreaks: There have been no documented cases of RMSF outside of the Americas, although the genus itself has been found across oceans. An outbreak occurred in Cordoba, Colombia with the first official report coming in 1937, where it was originally named Tobia fever after the village where it was first documented. In 2003 it reemerged in the same area, causing two fatalities which renewed interest in research and led to further identification of a 2005 outbreak on a military base outside Antioquia. Between February and March of 2007, a further four people died in the municipality of Los Cordobas. There were a total of 11 cases in a local population of 874 individuals resulting in a 1.25% prevalence and a 34% fatality rate, which was attributed to misdiagnosis and thus, lack of appropriate early antibiotic treatment.

Due to RMSF’s amorphous nature, it is believed that there has been a severe lack of reporting, and much underdiagnosing, resulting in numbers far below what is probably true.

Citation


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