

# Spotted Fevers

## (including Rocky Mountain Spotted Fever and Mediterranean Spotted Fever)

**Last Updated:** November 2012



the Center for  
Food Security  
& Public Health

IOWA STATE UNIVERSITY®

College of Veterinary Medicine  
Iowa State University  
Ames, Iowa 50011  
Phone: 515.294.7189  
Fax: 515.294.8259  
cfsph@iastate.edu  
www.cfsph.iastate.edu



INSTITUTE FOR  
INTERNATIONAL  
COOPERATION IN  
ANIMAL BIOLOGICS

Iowa State University  
College of Veterinary Medicine  
www.cfsph.iastate.edu/IICAB/

## Importance

Spotted fevers, which are caused by *Rickettsia* spp. in the spotted fever group (SFG), have been recognized in people for more than a hundred years. The clinical signs are broadly similar in all of these diseases, but the course ranges from mild and self-limited to severe and life-threatening. For a long time, spotted fevers were thought to be caused by only a few organisms, including *Rickettsia rickettsii* (Rocky Mountain spotted fever) in the Americas, *R. conorii* (Mediterranean spotted fever) in the Mediterranean region and *R. australis* (Queensland tick typhus) in Australia. Many additional species have been recognized as human pathogens since the 1980s. These infections are easily misidentified with commonly used diagnostic tests. For example, some illnesses once attributed to *R. rickettsii* are caused by *R. parkeri*, a less virulent organism.

Animals can be infected with SFG rickettsiae, and develop antibodies to these organisms. With the exception of Rocky Mountain spotted fever and possibly Mediterranean spotted fever in dogs, there is no strong evidence that these organisms are pathogenic in animals. It is nevertheless possible that illnesses have not been recognized, or have been attributed to another agent. Rocky Mountain spotted fever, which is a recognized illness among dogs in the North America, was only recently documented in dogs in South America.

## Etiology

Spotted fevers are caused by *Rickettsia* spp., which are pleomorphic, obligate intracellular, Gram negative coccobacilli in the family Rickettsiaceae and order Rickettsiales of the  $\alpha$ -Proteobacteria. The genus *Rickettsia* contains at least 25 officially validated species and many incompletely characterized organisms.

The spotted fever group of *Rickettsia* contains a number of human pathogens, most of which are transmitted by ticks. *R. rickettsii* causes Rocky Mountain spotted fever, named for the region of North America where it was first identified. This disease is also called Brazilian spotted fever in Brazil. *R. conorii* subsp. *conorii* is the agent of Mediterranean spotted fever, also known as boutonneuse fever. Other subspecies of *R. conorii* cause Israeli spotted fever (*R. conorii* subsp. *israelensis*), Astrakhan spotted fever (*R. conorii* subsp. *caspia*) and Indian tick typhus (*R. conorii* subsp. *indica*). An illness known as either TIBOLA (tick-borne lymphadenopathy) or DEBONEL (*Dermacentor*-borne necrosis erythema lymphadenopathy) can be caused by both *R. slovaca* and *R. raoultii*. Other named syndromes include African tick-bite fever (*R. africae*), Japanese (or Oriental) spotted fever (*R. japonica*), Queensland tick typhus (*R. australis*), Flinders Island spotted fever (*R. honei*), lymphangitis-associated rickettsiosis (*R. sibirica* subsp. *mongolitimonae*), Siberian or North Asian tick typhus (*R. sibirica* subsp. *sibirica*) and Far Eastern tick-borne rickettsiosis (*R. heilongjiangensis*). *R. parkeri* rickettsiosis (sometimes known as Tidewater spotted fever or American boutonneuse fever) is a recently-recognized illness in the Americas. *R. massiliae*, *R. helvetica*, *R. monacensis* and *R. aeschlimannii* are also known pathogens, while *Rickettsia* species 364D, *R. tamurae*, Candidatus *R. andeanae* and Candidatus *R. amblyommii* have been implicated in human illness.

Two pathogenic members of the SFG rickettsiae are transmitted by other arthropods. *R. felis* (formerly known as the ELB agent) causes a syndrome known as flea-borne spotted fever or cat flea typhus. *R. akari*, which is transmitted by mites, causes rickettsialpox.

Some SFG rickettsiae have been identified only in arthropods, and are of unknown pathogenicity for people and domesticated animals.

## Geographic Distribution

A few SFG rickettsiae seem to be cosmopolitan, while others have been found in only limited areas (Table 1). They are often focally distributed within an endemic region. The distribution of some organisms is poorly understood.

The two best characterized diseases, Rocky Mountain spotted fever (RMSF) and Mediterranean spotted fever (MSF), are limited to the Western or Eastern hemisphere, respectively. Rocky Mountain spotted fever occurs in North, Central and South

# Spotted Fevers

America. In the U.S., more than 60% of the cases are reported in five states (North Carolina, Oklahoma, Arkansas, Tennessee, and Missouri), with another focus of infection recently identified in the Southwest (Arizona). *R. parkeri*, which causes an illness that can be confused with RMSF, has been linked to clinical cases in the southeastern U.S., but might be more widely distributed in North America. It has also been associated with human illness in Uruguay, and it was found in ticks in Peru, Uruguay, Argentina and Brazil. Seropositive dogs were recently detected in Brazil. Several other pathogenic SFG rickettsiae, some of which are still poorly characterized, also occur in the Americas.

Mediterranean spotted fever is most common in the area surrounding the Mediterranean basin, including northern Africa, the Middle East and southern Europe. It can also be seen in northern and central Europe, in foci where its tick vector survives in dog kennels and houses. Clinical cases have been reported from other regions, such as Africa, but some cases are poorly documented and might be caused by other organisms. MSF usually occurs in small foci, and one area can be affected for years without spreading to nearby regions. Additional subspecies of *R. conorii* cause distinct illnesses in other regions, some of which overlap with the distribution of *R. conorii* subsp. *conorii*. Other SFG rickettsiae also occur in Europe, Asia and Africa, including areas where Mediterranean spotted fever is found.

**Table 1: Reported distribution of SFG rickettsiae**

<i>Organism (Disease)</i>	<i>Distribution</i>
<i>R. aeschlimannii</i>	Southern Europe, Africa. Organism also found in ticks in Kazakhstan
<i>R. africae</i> (African tick-bite fever)	Africa and the eastern Caribbean
<i>R. akari</i> (rickettsialpox)	Organism is cosmopolitan, including North America, Europe, Asia, Mexico, Africa. Disease reported especially in urban areas of northeastern U.S., but also in Europe (Croatia, Ukraine and Turkey), Korea, other areas
<i>R. australis</i> (Queensland tick typhus)	Australia
<i>R. conorii</i> subsp. <i>conorii</i> (Mediterranean spotted fever)	Mediterranean; also foci in northern and central Europe; cases reported in sub-Saharan Africa
<i>R. conorii</i> subsp. <i>indica</i> (Indian tick typhus)	Indian subcontinent
<i>R. conorii</i> subsp. <i>caspia</i> (Astrakhan spotted fever)	Russia (especially the Astrakhan region on the Caspian Sea), Kazakhstan; one case in Chad. Organism also found in ticks in Kosovo.
<i>R. conorii</i> subsp. <i>israelensis</i> (Israeli spotted fever)	Middle East, Portugal. Organism also found in ticks in Italy (Sicily).
<i>R. felis</i> (flea-borne spotted fever)	Possibly worldwide
<i>R. heilongjiangensis</i> (Far Eastern tick-borne rickettsiosis)	Russian Far East. Organism also found in ticks in China, possibly associated with human disease.
<i>R. helvetica</i>	Europe, Japan, Thailand, Laos
<i>R. honei</i> (Flinders Island spotted fever)	Australia; Nepal. Organism also found in ticks in Thailand, Sri Lanka, Italy, U.S. (Texas)
<i>R. japonica</i> (Japanese spotted fever)	Japan and south Korea, possibly other nearby regions
<i>R. massiliae</i>	Europe, Africa (emerging disease in the Mediterranean region). Organism also found in ticks in the U.S. and South America.
<i>R. monacensis</i>	Spain, Italy.
<i>R. parkeri</i>	U.S., Uruguay. Organism also found in ticks in Argentina, Brazil, Uruguay.
<i>R. raoultii</i> (TIBOLA/ DEBONEL)	Europe, Russia. Organism also found in China.
<i>R. rickettsii</i> (Rocky Mountain spotted fever)	western Canada, continental U.S., Mexico, Panama, Argentina, Brazil, Bolivia, Colombia, Costa Rica
<i>R. sibirica</i> subsp. <i>mongolitimonae</i> (lymphangitis-associated rickettsiosis)	Africa, Europe (France, Greece), China
<i>R. sibirica</i> subsp. <i>sibirica</i> (Siberian tick typhus)	Northern Asia, including parts of Russia. and China
<i>R. slovaca</i> (TIBOLA/ DEBONEL)	Europe, Russia. Organism also found in ticks in China. <i>R. slovaca</i> is associated with two tick species that are common from Europe to central Asia.

# Spotted Fevers

## Transmission

### Tick-borne spotted fevers

Ticks are the vectors for most SFG rickettsiae, and transmit them in saliva while feeding. Ticks must usually be attached for several hours before the bacteria are reactivated and pass to the vertebrate host. Transmission of *R. rickettsii* (Rocky Mountain spotted fever) by *Dermacentor andersoni* requires at least 4-6 hours attachment, although 10-24 hours is more usual. *Rhipicephalus sanguineus* (the dog tick) typically transmits *R. conorii* (Mediterranean spotted fever) after 20 hours. The minimum attachment time needed to reactivate some organisms is unknown. Transovarial and transstadial transmission has been demonstrated for some organisms (e.g., *R. rickettsii* in *Dermacentor andersoni*, *D. variabilis*, *R. sanguineus*, *Amblyomma cajennense* and *A. aureolatum*; and *R. conorii* in *Rh. sanguineus*). Other SFG rickettsiae are also thought to be transmitted by these routes.

Some known and proposed tick vectors for SFG rickettsiae are listed in Table 2. The most important vectors can vary with the region. *D. variabilis* (the American dog tick) and *D. andersoni* (the Rocky Mountain wood tick) transmit Rocky Mountain spotted fever in most of the U.S. and Canada, but *Rh. sanguineus* is the major vector in a focus of infection in Arizona. *Rh. sanguineus* is also thought to be important in Mexico. *Amblyomma cajennense* (the Cayenne tick) usually transmits RMSF to people in Central and South America, while *Am. aureolatum* (the yellow dog tick) is a vector in some urban areas of Brazil.

SFG rickettsiae can also be acquired by exposure to a crushed tick's tissues, fluids or feces, entering the body through breaks in the skin. Blood transfusions can transmit these organisms between people. In the laboratory, infections may occur after contamination of the mucous membranes, or in puncture wounds or cuts. Growing SFG rickettsiae in culture is particularly hazardous. Aerosol transmission of *R. rickettsii* has been reported after laboratory accidents.

**Table 2: Some known vectors for tick-borne SFG rickettsiae**

Organism (Disease)	Vectors
<i>R. aeschlimanii</i>	Mainly <i>Hyalomma marginatum</i> ; also <i>Rhipicephalus appendiculatus</i> , <i>Haemaphysalis punctata</i> , <i>Ixodes</i> spp.
<i>R. africae</i> (African tick-bite fever)	<i>Amblyomma hebraeum</i> , <i>Am. variegatum</i> , <i>Am. lepidum</i> , <i>Rh. appendiculatus</i> , <i>Rh. decoloratus</i>
<i>R. australis</i> (Queensland tick typhus)	<i>Ixodes holocyclus</i> , <i>I. tasmani</i> ; also found in <i>I. cornuatus</i>
<i>R. conorii</i> subsp. <i>conorii</i> (Mediterranean spotted fever)	Mainly <i>Rh. sanguineus</i> , also reported in <i>Ha. leachii</i> , <i>Ha. punctaleachi</i>
<i>R. conorii</i> subsp. <i>indica</i> (Indian tick typhus)	<i>Rh. sanguineus</i> , <i>Rh. microplus</i> , <i>Ha. leachii</i>
<i>R. conorii</i> subsp. <i>caspia</i> (Astrakhan spotted fever)	<i>Rh. pumilio</i> , <i>Rh. sanguineus</i>
<i>R. conorii</i> subsp. <i>israelensis</i> (Israeli spotted fever)	<i>Rh. sanguineus</i>
<i>R. heilongjiangensis</i> (Far Eastern tick-borne rickettsiosis)	<i>Ha. concinnae</i> , <i>Ha. japonica</i> , <i>Dermacentor silvarum</i>
<i>R. helvetica</i>	<i>I. ricinus</i> in Europe; also in <i>I. ovatus</i> , <i>I. persulcatus</i> , <i>I. monospinosus</i>
<i>R. honei</i> (Flinders Island spotted fever)	The reptile tick <i>Bothriocroton hydrosauri</i> is the principal vector; also in <i>Am. cajennense</i> , <i>I. granulatus</i> , <i>Ha. novaeguineae</i>
<i>R. japonica</i> (Japanese spotted fever)	<i>Ha. flava</i> and <i>Ha. hystericis</i> are probably the main vectors for humans in Japan; also in <i>D. taiwanensis</i> , <i>I. ovatus</i> , <i>Ha. longicornis</i>
<i>R. massiliae</i>	Thought to be <i>Rhipicephalus</i> spp. including <i>Rh. sanguineus</i> , <i>Rh. turanicus</i> , <i>Rh. muhsamae</i> , <i>Rh. lunulatus</i> , <i>Rh. sulcatus</i>
<i>R. monacensis</i>	<i>I. ricinus</i>
<i>R. parkeri</i>	<i>Am. maculatum</i> ; also found in <i>Am. americanum</i> , <i>Am. triste</i> and <i>Am. nodosum</i>
<i>R. raoultii</i> (TIBOLA/ DEBONEL)	<i>Rh. pumilio</i> , <i>D. nttalli</i> , <i>D. marginatus</i> , <i>D. silvarum</i> , <i>D. reticulatus</i>
<i>R. rickettsii</i> (Rocky Mountain spotted fever)	<i>D. andersoni</i> , <i>D. variabilis</i> in North America, <i>Am. cajennense</i> , <i>Am. aureolatum</i> in South America; <i>Rh. sanguineus</i> in Arizona, Mexico and South America; also found in <i>Am. imitator</i>
<i>R. sibirica</i> subsp. <i>mongolitimonae</i> (lymphangitis-associated rickettsiosis)	<i>Hy. asiaticum</i> , <i>Hy. truncatum</i>
<i>R. sibirica</i> subsp. <i>sibirica</i> (Siberian tick typhus)	<i>Dermacentor</i> spp. are probably the main vectors for humans ( <i>D. nuttalli</i> , <i>D. silvarum</i> , <i>D. marginatus</i> , <i>D. auratus</i> , <i>D. sinicus</i> , <i>D. pictus</i> ); also in other Ixodidae including <i>Ha. concinna</i> , <i>Ha. yeni</i> , <i>Ha. wellingtoni</i> and other species
<i>R. slovacica</i> (TIBOLA/ DEBONEL)	<i>D. marginatus</i> , <i>D. reticulatus</i>

# Spotted Fevers

## Flea-borne and mite-borne spotted fevers

Two SFG rickettsiae, *R. felis* and *R. akari*, are transmitted by arthropods other than ticks. *R. felis* has mainly been found in the cat flea, *Ctenocephalides felis*, which is currently the only arthropod known to be a biological vector. Transovarial and transstadial transmission has been reported in this flea. *R. felis* can also infect other fleas including *C. canis*, *C. orientis*, *Anomiopsyllus nudata*, *Archaeopsylla erinacei*, *Ctenophthalmus* sp., *Xenopsylla cheopis*, *X. brasiliensis*, *Ceratophyllus gallinae*, *Spilopsyllus cuniculi* and *Echidnophaga gallinacea*. The means of transmission to humans is still uncertain. *R. felis* was found in flea salivary glands in one study but not others. It has also been detected in flea feces. *C. felis* is found occasionally in other arthropods such as ticks, chiggers and mites, but these species might only be mechanical carriers after a blood meal.

*R. akari* is transmitted by the mite *Liponyssoides sanguineus*. This mite infests mice and other small rodents, but will bite humans, especially if its normal hosts are absent. Transovarial transmission of *R. akari* has been reported in *L. sanguineus*. *R. akari* has also been detected in ticks.

## Vertebrates as reservoirs for SFG rickettsiae

The idea that ticks act as both vectors and reservoirs for most of the SFG rickettsiae was proposed in the 1960s, and was generally accepted after that time. This idea has recently been questioned, in part because some species of *Rickettsia* (though not all) have detrimental effects on their tick vectors. *R. rickettsii* and *R. conorii* can decrease the survival, reproductive success or molting success of experimentally infected ticks, and are found in a very small percentage of the tick population in nature. This suggests that new lines of ticks must be reinfected from vertebrate hosts, to maintain these infections. Another argument for the existence of vertebrate reservoirs is that the vectors are sometimes more widely distributed than the organisms they carry. For example, the tick vector for *R. conorii* subsp. *conorii* is found worldwide between 50°N and 35°S, but Mediterranean spotted fever occurs in only part of this region. Vertebrates might act as reservoirs (or additional reservoirs) for an organism, or be amplifying hosts to infect additional ticks. This aspect of spotted fevers is still poorly understood and often speculative.

## Disinfection

Rickettsiae are obligate intracellular organisms, and do not survive for long periods outside their hosts. Species of *Rickettsia* (i.e., *R. rickettsii* and *R. akari*) are expected to be susceptible to 1% sodium hypochlorite, 70% ethanol, 2% glutaraldehyde, formaldehyde and phenol. In some cases, the efficacy of these disinfectants was extrapolated from their effects on other Gram negative bacteria. Ordinary household disinfectants including 70% isopropyl alcohol or 2% tincture of iodine can be used to disinfect a tick bite.

Rickettsiae can be destroyed by moist heat of 121° C for a minimum of 15 min, or dry heat of 160-170° C for an hour. *R. akari* is reported to be inactivated rapidly at 56°C. .

## Infections in Humans

### Incubation Period

Reported incubation periods for SFG rickettsioses range from one to 28 days. The incubation period for Rocky Mountain spotted fever (*R. rickettsii*) is usually 2 to 14 days (with a mean of 7 days) in the U.S., but one case series in Brazil estimated it to be one to 21 days, with a median of 12 days. Mediterranean spotted fever tends to become apparent in approximately 7 days, African tick bite fever in 5-7 days and rickettsialpox in 12-15 days. Other reported incubation periods are 2-9 days for Flinders Island spotted fever and 2-10 days for *R. parkeri* rickettsiosis and Japanese spotted fever.

### Clinical Signs

The general pattern of illness caused by SFG rickettsiae is similar: the affected individual usually develops a febrile illness, often followed by a rash. The form of the rash (e.g., maculopapular or papulovesicular) varies between diseases. An eschar (classically a painless black crusted ulcer with surrounding erythema) occurs at the inoculation site in many, but not all, spotted fevers. Multiple eschars are common in diseases where the person is typically bitten by more than one infected vector. Eschars are usually absent in Rocky Mountain spotted fever (*R. rickettsii*) and cat flea associated rickettsiosis (*R. felis*). Some spotted fevers (e.g., African tick-bite fever) are not life threatening and are usually mild, while others, such as Rocky Mountain spotted fever, are often severe. A variety of organ systems can be affected in complicated or severe cases.

The pattern of the rash, eschars and constitutional signs can sometimes suggest a diagnosis. For example, a patient with a mild illness, multiple eschars and a history of travel to the Caribbean is more likely to have African spotted fever than Rocky Mountain spotted fever.

### Rocky Mountain spotted fever (*R. rickettsii*)

Rocky Mountain spotted fever is a moderate to severe disease in most patients. The initial signs can include malaise, fever, chills, headache and myalgia. The fever is usually high and the headache severe. Gastrointestinal signs including nausea, anorexia, vomiting, diarrhea and abdominal pain (which may be severe) are common. Some patients develop edema, which can be generalized or limited to the face, periorbital region or extremities. Ocular lesions may include conjunctivitis, photophobia or petechiae, as well as ocular hemorrhages, optic disc edema or vascular occlusion in more severe cases. An eschar is not usually seen.

A nonpruritic macular rash, usually seen first on the wrists, forearms, ankles or scrotum, can appear from the

# Spotted Fevers

2nd to 14th day. Most patients in the U.S., but only half in Brazil, have a rash. The rash tends to develop sooner in children than adults. It spreads rapidly, often involving the palms or soles as well as the trunk and extremities. The spots initially blanch when pressed, but later may develop characteristic petechiae. A petechial rash is considered to be a sign of progression to severe RMSF. In the later stages, the petechiae can coalesce to form ecchymoses and may be followed by necrotic or gangrenous changes.

Other body systems are affected in some patients. Respiratory signs may range from coughing to pneumonia, pulmonary edema and acute respiratory distress. Jaundice can develop, and acute renal failure is possible in severely affected patients. Neurological signs, ranging from transient deafness or insomnia to tremors, ataxia, amnesia, paralysis, hallucinations or coma, can develop relatively soon after the onset of clinical signs. Encephalitis or meningitis has been reported in some cases. Hemorrhages are common, due to damage to the blood vessels. Some patients have visible hemorrhages, but bleeding can also occur in internal organs, such as the gastrointestinal tract. Coagulopathies and thromboses may cause impairments in circulation, which can sometimes result in gangrene. Various other complications such as mucosal ulcers, myocarditis (and cardiac arrhythmias), hypotension, shock and multi-organ failure are also possible. Severe illness with a rapidly deteriorating course can occur in patients with glucose-6-phosphate dehydrogenase deficiency, a sex-linked genetic condition that affects approximately 12% of African-American males in the U.S.

Although convalescence is usually rapid with early treatment, untreated patients may die within 1 to 2 weeks, and more severe cases often require hospitalization. Without treatment, the case fatality rate can be as high as 85% in some regions. Sequelae, particularly after severe disease, may include gangrene of the extremities and various neurological signs. Some, but not all, sequelae eventually resolve.

## ***Rickettsia parkeri rickettsiosis***

*R. parkeri* rickettsiosis seems to be a milder disease than Rocky Mountain spotted fever, although the symptoms are similar. A distinguishing feature is that eschars are seen in most cases of *R. parkeri* rickettsiosis. They are occasionally multiple. Fever, headache and myalgia are reported to be milder than in RMSF, and nausea, vomiting and other gastrointestinal signs were uncommon in one case series. A few patients had tender regional lymphadenopathy. Photophobia and neck stiffness have been reported, but seem to be infrequent. Most patients with *R. parkeri* rickettsiosis have a maculopapular, vesiculopapular or papulopustular rash, mainly on the trunk and extremities. In some cases, the palms or soles or face are also involved. A petechial rash is not characteristic, although a few scattered petechiae may occasionally be found around the eschar. Severe neurological signs were

not seen in one case series, and no deaths have been reported in treated patients.

## ***Mediterranean spotted fever (R. conorii subsp conorii)***

Like other spotted fevers, Mediterranean spotted fever begins as a febrile illness with nonspecific flu-like signs. Other symptoms can include an inoculation eschar (most often single), and a generalized maculopapular or purpuric rash, which usually involves the palms and soles. While almost all patients have a rash, an eschar was found in 20%–86% of patients in some early descriptions of MSF. Some eschars are atypical, resembling a furuncle or other skin lesion, and may be difficult to recognize. Regional lymphadenitis is not usually seen.

Although most cases of MSF are mild, severe and fatal cases are also seen. Complications can include renal, neurological, respiratory and cardiac conditions, as well as anemia, thrombocytopenia, phlebitis and ocular signs. Sequelae may include neurological deficits. Complications are more common with delayed treatment, or in older patients and those with debilitating diseases or glucose-6-phosphate dehydrogenase deficiency.

## ***Other R. conorii infections***

Astrakhan spotted fever (*R. conorii* subsp. *caspia*) and Indian tick typhus (*R. conorii* subsp. *indica*) are febrile illnesses, with eschar and rash, that resemble Mediterranean spotted fever.

The symptoms of Israeli spotted fever (*R. conorii* subsp. *israelensis*) are also similar to Mediterranean spotted fever, but some reports suggest this disease might be more severe. In one study, patients with Israeli spotted fever developed gastrointestinal signs (nausea, vomiting and diarrhea) more often than patients with MSF. In contrast, eschars are less common, and have been reported in 4% to 38% of patients.

## ***Japanese spotted fever (R. japonica)***

Although Japanese fever occurs in both children and adults, approximately 75% of the patients at one hospital were between 50 and 80 years of age. Many of these cases were severe. The fever was often high, and most patients had shaking chills, headache and an eschar. A rash began on the extremities and spread within a few hours to all parts of the body including the palms and soles. The rash usually became petechial after a few days, and disappeared within 2 weeks. Reported complications included cardiac signs, neurological signs, disseminated intravascular coagulation (DIC) and multiple organ failure.

## ***Queensland tick typhus (R. australis)***

Queensland tick typhus resembles other illnesses caused by SFG rickettsiae. Rash occurs in most cases. It can be either maculopapular or vesicular, and may resemble chickenpox. An eschar may also be seen. Although most cases seem to be mild and most patients recover without complications, a few cases have been severe or fatal.

# Spotted Fevers

Reported complications included renal dysfunction, respiratory failure, multiorgan failure and necrosis of the skin and extremities.

## **African tick bite fever (*R. africae*)**

African tick bite fever is relatively mild and self-limited. In addition to nonspecific flu-like signs, more than 90% of patients have one or more inoculation site eschars. Multiple eschars are common, and atypical eschars may be seen. Neck muscle myalgia and subjective neck stiffness, as well as regional lymphadenitis, are also frequent. Less than half of all patients develop a generalized maculopapular or vesicular rash. If it is present, the rash is usually most apparent near an eschar. Aphthous stomatitis (mouth blisters) or lymphangitis have also been reported. Complications are uncommon, but may include prolonged fever, reactive arthritis and cranial or peripheral neuropathy. Life-threatening illness and fatal cases have never been reported.

## **Flinders Island spotted fever (*R. honei*)**

Flinders Island spotted fever was first characterized on Flinders Island, Australia. This syndrome was described as a febrile illness of sudden onset, often followed by a maculopapular rash (without vesicles) on the trunk and limbs. An eschar was detected in approximately half of these patients. Most people recovered in 1-6 weeks even without antibiotics. No deaths were seen, although a third of the patients were hospitalized. Some *R. honei* infections reported in other geographic regions have differed from this description. In Nepal, a patient infected with *R. honei* developed a severe febrile illness that included diarrhea, severe arthralgia, hepatosplenomegaly, a purpuric rash, neurological signs, hypotension, tachycardia and hypoxia. Three patients in Thailand had a petechial maculopapular rash, in addition to a febrile illness, and one patient developed encephalopathy.

*R. honei* has been found in the blood of some chronically ill patients in Australia, but it is still uncertain whether it has any causative role.

## **TIBOLA/DEBONEL (*R. raoultii* and *R. slovaca*)**

The constitutional signs in TIBOLA/DEBONEL are generally reported to be mild, and fever and rash are uncommon. The eschar often occurs on the scalp, and localized alopecia may be seen at the site. Regional lymphadenopathy is relatively common and can be painful. Deaths have not been reported.

## **Lymphangitis-associated rickettsiosis (*R. sibirica* subsp. *mongolitimonae*)**

An unusual characteristic of *R. sibirica* subsp. *mongolitimonae* infections is the presence of enlarged regional lymph nodes and lymphangitis extending from the eschar(s) to the draining lymph node. Additional symptoms include fever and maculopapular rash. Multiple eschars are common.

## **Rickettsialpox (*R. akari*)**

Rickettsialpox is a relatively mild, self-limited disease. A single eschar occurs in more than 70% of cases. A febrile illness, often with a stiff neck, develops a few days later. Some patients also have a cough, nausea, vomiting or lymphadenopathy. A maculopapular rash develops on the trunk and extremities. It usually progresses to vesicles or pustules, and can resemble chickenpox. Fatal cases have not been documented.

## **Cat flea-associated rickettsiosis (*R. felis*)**

The syndrome caused by *R. felis* has not been completely characterized. In one case series, almost all patients had a fever, and most had a rash, which was usually maculopapular. Only a few patients had an eschar. Various nonspecific clinical signs (e.g., back pain and myalgia), as well as gastrointestinal signs and coughing, have also been reported. Most cases have been mild, but reported complications include pneumonia and neurological signs.

## **Other spotted fevers**

The characteristics of some spotted fevers are poorly understood, as only a few cases have been described. Some organisms appear to cause classical spotted fever signs, while others have been linked to mild illnesses that may not include a rash. Occasionally, reports have implicated members of the SFG rickettsiae in diseases that do not resemble spotted fevers.

## **Communicability**

SFG rickettsiae are not transmitted directly from person to person, with the exception of medical procedures such as blood transfusions.

Caution should be used when handling blood and tissue specimens that may contain these organisms, as well as ticks, their feces and tissues. In the laboratory, infections have been reported after accidental inoculation, contamination of the mucous membranes or exposure to aerosols.

## **Diagnostic Tests**

Spotted fevers are often diagnosed presumptively based on the symptoms and history, and treatment is begun before the diagnosis is confirmed with laboratory tests.

Most clinical cases are confirmed by serology. A fourfold rise in titer between acute and convalescent samples is considered to be diagnostic. Some cases may also be diagnosed based on single high titers. Immunofluorescence and immunoperoxidase assays are the most specific tests, but dot blot immunoassays and enzyme-linked immunosorbent assays (ELISAs) are also available. Some tests, such as ELISAs, are qualitative rather than quantitative, and cannot be used to demonstrate rising titers. The Weil-Felix test, based on cross-reactive antigens of *Proteus vulgaris*, is nonspecific and insensitive and has generally been abandoned where better tests are available. Antibodies to *R. rickettsii* do not usually appear until 6 to 10 days after the first clinical signs. Seroconversion may

# Spotted Fevers

occur even later in some diseases such as African tick-bite fever, where diagnostic titers often develop more than 3 weeks after the onset of clinical signs. Antibody titers may be low if antibiotics were given early. Some healthy people have antibodies to SFG rickettsiae.

SFG rickettsiae cross-react extensively, and the causative organism cannot be identified with ordinary serological tests. Most commercial immunofluorescence assays are based on a very limited selection of antigens (for example, *R. rickettsii* in the United States). These tests also detect antibodies to other SFG rickettsiae, and do not identify the organism to the species level. Tests that can distinguish antibodies to different *Rickettsia* species are usually available only at regional reference laboratories. They include comparisons of titers to different organisms, cross-absorption of sera and immunoblotting (Western blotting).

Rickettsial antigens or nucleic acids can sometimes be found in tissues and blood. Polymerase chain reaction (PCR) assays permit definitive identification of rickettsial species. They can also recognize novel SFG rickettsiae. Nucleic acids can be found in skin biopsies, especially of the eschar. In RMSF (where eschars are uncommon), the biopsy is taken from the rash. SFG rickettsiae can sometimes be found in blood samples, but rickettsemia is usually brief, and the organisms are often present at low levels. Direct immunofluorescence or immunoperoxidase staining can detect antigens in skin biopsies from living patients, or in tissues at autopsy. However, the organisms can be focally distributed and are not always found. As with serology, antibody-based tests only recognize the organisms as SFG rickettsiae and do not identify them to the species level.

Culture of the organism is usually reserved for unusual or severe cases, when there is a compelling reason to identify the species. This test is usually available only at reference laboratories. Culturing SFG rickettsiae is hazardous, and requires a biosafety level 3 laboratory. As obligate intracellular organisms, rickettsiae do not grow on ordinary bacterial media, and must be isolated in living cells. The centrifugation shell vial technique, using human embryonic lung fibroblasts, is often employed. Older techniques for isolation included animal inoculation into male guinea pigs and inoculation into embryonated eggs. The organisms can be found in the skin (especially the eschar) or other tissues, and sometimes in the blood (especially early in the course of disease). Samples must be received quickly at the laboratory for isolation to be successful.

## Treatment

Spotted fevers are usually treated without waiting for laboratory confirmation. The illness is less likely to be severe or fatal if antibiotics are begun early, and the response to treatment can be quicker. Treatment is not always necessary for some spotted fevers (e.g. rickettsialpox), but antibiotics may be given to shorten the illness.

Only a few antibiotics, such as tetracyclines, are effective against rickettsiae. Doxycycline is currently the drug of choice. Other drugs such as fluoroquinolones, chloramphenicol, josamycin or newer macrolides may also be used in some situations (e.g., people with allergies to tetracyclines). There is a risk of serious side effects with chloramphenicol. A recent study raised concerns about the effectiveness of fluoroquinolones in SFG rickettsioses, compared to doxycycline. Drug availability varies between countries.

## Prevention

Avoidance of tick bites is the cornerstone of prevention for tick-borne rickettsioses. Protective shoes and clothing (e.g., long-sleeved shirts and trousers tucked into socks) should be used in tick habitats. Ticks may be more visible on light-colored apparel. Clothing can be treated with acaricides such as permethrin. Tick repellents such as DEET are also helpful, but they are only effective for a short period against ticks, and must be reapplied periodically. For example, most tick repellents last less than 2 hours against *Amblyomma* spp. ticks. Clothing should be removed and decontaminated immediately after leaving a tick-infested environment.

People who enter tick habitats should check frequently for ticks, and remove them as soon as possible, using fine-tipped tweezers or gloved hands. If gloves are not available, the fingers can be shielded with a tissue or paper towel. Bare hands are not recommended, as there is a risk of exposure to the tick's tissue fluids or feces. The tick should not be squeezed, crushed or punctured. The U.S. Centers for Disease Control and Prevention (CDC) warns that tick removal techniques such as the use of hot matches or petroleum jelly may stimulate the tick to release additional saliva, and could increase the risk of infection. Tick bites should be disinfected after removal of the tick, and the hands should be washed with soap and water. The CDC recommends freezing the tick in a plastic bag, for identification in case of illness.

Ticks should be removed from pets, both to prevent dogs from becoming ill and to prevent ticks from entering the home. Some monthly flea preventatives for pets are also effective against ticks. Acaricides, biological controls and control of tick habitats can decrease the populations of tick vectors in a community. Dogs can act as sentinels for Rocky Mountain spotted fever in humans.

Two SFG rickettsiae are not transmitted by ticks. The risk of flea-borne spotted fever can be reduced by flea control on pets. Rickettsialpox is transmitted by a mite that is normally a parasite of mice and other small rodents. This mite may survive in the environment for up to two months, and humans are more likely to be bitten when the normal hosts have been destroyed. Concurrent acaricide treatment of the environment can eliminate these mites when wild rodents are eradicated.

There is currently no indication that prophylactic antibiotics can prevent spotted fevers after a tick bite, and some experimental evidence and observational studies suggest it would be ineffective.

## Morbidity and Mortality

The risk of infection varies with the abundance and location of host ticks in the environment, and with their tendency to feed on humans. Ticks such as *Rhipicephalus sanguineus* strongly prefer to feed on animals and rarely bite people. Human infections transmitted by such ticks (e.g., Mediterranean spotted fever) tend to be sporadic. Other ticks, such as *Amblyomma* spp., feed aggressively on most mammals. Diseases carried by these ticks, such as African spotted fever, can occur in clusters when groups of people (for instance, on a safari) enter tick-infested environments. The infection rate in ticks is also highly variable. For example, *R. parkeri* is found in 10-40% of its tick vectors, but *R. conorii* and *R. rickettsii* usually occur in less than 2%.

The precise morbidity and mortality rates for spotted fevers can sometimes be difficult to determine. At one time, all spotted fevers in the Americas were identified as either Rocky Mountain spotted fever or rickettsialpox, and many of the diseases in Europe were thought to be Mediterranean spotted fever. Even today, most illnesses are diagnosed with serological tests that do not identify SFG rickettsiae to the species level. The inclusion of other organisms could result in a disease appearing to be either milder or more severe than it truly is.

### Rocky Mountain spotted fever (*R. rickettsii*)

In the U.S., Rocky Mountain spotted fever usually occurs between April and October, coinciding with the tick season in affected areas. Most cases are sporadic, although clusters are occasionally seen. The number of confirmed and probable cases in the U.S. increased from an average of 3.0 per million population in 2000–2003, to 6.8 per million in 2004–2007 and 8 per million in 2008. Some of this increase might be due to better awareness, or to the adoption of a new, less stringent, case definition in surveillance. Infections with other organisms have undoubtedly been included in the statistics for RMSF. To reflect this, the reporting category was changed to “Spotted Fever Rickettsioses (including RMSF)” in 2010.

Before effective treatments were available, up to 63-87% of the cases in some parts of the U.S. and 75-80% of the cases in Brazil were fatal. Mortality from this disease has decreased steadily in the U.S. With modern antibiotics and supportive care, it was estimated to be approximately 3% (range 3-5%) between 1981 and 1998, and decreased to 1.4% (range 0.7–2.9%) in 1997–2002. The reason for the further decrease to 1.4% is not known, although some authors speculate that it might be related to the accidental inclusion of other diseases under “Rocky Mountain spotted fever.” Geographical variations in disease severity have

been reported, both within North America, and in comparisons between North and South America. In one region of Brazil, severe cases are common, and the average case fatality rate was 39% during 1995–2004. In contrast, the clinical course is milder, and the case fatality rate lower, in another part of Brazil. Geographical differences might be caused by the virulence of local strains of *R. rickettsii*, differences in treatment, or the distribution of other *Rickettsia* that can be confused with *R. rickettsii*.

### *R. parkeri rickettsiosis*

*R. parkeri rickettsiosis* is not the only illness that may be confused with Rocky Mountain spotted fever in the U.S.; however, it is the best characterized. This disease appears to be milder than RMSF. Approximately 33% of patients with *R. parkeri rickettsiosis* are hospitalized, compared to 75% of patients with RMSF. Neurological signs are also less common. In one case series, untreated patients with *R. parkeri rickettsiosis* were only moderately ill after 7–10 days of fever, and there were no deaths. In contrast, the illness usually becomes increasingly severe in untreated RMSF.

### Mediterranean spotted fever (*R. conorii* subsp. *conorii*)

Mediterranean spotted fever usually occurs in the spring and summer. The prevalence of this disease is reported to be 50 cases per 100,000 inhabitants in the Mediterranean region. In some areas (e.g., Italy and Portugal), the reported incidence has increased recently. MSF is transmitted by the dog tick *Rhipicephalus sanguineus*, and the risk of illness is associated with dog contact as well as tick burdens in the environment.

Most cases of MSF are mild. Before antibiotics were available, the case fatality rate was estimated to be 1-3%. However, severe illnesses (defined in a variety of ways) and deaths have been documented regularly in the literature since the 1980s. Complications are more common in older patients, those with other debilitating diseases, and cases with delayed treatment, but seem to be uncommon in children. In several case series, the rate of severe organ involvement ranged from less than 1% in children, to 5% in large French studies, to 15% to 20% in some reports from Algeria, Bulgaria and the Iberian Peninsula. Most studies have reported a case fatality rate between 0% and 3%, but studies from Portugal suggest it might be higher. In Portugal, the number of hospitalized MSF patients increased from 176 in 1994 to 446 in 2004. The overall case fatality rate in these hospitalized patients was 3-7%, but it was much higher at two hospitals. In one region, it peaked at 32% in 1997. A later study found that some of the patients in this area had Israeli spotted fever, rather than MSF. This study reported that the case fatality rate was 13% among these patients in 1994–2006, when only culture- or PCR-confirmed *R. conorii* subsp. *conorii* cases were included. Other SFG rickettsiae can also cause illnesses that can be confused with MSF.



## **Israeli spotted fever (*R. conorii* subsp. *israelensis*)**

Some studies suggest that *R. conorii* subsp. *israelensis* might be more virulent than *R. conorii* subsp. *conorii*, although this is still uncertain. A study from Portugal reported a case fatality rate of 29% in hospitalized patients with culture or PCR-confirmed Israeli spotted fever, compared to 13% in patients with similarly confirmed Mediterranean spotted fever.

## **Japanese spotted fever (*R. japonica*)**

More than 200 cases of Japanese spotted fever were reported between 1984 and 1998 in Japan. This disease has been described in both children and adults., but in one case series, 75% of the patients were between 50 and 80 years of age. Many of these cases were severe.

## **African tick bite fever *R. africae***

African tick bite fever is fairly common among travelers returning from southern Africa or the eastern Caribbean. Studies among Norwegian travelers to Africa reported an incidence of 4-5%. The prevalence of this disease in Africa is poorly understood. Although cases are rarely documented in some countries, the incidence was estimated to be 60–80 cases per 100,000 patients in some areas of Zimbabwe. African tick bite fever is likely to be underdiagnosed in some parts of Africa, due to the mildness of the clinical signs and the limited availability of medical care and/or diagnostic testing. As of 2012, complications appear to be uncommon, and life-threatening illness has not been reported.

## **Rickettsialpox**

Rickettsialpox is reported to be mild and self-limited, and fatalities have not been documented. Most cases of rickettsialpox were described between 1940 and 1950, with few published cases in the last 30 years. Cases tend to be more common in urban environments when wild rodents have been eradicated, and the mites seek other hosts.

## **Other illnesses**

Most cases of Queensland tick typhus (*R. australis*) are mild, but severe disease and deaths are possible. *R. felis* infections are also thought to be mild. No deaths were reported among patients with Flinders Island spotted fever (*R. honei*) on Flinders Island, Australia, even without antibiotic treatment. However, a recent *R. honei* case reported from Nepal was severe. TIBOLA/ DEBONEL (*R. slovaca* and *R. raoultii*) is unusual for a spotted fever in being more common in the winter. No deaths have been attributed to this disease, which is generally reported to be mild. Little is known about some spotted fevers, as only a few cases have been described.

## **Infections in Animals**

### **Species Affected**

#### **Infections**

SFG rickettsiae seem to be capable of infecting many species of mammals. Antibodies to this group of organisms have been reported in dogs, cats, horses, donkeys, mules, cattle, sheep, goats, pigs, rabbits and wild animals including deer, small mammals, carnivores and rodents. A few studies have demonstrated reactivity to a specific organism. Antibodies to *R. rickettsii* and *R. parkeri* were reported in dogs, horses and opossums; antibodies to *R. rickettsii*, *R. akari* and *R. felis* in cats; and antibodies to *R. japonica* in dogs and cats. Based on PCR and/or culture, organisms that have been detected in dogs include *R. conorii* subsp. *conorii*, *R. conorii* subsp. *israelensis*, *R. felis*, *R. parkeri* and *R. rickettsii*. *R. rickettsii* has also been found in wild rodents and some other small animals such as opossums (*Didelphis* spp.). Experimental infections with *R. conorii*, *R. rickettsii*, *R. parkeri* and *R. africae* have been established in domesticated mammals. Some species of birds were infected experimentally with *R. rickettsii*.

Little is known about potential amplifying or reservoir hosts for SFG rickettsiae. Rodents are thought to be amplifying hosts for *R. rickettsii*. Opossums might also amplify this organism, based on experimental studies. Rabbits (or small rodents living in rabbit burrows) were suggested as possible reservoir hosts for *R. conorii* subsp. *conorii*, based on fluctuations in the incidence of human MSF that coincided with changes in the wild rabbit population in France. Dogs have been proposed as possible amplifying hosts for *C. felis*.

#### **Clinical cases**

Rocky Mountain spotted fever occurs in dogs. Dogs might also be affected by Mediterranean spotted fever, but this is still uncertain. Other spotted fever agents have occasionally been implicated in illnesses, but there is no definitive evidence for their involvement.

### **Incubation Period**

In dogs, the incubation period for Rocky Mountain spotted fever is 2 to 14 days.

### **Clinical Signs**

#### **Rocky Mountain spotted fever (*R. rickettsii*)**

Dogs infected with *R. rickettsii* may remain asymptomatic or become mildly to severely ill. The clinical signs are highly variable, and may initially be nonspecific. Fever, anorexia and depression are the most commonly reported signs. Dogs may also have lymphadenopathy, a mucopurulent oculonasal discharge, gastrointestinal signs (abdominal pain, diarrhea, vomiting), respiratory signs (coughing, dyspnea) and joint or muscle pain. Some dogs develop edema on the face (e.g., the ears or lips), penile

# Spotted Fevers

sheath or extremities. Ocular signs, which may include focal retinal hemorrhages, chorioretinal exudate or retinal detachment, have been reported in some dogs. Thrombocytopenia is common but typically mild, and anemia may be seen. Epistaxis, petechial or ecchymotic hemorrhages, melena or hematuria occur in less than a quarter of all cases, and are generally due to vasculitis rather than low platelet numbers. Petechiae and ecchymoses tend to be found mainly on the oral, ocular and genital mucous membranes. Increased permeability of the blood vessels can cause hypotension and shock.

Neurological signs are relatively common in dogs with RMSF. They may follow or occur at the same time as the initial constitutional signs. Vestibular dysfunction is reported frequently, but other abnormalities including altered mental states, generalized or localized hyperesthesia, intention tremors of the head, ataxia, seizures, paraparesis or tetraparesis may be seen. Cardiac complications, renal failure, necrosis of the extremities and DIC have been reported in severe cases. The prognosis is usually good in treated dogs, although death is possible. Mortality can be higher in dogs with cardiovascular complications, active bleeding or neurological signs.

Few cases of RMSF have been described among dogs in South America. Two recently described cases in Brazil were similar to clinical cases reported in North America. One dog had fever, anorexia, diarrhea and hematochezia, followed by neurological signs including ataxia and vestibular syndrome with spontaneous nystagmus. Signs in the second dog included fever, anorexia, lethargy and vomiting. Dogs that were experimentally inoculated with a Brazilian strain of *R. rickettsii* developed fever, lethargy, anorexia and conjunctivitis, but no hemorrhagic, locomotor or neurological signs.

## **Mediterranean spotted fever (*R. conorii* subsp *conorii*)**

Although dogs can be infected with *R. conorii*, there is only limited evidence that they might become ill. Mild fever, anorexia and lethargy lasting 2–3 days, followed by spontaneous recovery, were associated with *R. conorii* infections in three Yorkshire terriers. Other case reports of potential MSF described fever, prostration, petechial rash and thrombocytopenia. Doxycycline resulted in rapid clinical improvement in some dogs. A study from Portugal reported that 68% of dogs with suspected tick-borne illness (e.g., fever, lymphadenopathy, gastrointestinal signs, thrombocytopenia and petechial rash) had antibodies to SFG rickettsiae, compared to 39% of healthy dogs. *R. conorii* subsp. *conorii* and *R. conorii* subsp. *israelensis* were detected in a few of these dogs by PCR, and some other tick-transmitted infections were ruled out. Experimentally infected dogs are often asymptomatic, but in one study, dogs infected with *R. conorii* subsp *conorii* developed mild fever, anorexia and lethargy. In this study,

inoculation of dogs with *R. conorii* subsp. *israelensis* resulted in milder signs in fewer animals.

## **Other spotted fevers**

One dog with clinical signs of fatigue, vomiting, and diarrhea had evidence of *R. felis* infection, by PCR. Whether the organism had a causative role is uncertain, and some other dogs infected with this organism have been asymptomatic. In Australia, *R. felis* DNA was detected in 9% of the dogs in an animal shelter, but infection was not associated with clinical signs.

In California, two dogs with signs of Rocky Mountain spotted fever had higher antibody titers to *R. massiliae* than *R. rickettsii*, *R. rhipicephali*, or 364D *Rickettsia*. PCR evidence for *R. massiliae* was found in many ticks on the property. Nucleic acids were not detected in the dogs.

In Tasmania, Australia, 59% of cats and 57% of dogs had antibodies to SFG rickettsiae, but there was no correlation between the animals' health and seropositivity. Similarly, a study from the U.S. found no statistically significant link between fever in cats, and antibodies to *Rickettsia* spp. Attempts to detect *Rickettsia* spp. DNA in these cats, using PCR, were unsuccessful.

No clinical signs that could be attributed to the organism were seen in calves inoculated with *R. parkeri*, or goats inoculated with *R. africae*. Cattle inoculated with *R. africae* developed only regional lymphadenopathy and inoculation site reactions.

## **Communicability**

SFG rickettsiae are not transmitted directly between animals, but some species have sufficient levels of rickettsemia to infect ticks or other vectors. Transmission might be possible in blood transfusions.

Animals can carry infected ticks or fleas, and may bring these vectors into closer contact with humans.

## **Diagnostic Tests**

In dogs, Rocky Mountain spotted fever is usually diagnosed retrospectively by serology. Indirect immunofluorescence is used most often, but ELISAs are also available. A fourfold rise in titer between acute and convalescent samples is diagnostic. A single high titer may also be suggestive; however, dogs can develop clinical signs before they become seropositive. Conversely, healthy dogs can have antibodies to SFG rickettsiae. Due to cross-reactivity, most serological tests cannot distinguish antibodies to different species of SFG rickettsiae. Such discriminatory tests are usually available only at reference laboratories. They include comparisons of titers to different organisms, cross-absorption of sera and immunoblotting (Western blotting).

Rickettsial antigens or nucleic acids may be found in tissues and blood. PCR permits definitive identification of rickettsial species. It can also recognize novel SFG rickettsiae. Direct immunofluorescence or immuno-

# Spotted Fevers

peroxidase staining can detect antigens. However, organisms can be focally distributed and are not always found. As with serology, immunostaining only recognizes the organisms as SFG rickettsiae, and does not identify them to the species level. Tests to detect antigens and nucleic acids may be available only at specialized laboratories, such as university or reference laboratories.

Isolation of SFG rickettsiae from tissues or blood is rarely done. Culture is available only at reference laboratories, as it is hazardous and requires biosafety level 3 conditions. *Rickettsia* spp. are obligate intracellular organisms, and must be isolated in cell cultures (or by older methods such as inoculation into male guinea pigs or embryonated eggs). Samples must be received quickly at the laboratory, for culture to be successful.

## Treatment

Only a limited number of antibiotics are effective against SFG rickettsiae. Tetracycline antibiotics, especially doxycycline, are the drugs of choice. Other antibiotics, such as chloramphenicol or fluoroquinolones can also be effective; however, chloramphenicol has health risks for people. A recent study in humans raised questions about the effectiveness of fluoroquinolones compared to doxycycline. Antibiotics are most effective given early in the disease. Supportive treatment may be needed for dehydration and other clinical signs.

## Prevention

Topical acaricides can be used to prevent tick bites. In tick-infested habitats, the animal's skin and hair coat should be checked frequently, and any ticks should be removed with fine tipped tweezers or gloved hands. If gloves or tweezers are not available, the fingers can be shielded with paper. Bare hands are not recommended, as there is a risk of exposure to the tick's tissue fluids or feces. The tick should not be squeezed, crushed or punctured, as its fluids may contain rickettsiae. The CDC warns against tick removal techniques such as the use of hot matches or petroleum jelly, which may stimulate the tick to release additional saliva and could increase the risk of infection. Acaricides, biological controls and habitat control can decrease tick populations in the environment.

## Morbidity and Mortality

Rocky Mountain spotted fever has been reported among dogs in both North and South America. Cases tend to be sporadic, and occur most often in animals less than three years old. Some dogs are infected asymptotically, while others develop mild to severe illness. German shepherds might become sick more often than other breeds, and English Springer spaniels with phosphofructokinase deficiency are thought to develop more severe disease. Antibiotics usually result in prompt improvement in cases without neurological signs or serious organ dysfunction; more severe infections may be slow to respond, and the dog

may be left with residual deficits. Case fatality rates vary, but are reported to be as high as 10%. Mortality can be higher in dogs with cardiovascular complications, active bleeding or neurological signs.

## Post Mortem Lesions [Click to view images](#)

Lesions reported in dogs include focal ischemic necrosis, thrombi and occlusions in blood vessels, and valvular endocarditis. Edema may be seen on the face, extremities or male genital organs. Pulmonary edema can also be found in some dogs. Ecchymoses and petechiae can occur in various organs including the brain, heart, testes and lymph nodes. Microscopically, vasculitis and perivascular inflammatory cell infiltrates may be seen in most body tissues.

## Internet Resources

---

Centers for Disease Control and Prevention (CDC)

<http://www.cdc.gov/rmsf/index.html>

International Veterinary Information Service (IVIS)

<http://www.ivis.org>

Public Health Agency of Canada, Pathogen Safety Data

Sheets <http://www.phac-aspc.gc.ca/lab-bio/res/psds-ftss/index-eng.php>

The Merck Manual

<http://www.merckmanuals.com/professional/index.html>

The Merck Veterinary Manual

<http://www.merckvetmanual.com/mvm/index.jsp>

## References

---

- Acha PN, Szyfres B (Pan American Health Organization [PAHO]). Zoonoses and communicable diseases common to man and animals. Volume 2. Chlamydioses, rickettsioses, and viroses. 3rd ed. Washington DC: PAHO; 2003. Scientific and Technical Publication No. 580. Rocky Mountain spotted fever; p. 32-8.
- Acha PN, Szyfres B (Pan American Health Organization [PAHO]). Zoonoses and communicable diseases common to man and animals. Volume 2. Parasitoses. 3rd ed. Washington DC: PAHO; 2003. Scientific and Technical Publication No. 580. Dermatitis caused by mites of animal origin. Other acariasis; p. 327-31.
- Adjemian JZ, Adjemian MK, Foley P, Chomel BB, Kasten RW, Foley JE. Evidence of multiple zoonotic agents in a wild rodent community in the eastern Sierra Nevada. *J Wildl Dis.* 2008;44(3):737-42.
- Alexandre N, Santos AS, Bacellar F, Boinas FJ, Nuncio MS, de Sousa R. Detection of *Rickettsia conorii* strains in Portuguese dogs (*Canis familiaris*). *Ticks Tick Borne Dis.* 2011;2(2):119-22.
- Aliaga L, Sánchez-Blázquez P, Rodríguez-Granger J, Sampedro A, Orozco M, Pastor J. Mediterranean spotted fever with encephalitis. *J Med Microbiol.* 2009;58(Pt 4):521-5.

- Angeloni VL. Rickettsial diseases [monograph online]. In: James WD, editor. *Military dermatology, Part III: Disease and the environment*. Available at: [http://www.wrampc.amedd.army.mil/fieldmed/dermatology/De rm\\_Textbook\\_Ch11.pdf](http://www.wrampc.amedd.army.mil/fieldmed/dermatology/De rm_Textbook_Ch11.pdf). \* Accessed 18 Aug 2004.
- Angerami RN, da Silva AM, Nascimento EM, Colombo S, Wada MY, dos Santos FC, Mancini DM, de Oliveira RC, Katz G, Martins EC, da Silva LJ. Brazilian spotted fever: two faces of a same disease? A comparative study of clinical aspects between an old and a new endemic area in Brazil. *Clin Microbiol Infect*. 2009;15 Suppl 2:207-8.
- Angerami RN, Resende MR, Feltrin AF, Katz G, Nascimento EM, Stucchi RS, Silva LJ. Brazilian spotted fever: a case series from an endemic area in southeastern Brazil: clinical aspects. *Ann N Y Acad Sci*. 2006;1078:252-4.
- Apperson CS, Engber B, Nicholson WL, Mead DG, Engel J, Yabsley MJ, Dail K, Johnson J, Watson W. Tick-borne diseases in North Carolina: Is “*Rickettsia amblyommii*” a possible cause of rickettsiosis reported as Rocky Mountain spotted fever? *Vector Borne Zoonotic Dis*. 2008;8(5): 597-606.
- Bayliss DB, Morris AK, Horta MC, Labruna MB, Radecki SV, Hawley JR, Brewer MM, Lappin MR. Prevalence of *Rickettsia* species antibodies and *Rickettsia* species DNA in the blood of cats with and without fever. *J Feline Med Surg*. 2009;11(4):266-70.
- Beeler E, Abramowicz KF, Zambrano ML, Sturgeon MM, Khalaf N, Hu R, Dasch GA, Ereemeeva ME. A focus of dogs and *Rickettsia massiliae*-infected *Rhipicephalus sanguineus* in California. *Am J Trop Med Hyg*. 2011;84(2):244-9.
- Bischof R, Rogers DG. Serologic survey of select infectious diseases in coyotes and raccoons in Nebraska. *J Wildl Dis*. 2005;41(4):787-91.
- Blanco JR, Oteo JA. Rickettsiosis in Europe. *Ann N Y Acad Sci*. 2006;1078:26-33.
- Botelho-Nevers E, Rovey C, Richet H, Raoult D. Analysis of risk factors for malignant Mediterranean spotted fever indicates that fluoroquinolone treatment has a deleterious effect. *J Antimicrob Chemother*. 2011;66(8):1821-30.
- Breitschwerdt EB, Davidson MG, Aucoin DP, Levy MG, Szabados NS, Hegarty BC, Kuehne AL, James RL. Efficacy of chloramphenicol, enrofloxacin, and tetracycline for treatment of experimental Rocky Mountain spotted fever in dogs. *Antimicrob Agents Chemother*. 1991;35:2375-81.
- Breitschwerdt EB, Hegarty BC, Maggi RG, Lantos PM, Aslett DM, Bradley JM. *Rickettsia rickettsii* transmission by a lone star tick, North Carolina. *Emerg Infect Dis*. 2011;17(5):873-5.
- Breitschwerdt EB, Meuten DJ, Walker DH, Levy M, Kennedy K, King M, Curtis B. Canine Rocky Mountain spotted fever: A kennel epizootic. *Am J Vet Res*. 1985;46:2124-2128.
- Breitschwerdt EB, Papich MG, Hegarty BC, Gilger B, Hancock SI, Davidson MG. Efficacy of doxycycline, azithromycin, or trovafloxacin for treatment of experimental Rocky Mountain spotted fever in dogs. *Antimicrob Agents Chemother*. 1999;43(4):813-21.
- Brouqui P, Parola P, Fournier PE, Raoult D. Spotted fever rickettsioses in southern and eastern Europe. *FEMS Immunol Med Microbiol*. 2007;49(1):2-12.
- Baltadzhiev IG, Popivanova NI. Some epidemiological features of the Mediterranean spotted fever re-emerging in Bulgaria. *Folia Med (Plovdiv)*. 2012;54(1):36-43.
- Buckingham SC, Marshall GS, Schutze GE, Woods CR, Jackson MA, Patterson LE, Jacobs RF. Tick-borne Infections in Children Study Group. Clinical and laboratory features, hospital course, and outcome of Rocky Mountain spotted fever in children. *J Pediatr*. 2007;150(2):180-4, 184.
- Burgdorfer W, Friedhoff KT, Lancaster JL Jr. Natural history of tick-borne spotted fever in the USA. Susceptibility of small mammals to virulent *Rickettsia rickettsii*. *Bull World Health Organ*. 1966;35(2):149-53.
- Case JB, Chomel B, Nicholson W, Foley JE. Serological survey of vector-borne zoonotic pathogens in pet cats and cats from animal shelters and feral colonies. *J Feline Med Surg*. 2006;8(2):111-7.
- Camer GA, Lim CW. Detection of spotted fever and typhus group rickettsial infection in wild raccoon dogs (*Nyctereutes procyonoides koreensis*) in Chonbuk Province, Korea. *J Zoo Wildl Med*. 2008;39(2):145-7.
- Castellaw AH, Cheney EF, Varela-Stokes AS. Tick-borne disease agents in various wildlife from Mississippi. *Vector Borne Zoonotic Dis*. 2011;11(4):439-42.
- Centers for Disease Control and Prevention [CDC]. Rocky Mountain spotted fever [online]. CDC; 2010 Nov. Available at: <http://www.cdc.gov/rmsf/index.html>. Accessed 12 Oct 2012.
- Centers for Disease Control and Prevention [CDC]. Rocky Mountain spotted fever and animals [online]. CDC; 2010 Jul. Available at: <http://www.cdc.gov/healthypets/diseases/rockymountain.htm>. Accessed 10 Oct 2012.
- Centers for Disease Control and Prevention [CDC]. Rocky Mountain spotted fever (*Rickettsia rickettsii*). 2004 case definition [online]. CDC; 2003 Feb. Available at <http://www.cdc.gov/epo/dphsi/casedef/rockycurrent.htm>. \* Accessed 10 Aug 2004.
- Chung MH, Lee SH, Kim MJ, Lee JH, Kim ES, Kim MK, Park MY, Kang JS. Japanese spotted fever, South Korea. *Emerg Infect Dis*. 2006;12(7):1122-4.
- Comer KM. Rocky Mountain spotted fever. *Vet Clin North Am Small Anim Pract*. 1991;21:27-44.
- Cragun WC, Bartlett BL, Ellis MW, Hoover AZ, Tyring SK, Mendoza N, Vento TJ, Nicholson WL, Ereemeeva ME, Olano JP, Rapini RP, Paddock CD. The expanding spectrum of eschar-associated rickettsioses in the United States. *Arch Dermatol*. 2010;146(6):641-8.
- Dantas-Torres F. Rocky Mountain spotted fever. *Lancet Infect Dis*. 2007;7(11):724-32.
- Demeester R, Claus M, Hildebrand M, Vlieghe E, Bottieau E. Diversity of life-threatening complications due to Mediterranean spotted fever in returning travelers. *J Travel Med*. 2010;17(2):100-4.
- Fournier PE, Raoult D. Current knowledge on phylogeny and taxonomy of *Rickettsia* spp. *Ann NY Acad Sci*. 2009;1166: 1–11.
- Freitas MC, Grycajuk M, Molento MB, Bonacin J, Labruna MB, Pacheco Rde C, Moraes-Filho J, Deconto I, Biondo AW. Brazilian spotted fever in cart horses in a non-endemic area in Southern Brazil. *Rev Bras Parasitol Vet*. 2010;19(2):130-1.
- Fuentes L. Ecological study of Rocky Mountain spotted fever in Costa Rica. *Am J Trop Med Hyg*. 1986;35(1):192-6.
- Gayle A. Tick-borne diseases. *Am Fam Physician*. 2001;64: 461-6,8.

- Graves S, Stenos J. *Rickettsia honei*: a spotted fever group *Rickettsia* on three continents. *Ann N Y Acad Sci*. 2003;990:62-6.
- Graves S, Stenos J. Rickettsioses in Australia. *Ann N Y Acad Sci*. 2009;1166:151-5.
- Graves S, Unsworth N, Stenos J. Rickettsioses in Australia. *Ann N Y Acad Sci*. 2006;1078:74-9.
- Greene CE. Rocky Mountain spotted fever and ehrlichiosis. In: Kirk RW, editor. *Current veterinary therapy IX*. Philadelphia: WB Saunders; 1986. p. 1080-4.
- Harrus S, Lior Y, Ephros M, Grisaru-Soen G, Keysary A, Strenger C, Jongejan F, Waner T, Baneth G. *Rickettsia conorii* in humans and dogs: a seroepidemiologic survey of two rural villages in Israel. *Am J Trop Med Hyg*. 2007;77(1):133-5.
- Henke SE, Pence DB, Demarais S, Johnson JR. Serologic survey of selected zoonotic disease agents in black-tailed jack rabbits from western Texas. *J Wildl Dis*. 1990;26(1):107-11.
- Hii SF, Kopp SR, Thompson MF, O'Leary CA, Rees RL, Traub RJ. Molecular evidence of *Rickettsia felis* infection in dogs from Northern Territory, Australia. *Parasit Vectors*. 2011;4:198-1012.
- Horta MC, Labruna MB, Pinter A, Linardi PM, Schumaker TT. *Rickettsia* infection in five areas of the state of São Paulo, Brazil. *Mem Inst Oswaldo Cruz*. 2007;102(7):793-801.
- Horta MC, Moraes-Filho J, Casagrande RA, Saito TB, Rosa SC, Ogrzewalska M, Matushima ER, Labruna MB. Experimental infection of opossums *Didelphis aurita* by *Rickettsia rickettsii* and evaluation of the transmission of the infection to ticks *Amblyomma cajennense*. *Vector Borne Zoonotic Dis*. 2009;9(1):109-18.
- Hoshina K, Itogawa H, Itagaki A, Gomyoda M, Uchida T. [Serosurvey for spotted fever group rickettsial infection in vertebrates in Shimane Prefecture: abstract]. *Kansenshokaku Zasshi*. 1995;69(5):524-31.
- Hribnik TN, Barr SC. Canine Rocky Mountain spotted fever. In: Kirk RW, editor. *Current veterinary therapy X*. Philadelphia: WB Saunders; 1989. p. 421-2.
- Ibarra V, Oteo JA, Portillo A, Santibáñez S, Blanco JR, Metola L, Eiros JM, Pérez-Martínez L, Sanz M. *Rickettsia slovaca* infection: DEBONEL/TIBOLA. *Ann N Y Acad Sci*. 2006;1078:206-14.
- Imaoka K, Kaneko S, Tabara K, Kusatake K, Morita E. The first human case of *Rickettsia tamurae* infection in Japan. *Case Rep Dermatol*. 2011;3(1):68-73.
- Izzard L, Cox E, Stenos J, Waterston M, Fenwick S, Graves S. Serological prevalence study of exposure of cats and dogs in Launceston, Tasmania, Australia to spotted fever group rickettsiae. *Aust Vet J*. 2010;88(1-2):29-31.
- Jensenius M, Fournier PE, Kelly P, Myrvang B, Raoult D. African tick bite fever. *Lancet Infect Dis*. 2003;3(9):557-64.
- Jensenius M, Fournier PE, Raoult D. Rickettsioses and the international traveler. *Clin Infect Dis*. 2004;39(10):1493-9.
- Jiang J, Stromdahl EY, Richards AL. Detection of *Rickettsia parkeri* and Candidatus *Rickettsia andeanae* in *Amblyomma maculatum* Gulf Coast ticks collected from humans in the United States. *Vector Borne Zoonotic Dis*. 2012;12(3):175-82.
- Kahn CM, Line S, editors. *The Merck veterinary manual*. 10th ed. Whitehouse Station, NJ: Merck and Co; 2010. Rocky Mountain spotted fever; p 731-2.
- Kelly P, Lucas H, Beati L, Yowell C, Mahan S, Dame J. *Rickettsia africae* in *Amblyomma variegatum* and domestic ruminants on eight Caribbean islands. *J Parasitol*. 2010;96(6):1086-8.
- Kidd L, Maggi R, Diniz PP, Hegarty B, Tucker M, Breitschwerdt E. Evaluation of conventional and real-time PCR assays for detection and differentiation of Spotted Fever Group *Rickettsia* in dog blood. *Vet Microbiol*. 2008;129(3-4):294-303.
- Labruna MB, Kamakura O, Moraes-Filho J, Horta MC, Pacheco RC. Rocky Mountain spotted fever in dogs, Brazil. *Emerg Infect Dis*. 2009;15(3):458-60.
- Labruna MB, Ogrzewalska M, Soares JF, Martins TF, Soares HS, Moraes-Filho J, Nieri-Bastos FA, Almeida AP, Pinter A. Experimental infection of *Amblyomma aureolatum* ticks with *Rickettsia rickettsii*. *Emerg Infect Dis*. 2011;17(5):829-34.
- Letaïef A. Epidemiology of rickettsioses in North Africa. *Ann N Y Acad Sci*. 2006;1078:34-41.
- Levin ML, Killmaster LF, Zemtsova GE. Domestic dogs (*Canis familiaris*) as reservoir hosts for *Rickettsia conorii*. *Vector Borne Zoonotic Dis*. 2012;12(1):28-33.
- Lin L, Decker CF. Rocky Mountain spotted fever. *Dis Mon*. 2012;58(6):361-9.
- Lundgren DL, Thorpe BD, Haskell CD. Infectious diseases in wild animals in Utah. VI. Experimental infection of birds with *Rickettsia rickettsii*. *J Bacteriol*. 1966;91(3):963-6.
- Madeddu G, Mancini F, Caddeo A, Ciervo A, Babudieri S, Maida I, Fiori ML, Rezza G, Mura MS. *Rickettsia monacensis* as cause of Mediterranean spotted fever-like illness, Italy. *Emerg Infect Dis*. 2012;18(4):702-4.
- Magnarelli LA, Anderson JF, Burgdorfer W. Rocky mountain spotted fever in Connecticut: human cases, spotted-fever group rickettsiae in ticks, and antibodies in mammals. *Am J Epidemiol*. 1979;110(2):148-55.
- Magnarelli LA, Anderson JF, Philip RN, Burgdorfer W, Casper EA. Endemicity of spotted fever group rickettsiae in Connecticut. *Am J Trop Med Hyg*. 1981;30(3):715-21.
- Mahara F. Rickettsioses in Japan and the far East. *Ann N Y Acad Sci*. 2006;1078:60-73.
- Matthewman L, Kelly P, Hayter D, Downie S, Wray K, Bryson N, Rycroft A, Raoult D. Domestic cats as indicators of the presence of spotted fever and typhus group rickettsiae. *Eur J Epidemiol*. 1997;13(1):109-11.
- McBride WJH, Hanson JP, Miller R, Wenck D. Severe spotted fever group rickettsiosis, Australia. *Emerg Infect Dis*. 2007;13(11): 1742-4.
- McClain D, Dana AN, Goldenberg G. Mite infestations. *Dermatol Ther*. 2009;22(4):327-46.
- McQuiston JH, Guerra MA, Watts MR, Lawaczek E, Levy C, Nicholson WL, Adjemian J, Swerdlow DL. Evidence of exposure to spotted fever group rickettsiae among Arizona dogs outside a previously documented outbreak area. *Zoonoses Public Health*. 2011;58(2):85-92.
- McQuiston JH, Paddock CD, Singleton J Jr, Wheeling JT, Zaki SR, Childs JE. Imported spotted fever rickettsioses in United States travelers returning from Africa: a summary of cases confirmed by laboratory testing at the Centers for Disease Control and Prevention, 1999-2002. *Am J Trop Med Hyg*. 2004;70(1):98-101.

- Mikszewski JS, Vite CH. Central nervous system dysfunction associated with Rocky Mountain spotted fever infection in five dogs. *J Am Anim Hosp Assoc.* 2005;41(4):259-66.
- Moraes-Filho J, Pinter A, Pacheco RC, Gutmann TB, Barbosa SO, Gonzáles MA, Muraro MA, Cecílio SR, Labruna MB. New epidemiological data on Brazilian spotted fever in an endemic area of the state of São Paulo, Brazil. *Vector Borne Zoonotic Dis.* 2009;9(1):73-8.
- Murphy H, Renvoise A, Pandey P, Parola P, Raoult D. *Rickettsia honei* infection in human, Nepal, 2009. *Emerg Infect Dis.* 2011;17(10):1865-7.
- Nicholson WL, Allen KE, McQuiston JH, Breitschwerdt EB, Little SE. The increasing recognition of rickettsial pathogens in dogs and people. *Trends Parasitol.* 2010;26(4):205-12.
- Nicholson WL, Gordon R, Demma LJ. Spotted fever group rickettsial infection in dogs from eastern Arizona: how long has it been there? *Ann N Y Acad Sci.* 2006;1078:519-22.
- Nilsson K. Septicaemia with *Rickettsia helvetica* in a patient with acute febrile illness, rash and myasthenia. *J Infect.* 2009;58(1):79-82.
- Oliveira KA, Pinter A, Medina-Sanchez A, Boppana VD, Wikel SK, Saito TB, Shelite T, Blanton L, Popov V, Teel PD, Walker DH, Galvao MA, Mafra C, Bouyer DH. *Amblyomma imitator* ticks as vectors of *Rickettsia rickettsii*, Mexico. *Emerg Infect Dis.* 2010;16(8):1282-4.
- Openshaw JJ, Swerdlow DL, Krebs JW, Holman RC, Mandel E, Harvey A, Haberling D, Massung RF, McQuiston JH. Rocky mountain spotted fever in the United States, 2000-2007: interpreting contemporary increases in incidence. *Am J Trop Med Hyg.* 2010;83(1):174-82.
- Paddock CD. The Science and fiction of emerging rickettsioses. *Ann NY Acad Sci.* 2009;1166: 133-43.
- Paddock CD, Brenner O, Vaid C, Boyd DB, Berg JM, Joseph RJ, Zaki SR, Childs JE. Concurrent Rocky Mountain spotted fever in a dog and its owner. *Am J Trop Med Hyg.* 2002;66: 197-9.
- Paddock CD, Finley RW, Wright CS, Robinson HN, Schrodt BJ, Lane CC, Ekenna O, Blass MA, Tamminga CL, Ohl CA, McLellan SL, Goddard J, Holman RC, Openshaw JJ, Sumner JW, Zaki SR, Eremeeva ME. *Rickettsia parkeri* rickettsiosis and its clinical distinction from Rocky Mountain spotted fever. *Clin Infect Dis.* 2008;47(9):1188-96.
- Paddock CD, Fournier PE, Sumner JW, Goddard J, Elshenawy Y, Metcalfe MG, Loftis AD, Varela-Stokes A. Isolation of *Rickettsia parkeri* and identification of a novel spotted fever group *Rickettsia* sp. from Gulf Coast ticks (*Amblyomma maculatum*) in the United States. *Appl Environ Microbiol.* 2010;76(9):2689-96.
- Parola P. *Rickettsia felis*: from a rare disease in the USA to a common cause of fever in sub-Saharan Africa. *Clin Microbiol Infect.* 2011;17(7):996-1000.
- Parola P. Rickettsioses in sub-Saharan Africa. *Ann N Y Acad Sci.* 2006;1078:42-7.
- Parola P, Davoust B, Raoult D. Tick- and flea-borne rickettsial emerging zoonoses. *Vet Res.* 2005;36:469-92.
- Parola P, Raoult D. Tropical rickettsioses. *Clin Dermatol.* 2006;24(3):191-200.
- Parola P, Socolovschi C, Raoult D. Deciphering the relationships between *Rickettsia conorii conorii* and *Rhipicephalus sanguineus* in the ecology and epidemiology of mediterranean spotted fever. *Ann NY Acad Sci.* 2009;1166:49-54.
- Piranda EM, Faccini JL, Pinter A, Saito TB, Pacheco RC, Hagiwara MK, Labruna MB. Experimental infection of dogs with a Brazilian strain of *Rickettsia rickettsii*: clinical and laboratory findings. *Mem Inst Oswaldo Cruz.* 2008;103(7):696-701.
- Portillo A, Pérez-Martínez L, Santibáñez S, Blanco JR, Ibarra V, Oteo JA. Detection of *Rickettsia africana* in *Rhipicephalus (Boophilus) decoloratus* ticks from the Republic of Botswana, South Africa. *Am J Trop Med Hyg.* 2007;77(2):376-7.
- Pretorius AM, Jensenius M, Birtles RJ. Update on spotted fever group Rickettsiae in South Africa. *Vector Borne Zoonotic Dis.* 2004;4(3):249-60.
- Public Health Agency of Canada. Pathogen Safety Data Sheet – *Rickettsia akari*. Pathogen Regulation Directorate, Public Health Agency of Canada; 2011 Dec. Available at: <http://www.phac-aspc.gc.ca/lab-bio/res/psds-ftss/rickettsia-akari-eng.php>. Accessed 10 Oct 2012.
- Public Health Agency of Canada. Pathogen Safety Data Sheet – *Rickettsia rickettsii*. Pathogen Regulation Directorate, Public Health Agency of Canada; 2010 Jul. Available at: <http://www.phac-aspc.gc.ca/lab-bio/res/psds-ftss/rickettsia-rickettsii-eng.php>. Accessed 10 Oct 2012.
- Raoult D, Parola P. Rocky Mountain spotted fever in the USA: a benign disease or a common diagnostic error? *Lancet Infect Dis.* 2008;8(10):587-9.
- Rovero C, Brouqui P, Raoult D. Questions on Mediterranean spotted fever a century after its discovery. *Emerg Infect Dis.* 2008;14(9):1360-7.
- Schex S, Dobler G, Riehm J, Müller J, Essbauer S. *Rickettsia* spp. in wild small mammals in Lower Bavaria, South-Eastern Germany. *Vector Borne Zoonotic Dis.* 2011;11(5):493-502.
- Soares JF, Soares HS, Barbieri AM, Labruna MB. Experimental infection of the tick *Amblyomma cajennense*, Cayenne tick, with *Rickettsia rickettsii*, the agent of Rocky Mountain spotted fever. *Med Vet Entomol.* 2012;26(2):139-51.
- Solano-Gallego L, Hegarty B, Espada Y, Llull J, Breitschwerdt E. Serological and molecular evidence of exposure to arthropod-borne organisms in cats from northeastern Spain. *Vet Microbiol.* 2006;118(3-4):274-7.
- Sousa R de, França A, Dória Nòbrega S, Belo A, Amaro M, Abreu T, Poças J, Proença P, Vaz J, Torgal J, Bacellar F, Ismail N, Walker DH. Host- and microbe-related risk factors for and pathophysiology of fatal *Rickettsia conorii* infection in Portuguese patients. *J Infect Dis.* 2008;198(4):576-85.
- Tabuchi M, Jilintai, Sakata Y, Miyazaki N, Inokuma H. Serological survey of *Rickettsia japonica* infection in dogs and cats in Japan. *Clin Vaccine Immunol.* 2007;14(11):1526-8.
- Tarasevich IV, Mediannikov OY. Rickettsial diseases in Russia. *Ann N Y Acad Sci.* 2006;1078:48-59.
- Tian ZC, Liu GY, Shen H, Xie JR, Luo J, Tian MY. First report on the occurrence of *Rickettsia slovaca* and *Rickettsia raoultii* in *Dermacentor silvarum* in China. *Parasit Vectors.* 2012;19:5:19.
- Tomassone L, Conte V, Parrilla G, De Meneghi D. *Rickettsia* infection in dogs and *Rickettsia parkeri* in *Amblyomma tigrinum* ticks, Cochabamba Department, Bolivia. *Vector Borne Zoonotic Dis.* 2010; 10(10): 953-8.

# Spotted Fevers

- Tribaldos M, Zaldivar Y, Bermudez S, Samudio F, Mendoza Y, Martinez AA, Villalobos R, Eremeeva ME, Paddock CD, Page K, Smith RE, Pascale JM. Rocky Mountain spotted fever in Panama: a cluster description. *J Infect Dev Ctries.* 2011;5(10):737-41.
- Varela AS. Tick-borne ehrlichiae and rickettsiae. In: Bowman DD. Companion and exotic animal parasitology. Ithaca, NY: International Veterinary Information Service [IVIS]; 2003. Available at: [http://www.ivis.org/advances/parasit\\_Bowman/varela/chapter\\_frm.asp?LA=1](http://www.ivis.org/advances/parasit_Bowman/varela/chapter_frm.asp?LA=1). Accessed 11 Aug 2004.
- Vite CH, editor. Braund's Clinical neurology in small animals - localization, diagnosis and treatment. Ithaca, NY: International Veterinary Information Service (IVIS); 2005. Inflammatory diseases of the central nervous system: Rickettsial meningoencephalitis. Available at: [http://www.ivis.org/advances/Vite/braund27/chapter\\_frm.asp](http://www.ivis.org/advances/Vite/braund27/chapter_frm.asp). Accessed 19 Oct 2012.
- Walker DH. Rickettsiae [monograph online]. In Baron S, editor. *Medical Microbiology*. 4th ed. New York: Churchill Livingstone; 1996. Available at: <http://www.gsbs.utmb.edu/microbook/>. \* Accessed 10 Aug 2004.
- Warner RD, Marsh WW. Rocky Mountain spotted fever. *J Am Vet Med Assoc.* 2002;221:1413-7.
- Ybañez AP, Sato F, Nambo Y, Fukui T, Masuzawa T, Ohashi N, Matsumoto K, Kishimoto T, Inokuma H. Survey on tick-borne pathogens in Thoroughbred horses in the Hidaka District, Hokkaido, Japan. *J Vet Med Sci.* 2012 Aug 10. [Epub ahead of print]
- Znazen A, Hammami B, Lahiani D, Ben Jemaa M, Hammami A. Israeli spotted fever, Tunisia. *Emerg Infect Dis.* 2011;17(7):1328-30.

\*Link defunct as of 2012