Spotted Fevers Including Rocky Mountain Spotted Fever and Mediterranean Spotted Fever

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Importance

Spotted fevers, which are caused by rickettsiae in the spotted fever group (SFG), have broadly similar clinical signs but a course that can range from mild and self-limited to severe and life-threatening. For a long time, these diseases were thought to be caused by only a few organisms such as *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. However, many additional species have been recognized as human pathogens since the 1980s, and multiple organisms are now known to circulate in many areas. Because diagnosis is often based on serological tests, which cross-react, some causative organisms may remain unrecognized. For example, some illnesses in North America once attributed to *R. rickettsii* are now known to be caused by *R. parkeri* or *R. philipii*, which tend to cause milder illnesses than Rocky Mountain spotted fever (RMSF).

Animals can also be infected with SFG rickettsiae, but with the exception of RMSF and possibly Mediterranean spotted fever (MSF) in dogs, there is no strong evidence that these organisms cause any significant illnesses.

Etiology

Spotted fevers are caused by members of the spotted fever group (SFG) in the genus *Rickettsia* (family Rickettsiaceae). These organisms are pleomorphic, obligate intracellular, Gram negative coccobacilli and include both known pathogens and organisms of unknown clinical significance. A few species (e.g., *R. felis*, *R. akari*, *R. australis*) are sometimes classified into a 'transitional group' of rickettsiae, which is considered distinct from both SFG rickettsiae and typhus group rickettsiae. However, this distinction is irrelevant for clinical purposes, and this factsheet uses 'SFG rickettsiae' for all of the organisms that cause spotted fevers.

Two of the most important pathogens are *R. rickettsii*, which causes Rocky Mountain spotted fever (also called Brazilian spotted fever), and *R. conorii* subsp. *conorii*, the agent of Mediterranean spotted fever (boutonneuse fever). More recently recognized subspecies of *R. conorii* are the agents of Israeli spotted fever (*R. conorii* subsp. *israelensis*), Astrakhan spotted fever (*R. conorii* subsp. *caspia*) and Indian tick typhus (*R. conorii* subsp. *indica*). *R. parkeri* causes an illness which has been termed Tidewater spotted fever, American boutonneuse fever or *R parkeri* rickettsiosis. A closely related organism, called *R. parkeri* strain Atlantic rainforest or *Rickettsia* spp. strain Atlantic rainforest, has been reported from parts of South America. *R. philipii* (formerly *Rickettsia* species 364D) causes Pacific Coast tick fever.

Other named syndromes include African tick-bite fever (*R. africae*), Japanese (or Oriental) spotted fever (*R. japonica*), Queensland tick typhus (*R. australis*), Flinders Island or Australian spotted fever (*R. honei*), Siberian or North Asian tick typhus (*R. sibirica* subsp. *sibirica*) and Far Eastern tick-borne rickettsiosis (*R. heilongjiangensis*). A syndrome known as lymphangitis-associated rickettsiosis is often caused by *R. sibirica* subsp. *mongolitimonae*, though other SFG rickettsiae have also been found occasionally. Another distinctive illness is known by various acronyms including TIBOLA (tick-borne lymphadenopathy), DEBONEL (*Dermacentor*-borne necrosis erythema lymphadenopathy) and SENLAT (scalp eschar neck lymphadenopathy), and occurs after a tick bite on the head. It was originally attributed to *R. slovaca* and *R. raoultii*, but other species, such as *R. sibirica mongolitimonae* and *R. massiliae*, have been identified in some cases. *R. helvetica*, *R. monacensis* and *R. aeschlimannii* are also known pathogens, and *R. tamurae*, *R. amblyommatis* and Candidatus *R. andeanae* were the proposed agents in a few spotted fever cases.

All of the agents above are tick-borne, but two spotted fevers are transmitted by other arthropods. *R. akari*, which uses *Liponyssoides* mites as its vector, causes rickettsialpox, and *R. felis* (formerly known as the ELB agent) is associated with a syndrome known as flea-borne spotted fever or cat flea typhus. Some authors consider *R. felis* to be a significant pathogen. Others note that it can be found in a wide variety of common arthropods, including some that do not feed on mammals (e.g., booklice), and that its nucleic acids are often found in asymptomatic people and in illnesses that could have another cause, and question its importance.

Species Affected

Evidence for infections with SFG rickettsiae has been found in many animals including dogs, cats, equids, cattle, sheep, goats, pigs and rabbits, as well as some wildlife such as wild boars, opossums, various carnivores and cervids, rodents and other small mammals, bats, and even some birds and reptiles. However, *R. rickettsii*, which causes Rocky Mountain spotted fever in dogs, is the only organism known to be a significant pathogen in naturally infected animals. Limited evidence suggests that *R. conorii* (Mediterranean spotted fever) might cause occasional mild illnesses in this species, and a few clinical case reports, with varying levels of evidence, have proposed a causative role for *R. felis, R. akari*, *R. massiliae* and a novel SFG rickettsia in dogs, and *R. rickettsii* or another rickettsia in one horse. Guinea pigs, which are often used as an animal model for SFG rickettsiae, can develop severe illnesses when experimentally infected.

The reservoir or amplifying hosts for SFG rickettsiae are not known, though experimentally infected animals, including dogs inoculated with *R. felis, R. conorii* or *R. rickettsii,* sometimes develop rickettsemia sufficient to infect arthropod vectors. Animals that have been suggested as possible reservoir hosts for some organisms include various wild rodents, opossums, rabbits and dogs. Reptiles were proposed to host *R. honei*, based on finding this organism in the reptile-associated tick *Aponomma hydrosaur*. The arthropod vectors for SFG rickettsiae also seem to be capable of maintaining some organisms indefinitely, thus possibly acting as both vector and reservoir.

Zoonotic potential

All of the pathogenic members of the spotted fever group affect humans. However, these organisms are not transmitted directly between hosts, including from animals to humans.

Geographic Distribution

Some SFG rickettsiae, such as *R. felis, R. akari* and *R. massiliae*, are cosmopolitan and can be found on most continents, while others seem to have a more limited distribution. The distribution of many organisms is still incompletely understood.

Species known to occur only in the Eastern Hemisphere include *R. conorii* subsp. *conorii*, the usual cause of Mediterranean spotted fever in Europe. This organism has also been found in ticks and/or clinical cases in China, Africa and other locations. The other three subspecies of *R. conorii* were originally reported to cause MSF-like diseases in the locations reflected in their names (e.g., Indian tick typhus), but they are now known to be more widely distributed, and have been detected in Europe as well as other locations. *R. japonica* has, to date, been found only in parts of Asia (e.g., Japan, China and Thailand), while *R. australis* seems to be limited to Australia. Some other SFG rickettsiae that have been identified in parts of Europe, Asia and/or Africa include *R. aeschlimannii*, *R. heilongjiangensis*, *R. slovaca*, *R. raoultii*, *R. monacensis*, *R. sibirica* subsp. *mongolitimonae* and *R. sibirica* subsp. *sibirica*.

R. rickettsiae causes Rocky Mountain spotted fever in parts of North, Central and South America. *R. parkeri* is also endemic at various sites in the Americas, and *R. philipii* has been found on the West Coast of North America. Some SFG rickettsiae previously thought to be limited to the Eastern Hemisphere (e.g., *R. slovaca, R. monacensis)* have now been identified in ticks in the Americas and might cause some clinical cases currently attributed to other organisms.

R. africae occurs in Africa, but it also circulates on some Caribbean islands, most likely introduced in *Amblyomma* ticks. This organism was recently recognized in ticks in parts of the Middle East, India and New Caledonia, and probably occurs in other locations. *R. honei*, originally detected on Flinders Island, Australia, was later found in other parts of Australia and in Thailand, with a single case that seemed to be locally acquired in the U.S. (Texas).

Transmission

Ticks are the vectors for most SFG rickettsiae. Each organism has one or more principal vectors, which may differ between regions. *R. rickettsii*, for instance, is often transmitted by *Dermacentor variabilis* and *D. andersoni* in the U.S. and Canada, but *Rhipicephalus sanguineus* is important in Mexico and parts of Arizona, and *Amblyomma* spp. often transmit this organism in South America. Ticks usually transmit SFG rickettsiae in bites; but organisms in a tick's crushed tissues or feces can enter the body through mucous membranes or breaks in the skin. Transmission seems to be influenced both by how long the tick has been attached, and whether it was "fed," i.e., previously received a blood meal. *R. rickettsii* usually causes severe signs in guinea pigs only when infected *D. variabilis* ticks have been attached for more than 8-12 hours if they are unfed; however, this can occur within 2 hours if the ticks already fed on another animal. Recent studies suggest that ticks actually begin transmitting *R. rickettsii* within an hour, perhaps even minutes, of attachment even when unfed, though the likelihood of illness, as well as its severity, increases with time as the dose of rickettsia becomes larger. Some organisms, including *R. rickettsii* and *R. conorii*, are known to be transmitted transovarially and transstadially in ticks.

R. akari is usually transmitted by the mite *Liponyssoides sanguineus*, which normally infests mice and other small rodents but will bite other species, especially if its normal hosts are absent. Transovarial transmission has been demonstrated in this vector. *R. akari* has also been found occasionally in ticks. The cat flea, *Ctenocephalides felis*, (which also infest hosts other than cats) is thought to be the primary biological vector for *R. felis*. This organism has also been found in other species of fleas, ticks, mites, mosquitoes, chiggers and other arthropods, including some that do not feed on vertebrates, such as the booklouse *Liposcelis bostrychophila*. How fleas transmit *R. felis* is still uncertain, but it has been detected in flea feces, and one study found it in flea salivary glands. Both transovarial and transstadial transmission have been reported in *C. felis*.

SFG rickettsiae are normally not transmitted directly between animals or people, other than in procedures such as blood transfusions. However, infections can be acquired through mucous membranes or broken skin in the laboratory, including via aerosols after laboratory accidents. Rickettsiae are obligate intracellular pathogens and do not survive for long outside the host.

Disinfection

Agents expected or known to be effective against rickettsiae include sodium hypochlorite, 70% ethanol and phenols, as well as 2% glutaraldehyde, formaldehyde and β-propiolactone. Heat of 56ºC is also expected to be effective, based on experiments with *R. akari* and *R. honei*, which were rapidly inactivated at this temperature, *R. honei* in 5 minutes.

Infections in Animals

Incubation Period

The estimated incubation period for Rocky Mountain spotted fever in dogs is 2-14 days.

Clinical Signs

Rocky Mountain spotted fever (R. rickettsii)

Dogs infected with *R. rickettsii* may remain asymptomatic or become mildly to severely ill. Clinical signs, which are variable, include fever and other nonspecific signs of illness (e.g., anorexia, depression) and, in some cases, conjunctivitis, gastrointestinal signs (abdominal pain, diarrhea, vomiting), respiratory signs, and joint or muscle pain. Thrombocytopenia is common but typically mild, and some dogs may be anemic. A macular or maculopapular rash seems to have been reported only in some experimentally infected dogs. However, naturally infected dogs may develop petechiae or ecchymoses on the mucous membranes or skin, and edema on the ears, lips or other parts of the face, the penile sheath and/or extremities. Complications can include ocular signs, (e.g., focal retinal hemorrhages, uveitis, retinitis), hemorrhages (epistaxis, melena, hematuria), neurological signs of varying severity, cardiac involvement, renal failure, necrosis of the extremities, disseminated intravascular coagulation, hypotension and shock. While the prognosis is usually good in treated dogs without significant complications, severe cases may be fatal.

An acute febrile illness in a 20-year-old horse, which was characterized by nonspecific clinical signs and responded to tetracyclines, was reported as a possible rickettsial illness. Seroconversion was not demonstrated, but serological titers to *R. rickettsii* declined rapidly beginning 4 days after treatment, the first day a serum sample was collected. The significance of this finding is unclear, and titers to rickettsiae in dogs do not usually decline for several months or more after the illness. Horses experimentally infected with *R. rickettsii* did not develop any clinical signs.

Other spotted fevers in animals

Most dogs, cats and livestock experimentally infected with various SFG rickettsiae remain asymptomatic, except for transient fevers or inoculation site reactions in some individuals. However, one study demonstrated that pretreatment of two dogs with cyclosporine resulted in the development of a fever, depression and anorexia when they were inoculated with a high dose of *R. japonica*, while healthy dogs given the same dose of the organism did not become ill. Cyclosporine was stopped on the day of the inoculation, and both animals recovered spontaneously by 5 days. Although this study suggests that some SFG rickettsiae other than *R. rickettsii* might affect animals in poor health, it has been difficult to demonstrate this in naturally infected animals. Issues include the high prevalence of subclinical infections, as well as the presence of multiple agents in ticks, which could result in an animal acquiring an incidental rickettsial infection together with the agent that is actually causing the disease.

As of 2023, there are only a few published case reports, all in dogs, of possible spotted fevers other than RMSF. Mild fever, anorexia and lethargy for 2–3 days, followed by spontaneous recovery, was associated with *R. conorii* infections (Mediterranean spotted fever) in three Yorkshire terriers. A few other reports of possible MSF described fever, prostration, petechial rash and thrombocytopenia. Dogs experimentally infected with *R. conorii* are usually asymptomatic, though one group reported that some dogs developed mild fever, anorexia and lethargy. Seroconversion has been seen in both febrile and asymptomatic dogs in endemic regions.

A R. massiliae infection was proposed in two dogs that had signs of RMSF but higher antibody titers to this organism than to R. rickettsii, R. rhipicephali, or R. philipii. Nucleic acids of R. massiliae were found in ticks on the property, but a PCR test on the dogs was negative. In another case report, a young dog with an acute illness characterized by nonspecific signs, vomiting and melena was PCR positive for R. akari and responded to doxycycline. One paper reported finding the nucleic acids of a novel Rickettsia in three dogs that had clinical signs consistent with a rickettsial illness (as well as other diseases). Two of the dogs seroconverted to SFG rickettsiae. Another dog with fatigue, vomiting, and diarrhea had R. felis nucleic acids. Dogs inoculated with this organism have mostly been asymptomatic, though one study reported mild diarrhea and decreased appetite in a few animals and petechiae on the oral mucous membranes of one. Whether this was from R. felis or had another cause was unclear.

Post Mortem Lesions

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In addition to the externally visible lesions, dogs with RMSF may have pulmonary edema, focal ischemic necrosis, thrombi and occlusions in blood vessels, and valvular endocarditis. Ecchymoses and petechiae may be found in internal organs including the brain, heart, testes and lymph nodes, as well as the skin and mucous membranes. Microscopically, vasculitis and perivascular inflammatory cell infiltrates may be seen in many tissues.

Diagnostic Tests

Rocky Mountain spotted fever in dogs is usually diagnosed by serology, using indirect immunofluorescence or ELISAs. A fourfold rise in antibody titers is diagnostic. A single high titer may also be suggestive; however, healthy dogs sometimes have antibodies to this or other rickettsiae, while sick dogs may not have detectable titers when they are first seen. The commonly used serological tests cannot distinguish antibody reactions to different organisms, but discriminatory tests (e.g., immunoblotting, comparison of titers to different rickettsiae, cross-absorption of sera) might be available at some reference laboratories.

Rickettsiae, their nucleic acids and antigens can be detected in tissues, including swabs or biopsies of the eschar, and they may sometimes be found in blood, especially during the early stages of the illness. A variety of PCR tests have been developed, with varying levels of specificity for individual organisms. Immunostaining can identify rickettsial antigens in tissues, though the organisms are focally distributed and may be missed. Culture, which requires biosafety level 3 conditions and live mammalian cells to grow the rickettsiae, is only available at reference laboratories and is rarely done. Older techniques to isolate rickettsiae, now rarely used, include animal inoculation into male guinea pigs and inoculation into embryonated eggs. Samples must be received quickly at the laboratory for culture to be successful.

Treatment

Only a few antibiotics, such as tetracyclines, are effective in treating rickettsiae. Treatment is most effective when begun early.

Control

Disease reporting

Veterinarians who suspect an animal is infected with a member of the SFG rickettsiae should follow their national and/or local guidelines for disease reporting.

Prevention

Topical acaricides or monthly flea preventatives can help prevent tick bites. Any attached ticks should be removed as soon as possible to reduce the risk of illness. Environmental controls for ticks include acaricides, biological controls and habitat modification; however, adverse effects on other arthropods and the possibility of promoting acaricide resistance should be taken into consideration.

Morbidity and Mortality

Most infections with SFG rickettsiae in animals seem to be asymptomatic. Rocky Mountain spotted fever cases in dogs tend to be sporadic, are seen most often in young animals, and range from subclinical to severe. Some reports have suggested that German shepherds might become sick more often than other breeds, and English Springer spaniels with phosphofructokinase deficiency are thought to develop more severe illnesses. Antibiotics usually result in prompt improvement in cases without neurological signs or serious organ dysfunction, but more severe cases may be slow to respond, and some dog may be left with residual neurological deficits or other issues. Mortality is higher in dogs with cardiovascular complications, active bleeding or neurological signs.

Infections in Humans

Incubation Period

Reported incubation periods for SFG rickettsioses range from one to 28 days and may vary with the organism, but most illnesses become apparent within a week or two.

Clinical Signs

The illnesses caused by SFG rickettsiae are broadly similar and are usually characterized by a febrile illness that is often accompanied by a rash and, in some cases, an eschar at the inoculation site. Eschars, which classically appear as a painless black crusted ulcer surrounded by erythema, are common in some spotted fevers, but typically absent in others. Multiple eschars may be found in diseases where the person is often bitten by more than one infected tick. Severe illnesses can include signs of vasculitis and renal, neurological, respiratory and cardiac complications. The pattern of the rash and eschars, together with the severity of the illness and the geographic location, can sometimes suggest a particular spotted fever. A few syndromes, such as lymphangitis-associated rickettsiosis or TIBOLA, also have distinctive clinical features.

Rocky Mountain spotted fever (R. rickettsii)

RMSF often begins as a nonspecific illness, with fever (often high), chills, malaise, headache, myalgia and anorexia. Gastrointestinal signs such as nausea, vomiting, diarrhea and abdominal pain are common, and some patients develop edema, which may either be generalized or limited to the face, periorbital region or extremities. There is usually no eschar. A nonpruritic macular rash, often seen first on the wrists, forearms, ankles or scrotum, can appear from the 2nd to 14th day and may spread rapidly. It frequently affects the palms or soles as well as the trunk and extremities, especially later in the disease. The face is usually spared. While the rash initially blanches on pressure, it may eventually become petechial, which is considered a sign of progression to severe RMSF. Petechiae, which can also appear on mucous membranes, sometimes coalesce to form ecchymoses.

Some patients develop ocular signs (e.g., conjunctivitis, optic disc edema, retinitis), respiratory signs ranging from a cough to acute respiratory distress, neurological signs of varying severity (e.g., transient deafness, tremors, paralysis), jaundice, acute renal failure, gangrene, myocarditis, hypotension, shock or multi-organ failure. Although patients in the early stages usually recover quickly with treatment, untreated cases may be fatal within a week or two.

Neurological signs sometimes persist after recovery, though some eventually resolve. Serological surveillance and outbreak reports suggest that subclinical infections and mild illnesses also occur in endemic regions, though cross-reactivity between rickettsiae can make it difficult to definitively attribute these cases to *R. rickettsii*.

Rickettsia parkeri rickettsiosis

R. parkeri rickettsiosis resembles Rocky Mountain spotted fever, with which it was initially confused, but gastrointestinal signs seem to be uncommon, and most patients have eschars, which are occasionally multiple. Although many patients have a maculopapular, vesiculopapular or papulopustular rash on the trunk and extremities, a petechial rash is not characteristic of this disease. Overall, this illness tends to be milder than RMSF, though severe cases are possible.

Mediterranean spotted fever (*R. conorii* subsp. *conorii*) and other illnesses caused by *R. conorii*

Like other spotted fevers, Mediterranean spotted fever begins as a febrile illness with nonspecific flu-like signs. Patients often have an eschar, which is most often single, and tend to develop a generalized maculopapular or purpuric rash, which usually includes the palms and soles. Although most cases are relatively mild, severe illnesses with complications similar to RMSF are possible.

Astrakhan spotted fever (*R. conorii* subsp. *caspia*), Indian tick typhus (*R. conorii* subsp. *indica*) and Israeli spotted fever (*R. conorii* subsp. *israelensis*) resemble Mediterranean spotted fever; however, eschars seem to be less common in Israeli and Astrakhan spotted fevers, and Israeli spotted fever appears to be more severe than the other illnesses caused by *R. conorii*.

Japanese spotted fever (*R. japonica*)

Some reports suggest that Japanese spotted fever may disproportionately affect older adults, and can be severe in this population. The clinical signs may include high fever, headache, gastrointestinal signs, a cough/ sore throat and/or erythema on the extremities, as well as an eschar and a rash. In one case series, the rash often became petechial after a few days, but often disappeared within 2 weeks. Reported complications are similar to those in severe RMSF.

Queensland tick typhus (*R. australis*)

Some patients with Queensland tick typhus have an eschar, and enlargement of the draining lymph node is common. Most also develop a rash, which is often macular or maculopapular but can be vesicular or pustular and may resemble chickenpox. Petechial rashes are rare. Most cases of Queensland tick typhus seem to be mild and patients generally recover without complications, though severe or fatal cases are seen occasionally.

African tick bite fever (*R. africae*)

African tick bite fever is usually a relatively mild and self-limited disease, and complications are uncommon. In addition to nonspecific flu-like signs, many patients have neck muscle myalgia, subjective neck stiffness and regional lymphadenopathy. Aphthous stomatitis (mouth blisters) and lymphangitis have also been reported. Most patients have at least one eschar, and multiple eschars are common. Less than half develop a generalized maculopapular or vesicular rash. Pustular or purpuric rashes are rare.

Flinders Island spotted fever (*R. honei*)

Flinders Island spotted fever cases reported in Australia were described as a febrile illness with a maculopapular rash on the trunk and limbs. Some patients had an eschar. Most recovered in 1-6 weeks even without antibiotics, and no deaths were seen, although some people were hospitalized. A patient in the U.S., infected in India, had a similar illness. However, four patients reported from Thailand and Nepal developed more severe cases with petechial or purpuric rashes and, in some cases, neurological signs, gastrointestinal signs, hypotension and hypoxia.

Pacific Coast tick fever (*R. philipii*)

Relatively few cases of Pacific coast fever have been published, but most of these cases were relatively mild, with few hospitalizations. Most people had an eschar, which was occasionally multiple, but rashes seem to be uncommon and may be limited in extent.

Lymphangitis-associated rickettsiosis (*R. sibirica* subsp. *mongolitimonae* and other agents)

Lymphangitis-associated rickettsiosis (LAR) is characterized by lymphangitis extending from the eschar(s) to the draining lymph node, which is enlarged. Multiple eschars are common, and there may also be a maculopapular rash. While this illness is often mild, more severe cases with neurological signs or renal disease have been reported.

R. sibirica subsp. *mongolitimonae* can also cause a more typical spotted fever with rash but no lymphangitis and lymphadenopathy, while other rickettsiae, such as *R. africae*, have occasionally been found in LAR.

TIBOLA (*R. slovaca*, *R. raoultii* and other agents)

TIBOLA is often seen in children, though adults are also affected. The site of the bite, on the scalp, may be responsible for most of the symptoms. An eschar is usually present, and localized alopecia may be found at its site. Constitutional signs are generally reported to be mild and flu-like, and only a minority of patients have fever and/or a rash. Regional lymphadenopathy, which is often cervical, is relatively common and can be painful. Deaths have not been reported.

Some of the organisms associated with TIBOLA can also cause more typical spotted fevers. *R. raoultii* infections in China can be relatively severe, and eschars and rashes appear to be uncommon.

Rickettsialpox (*R. akari*)

Rickettsialpox is a relatively mild, often self-limited, febrile illness. Many patients have a stiff neck, and some also have a cough, nausea, vomiting or lymphadenopathy. A single eschar is common, and a maculopapular rash develops on the trunk and extremities, usually progresses to vesicles or pustules, and can resemble chickenpox.

Cat flea–associated rickettsiosis (R. felis)

The syndrome caused by *R. felis* is incompletely understood, though most cases seem to be relatively mild. Nonspecific signs of illness, with or without fever, as well as gastrointestinal and/or respiratory signs, have been described in patients. Some only had a fever. Eschars appear to be uncommon, but most patients in one case series had a maculopapular rash. Complications such as neurological signs seem to be infrequent. Two illnesses in infants characterized by generalized skin vesicles and ulcers were also attributed to *R. felis*, based on PCR of the skin lesions; however, this diagnosis has been questioned because these signs are not typical of rickettsioses, an infant tested for antibodies did not seroconvert, and false positive PCR reactions are possible from *R. felis* in the environment.

Diagnostic Tests

Most cases in humans are confirmed by serology, which has the same limitations as serological testing in animals and requires a fourfold rise in titer for a definitive diagnosis. Seroconversion can be slow in some diseases such as African tick-bite fever. Antigen detection tests do not seem to be widely available, but PCR may identify the organisms in eschar swabs, biopsies of the eschar or rash, or postmortem samples of internal organs. Organisms are usually detectable for only a short time in blood and often occur at low levels, especially in milder cases. Culture is generally reserved for cases when there is a compelling reason to identify the species, such as an unusual illness. Performing multiple tests (e.g., PCR and serology) increases the likelihood of a diagnosis.

Treatment

Spotted fevers are often treated with antibiotics without waiting for laboratory confirmation, particularly in diseases such as RMSF where patients can deteriorate rapidly. Antibiotics are not always necessary for some of the milder spotted fevers, but may be given to shorten the illness

Control

Measures such as repellents and appropriate clothing (e.g., long pants tucked into boots) can reduce the incidence of tick bites. Any attached ticks should be removed as soon as possible. Flea and tick control programs for pets decrease the likelihood that they will carry arthropods into the house. Concurrent acaricide treatment during rodent eradication programs helps reduce the risk that their mites, which may survive up to 2 months, will bite people and transmit rickettsialpox.

Morbidity and Mortality

The risk of becoming infected with SFG rickettsiae is influenced by the percentage of infected vectors, their abundance and location in the environment, and their tendency to feed on humans. *R. conorii* and *R. rickettsii* are usually found in less than 1-2% of their tick vectors, but other species of *Rickettsia* can be more prevalent. African tick bite fever, which is carried in ticks that feed aggressively and indiscriminately, sometimes occurs as clusters of cases when groups of people enter tick-infested environments.

Spotted fevers vary in severity. Some organisms, in particular *R. rickettsii*, regularly cause life-threatening illnesses, but cases caused by agents such as *R africae* or *R. akari* are often fairly mild. Host factors such as general health, age and genetic susceptibility (e.g., glucose-6-phosphate dehydrogenase deficiency) can also be a factor. Morbidity and mortality rates for a specific organism can be difficult to estimate accurately, as multiple SFG rickettsiae often circulate in an area and most cases are diagnosed with serological tests that do not identify the species. Current estimates of the case fatality rate for untreated RMSF from North American sources are often in the range of 20-25%, though some estimates from small case series in Mexico and South America suggest a CFR of 30-40% if treatment is delayed. The case fatality rate for treated cases in the U.S. has been falling since the 1980s and 1990s, when it was estimated to be around 3-5%, and was < 1% in 2008-2012. However, this value is probably affected by mandatory reporting and increased awareness, together with the inclusion of all organisms in a single reporting category of "spotted fever rickettsiosis" since 2009. The estimated CFR for untreated Mediterranean spotted fever is < 3%, while deaths appear to be very rare in rickettsialpox, African spotted fever or *R. felis* infections.

Relatively little is known about the incidence of asymptomatic infections and mild illnesses from SFG rickettsiae; however, subclinical seroconversion to *R. parkeri* and *R. rickettsii* has been documented in people exposed to ticks, and serological studies have found exposure rates to SFG rickettsiae ranging from < 5% to 20-55%, depending on the location and risk factors for tick exposure, such as forestry work.

Internet Resources

eMedicine. Rocky Mountain spotted fever

eMedicine. Mediterranean spotted fever

Public Health Agency of Canada. Pathogen Safety Data Sheets

The Merck Manual

The Merck Veterinary Manual

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