Emerging Spotted Fever Rickettsioses in the United States

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KEYWORDS

• *Rickettsia* • Canine • Feline • Vasculitis • Thrombocytopenia

KEY POINTS

- Rocky Mountain spotted fever (RMSF), caused by *Rickettsia rickettsii*, causes acute, potentially fatal, febrile disease in dogs, similar to the disease it causes in people.
- Both PCR and serology may be negative at the time of presentation when dogs are ill.
- Empiric treatment of suspected cases with doxycycline before confirming the diagnosis is important.
- The role of other spotted fever group rickettsia as disease-causing agents in dogs, cats, and people in the United States is being elucidated.
- Preventing parasitism of dogs and cats by fleas and ticks is important for human and animal health.

Abbreviations	
RMSF	Rocky Mountain Spotted Fever
PCR	Polymerase Chain Reaction
SFG	Spotted Fever Group
TG	Typhus Group
CDC	Center for Disease Control and Prevention
aPTT	activated Partial Thromboplastin Time
PT	Prothrombin Time
DIC	Disseminated Intravascular Coagulation

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INTRODUCTION

Rickettsia species are obligately intracellular alpha-proteobacteria belonging to the genus *Rickettsia,* family *Rickettsiaceae,* and order *Rickettsiales*. There are currently 29 named species of *Rickettsia,* with many more proposed species based primarily on genotypic characterization (http://www.bacterio.net/)[1]. *Rickettsia* spp. have historically been divided into the spotted fever group (SFG) the typhus group (TG), and an ancestral group. The division between the spotted fever and typhus groups is based on clinically relevant genotypic and phenotypic characteristics. These include, but are not limited to, differences in disease manifestations, the host's serologic response to the organisms, and the types of vectors that transmit them.

Most of the SFG *Rickettsia* are tick-transmitted, while members of the TG are flea or louse transmitted. *Rickettsia felis* and *Rickettsia akari* have been considered, and are still referred to by some, as members of the SFG. However, they share genotypic and clinically relevant features with both the SFG and TG *Rickettsia*. For example, *R. felis* and *R. akari* are flea and mite transmitted, respectively, and the diseases they cause in people are distinct from other spotted fever rickettsioses. In 2008 it was proposed that be placed in a separate "transitional" group based on phylogenomic analysis.[2] A recent analysis of genomic evolution of arthropod-associated *Rickettsia* suggests that these organisms may belong to a phylogenetically distinct spotted fever group.[3]

Historically, SFG *Rickettsia* have been considered pathogenic or nonpathogenic. The most well-described pathogenic SFG *Rickettsia* that infects people and dogs in the Americas is *R. rickettsii*, the cause of Rocky Mountain spotted fever (RMSF). In Europe, Africa, Asia, and the Middle East, *Rickettsia conorii* is responsible for causing similarly severe spotted fever rickettsioses, Mediterranean spotted fever. Mediterranean Spotted Fever has also been described in dogs.[4,5] Infections with several other species of SFG *Rickettsia* have been described in people with spotted-fever-like illnesses in recent years.[1,6–14] Thus, the spotted fever rickettsioses are considered important emerging infectious diseases in the United States and globally.[1,15] Some of these novel rickettsioses are caused by newly discovered species while others have been associated with species previously thought to be nonpathogenic endosymbionts of ticks. Disease caused by "classic" SFG *Rickettsia* like *R. rickettsii* is also considered "emerging" due to increasing prevalence in expanding geographic locales.[13,14,16]

CANINE ROCKY MOUNTAIN SPOTTED FEVER

Epidemiology

Illness caused by *R. rickettsii* is very well characterized in dogs and is quite similar to Rocky Mountain spotted fever (RMSF) in people. *Rickettsia rickettsii* is transmitted by several hard (Ixodid) ticks including *Dermacentor variabilis* (American dog tick), *Dermacentor andersoni* (Rocky Mountain wood tick), *Amblyomma americanum* (lone star tick), *Amblyomma cajennense* (Cayenne tick), and *Rhipicephalus sanguineus* (brown dog tick). Historically, the geographic distribution of RMSF in the United States has primarily followed that of its primary tick vectors in the region, *D. variabilis* and *D. andersoni.* According to the Center for Disease Control and Prevention (CDC), Arkansas, Missouri, North Carolina, Tennessee, and Virginia account for most cases (cdc.gov and **Fig. 1**).Most cases of canine and human RMSF are reported from spring to late summer, months of peak *Dermacentor* tick activity. Dogs living outdoors, particularly those with access to shrubs and high grass, are at increased risk.

Increasing travel and the effects of climate change on tick populations and habitats are changing the geographic distribution of RMSF and other emerging infectious

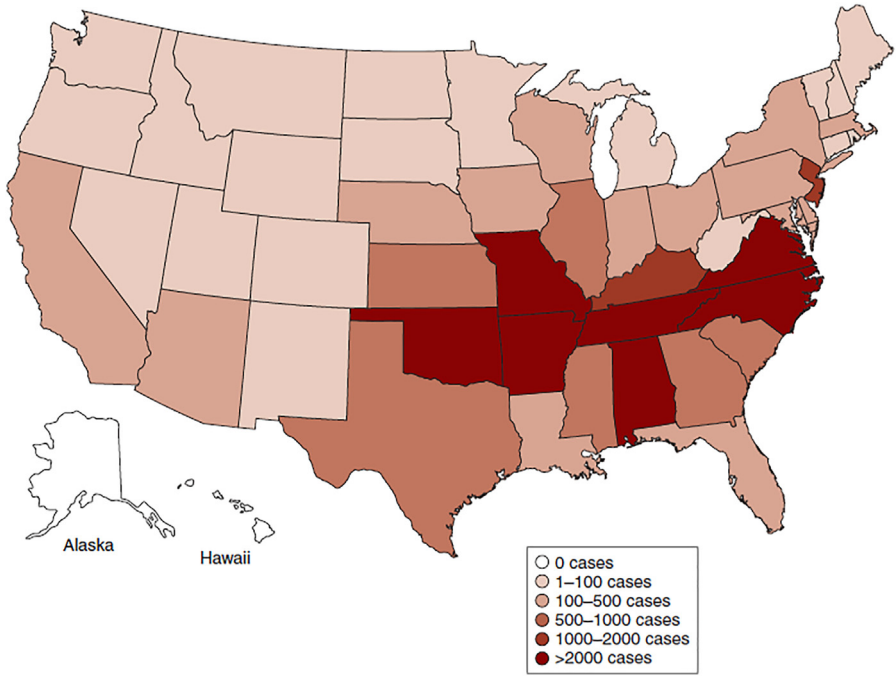


Fig. 1. Geographic distribution of the incidence of spotted fever group rickettsioses in people in the United States, 2010 to 2019. (Used with permission from Ch 46. Spotted Fever Rickettsioses, Flea-borne rickettsioses and Typhus. Kidd L., Breitschwerdt EB. Greene's Infectious Diseases of the Dog and Cat 5th Edition. Ed. JE Sykes Elsevier 2022.)

diseases. For example, in the early 2000s, a fatal outbreak of RMSF in people occurred in a nonendemic area of Arizona.[16] The outbreak was caused by *Rh. sanguineus*. Retrospectively, it was shown that infection existed in the dog population before the fatal outbreak in people.[17] The seasonal incidence of cases in this region is longer than in other regions of the United States.(cdc.gov/rmsf/stats) This is thought to be due to differences in the activity of *Rh. sanguineus* compared with *Dermacentor* ticks.

Rhipicephalus sanguineus is also the primary vector of *R. rickettsii* in Mexico. In South America, *Amblyomma* species are the main vectors. *Amblyomma* ticks are also potential vectors in the United States.[18,19] Veterinarians should consider the possibility of transmission by novel vectors if dogs present with clinical signs of RMSF in nonendemic areas or at an unusual time of year.

Pathophysiology

Rickettsia rickettsii infects endothelial cells. The resulting vasculitis contributes to the development of disordered primary hemostasis, tissue edema, hypovolemia, and microthrombosis. Thrombocytopenia is common and occurs due to vasculitis and possibly immune-mediated platelet destruction.[20] Increased vascular permeability and associated edema and hypovolemia result from the disruption of adherens junctions, endothelial cell death, and expression of inflammatory cytokines. Organisms also induce changes in platelet adherence to endothelium, increased tissue factor expression, increased plasminogen activator inhibitor and cause the release of von-Willebrand factor, all of which likely contribute to microthrombosis.[21,22]

Clinical findings

Rocky Mountain spotted fever is an acute disease. Chronic infection has not been documented in naturally infected dogs. However, recrudescence of infection has been documented in experimentally infected dogs.[23] Low numbers of *Rickettsia* circulate in blood free or in detached endothelial cells for a short period of time after infection. This is the time that clinical signs are observed. Coinfection with other vector-borne agents is common and should be considered if the clinical presentation is atypical, there is an incomplete response to doxycycline therapy or if clinical signs have been present chronically.

Because *R. rickettsii* infects endothelial cells, vasculitis is the major clinical sign associated with infection. Due to variation in the extent and severity of vascular injury among dogs, a range of signs can occur, and disease manifestations are initially mild and nonspecific. The nonspecific nature of the clinical signs makes diagnosis difficult. This is very important because a delay in diagnosis and appropriate antimicrobial therapy dramatically increases morbidity and mortality in people and in dogs.[24,25] Therefore, the clinician must have a high index of suspicion to correctly diagnose and treat this

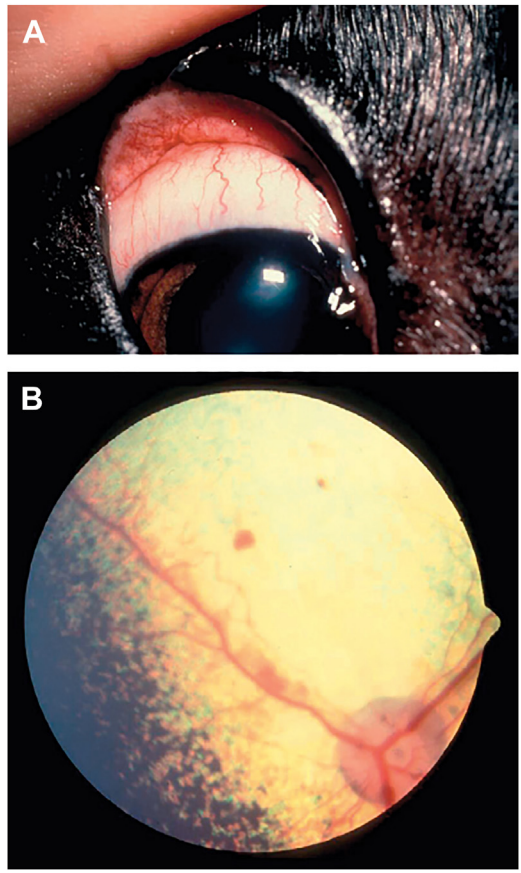


Fig. 2. Ocular complications in dogs with RMSF. *(A)*, Conjunctival hyperemia and scleral injection. *(B)*, Retinal hemorrhages. (Used with permission from Ch 46. Spotted Fever Rickettsioses, Flea-borne rickettsioses and Typhus. Kidd L., Breitschwerdt EB. Greene's Infectious Diseases of the Dog and Cat 5th Edition. Ed. JE Sykes Elsevier 2022.)

disease. This can be difficult because there is often no known history of a tick bite.[24] Lethargy and anorexia are common and may be the only clinical signs. Vomiting and diarrhea occur frequently, which is case context that unfortunately can lead clinicians down a diagnostic path that does not include testing for vector-borne disease. Melena may also occur. Central nervous system abnormalities including vestibular disease and seizures may be observed. Dramatic and rapid weight loss has been described.

Fever and ocular abnormalities are common physical examination findings. Ocular signs may include mucopurulent discharge, scleral and conjunctival injection and hemorrhage, conjunctivitis, uveitis, retinal hemorrhage, and retinitis (Fig. 2). Lymphadenomegaly, splenomegaly, nasal discharge, epistaxis, tachypnea, dyspnea, petechiae, ecchymosis, peripheral edema, hyperemia, and necrosis may occur. Cutaneous lesions are not always present in dogs or people. Orchitis and scrotal edema, hyperemia, and epididymal pain are common in intact male dogs. Generalized myalgia and arthralgia can be observed. Central nervous system abnormalities can be focal or generalized and include paraparesis, tetraparesis, ataxia, hyperesthesia, central or peripheral vestibular signs, stupor, seizures, and/or coma. Arrhythmias may be noted. Microvascular hemorrhage, thrombosis, hypotension, oliguric renal failure, cardiovascular collapse, and brain death can occur in severe cases. Thoracic radiographs may show an unstructured interstitial pattern.[26]

Laboratory testing

Importantly, treatment must be instituted before definitive diagnostic tests confirm infection. Because direct inoculation into blood or aerosolization can cause infection, all specimens should be handled with care and marked clearly as biohazards. Avoid needle sticks, contact with cuts in the skin, and aerosolization of rickettsemic blood.

Complete blood counts commonly show thrombocytopenia but it does not occur in all dogs with RMSF. Leukopenia or leukocytosis may be observed. Neutrophils may have toxic change. Nonregenerative anemia may be present. Serum biochemical abnormalities may include hypoalbuminemia, elevated alkaline phosphatase, hyponatremia, and mild hyperbilirubinemia. Prolonged aPTT, PT, and elevated fibrinogen and fibrin degradation products may occur. DIC is uncommon. Urinalysis results are variable and may include proteinuria, hematuria, bilirubinuria, and pyuria. Granular casts can be observed. Cerebral spinal fluid analysis may reveal a mixed cellular, neutrophilic, or lymphocytic pleocytosis. Arthrocentesis may reveal neutrophilic polyarthritis.

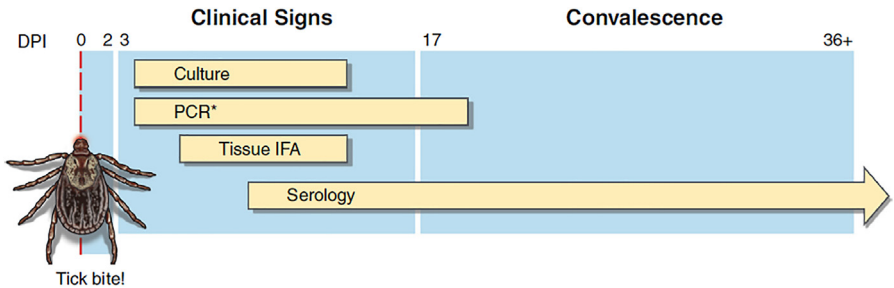


Fig. 3. Timing in relation to day postinfection (DPI) that clinical signs and diagnostic tests for *Rickettsia rickettsii* may be positive in an infected dog. *Further studies are needed to determine exactly how DNA can be detected in peripheral blood after infection. (Used with permission from Ch 46. Spotted Fever Rickettsioses, Flea-borne rickettsioses and Typhus. Kidd L., Breitschwerdt EB. Greene's Infectious Diseases of the Dog and Cat 5th Edition. Ed. JE Sykes Elsevier 2022.)

Cytologic examination of enlarged lymph nodes is consistent with reactive lymphoid hyperplasia.

Active infection with an SFG *Rickettsia* is confirmed in a patient with compatible acute clinical signs and demonstration of the organism using PCR or immunohistochemistry, or documentation of seroconversion. Importantly, serology and PCR can be negative at the time of testing because clinical signs can occur before seroconversion, and organisms circulate transiently in blood in low number (**Fig. 3**).[27] Infection also cannot be definitively diagnosed by documenting a single positive titer because of cross-reactivity with nonpathogenic SFG *Rickettsia* and the potential for long-lived antibody levels after infection. Therefore, documenting a four-fold change in titer is necessary to confirm acute infection with SFG *Rickettsia* using serology. That said, a single high titer in the context of acute and compatible clinical signs and appropriate response to therapy is suggestive of infection.[24] It is important to note that most antibody-based diagnostic tests do not differentiate among species of SFG *Rickettsia*. Some PCR tests can differentiate among species infecting *Rickettsia* while others only amplify conserved rickettsial DNA targets. Veterinarians should check with their laboratory regarding the sensitivity and specificity of a given PCR, keeping in mind that in vitro (absolute) sensitivity is higher than in vivo sensitivity due to the low circulating copy number of *Rickettsia* in blood (see **Fig. 3**). Importantly, a negative PCR test and negative serologic test do not rule out infection or the need for immediate antimicrobial treatment.

Treatment

Appropriate antibiotic therapy must be immediately instituted based on clinical suspicion before diagnostic tests confirm infection. Inappropriate or delayed antibiotic therapy may increase morbidity and mortality.[24] A recent analysis of the human literature showed mortality increased from 4% for patients receiving doxycycline within the first 5 days of illness to 35% when treatment was delayed beyond day five.[28] Treating with an antibiotic that is not effective also allows rapid progression. Some antibiotics such as trimethoprim sulfa may worsen disease in people. Doxycycline (5 mg/kg PO BID) is the treatment of choice. It is highly effective at eliminating *R. rickettsii* in dogs. Furthermore, doxycycline provides effective empiric therapy for *A. phagocytophilum*, *Ehrlichia spp*, and *Borrelia burgdorferi,* agents that are differential diagnoses or may coinfect patients with RMSF. Enrofloxacin has been shown to be effective against *R. rickettsii* in experimentally infected dogs, but it is not effective against *Ehrlichia canis*, a differential diagnosis or possible coinfecting agent.[29,30] Chloramphenicol was effective in experimentally infected dogs.[29] However, in people, it may be less effective than doxycycline.[25] It also has less efficacy against possible coinfecting agents. Dental abnormalities including tooth discoloration and enamel hypoplasia have not been observed in children with RMSF treated with doxycycline at a low dose for 7 to 10 days.[31] Therefore, it is the treatment of choice for RMSF in children. https://www.cdc.gov/rmsf/treatment/index.html In fact, the CDC warns clinicians "Healthcare providers should be cautions when exploring treatments other than doxycycline." https://www.cdc.gov/rmsf/treatment/index.html.

The duration of therapy for RMSF in dogs is short, with 7 days being adequate in most cases. Treatment a few days past defervescence is recommended. A longer course of (doxycycline) therapy is recommended for patients coinfected with an *E spp*. or *B. burgdorferi*. Owners should be warned of the potential, yet possibly low, risk of dental abnormalities if doxycycline is used short term to treat RMSF in puppies.

Many patients require hospitalization. Intravenous antibiotic therapy may be necessary for debilitated patients. Aggressive supportive care for complications such as

thrombosis, central nervous system deficits, and gastrointestinal signs may be necessary. Due to the loss in vascular integrity, fluids should be administered with caution and colloids may be warranted in some cases.

The use of corticosteroids in dogs with RMSF is controversial. Anti-inflammatory and immunosuppressive doses did not affect the overall outcome of experimentally infected dogs, but rickettsemia was longer in dogs concurrently treated with doxycycline and immunosuppressive doses of corticosteroids.[32] Of note, the duration of rickettsemia, which was documented using a culture technique, was not determined beyond 10 days postinfection in that study. Anti-inflammatory doses of corticosteroids have been used in dogs with severe CNS manifestations and may be necessary topically or systemically for the treatment of ocular abnormalities.

Response to appropriate antibiotic therapy is very rapid (24–48 hours). Coinfection with *B. burgdorferi, Ehrlichia spp, Babesia spp,* and *Bartonella spp* or other agents should be considered in dogs with severe or prolonged clinical signs and dogs that fail to respond to doxycycline. Residual central nervous system and other deficits may occur in severely affected patients. A convalescent serum sample should be drawn 2 to 3 weeks after the initial serologic sample in PCR-negative patients to confirm infection.

Prognosis

The prognosis is good to excellent if the disease is diagnosed and treated with appropriate antibiotics and supportive care early in the course of illness.

Public health implications

Human spotted fever rickettsioses are reportable diseases in the United States. The same is true for dogs in some counties. Dogs are sentinels for spotted fever rickettsioses in people. It is important for veterinarians to communicate with owners and physicians that infection in a dog may precede tick-transmitted infection to owners or neighbors. It is well established that people living near dogs and with dogs in endemic areas are at increased risk for acquiring RMSF. This results from human exposure to the same environments whereby the dogs acquire ticks, and through interactions with tick-infested dogs. Instruct clients to remove ticks properly and avoid crushing to prevent exposure to infected hemolymph. See http://www.cdc.gov/ticks/removing_a_tick.html for CDC guidelines on appropriate tick removal. Educating owners regarding the importance of tick control and prevention for people, pets, and the environment is critical. In cases whereby *Rh. sanguineus* is the vector, environmental control is particularly important given its proclivity to live within housing structures.

EMERGING SPOTTED FEVER GROUP RICKETTSIOSES IN THE UNITED STATES

The classic geographic distribution of RMSF has been changing, and novel vectors may be contributing to this phenomenon. As mentioned above, RMSF is now present in the Southwest due to *Rh. sanguineus*, a novel vector for *R. rickettsii* in the United States. *Rh. sanguineus* is the primary vector of *R. rickettsii* in Mexico, and an ongoing outbreak in people in Mexicali Mexico, which borders southern California was associated with this tick species, and again, dogs.[33,34] Interestingly, no *R. rickettsii* DNA was amplified from *Rh. sanguineus* ticks collected from dogs at an animal shelter in Imperial county California, just North of the Mexico/California border.[35] In contrast, SFG *Rickettsia*, including *R. rickettsii*, *Rickettsia massiliae*, and *Rickettsia parkeri*, were amplified from *Rh. sanguineus* ticks parasitizing dogs participating in a Mexican government sterilization program near the same region.[36] In addition, a recent serosurvey

showed that 12.2% of 752 dogs residing in Imperial county California were seroreactive to SFG *Rickettsia*.[33] Dogs close to the border and taken across the border were significantly more likely to be seroreactive. Genetic differences among lineages of *Rh. sanguineus* and environmental factors may contribute to differences in the prevalence of SFG *Rickettsia* infecting ticks in different, but relatively close, geographic locales.[37]

In South America, *Amblyomma* species are the main vector for *R. rickettsii*. In 2011, *A. americanum* was implicated in the transmission of *R. rickettsii* to a person in North Carolina, and recently this tick was shown to be a competent vector.[18,19] As mentioned above, veterinarians should consider the possibility of transmission by novel vectors if dogs present with clinical signs of RMSF in nonendemic areas or at an unusual time of year.

Spotted fever group (SFG) *Rickettsia* other than *R. rickettsii* have also been implicated as spotted-fever like illness causing agents in people in the United States. Clinical signs of infection with other SFG *Rickettsia* can differ from RMSF. *Rickettsia parkeri* is an SFG *Rickettsia* that is most commonly found in the United States in *Amblyomma maculatum* (Gulf Coast tick). Infection has been increasingly recognized in people in the United States. Because diagnosis is often based on serologic testing, which is not species specific, it is thought that some cases reported to the CDC in previous years as being RMSF were actually infections with this agent.[13] In contrast to RMSF, infection in people is usually associated with the formation of an eschar, a localized inflammatory and necrotic skin lesion with a black crust that forms at the site of the tick bite. The formation of eschars has been associated with other SFG *Rickettsia* infections, and their formation is inversely associated with disease severity.[38] Generally speaking, *R. parkeri* is thought to cause a milder illness than *R. rickettsii* in people. *Rickettsia parkeri* was also recently amplified from ill people after hiking in southern Arizona.[39] The suspected vector was *Amblyomma triste*, a Neotropical species recently recognized in the United States. *Rickettsia parkeri* was amplified using PCR from 13% of 93 dogs residing in shelters in Southern Louisiana.[40] The dogs did not have clinical signs of illness, whether hematologic or other abnormalities were present was not investigated. DNA from *R. parkeri* has also been recently amplified from *Rh. sanguineus* parasitizing dogs at the United States Mexico border.[36]

R. massiliae, another *SFG Rickettsia* has been implicated as a disease-causing agent in people in the United States and elsewhere. Recently, infection with *R. massiliae* was suspected in ill, seropositive dogs infested with *R. massiliae* infected *Rh. sanguineus* ticks in Los Angeles county California.[11] This species of SFG *Rickettsia* has also been amplified from *Rh. sanguineus* ticks in Arizona, the US–Mexico Border, and the Eastern United States.[36,41,42]

Rickettsia amblyommatis (formerly *Can*. Rickettsia amblyommii), and *R. montanensis*, (Formerly *Rickettsia montana*) are thought to be nonpathogenic endosymbionts of ticks. Exposure is common in dogs in areas endemic to *R. rickettsii*, which can complicate serodiagnosis of RMSF due to crossreactivity.[43] Recent evidence suggests that these organisms may be capable of causing illness in some people.[44,45] Experimental infection of beagles with *R. montana* (*R. montanensis*) did not result in seroconversion or illness.[46] DNA from *R. amblyommii* and *R. montanensis* was recently amplified from the blood of 2 naturally infected dogs who did not seem clinically ill.[47] Taken together, these data suggest that if these organisms can cause disease in dogs it is uncommon.

Pacific Coast Fever is another spotted fever rickettsioses of increasing importance in the Western United States' people.[38] It is caused by *Rickettsia* strain 364D (proposed name *R. philipii*), and transmitted by *Dermacentor occidentalis*, the Pacific

Coast Tick. The disease is less severe than RMSF and, like other milder spotted fever rickettsioses, is often associated with an eschar at the region of the tick bite. Whether this organism infects or causes illness in dogs is not known.

Recently, infection with a novel SFG *Rickettsia* closely related to *R. massiliae* and *R. heilongjiangensis* was documented in three dogs in the United States with clinical signs and laboratory abnormalities associated with RMSF.[48] In addition, several SFG *Rickettsia* were identified in large study of *Dermacentor* ticks parasitizing dogs and cats in the United States.[49] *Rickettsia* species were identified in 12.5% of ticks and included *R. montanensis*, *R. bellii*, *R. rhipicephali*, *R. peacocki*, *R. amblyommatis*, *R. cooleyi*, and unclassified *Rickettsia* species. Whether these agents might cause disease in individual patients continues to be elucidated.

SPOTTED FEVER RICKETTSIOSES IN CATS

Although antibodies to *R. rickettsii* are detected in cats in endemic areas, active infection and associated clinical signs have not been documented. Antibodies to several other SFG *Rickettsia* have been detected in cats, and recently, DNA from some SFG *Rickettsia* species most closely resembling *R. massiliae* Bar29 and *R. conorii* has been amplified from naturally infected cats.[50] DNA from "*Candidatus* Rickettsia senegalensis" was also recently amplified from the blood of 2 cats in Riverside county CA.[51] The ability of SFG *Rickettsia* to cause disease in cats is not known.

RICKETTSIA AKARI AND *RICKETTSIA FELIS* INFECTIONS IN DOGS AND CATS

Although there is an ongoing debate over whether *R. akari* and *R. felis* belong in the same phylogenetic group as other SFG rickettsia, the disease they cause in people is similar to other spotted fever rickettsioses.[2,3] *Rickettsia akari* is transmitted by mites primarily in urban areas. Exposure to *R. akari* has been documented in dogs from New York City.[52] In addition, *R. akari* DNA was amplified from the peripheral blood of an 8-month old dog from Mexico with clinical and laboratory abnormalities similar to RMSF that were rapidly doxycycline responsive.[53] The organism was also amplified from 2 *Rh. sanguineus* ticks parasitizing the dog, prompting the authors to suggest that a vector other than mites may be possible.

Rickettsia felis is primarily transmitted by *Ctenocephalides felis* in the continental United States. The disease is endemic in Southern and Central Texas and California. In people, it causes disease similar to that caused by a typhus group *Rickettsia*, *R. typhi*. However, despite its vector, as mentioned above, it is more closely genetically related to SFG *Rickettsia* so it is included in this article. Opossums are an important reservoir as they live in close proximity to humans and cats and harbor high loads of cat fleas. Indoor/outdoor cats may be infested with cat fleas which then infect the cat's human companions.[54] Although experimental and natural exposure and infection have been documented in cats and dogs, the role of it as a disease-causing agent in companion animals is not well defined.[51,55,56] However, it is clear that flea control and reducing exposure to opossums is absolutely essential to reduce the zoonotic risk of illness in people.

SUMMARY

Rocky Mountain spotted fever causes an acute febrile illness in dogs and people. Both PCR and serology may be negative at the time of presentation. Doxycycline therapy must be initiated based on clinical suspicion to prevent death and morbidity. Response to therapy is very rapid. Dogs are sentinels for disease in people. The geographic distribution of RMSF is expanding. The role of other SFG *Rickettsia* as

disease-causing agents in cats and dogs continues to be elucidated. Flea and tick control is important from a One Health perspective to protect dogs, cats, and their human companions.

CLINICS CARE POINTS

- Rocky Mountain spotted fever, caused by *R. rickettsii* causes a febrile, acute illness in dogs.
- Dogs are sentinels for infection in their human companions; therefore, notify clients to contact a physician immediately if they feel ill when RMSF is suspected in a canine patient.
- Both PCR and serologic testing may be negative when dogs are clinically ill.
- Doxycycline must be started immediately based on clinical suspicion.
- Combining PCR with serologic testing, repeat testing using PCR, and testing convalescent serum for seroconversion may be necessary to confirm the diagnosis.
- The prognosis is excellent if appropriate antimicrobial therapy is begun in a timely fashion.
- Infection from exposure to novel vectors or with novel agents should be considered if cases present in unusual geographic locales or times of year.

DISCLOSURE

Paid speaker and consultant for Zoetis and IDEXX laboratories. Currently employed at Zoetis.

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