

## Rocky Mountain Spotted Fever (RMSF)

### ORGANISM:

Rickettsia is a genus of intracellular bacteria that causes the infections RMSF and associated Rickettsial Spotted Fevers. *R. rickettsii* is the species responsible for RMSF.

### VECTOR & DISTRIBUTION:

Primary vectors include the Rocky Mountain Wood Tick, the American Dog Tick and the Brown Dog Tick. Therefore, the area at risk includes the entire continental United States and Mexico.

### SYMPTOMS:

Early symptoms of RMSF include:

- Fever • Headache • Nausea/Vomiting/Anorexia • Myalgia • Abdominal pain

RMSF is the most severe of the rickettsiosis in the United States and can be rapidly progressive.

### DIAGNOSIS:

Since many patients do NOT recall a tick bite, this CANNOT be a basis for treatment. The classic triad of tick bite/fever/petechial rash is not always reliable to identify at-risk patients early enough to prevent severe sequela.

Late complications include vasculitis, neurologic symptoms, internal organ damage and severe peripheral circulatory problems.

### LAB TESTING:

Laboratory findings can include thrombocytopenia, hyponatremia and elevated hepatic transaminases, but these are frequently not apparent early in the course. Confirmation is by IgG IFA assays performed on acute and convalescent serum.

### TREATMENT:

Doxycycline is the only approved treatment for RMSF and most of the Rickettsial infections, and should be preferred for adult, pediatric and pregnant patients.

## Powassan Virus

### ORGANISM:

Powassan Virus (POWV) is a neurovirulent flavivirus.

### VECTOR & DISTRIBUTION:

It is carried by multiple species of the Ixodes and Dermacentor tick. This rare but very serious disease is commonly contracted in the Northern and Midwest regions of the U.S. during the spring, summer, and fall. Expansion is predicted across much of Canada and the US.

### SYMPTOMS:

Early signs and symptoms include:

- Fever • Severe headache • Vomiting
- Weakness leading to confusion, difficulty speaking, loss of coordination, seizures



POWV frequently progresses to encephalitis and/or meningitis, which typically leads to chronic neurological deficit or death.

### DIAGNOSIS:

POWV diagnosis requires a detailed history of possible exposure, signs and symptoms – and a high clinical suspicion. As the virus is contained in the tick's saliva, transmission can occur within minutes of a bite. Confirmation by laboratory testing may include both blood and spinal fluid.

### TREATMENT:

Currently, there is no treatment protocol for POWV and therapy is primarily supportive.

## Tularemia

### ORGANISM:

This rare and infectious disease is caused by *Francisella tularensis*.

### VECTOR & DISTRIBUTION:

Tularemia has become evident worldwide, mainly in rural areas. It is spread by insect bites, deer flies, dog ticks, wood ticks, lone star ticks, and exposure to sick or dead animals. Occasionally, it can be spread by airborne bacteria found in soil, contaminated food or water, or and by eating or handling undercooked meat of an infected animal.

### SYMPTOMS:

The disease commonly attacks the:

- Skin • Eyes • Lymph nodes • Lungs

Typically, exposed individuals become sick within three to five days, although it can take as long as 14. Illness ranges from mild to life-threatening. Symptoms include:

- Swollen and painful lymph glands • Fever/Chills • Headache • Exhaustion

At times, a skin ulcer can develop at the site of infection.

### DIAGNOSIS:

A presumptive diagnosis of tularemia may be made through testing of specimens using direct fluorescent antibody, immunohistochemical staining, or PCR. Confirmation may be made by culture or acute and convalescent serology.

### TREATMENT:

This infectious disease can be treated effectively with antibiotics, including doxycycline or IV gentamicin, if diagnosed early.

## Mycoplasmas

### ORGANISM:

Mycoplasmas are small, self-replicating organisms found as both commensal and pathogenic bacteria in humans.

### VECTOR & DISTRIBUTION:

Mycoplasma species are distributed throughout the United States. Direct exposure is the most accepted method of transmission. Certain Mycoplasma species, particularly *M. fermentans*, have been identified in blood-sucking arthropods, including Ixodes ticks. Reactivation is possible when the immune system is under attack, such as with *Borrelia* infection.

### SYMPTOMS:

Early systemic symptoms include fatigue and myalgias. In addition to atypical pneumonia, *M. pneumoniae* can also induce autoimmune hemolytic anemia. Late complications may involve the neurologic, cardiovascular, hematologic, gastrointestinal and integumentary systems and include:

- Pericarditis/Myocarditis • Nephritis • Encephalitis • Meningitis

This and other Mycoplasma species can also infect:

- Genitourinary system • Central nervous system • Joints

NOTE: These can persist even after treatment with antibiotics.

### DIAGNOSIS:

Once suspected, diagnosis can be confirmed by antibody testing or PCR. This is complicated by the fact that there are many species of Mycoplasma that can cause disease in humans and most testing is species-specific.

### TREATMENT:

Because Mycoplasma species do not have a cell wall, they are resistant to many antimicrobials.

Antibiotics targeting bacterial rRNA in ribosomal complexes are used, including macrolides, tetracyclines, ketolides, and fluoroquinolones which are bactericidal rather than bacteriostatic.

# Tick-Borne Diseases other than Lyme

## What You Need To Know



## Increasing Awareness for Lyme and Tick-Borne Co-Infections



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Many tick species are reservoirs or “cesspools” for multiple organisms such as *Borrelia*, *Bartonella*, *Babesia*, *Ehrlichia*, *Anaplasma*, *Chlamydia*, *Mycoplasma* species and viruses such as Powassan. These organisms are often referred to as “co-infections,” however, each infection represents a distinct organism, a characteristic pathology and a separate diagnosis. Multiple concurrent infections can amplify patient presentation and may contribute to persistent symptoms and treatment failure. As with Lyme Disease, all tick-borne infections can present with symptoms that are often not explained by common laboratory testing. Critical attention to patient history and the practitioner’s clinical judgment are vital to covering the full scope of a tick-borne disease.

The intent of this publication is to increase awareness among practitioners of the prevalence and presentation of the tick-borne infections frequently associated with Lyme disease, but often independent of Lyme. Please note that the signs and symptoms described in this brochure may be altered significantly in the presence of Lyme or other infections.

## Bartonella

### ORGANISM:

*Bartonella* is a genus of small gram-negative intracellular organisms. Dozens of species have been identified, but three species are responsible for the majority of human *Bartonella* infections.

### VECTOR & DISTRIBUTION:

The distribution of *Bartonella* species is worldwide; anywhere fleas, lice and ticks are found. Primary tick vector is the black-legged tick, the primary vector of Lyme disease.

### SYMPTOMS:

Symptoms are frequently neurological/psychological. They may involve a combination of body systems and include:

- Headaches, frequently frontal
- Numbness/Tingling
- Brain fog
- Muscle twitching
- Shin pain/Bone pain
- Irritability/Rage
- Anxiety/Depression
- GERD/Abdominal pain/Diarrhea
- Pain in the soles of the feet when arising
- Skin striae resembling stretch marks, intensely red or purple, that do not follow skin planes and are not caused by weight gain
- Endocarditis /Heart valve damage are rare complications

### DIAGNOSIS:

Vascular Endothelial Growth Factor (VEGF) may be elevated in active infection. Clinical suspicion may be confirmed by serologies including immunoblots, FISH assay and PCR.

### TREATMENT:

Oral treatment includes tetracyclines, macrolides and rifampin.

## Tick-Borne Relapsing Fever (TBRF)

### ORGANISM:

TBRF is caused by at least 16 species of *Borrelia* – four of which cause the majority of illness: *B. hermsii* (most common), *B. parkerii*, and *B. turicatae* (most likely to present with neurologic involvement). *B. miyamotoi* is a recent addition to this group. Because of characteristic DNA rearrangement, their antigenic variation allows them to evade the host immune response and cause relapsing episodes of symptoms.

### VECTOR & DISTRIBUTION:

These *Borrelia* species have been found in a variety of hard-and soft-bodied ticks. Cases of TBRF have been found throughout the United States. Some species of TBRF can be transmitted from tick to host in a matter of minutes.

### SYMPTOMS:

Classic descriptions of TBRF include febrile episodes are accompanied by multiple, non-specific symptoms:

- Headache
- Myalgias
- Arthralgias
- Nausea/Vomiting
- Abdominal pain
- Dry cough
- Rash
- Jaundice
- Hepatosplenomegaly lasting about three days separated by 7-day afebrile periods

The end of a febrile episode follows a sequence of events, called a “crisis” in which very high temperatures, delirium and tachycardia are followed by drenching sweats and transient hypotension as body temperature rapidly decreases.

However, recent surveys have demonstrated that TBRF may present identically to Lyme disease, which makes diagnosis difficult as Lyme tests generally do not detect TBRF.

### DIAGNOSIS & TREATMENT:

- Rarely, the organism can be visualized in the blood during febrile spikes. More reliable testing includes immunoblotting and PCR.
- TBRF has been associated with poor pregnancy outcomes, with maternal-fetal transmission being possible.
- Treatments include penicillins, cephalosporins, tetracyclines, and macrolides.

## Babesia

### ORGANISM:

*Babesia microti* – a “malaria-like” intraerythrocytic protozoan parasite. It often accompanies infections with *Borrelia burgdorferi*, the bacteria that causes Lyme disease, which is what makes it a “co-infection.” Two detectable species dominate in the USA: *B. microti* and *B. duncani*, but cases of a distinct midwestern strain, “MO-1” are being reported.

### VECTOR & DISTRIBUTION:

It is transmitted from an infected *Ixodes scapularis* or “deer tick” bite. Multiple species are most commonly found in the Pacific Northwest and Atlantic coastal and Midwestern parts of the United States, parts of Europe, and is currently spreading throughout the world (CDC, 2018).

### SYMPTOMS:

Patients with *Babesia* display “flu-like” symptoms such as:

- Fever/Chills/Sweats/Body aches
- Headache, frequently at vertex
- Dizziness
- Loss of appetite/Nausea
- Chest pain/Palpitations
- Air hunger
- Fatigue

When *Babesia* co-infect a Lyme patient, Lyme may become more severe and more treatment-resistant.

If left untreated, patients can develop complications, such as:

- Low blood pressure
- Hemolysis
- Thrombocytopenia
- Disseminated intravascular coagulation (DIC)
- Malfunction of vital organs
- Death

### DIAGNOSIS:

If you suspect a patient is infected with *Babesia*, serology, fluorescence in situ hybridization (FISH) and polymerase chain reaction (PCR)-based tests are available for *B. microti* and *B. duncani* and since both manifest similarly, testing for both is warranted. Asymptomatic patients usually require no treatment. According to the 2019 Merck Manual, diagnosis and treatment should be started if a patient starts to display:

- High fever
- Rapidly increasing parasitemia
- Falling hematocrit

### TREATMENT:

Treatment may include atovaquone, malarone, nitazoxanide and several other natural and pharmaceutical antiparasitics.

## Anaplasma Phagocytophilum

### ORGANISM:

*Anaplasma phagocytophilum* is an obligate intracellular gram-negative bacteria of the order Rickettsiales.

### VECTOR & DISTRIBUTION:

Black-legged ticks, *Ixodes scapularis* and *Ixodes pacificus*. Distribution includes most of the U.S. east of the Rockies, the Pacific coast and temperate eastern Canada.

### SYMPTOMS:

In the early stages, within 1-2 weeks after the tick bite, mild to moderate symptoms include:

- Severe headaches
- Fevers & chills
- Myalgias

Symptoms can progress to severe respiratory failure, disseminated intravascular coagulation (DIC), organ failure, and death, if untreated.

Risk factors for severe illness include:

- Delayed treatment
- Older age
- Patients with weakened immune systems

A rash is rarely reported with this infection (<10% of cases). Therefore, presence of a rash may indicate a co-infection with other tick-borne pathogens.

### DIAGNOSIS:

- Patient history of suspected tick bite/exposure/travel history with developing symptoms
- General lab findings of anemia, thrombocytopenia, and elevated liver transaminases
- PCR and IFA testing results are unreliable to diagnose in a timely manner but are useful for confirmation.

### TREATMENT:

To prevent progression to severe, life-threatening disease, start treatment if pathogen is suspected.

- Doxycycline is drug of choice for treatment in all ages.
- Short courses have not been shown to be harmful in children.

## Ehrlichia

### ORGANISM:

*Ehrlichia chaffeensis* is an obligate intracellular, gram-negative species of Rickettsiales bacteria which is responsible for Human Monocytic Ehrlichiosis.

### VECTOR & DISTRIBUTION:

The primary vector, the Lone Star Tick, can be found across the southeastern and Atlantic Coastal U.S. and stretching as far north as Maine and Minnesota. *Ehrlichia muris*-like agent (EML) is a species recently found in patients in Wisconsin and Minnesota and the vector is the black-legged tick, *Ixodes scapularis*.

### SYMPTOMS:

Within 5-14 days after the tick bite, if known, early symptoms of all species include:

- Fever
- Headache
- Myalgias
- Malaise
- GI symptoms include nausea, vomiting and anorexia
- Rashes appear in less than 30% of adults, and 60% of children

Late complications can include:

- ARDS
- Toxic or septic shock-like syndromes
- Renal failure
- Hepatic failure
- Coagulopathies

### DIAGNOSIS:

Laboratory studies may reveal relative lymphopenia, thrombocytopenia, elevated serum transaminases, elevated C reactive protein and hyponatremia. Confirmation may rely on a single elevated Ig G immunofluorescent antibody (IFA) titer or paired acute and convalescent IFA titers.

### TREATMENT:

Treatment should begin early, based on clinical suspicion – delay can lead to increased morbidity and mortality.

- Doxycycline is the treatment of choice for Ehrlichia, as it is for most Rickettsial infections.