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# Spotted Fever Rickettsiosis in Dogs: An Update

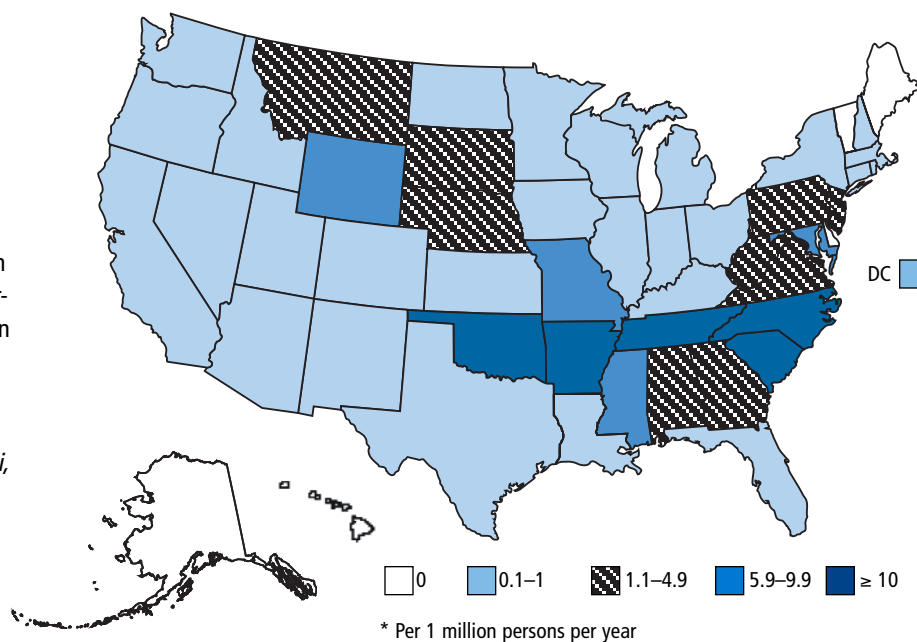
## **P** Profile

### Definitions

Spotted fever group (SFG) *Rickettsia* are small, vector-borne, obligately intracellular bacteria. There are more than 20 species belonging to this group and most have been discovered recently. SFG *Rickettsia* are important causes of emerging infectious disease in people.<sup>1</sup>

*Rickettsia rickettsii*, the cause of Rocky Mountain spotted fever (RMSF) and *R. conorii*, the cause of Mediterranean spotted fever, have been shown to infect and cause disease in dogs.<sup>2,3</sup> In addition, dogs are sentinels for *R. rickettsii* and *R. conorii* infection in people.<sup>4-6</sup> Canine RMSF is well characterized and the focus of this article; however, veterinarians should be aware that infection with novel species in dogs is likely.

**Incidence/Prevalence.** The incidence of rickettsioses in people is increasing due to disease caused by species previously thought to be nonpathogenic, new forms of disease caused by recently discovered species, and spread into nonendemic regions by novel vectors. Human RMSF is a reportable disease in the U.S. Counties in some states also require reporting for dogs, particularly during suspected outbreaks. Signs of illness may become evident in dogs before or coinciding with infection in people living in the same household, and exposure can be detected in



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**Average annual incidence of RMSF reported by state: 1997–2002**  
Courtesy Centers for Disease Control and Prevention

dog populations before human epidemics.<sup>4,5,7</sup> Veterinarians, therefore, play a pivotal role in preventing illness in both dogs and people.

**Geographic Distribution.** The geographic distribution of RMSF is expanding. Historically, most cases occur in the southeast and south central U.S. (Figure 1). Disease distribution followed the primary vectors, *Dermacentor variabilis* and *D. andersonii*. However, *Rhipicephalus sanguineus*, a tick that normally prefers to feed on dogs and is ubiqui-

tously distributed, caused a recent outbreak of RMSF in people in a nonendemic area of Arizona.<sup>8</sup> Furthermore, other tick species in the U.S. are also infected with *R. rickettsii*. Veterinarians practicing in nonendemic areas should be vigilant for disease caused by novel tick vectors.<sup>9</sup>

### Signalment

Young and purebred dogs are overrepresented in some studies. Severe disease may occur in English springer spaniels with phosphofructokinase deficiency and in German

RMSF = Rocky Mountain spotted fever; SFG = spotted fever group

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shepherd dogs. No sex predilection has been definitively documented.<sup>3,10</sup>

### Risk Factors

Although disease can occur any time of year, most cases of RMSF are reported from April through October, months of peak tick activity. Dogs living outdoors are at increased risk.<sup>3,10</sup>

### Pathophysiology

Tick feeding activates the organism, which is transmitted in saliva. Because the organism infects endothelial cells, clinical signs are consistent with vasculitis—manifesting as disordered primary hemostasis, edema, and microthrombosis. Thrombocytopenia is common due to vasculitis and immune-mediated platelet destruction. Low numbers of organisms circulate in blood for a short period of time after infection (13 days). This period corresponds to the time that clinical signs are observed.<sup>11,12</sup> Accordingly, RMSF is an acute disease; chronic infection has not been documented in dogs. Antibody titers may be long-lived, and immunity to infection is likely lifelong.

### Signs

A range of signs can occur that may be non-specific.

**History.** Often, there is no known history of a tick bite. Lethargy and anorexia are common and can be the only presenting complaints. Vomiting and diarrhea may be reported. Melena may be observed, as well as various central nervous system (CNS) abnormalities, including vestibular disease and seizures. Dramatic and rapid weight loss has been described.<sup>3,10,13</sup>

### Physical Examination.

- Fever is often present, but not always.
- Ocular signs are frequently observed, and may include discharge, scleral and con-

junctival injection and hemorrhage, conjunctivitis, uveitis, retinal hemorrhage, and retinitis (**Figure 2**).

- Lymphadenomegaly is common.
- Respiratory abnormalities include nasal discharge, epistaxis, tachypnea, and dyspnea.
- Mucocutaneous and cutaneous abnormalities include petechiae, ecchymosis, edema, hyperemia, and necrosis.
- Orchitis and scrotal edema, hyperemia, and epididymal pain are common in intact dogs.
- Generalized myalgia and arthralgia can be observed.
- CNS abnormalities, which can be focal or generalized, include hyperesthesia, ataxia, vestibular signs, stupor, seizures, and coma.
- Arrhythmias may be noted.
- Microvascular hemorrhage, thrombosis, hypotension, oliguric renal failure, cardiovascular collapse, and brain death occur terminally.<sup>3,10,13</sup>

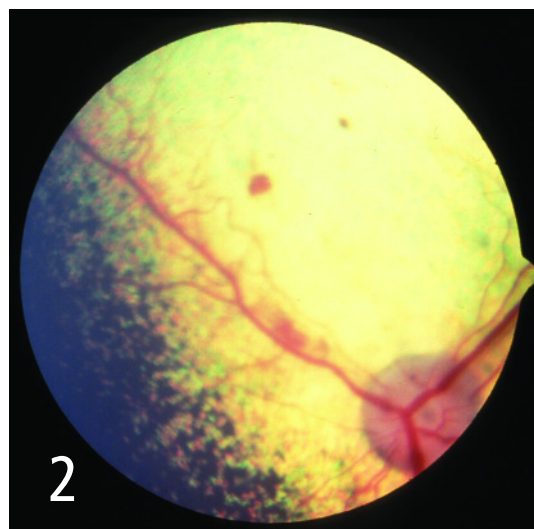


### Diagnosis

A high index of suspicion based on clinical signs is necessary because treatment must be instituted before definitive diagnostic tests confirm infection.<sup>3,11</sup>

### Differential Diagnosis

- Infection with other tick-borne agents (eg, *A phagocytophilum*; *Ehrlichia*, *Bartonella*, and *Babesia* species; *Borrelia burgdorferi*)<sup>3</sup>
- Sepsis, systemic inflammatory response syndrome (SIRS)
- *Leptospirosis*
- Other causes of vasculitis and thrombocytopenia
- Other causes of CNS disease



Retinal hemorrhages in a dog with RMSF

### Laboratory Findings

(Most frequently encountered findings are marked with an asterisk.<sup>3,13</sup>)

- Thrombocytopenia most common (83% of patients)\*
- Leukocytosis (neutrophils may have toxic change)\*
- Nonregenerative anemia
- Hypoalbuminemia\*
- Elevated alkaline phosphatase\*
- Hyponatremia
- Hyperbilirubinemia
- Coagulation abnormalities
  - Prolonged prothrombin time
  - Prolonged activated partial thromboplastin time\*
  - Elevated fibrinogen\*
  - Elevated fibrinogen degradation products
  - Disseminated intravascular coagulation (uncommon)
- Proteinuria
- Hematuria\*
- Bilirubinuria\*
- Pyuria
- Mixed-cell pleocytosis
- Neutrophilic polyarthritis

CNS = central nervous system; DIC = disseminated intravascular coagulation; PCR = polymerase chain reaction; RMSF = Rocky Mountain spotted fever; SFG = spotted fever group; SIRS = systemic inflammatory response syndrome

## Imaging

- Findings depend on organs involved.
- Thoracic radiographs may show an unstructured interstitial pattern.

## Diagnostic Tests

General considerations:

- Handle specimens with care and mark clearly as biohazards.
- Contact with or aerosolization of rickettsemic blood should be avoided.
- Most tests do not differentiate among species of SFG *Rickettsia*:
  - Species presumed based on geographic locale (eg, seropositive patients are presumed to be infected with *R. rickettsii* in the western hemisphere).
  - Other species of SFG *Rickettsia* are present in the United States.<sup>14</sup>
  - Novel species will not be recognized with routine diagnostic testing.

## Serology

### Microimmunofluorescence

- Microimmunofluorescence testing of acute and convalescent samples documenting a fourfold change in titer is the gold standard for diagnosis.
- Do not rule out diagnosis based on a single negative titer.
  - Can be negative acutely<sup>3,11</sup>
  - Clinical signs can occur before seroconversion.
- A positive titer does not confirm active infection.
  - Antibodies cross-react among other SFG *Rickettsia*.
  - Exposure to other nonpathogenic (or less pathogenic) *Rickettsia* symbionts of ticks is common.<sup>14,15</sup>
  - Cross-reactivity occurs in dogs and people infected with *Bartonella henselae*.<sup>16</sup>
  - Previous infection with *R. rickettsii* can result in long-lived antibody titers.<sup>11,17</sup>

### Polymerase Chain Reaction (PCR)

- PCR can be used to detect infection in

some acutely infected seronegative dogs.

- Negative PCR does not rule out infection; low numbers of organisms circulate for a short period of time.
- A sensitive PCR that detects and differentiates among SFG *Rickettsia* infecting dog blood has been described.<sup>18</sup>
- Studies regarding the sensitivity and specificity of other PCR assays used in dogs have not been published.

### Immunohistochemistry/Gimenez Staining

- Can confirm infection using tissue samples.
- Does not differentiate species.



## Treatment

### Inpatient or Outpatient

Most patients require hospitalization.

### Medical Therapy

The general medical approach to therapy is outlined in **Medications**.

Inappropriate antibiotic therapy may increase morbidity and mortality.<sup>3</sup> The use of trimethoprim-sulfamethoxazole may even worsen the disease. Delaying therapy also increases the risk for complications; therefore, therapy must begin based on clinical suspicion before diagnostic tests confirm infection. Aggressive supportive care for complications such as DIC and thrombosis may be necessary. Cautious use of fluids and colloids may be warranted in some cases; however, avoid exacerbation of edema.



## Medications

### Antibiotics

#### Doxycycline

(5 mg/kg PO Q 12 H for 7–14 days)

- Treatment of choice
- Parenteral administration may be necessary transiently in debilitated patients or

those with vomiting.

- Effective empiric therapy for *A. phagocytophilum*, *B. burgdorferi*, and *Ehrlichia* infections (differential diagnoses for RMSF)
- Coinfection may require a longer treatment course.
- Theoretical risk for tooth discoloration in puppies not well documented.

### Chloramphenicol

(15–30 mg/kg PO Q 8 H for 7–14 days)

- Effective in experimentally infected dogs
- Parenteral administration may be necessary transiently in debilitated patients or those with vomiting.
- May be less effective than doxycycline for treating RMSF in people, and less effective against *E. chaffeensis* and *A. phagocytophilum* (differential diagnoses for RMSF) than doxycycline (*in vitro*)<sup>19</sup>
- Has been suggested for use in infected puppies, but caution is warranted.
- Adverse side effects
  - Bone marrow suppression
  - Risk to humans: Aplastic anemia (wear gloves)

### Enrofloxacin

(5 mg/kg PO Q 12 H for 7–14 days)

- Effective in experimentally infected dogs
- Not for use in young animals (cartilage abnormalities)
- Not effective against *E. canis* (differential diagnosis for RMSF)<sup>20</sup>

### Corticosteroids

- Controversial; antiinflammatory and immunosuppressive doses did not affect outcome but rickettsemia was prolonged in sublethally experimentally infected dogs.<sup>21</sup>
- Antiinflammatory doses have been used in dogs with severe CNS manifestations and may also be necessary in dogs with ocular abnormalities.<sup>13, 22</sup>

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## Follow-Up

- Response to appropriate antibiotic therapy is very rapid (24–48 hours).
- Coinfection with *B burgdorferi*, *E canis*, *E ewingii*, *E chaffeensis*, *Babesia canis*, and *Bartonella* species should be considered in dogs with severe or prolonged clinical signs.<sup>3</sup>
- Residual CNS and other deficits may occur in severely affected patients.
- Convalescent titers should be drawn 2 to 3 weeks after initial sample.

## Prognosis

The prognosis for dogs with RMSF is good to excellent if diagnosed and treated with appropriate antibiotics and supportive care early.<sup>3,13</sup>



## In General

## Relative Cost

Diagnostic workup and treatment: \$\$–\$\$\$

### Cost Key

\$ = < \$100	\$\$\$\$ = \$500–\$1000
\$\$ = \$100–\$250	\$\$\$\$\$ = > \$1000
\$\$\$ = \$250–\$500	

## Client Education

- Communicate with owners and physicians that infections in dogs may precede tick-transmitted infection in owners.
- Instruct clients to remove ticks properly and avoid crushing to prevent exposure to infected hemolymph (details on proper removal techniques are available at [cdc.gov/ncidod/lyme/ld\\_tickremoval.htm](http://cdc.gov/ncidod/lyme/ld_tickremoval.htm)).
- Educate regarding use of tick control and prevention for owners and pets

EDTA = ethylenediaminetetraacetic acid; PCR = polymerase chain reaction; RMSF = Rocky Mountain spotted fever; SFG = spotted fever group



## Diagnosis & Treatment

Clinical signs and laboratory abnormalities consistent with RMSF\*



Collect EDTA for PCR# and serum for serologic testing+

Consider testing for other tickborne agents



Treat with doxycycline and supportive care++



Collect convalescent serum sample 21–28 days after presentation



4-fold change in titer or positive PCR = diagnosis confirmed

\* If atypical or severe signs are observed, test for coinfection and consider sequencing PCR product for *Rickettsia* species identification

# Negative PCR does not rule out infection  
+ Negative acute serology does not rule out infection

++ If response to therapy is not rapid, test for coinfection and revisit diagnosis

## Future Considerations

Novel and well characterized species of SFG *Rickettsia* are important causes of emerging infectious disease in dogs and people. Furthermore, *R rickettsii* is considered a potential bioterrorist agent.<sup>22</sup> Because dogs are sentinels for infection, veterinarians can play an important role in detecting, defining, and preventing illness in their canine patients and their human companions. ■

See Aids & Resources, back page, for references, contacts, and appendices.

Article archived on [cliniciansbrief.com](http://cliniciansbrief.com)

## Hematology Analyzer

The new **VET FOCUS 5**

from Scil Animal Care

Company GmbH ([scilvet.com](http://scilvet.com))

promises precise, accurate blood analysis in 2 minutes for about \$2 per sample. The analyzer hits cells with 2 electrical currents: the first—low-voltage impedance for cell counting and sizing—is followed by a high-voltage current that reviews the internal cell complexity, providing a 5-part white blood cell differential. The analyzer also features proprietary diluents and lyses that allow multiple-species analysis.—Press release 3/2009



## Online Pharmacy Accreditation

The National Association of Boards of Pharmacy ([nabp.net](http://nabp.net)) recently launched Veterinary Verified Internet Pharmacy Practice Sites (Vet-VIPPS), a program to accredit online veterinary pharmacies. Pharmacies displaying the seal must demonstrate they meet criteria for protection of patient privacy, authentication and security of prescription orders, adhere to a quality assurance policy, and provide meaningful consultation between clients and pharmacists.—Press release 3/2009

## Rapid Rabies Screen

**RABIES RAPID** (rapid antibody portable immunodetection) by Dyne Immune, LLC ([dyneimmune.com](http://dyneimmune.com)) detects the presence of rabies in animal saliva within 30 minutes. According to Dyne

Immune CEO V. James DeFranco, MD, "The screen allows veterinarians, animal control officers, and other professionals to check for rabies in animals that are still alive, eliminating the long wait (10 to 14 days) and hefty price tag associated with typical postmortem rabies testing." —Press release 2/2009

