Rocky Mountain Spotted Fever (RMSF)
RMSF is a serious illness that can be fatal in the first eight days of symptoms if not treated correctly, even in previously healthy people. The progression of the disease varies greatly. RMSF is caused by *Rickettsia rickettsii*. Symptoms typically begin 2-14 days after the bite of an infected tick. A tick bite is usually painless and about half of the people who develop RMSF do not remember being bitten. RMSF frequently begins as sudden onset of fever & headache. Treatment is most effective at preventing death if started in the first five days of symptoms. Diagnostic tests, especially tests based on the detection of antibodies, will frequently appear negative in the first 7-10 days of illness. There is no test available at this time that can provide a conclusive result in time to make important decisions about treatment.

Physician Diagnosis
Providers often must use their judgment to treat patients based on clinical suspicion alone, relying on important information (such as recent tick bites, exposure to high grass and tick-infested areas, contact with dogs, similar illnesses in family members or pets, or history of recent travel to areas of high incidence) in the patient’s history and physical examination to aid clinical suspicion.

Clues such as a low platelet count (thrombocytopenia), low sodium levels (hyponatremia), or elevated liver enzyme levels are often helpful predictors of RMSF but may not be present in all patients. After a suspect diagnosis is made on clinical suspicion and treatment has begun, specialized laboratory testing should be used to confirm the diagnosis of RMSF. Treatment should never be delayed pending the receipt of laboratory test results, or be withheld on the basis of an initial negative finding for *R. rickettsii*.

Infection in Children
Children with RMSF infection may experience nausea, vomiting, and loss of appetite. Children are less likely to report a headache, but more likely to develop an early rash than adults. Other frequently observed signs and symptoms in children with RMSF are abdominal pain, altered mental status, and conjunctival injection. Occasionally, symptoms like cough, sore throat, and diarrhea may be seen, and can lead to misdiagnosis.

Common symptoms Note: Risk of misdiagnosis when no rash or atypical rash are present
Few people develop all symptoms Number & combination of symptoms varies greatly.

- Fever
- Rash 2-5 days after fever
  - May be absent (below)
- Headache
- Nausea
- Vomiting
- Acute abdominal pain
  - May mimic appendicitis,
  - Muscle pain
  - Lack of appetite
  - Conjunctival infection
    (red eyes)

**Classic case:**
Rash 2-5 days after fever onset
- Small, flat, pink, non-itchy spots (macules)
- Wrists, forearms, ankles
- Spreads to trunk, sometimes the palms & soles

* Rash
90% of RMSF patients develop some type of rash, some after treatment should have already begun. Considering RMSF if other signs and symptoms support a diagnosis is important, even if a rash is not present. The red to purple, spotted (petechial) rash of RMSF isn’t usually seen until the 6th day or later after onset of symptoms & occurs in 35-60% of patients with the infection. This is a sign of progression to severe disease. Every attempt should be made to begin treatment before petechiae develop.
Laboratory Confirmation

*R. rickettsii* infects the endothelial cells that line blood vessels, and doesn't circulate in large numbers in the blood unless the patient has progressed to a very severe infection. Hence, blood specimens (whole blood, serum) are not always useful for detection through polymerase chain reaction (PCR) or culture. PCR or immuno-histochemical (IHC) staining can be performed on a skin biopsy taken from a rash site. This can often deliver a rapid result with good sensitivity (70%) when applied to tissue specimens collected during the acute phase of illness and before antibiotic treatment has been started, but a negative result should not be used to guide treatment decisions. PCR, culture, and IHC can also be applied to autopsy specimens (liver, spleen, kidney, etc.). Routine hospital blood cultures cannot detect *R. rickettsii*.

During RMSF infection, antibodies develop, with detectable antibody titers usually observed by 7-10 days after illness onset. Note: antibodies are not detectable in the first week of illness in 85% of patients (the critical period), and a negative test during this time does not rule out RMSF as a cause of illness.

The gold standard serologic test for diagnosis of RMSF is the indirect immunofluorescence assay (IFA) with *R. rickettsii* antigen, performed on two paired serum samples to demonstrate a significant (four-fold) rise in antibody titers. The first sample should be taken as early in the disease as possible, preferably in the first week of symptoms, and the second sample should be taken 2 to 4 weeks later. In most RMSF cases, the first IgG IFA titer is typically low or negative, and the second typically shows a significant (fourfold) increase in IgG antibody levels. IgM antibodies usually rise at the same time as IgG near the end of the first week of illness and remain elevated for months or even years. Also, IgM antibodies are less specific than IgG antibodies and more likely to result in a false positive. For these reasons, physicians requesting IgM serologic titers should also request a concurrent IgG titer.

Both IgM and IgG levels may remain elevated for months or longer. Up to 10% of currently healthy people in some areas may have elevated antibody titers due to past exposure to *R. rickettsii* or similar organisms. Therefore, if only one sample is tested it can be difficult to interpret, whereas two paired samples taken weeks apart demonstrating a significant (four-fold) rise in antibody titer provide the best evidence for a correct diagnosis of RMSF.

Treatment

Doxycycline is the first line treatment for adults & children of all ages and should be initiated immediately. Treatment is most effective at preventing death if doxycycline is started in the first 5 days of symptoms. Treatment, therefore, must be based on clinical suspicion alone. Use of antibiotics other than doxycycline is associated with a higher risk of fatal outcome.

If the patient is treated within the first 5 days of the disease, fever generally subsides within 24-72 hours. Failure to respond to doxycycline suggests that the patient’s condition might not be RMSF. Severely ill patients may require longer periods before their fever resolves, especially if they have experienced damage to multiple organ systems. Doxycycline resistance or relapse after the completion of recommended course of treatment has not been documented to occur.

Recommended Dosage

Doxycycline is the first line treatment for adults and children of all ages:

- **Adults:** 100 mg every 12 hours
- **Children under 45 kg (100 lbs):** 2.2 mg/kg body weight given twice a day

Patients should be treated for at least 3 days after the fever subsides and until there is evidence of clinical improvement. Standard duration of treatment is 7-14 days.
Treating Children
The use of doxycycline to treat suspected RMSF in children is standard practice recommended by both CDC and the AAP Committee on Infectious Diseases. Use of antibiotics other than doxycycline increases the risk of patient death. Unlike older tetracyclines, the recommended dose and duration of medication needed to treat RMSF has not been shown to cause staining of permanent teeth, even when five courses are given before the age of eight. Healthcare providers should use doxycycline as the first-line treatment for suspected Rocky Mountain spotted fever in patients of all ages.

Other Treatments
In cases of life threatening allergies to doxycycline and in some pregnant patients for whom the clinical course of RMSF appears mild, chloramphenicol may be considered as an alternative antibiotic. Oral formulations of chloramphenicol are not available in the United States, and use of this drug carries the potential for other adverse risks, such as aplastic anemia and Grey baby syndrome. Furthermore, the risk for fatal outcome is elevated in patients who are treated with chloramphenicol compared to those treated with doxycycline. Other antibiotics, including broad spectrum antibiotics are not effective against R. rickettsii, and the use of sulfa drugs may worsen infection.

There is no evidence that prophylaxis (preventive treatment) is effective. It may simply delay onset.

Other Considerations
The clinical presentation for RMSF can also resemble other tick-borne diseases, such as ehrlichiosis and anaplasmosis. Similar to RMSF, these infections respond well to treatment with doxycycline. Providers should order diagnostic tests for additional agents if clinical history and geographic association warrant.

Long-term Health Problems
Patients who had a particularly severe infection requiring prolonged hospitalization may have long-term health problems caused by this disease. *Rickettsia rickettsii* infects the endothelial cells that line the blood vessels, resulting in "vasculitis", and bleeding or clotting in the brain or other vital organs may occur. Loss of fluid from damaged vessels can result in loss of circulation to the extremities and could ultimately lead to amputation. Severe vasculitis in the first two weeks of illness may also result in permanent long-term health problems such as profound neurological deficits, or damage to internal organs. Those who do not have this kind of vascular damage in the initial stages of the disease typically recover fully within several days to months.

For more in-depth information about signs and symptoms of RMSF, please visit http://www.cdc.gov/mmwr/preview/mmwrhtml/rr5504a1.htm

Source: CDC.gov