Anaplasmosis

**Pathogen(s):** Anaplasma phagocytophilum (formerly Human Granulocytic Ehrlichiosis, HGE)

**Location:** The Upper Midwest and Northeast United States overlapping with the geographic distribution of Lyme disease and other diseases transmitted by the Blacklegged tick (Ixodes scapularis).

**Peak Infections:** June through August

**Vector:** Blacklegged ticks (Ixodes scapularis)

**Incubation Period:** 5-14 days

**Signs & Symptoms:** Fever, chills, rigors, severe headache, myalgia, gastrointestinal symptoms (nausea, vomiting, diarrhea, and anorexia) and rash (<10%). Few people will develop all symptoms and the number and combination of symptoms varies greatly between patients.

**Laboratory findings:** Mild anemia, leukopenia (characterized by relative and absolute lymphopenia and left shift), Thrombocytopenia, mild to moderate elevations in hepatic transaminases. PCR testing is most sensitive during the first week of illness. Antibody-based testing for a rise in IgM (increase 2-3 days after illness) and IgG (typically up to a 4-fold increase 7-10 days after illness). Samples should be taken within the first week of illness. A second sample should be taken 2-4 weeks later.

**MDL Test Code(s):**
- 441 *Ehrlichia chaffeensis* (HME) & *Anaplasma phagocytophilum* (HGE) by Real-Time PCR
- 439 *Anaplasma phagocytophilum* IgG/IgM by IFA

**Treatment (1, 3):**
- Adults: 100 mg doxycycline twice per day (100 mg/dose max), orally or IV for 10-14 days.
- Children (weighing <100 lbs, 45.4 kg): 2.2 mg/kg doxycycline twice per day (100 mg/dose max), orally or IV for 10-14 days. (1, 3)

**Comments:** Anaplasmosis is less severe and life-threatening than rickettsial diseases such as Rocky Mountain spotted fever or *E. chaffeensis* ehrlichiosis. Due to the common tick vector, co-infection with *Anaplasma phagocytophilum*, *Borrelia burgdorferi*, *Babesia microti* or Powassan virus is possible. Illness may be marked by a more severe course or incomplete response to treatment. Severity increases with advanced age, immunosuppression, co-morbid medical conditions and delay in diagnosis and treatment.
Ehrlichiosis

Pathogen(s):  
Ehrlichia chaffeensis, Ehrlichia ewingii, and Ehrlichia muris eauclairensis (Human Monocytic Ehrlichiosis, HME)

Location:  
The Southeastern and South Central United States, from the East Coast to Texas, overlapping with the geographic distribution of Rocky Mountain spotted fever rickettsiosis. The Lone Star tick (Amblyomma americanum) is primarily responsible for the transmission of E. chaffeensis and E. ewingii. Oklahoma, Missouri, and Arkansas account for 35% of E. chaffeensis infections. There have been >115 cases of E. muris eauclairensis ehrlichiosis since 2009. The blacklegged tick (Ixodes scapularis) is associated with the transmission of this new subspecies.

Peak Infections:  
June through August

Vector:  
Lone Star tick (Amblyomma americanum) - transmits E. chaffeensis and E. ewingii.  
Blacklegged tick (Ixodes scapularis) - transmits E. muris eauclairensis.

Incubation Period:  
1 – 2 weeks

Signs & Symptoms:  
The three species of Ehrlichia have similar clinical presentations: fever, chills, headaches, malaise, muscle pain, gastrointestinal symptoms (nausea, vomiting, diarrhea, and anorexia), altered mental status, and rash (more common among children). E. chaffeensis can be more severe and cause fatal illness.

Laboratory findings:  
Thrombocytopenia, leukopenia (absolute), during the first week of clinical disease. Later in the illness, anemia and mild to moderate elevations in hepatic transaminases. During the acute stages of illness, morulae can be detected in ~20% of patients. E. chaffeensis commonly infects monocytes whereas E. ewingii commonly infects granulocytes. PCR testing is most sensitive during the first week of illness. Antibody-based testing for a rise in IgM (increase 2-3 days after illness) and IgG (typically up to a 4-fold increase 7-10 days after illness). Samples should be taken within the first week of illness. A second sample should be taken 2-4 weeks later.

MDL Test Code(s):  
441 Ehrlichia chaffeensis (HME) & Anaplasma phagocytophilum (HGE) by Real-Time PCR

Future MDL Tests:  
Ehrlichia ewingii by Real-Time PCR  
Ehrlichia muris eauclairensis by Real-Time PCR

Treatment (1, 3):  
Adults: 100 mg doxycycline twice per day (100 mg/dose max), orally or IV for 10-14 days.  
Children (weighing <100 lbs, 45.4 kg): 2.2 mg/kg doxycycline twice per day (100 mg/dose max), orally or IV for 10-14 days. (1, 3)

Comments:  
E. chaffeensis ehrlichiosis can cause fatal illness, whereas no deaths have been reported for E. ewingii or E. muris eauclairensis ehrlichiosis. Cases of E. chaffeensis ehrlichiosis generally increase with age; however, case-fatality rates are highest among children aged <10 years and adults aged ≥ 70 years.
Babesiosis

Pathogen(s): Babesia microti, Babesia duncani (WA-1), and B. divergens-like (MO1)

Location: The Upper Midwest (Wisconsin and Minnesota) and Northeast (New England, New York and New Jersey) United States, overlapping with the geographic distribution of Lyme disease and other diseases transmitted by the blacklegged tick (Ixodes scapularis). Sporadic cases of infection caused by B. duncani (WA-1) and B. divergens-like (MO1) have been detected in other U.S. regions, including the West Coast. Additionally, cases of blood transfusion-associated Babesiosis have been reported.

Peak Infections: June through August

Vector: Blacklegged tick (Ixodes scapularis)

Incubation Period: 1 – 9+ weeks

Signs & Symptoms: A wide range of signs and symptoms, from asymptomatic to life threatening. Clinical manifestations, if any, usually develop within several weeks after exposure. They may also develop or recur months later. S&S include fever, chills, headaches, myalgia, arthralgia, gastrointestinal symptoms (nausea, anorexia, vomiting, and diarrhea), dark urine, and rash (<10%). Less common S&S include cough, sore throat, emotional lability, depression, photophobia, and conjunctival injection. Mild splenomegaly, mild hepatomegaly, or jaundice may occur in some patients. Severe cases may be associated with thrombocytopenia, disseminated intravascular coagulation, hemodynamic instability, acute respiratory distress, renal failure, hepatic compromise, altered mental status, and death.

Laboratory findings: Decreased hematocrit due to hemolytic anemia, thrombocytopenia, mildly elevated hepatic transaminase values, elevated serum creatinine and blood urea nitrogen (BUN) values.

MDL Test Code(s):
- 410 Babesia microti by Real-Time PCR
- 440 Babesia microti IgG/IgM by IFA
- 431 Babesia duncani (WA-1) by Real-Time PCR

Future MDL Tests:
- Babesia duncani (WA-1) IgG/IgM by IFA
- Babesia divergens-like (MO1) by Real-Time PCR

Treatment (1, 3):
Adult combination therapy: 750 mg atovaquone orally every 12 hrs PLUS 500-1000 mg azithromycin orally on day 1, followed by 250-1000 mg (1000 mg/dose max) daily for 7-10 days OR 300-600 mg clindamycin IV every 6 hrs OR 600 mg orally every 8 hrs PLUS 650 mg quinine orally every 6-8 hrs for 7-10 days (standard for severely ill patients).

NOTE: Most persons without clinical manifestations of infection do not require treatment unless the patient has demonstrable parasitemia for more than 3 months.

Comments: Babesiosis is caused by a parasite, transmitted by the blacklegged tick, that infects the red blood cells of the host. Treatment is based on patient age, clinical status, immunocompetence, splenic function, comorbidities, pregnancy status, other medications, and allergies. Expert consultation is recommended for persons who have or are at-risk for severe or relapsing infection or who are at either extreme of the age spectrum.
Borreliosis
Lyme Disease

Figure 7: Geographic map of Lyme disease reported to CDC, U.S., 2016 (1).

Figure 8: Various presentations of Erythema migrans rash (6).

Pathogen(s): Borrelia burgdorferi and Borrelia mayonii
Location: B. burgdorferi associated Lyme disease found in the Upper Midwest (Wisconsin and Minnesota) and Northeast (New England, Delaware, Maryland, New Jersey, New York, Pennsylvania, and Virginia) United States accounts for 95% of cases. B. mayonii is a new emerging species of Borrelia associated with Lyme disease located in the Upper Midwest.

Peak Infections: May through September, although cases have been reported year-round.
Vector: Blacklegged ticks (Ixodes scapularis) and Western blacklegged ticks (Ixodes pacificus)
Incubation Period: 3 - 30 days
Signs & Symptoms:
Localized Early Stage: 70-80% of patients have erythema migrans (EM), a red ring-like or homogenous expanding rash. Also, flu-like symptoms with malaise, headaches, fever, myalgia, arthralgia, and lymphadenopathy. Serologic testing may be insensitive during this early stage.
Disseminated Stage: Multiple secondary annular rashes, flu-like symptoms, lymphadenopathy; rheumatologic manifestations such as transient, migratory arthritis and effusion in one or multiple joints; migratory pain in tendons, bursae, muscle, and bones; Baker’s cyst; cardiac manifestations such as conduction abnormalities (e.g. atrioventricular node block), myocarditis, and pericarditis; neurologic manifestations such as Bell’s palsy or other cranial neuropathy, meningitis, motor and sensory radiculoneuropathy, mononeuritis multiplex, subtle cognitive difficulties, encephalitis, encephalomyelitis, subtle encephalopathy, pseudotumor cerebri (rare), Conjunctivitis, keratitis, uveitis, mild hepatitis, and splenomegaly have been reported. The disseminated stage should be positive for serology.

Laboratory findings: Elevated erythrocyte sedimentation rate, mildly elevated hepatic transaminases, microscopic hematuria or proteinuria. In Lyme meningitis, CSF typically shows lymphocytic pleocytosis, slightly elevated protein, and normal glucose.

MDL Test Code(s): 305 Borrelia burgdorferi (United States) by Real-Time PCR
440 Lyme disease IgG/IgM by ELISA
417 Lyme disease C6 Peptide by ELISA
313 Lyme disease by Western blot (IgG/IgM)
424 Borrelia afzelii (Europe) by Real-Time PCR
441 Borrelia afzelii (Europe) by Western blot (IgG/IgM)
425 Borrelia garinii (Europe) by Real-Time PCR
442 Borrelia garinii (Europe) by Western blot (IgG/IgM)

Future MDL Tests: Borrelia mayonii (United States) by Real-Time PCR

Treatment (1, 3):
Localized Early Stage: Adult therapy: 100 mg doxycycline twice per day, orally for 10-21 days OR 500 mg cefuroxime axetil twice per day, orally for 14-21 days OR 500 mg amoxicillin three times per day, orally for 14-21 days.
Children therapy: 50 mg/kg per day amoxicillin, orally, divided into 3 doses (500 mg per dose max) for 14-21 days OR 4 mg/kg per day doxycycline, orally, divided into 2 doses (100 mg per dose max) for 10-21 days OR 30 mg/kg per day cefuroxime axetil, orally, divided into 2 doses (500 mg per dose max) for 14-21 days.
For Doxycycline, Stupica et al., 2012 suggest the efficacy of shorter courses (10 days vs. 15 days) of treatment for early Lyme disease.

**Disseminated Stage:**

If patients are intolerant of amoxicillin, cefuroxime axetil, and doxycycline, it’s possible to use macrolides azithromycin, clarithromycin, or erythromycin. These antibiotics have a lower efficacy rate, so patients should be closely monitored to ensure symptoms resolve.

**Comments:**

More than 300,000 new cases are reported annually. Due to the common tick vector, co-infection with *Anaplasma phagocytophilum*, *Borrelia burgdorferi*, *Babesia microti*, *Bartonella henselae* or Powassan virus is possible. In particular, *B. microti* and/or *A. phagocytophilum* should be considered if the patient has more severe symptoms than commonly observed with Lyme disease alone. Patients who have a high-grade fever for more than 48 hrs despite appropriate antibiotic therapy or who have unexplained leukopenia, thrombocytopenia or anemia are also at-risk. Co-infection should be considered in patients whose EM skin lesions have resolved but still show persistent flu-like symptoms.

**Tick-borne Relapsing Fever (TBRF): Western Soft Tick**

![Map of Tick-borne Relapsing Fever](image)

**Pathogen(s):** *Borrelia hermsii*, *Borrelia turicatae*, and *Borrelia parkeri*

**Location:** Mostly seen in 14 western states: Arizona, California, Colorado, Idaho, Kansas, Montana, Nevada, New Mexico, Oklahoma, Oregon, Texas, Utah, Washington, and Wyoming. Many cases of TBRF occur in rodent-infested cabins. TBRF may be associated with cave exposure.

**Peak Infections:** Summer and occasionally winter, when fires warm cabin walls and activate resting ticks.

**Vector:** Soft bodied ticks (*Ornithodoros* spp.).

**Incubation Period:** ~ 7 days, followed by recurring febrile episodes that last 3 days and separated by afebrile periods of ~ 7 days.

**Signs & Symptoms:** Relapsing fever, headaches, myalgia, chills, nausea, vomiting, arthralgia, and facial palsy (rare).

**Laboratory findings:** Normal to increased white blood cell count with a left shift, mildly increased serum bilirubin, mild to moderate thrombocytopenia, elevated erythrocyte sedimentation rate, slightly prolonged prothrombin time, and partial thromboplastin time.

**MDL Test Code(s):** 360 *Borrelia turicatae* by Real-Time PCR

**Future MDL Tests:** *Borrelia hermsii* by Real-Time PCR

**Borrelia parkeri** by Real-Time PCR

**Treatment (1):**

Adults: 500 mg tetracycline four times per day, orally for 10 days OR 500 mg erythromycin four times per day, orally for 10 days OR for CNS involvement, 2 g ceftriaxone per day, IV for 10-14 days.

Children: 12.5 mg/kg erythromycin four times per day, orally (2 g/day max) for 10 days.

**Comments:** During the first 2-4 hours of treatment, all patients should be observed for a Jarisch-Herxheimer reaction. Acute respiratory distress syndrome requiring intubation has occurred in several patients undergoing TBRF treatment.
**Tick-borne Relapsing Fever (TBRF): Eastern Hard Tick**

Pathogen(s): *Borrelia miyamotoi*

Location: The Upper Midwest, Northeast, and mid-Atlantic United States, in places where Lyme Disease is endemic. Many cases of TBRF occur in rodent-infested cabins. In Texas, TBRF may be associated with cave exposure.

Peak Infections: July and August.

Vector: May be spread by larval blacklegged tick (*Ixodes scapularis*).

Incubation Period: Days to weeks.

Signs & Symptoms: Fever, chills, fatigue, severe headaches, arthralgia, and myalgia. Uncommon symptoms include dizziness, confusion, vertigo, rash, dyspnea, nausea, abdominal pain, diarrhea, and anorexia.

Laboratory findings: Leukopenia, thrombocytopenia, elevated hepatic transaminase values. PCR testing for active infection, and antibody-based testing including C6 peptide Lyme disease ELISA test may be positive.

MDL Test Code(s): 443 *Borrelia miyamotoi* by Real-Time PCR

Treatment (1): There are no comprehensive studies to evaluate treatment regimens. Published case series report successful treatment with antibiotics and dosages used for Lyme disease.

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**Southern Tick-Associated Rash Illness (STARI)**

Pathogen(s): *Borrelia lonestari* (the putative *Borrelia* species associated with STARI as discussed in the literature, although the definitive cause of STARI is currently unknown)

Location: Central Texas and Oklahoma, eastward across the South, and along the Atlantic coast of the United States, as far north as Maine.

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**Rickettsiosis**

**Pathogen(s):** *Rickettsia rickettsii*

**Location:** Throughout the United States. North Carolina, Oklahoma, Arkansas, Tennessee, and Missouri account for >60% of the cases. Recently, areas of Arizona have had >360 cases with 21 fatalities.

**Peak Infections:** May through July with 90% of cases reported from April through September.

**Vector:** American dog tick (*Dermacentor variabilis*), transmits RMSF in the eastern, central, and western states. Brown dog tick (*Rhipicephalus sanguineus*) transmits RMSF in the Southwest. Rocky Mountain wood tick (*Dermacentor andersoni*) transmits RMSF in the Rocky Mountain states.

**Incubation Period:** 3-12 days

**Peak Infections:** June through August

**Vector:** Lone Star tick (*Amblyomma americanum*)

**Incubation Period:** 1 - 2 weeks

**Signs & Symptoms:** An expanding bull’s eye rash (~3 inches in diameter) that develops around the site of the tick bite. Patients can also experience fatigue, headaches, fever, joint pain, and muscle pain within 30 days of the bite. Saliva from the Lone Star tick can be irritating, therefore redness and discomfort at the bite site does not necessarily indicate infection.

**Laboratory findings:** Lyme disease testing is negative, since the Lone Star tick does not carry and transmit *Borrelia burgdorferi*.

**MDL Test Code(s):** 440 *Borrelia lonestari* by Real-Time PCR

**Treatment (1):** Unknown. However, the signs and symptoms of STRI often resemble early Lyme disease, so physicians will often treat it with Lyme disease oral antibiotics.

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**Spotted Fever Group Rickettsiosis**

**Rickettsia rickettsii** *(Rocky Mountain spotted fever, RMSF)*

**Figure 14:** Geographic map of spotted fever rickettsiosis (including Rocky Mountain spotted fever) reported to CDC, U.S., 2016 [1].

**Pathogen(s):** *Rickettsia rickettsii*

**Location:** Throughout the United States. North Carolina, Oklahoma, Arkansas, Tennessee, and Missouri account for >60% of the cases. Recently, areas of Arizona have had >360 cases with 21 fatalities.

**Peak Infections:** May through July with 90% of cases reported from April through September.

**Vector:** American dog tick (*Dermacentor variabilis*), transmits RMSF in the eastern, central, and western states. Brown dog tick (*Rhipicephalus sanguineus*) transmits RMSF in the Southwest. Rocky Mountain wood tick (*Dermacentor andersoni*) transmits RMSF in the Rocky Mountain states.

**Incubation Period:** 3-12 days

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**Figure 15:** Early stage maculopapular rash. Photo/CDC (3).

**Figure 16:** Late stage petechial rash. Photo/CDC (3).
Signs & Symptoms: Early symptoms (1-4 days) include high fever, severe headaches, malaise, myalgia, edema around the eyes and on the back of the hands, gastrointestinal symptoms (nausea, vomiting, and anorexia). Later symptoms (≥5 days) include altered mental status, coma, cerebral edema, respiratory compromise, or pulmonary edema and ARDS, necrosis requiring amputation, and multiorgan system damage (such as CNS and renal failure). A rash typically appears 2-5 days after onset of symptoms, however ~10% of RMSF patients never develop a rash. The decision to treat should not be based on the presence of a rash. Early maculopapular rashes consist of small, flat, pink, non-itchy spots that initially appear on the wrists, forearms, and ankles. These spread to the trunk and sometimes palms and soles. Late petechial rashes consist of red to purple spots, which are not seen until ≥6 days after the onset of symptoms. Petechial rashes are considered a progression to severe disease. Every attempt should be made to begin treatment before this develops.

Laboratory findings: Thrombocytopenia, elevated hepatic transaminases, and hyponatremia. (Laboratory values are often within normal limits in early illness).

MDL Test Code(s): 446 Rickettsia species (Rickettsiosis) by Real-Time PCR

Future MDL Tests: Rickettsia rickettsii by Real-Time PCR

Treatment (1, 3):
Adult: 100 mg doxycycline twice per day, orally or IV (100 mg/dose max) for at least 3 days after the fever subsides and until evidence of clinical improvement. Minimum course of treatment is 5-7 days.
Children: 2.2 mg/kg per dose doxycycline twice per day, orally or IV (100 mg/dose max) for at least 3 days after the fever subsides and until evidence of clinical improvement. Minimum course of treatment is 5-7 days.

Comments: RMSF (5-10% fatality rate) can be rapidly fatal if not treated within the first 5 days of symptoms. (fatality rate, 5-10%). Before antibiotics were available, case fatality rates ranged from 20-80%. Antibiotic therapy should not be delayed while waiting for a confirmation of the diagnosis via laboratory testing.

Rickettsia parkeri Rickettsiosis

Pathogen(s): Rickettsia parkeri
Location: The Southeast and mid-Atlantic United States, and parts of southern Arizona.
Peak Infections: July to September, but can occur April to October
Vector: Gulf Coast tick (Amblyomma maculatum)
Incubation Period: 2-10 days
Signs & Symptoms: R. parkeri rickettsiosis has overlapping symptoms with RMSF, but less severe. It’s almost always associated with an inoculation eschar (ulcerated, necrotic lesion) at the site of tick attachment. Several days after an eschar appears, so do fevers, headaches, rashes (sparse maculopapular or papulovesicular eruptions on the trunk and extremities), and muscle aches.

Laboratory findings: Mildly elevated hepatic transaminases, mild leukopenia, and mild thrombocytopenia (less common).

MDL Test Code(s): 446 Rickettsia species (Rickettsiosis) by Real-Time PCR
448 Rickettsia parkeri by Real-Time PCR

Treatment (1, 3):
Adults: 100 mg doxycycline twice per day (100 mg/dose max), orally or IV for at least 3 days after the fever subsides, and until evidence of clinical improvement. Minimum course of treatment is 5-7 days.
Children: 2.2 mg/kg per dose doxycycline twice per day (100 mg/dose max), orally or IV for at least 3 days after the fever subsides, and until evidence of clinical improvement. Minimum course of treatment is 5-7 days.
Pacific Coast Tick Fever: *Rickettsia philipii* (364D)

**Pathogen(s):** *Rickettsia philipii* (364D)

**Location:** *R. philipii* (364D) rickettsiosis is transmitted by the Pacific Coast tick. All 10 reported cases occurred in California.

**Peak Infections:** July to September

**Vector:** Pacific Coast tick (*Dermacentor occidentalis*) ranges from California to Oregon.

**Incubation Period:** 2-10 days

**Signs & Symptoms:** *R. philipii* (364D) rickettsiosis has overlapping symptoms with RMSF but less severe. Almost always associated with an inoculation eschar (ulcerated, necrotic lesion) at the site of tick attachment. Several days after an eschar appears, fever, headache, rash (sparse maculopapular or papulovesicular eruptions on the trunk and extremities), and muscle aches.

**Laboratory findings:** Mildly elevated hepatic transaminases, mild leukopenia, and mild thrombocytopenia (less common).

**MDL Test Code(s):** 446 *Rickettsia species* (Rickettsiosis) by Real-Time PCR

**Treatment** (1, 3):
- Adult: Doxycycline 100 mg twice per day, orally or IV (100 mg/dose max) for at least 3 days after the fever subsides and until evidence of clinical improvement. Minimum course of treatment is 5-7 days.
- Children: Doxycycline 2.2 mg/kg per dose twice per day, orally or IV (100 mg/dose max) for at least 3 days after the fever subsides and until evidence of clinical improvement. Minimum course of treatment is 5-7 days.

**Comments:** RMSF antibody tests are available and may cross-react with *R. philipii*.

Tularemia

**Figure 19:** Rickettsia philipii associated rash (3).

**Figure 20:** Echar on a patient with Rickettsia species 364D rickettsiosis (3).

**Figure 21:** Geographic map of Tularemia reported to CDC, U.S., 2016 (1).

**Figure 22:** An ulcer caused by *Francisella tularensis* (12).

**Figure 23:** Glandular Tularemia (13).
**Pathogen(s):** *Francisella tularensis* subspecies *tularensis* and *Francisella tularensis* subspecies *holarctica*

**Location:** Mainland United States. Most commonly, in the South Central United States, Pacific Northwest, and parts of Massachusetts including Martha’s Vineyard.

**Peak Infections:** June through August

**Vector:** The American dog tick (*Dermacentor variabilis*), the Rocky Mountain wood tick (*Dermacentor andersoni*) and Lone Star tick (*Amblyomma americanum*). The deer fly (*Chrysops spp.*) can also transmit tularemia. Tularemia is highly infectious and can also be transmitted by handling infected animals, inhalation, and ingesting undercooked meat or contaminated water.

**Incubation Period:** 3-5 days (with a range of 1-21 days)

**Signs & Symptoms:** Fever, headaches, malaise, fatigue, anorexia, myalgia, chest discomfort, cough, sore throat, vomiting diarrhea, abdominal pain. Ulceroglandular S&S include localized lymphadenopathy and cutaneous ulcers at the infection site (not always present). Oculoglandular S&S include photophobia, conjunctivitis, preauricular submandibular, or cervical lymphadenopathy. Oropharyngeal S&S include severe throat pain, exudative pharyngitis, or tonsillitis, cervical, periparotid and/or retropharyngeal lymphadenopathy. Febrile symptoms may resemble typhoid fever.

**Laboratory findings:** Elevated hepatic transaminases, elevated creatine phosphokinase. Leukocyte count and sedimentation rate, thrombocytopenia, and hyponatremia may be normal or elevated. Myoglobinuria and sterile pyuria may or may not be present.

**MDL Test Code(s):** 360 *Francisella tularensis* (subspecies *tularensis* & *holarctica*) by Real-Time PCR

**Future MDL Tests:** *Francisella tularensis* IgG/IgM by ELISA

**Treatment (1):** Adults: streptomycin 1 g IM twice daily (2 g per day max) for a minimum of 10 days OR doxycycline 100 mg IV or PO twice daily for 14-21 days. Not FDA approved, but shown to be successful: gentamicin 5 mg/kg IM or IV daily (monitor serum drug levels; peak serum levels of at least 5mcg/ml) OR ciprofloxacin 400 mg IV or 500 mg PO twice daily for 10-14 days.

Children: streptomycin 15 mg/kg IM twice daily (2 g per day max) for a minimum of 10 days. Not FDA approved, but shown to be successful: gentamicin 2.5 mg/kg IM or IV 3 times daily (monitor serum drug levels; once daily dosing could be considered with a pediatric infectious disease specialist and a pharmacist) for a minimum of 10 days OR ciprofloxacin 15 mg/kg IV or PO twice daily (800 mg per day max) for 10 days.

**Comments:** Gentamicin or streptomycin is preferred for treatment of severe tularemia. Doses should be adjusted for renal insufficiency. Chloramphenicol may be added to streptomycin to treat meningitis.

**Tick Borne Viruses**

**Bourbon virus**

**Pathogen(s):** Bourbon virus

**Location:** The Midwest and southern United States. (The virus was first identified in 2014 in an infected patient from Bourbon County, Kansas.)

**Peak Infections:** Not known

**Vector:** Lone Star Tick (*Amblyomma americanum*) is suspected

**Incubation Period:** Not known

**Signs & Symptoms:** Fever, fatigue, anorexia, nausea, vomiting, and maculopapular rash. Some patients infected with Bourbon virus have died during their acute illness.

**Laboratory findings:** Leukopenia and thrombocytopenia

**Future MDL Tests:** Bourbon virus by Real-Time PCR
Colorado Tick Fever virus

Pathogen(s): Colorado Tick Fever Virus
Location: The western United States, primarily Colorado, Utah, Montana, and Wyoming, at high altitudes of 4,000 to 10,000 feet above sea level.
Peak Infections: Not known
Vector: Rocky Mountain wood tick (Dermacentor andersoni). Although rare, the virus can also be transmitted via blood transfusions.
Incubation Period: 1-14 days
Signs & Symptoms: Fever, chills, headaches, myalgia. Some patients have sore throat, vomiting, abdominal pain, or skin rash. About 50% of patients have a biphasic fever. Rare cases of severe disease effect the central nervous system with symptoms of stiff neck and confusion.
Laboratory findings: Leukopenia and moderate thrombocytopenia
MDL Test Code(s): Colorado Tick Fever virus by Real-Time PCR
Treatment (1): There are no vaccines or medications to prevent or treat CTF virus infection. Supportive care is recommended. Patients with confirmed CTF should defer blood and bone marrow donation for at least 6 months after recovery.
Comments: There have been a total of 83 cases reported from 2002 to 2012. Patients with confirmed CTF should defer blood and bone marrow donations for at least 6 months after recovery. The Rocky Mountain wood tick (Dermacentor andersoni) can transmit Rickettsia rickettsii (Rocky Mountain spotted fever), Colorado tick fever virus (Colorado tick fever) and Francisella tularensis (Tularemia).

Heartland virus (Phlebovirus)

Figure 24: Geographic map of Dermacentor andersoni ticks for confirmed and probable Colorado Tick Fever (CTF) virus disease cases, United States, 2002–2012 (14).

Figure 25: Geographic map of Heartland virus disease cases by state as of September 2018 (15).
**Powassan virus**

![Geographic map of Powassan virus neuroinvasive disease cases reported by year, 2008-2017 (16).](image)

| Pathogen(s): | Heartland virus (Phlebovirus) |
| Location: | The Midwest (Arkansas, Indiana, Illinois, Kansas, Missouri, and Oklahoma) and southern United States (Georgia, Kentucky, North Carolina, and Tennessee). |
| Peak Infections: | May through September |
| Vector: | Lone Star tick (Amblyomma americanum) |
| Incubation Period: | Specific ranges are unknown, but most patients report a tick bite 2 weeks prior to illness. |
| Signs & Symptoms: | Fever, fatigue, decreased appetite, headaches, nausea, diarrhea, muscle pain, and joint pain. |
| Laboratory findings: | Leukopenia, thrombocytopenia and mild to moderate elevation of liver transaminases. |
| MDL Test Code(s): | Heartland virus (Phlebovirus) by Real-Time PCR |
| Treatment (1): | There are no vaccines or medications to prevent or treat Heartland virus infection. Many patients have required hospitalization. With supportive care, most patients have fully recovered; however, a few older individuals with comorbidities have died. |
| Comments: | The Lone Star tick can transmit *Ehrlichia chaffeensis* and *E. ewingii* (Ehrlichiosis), *Francisella tularensis* (Tularemia), Heartland virus (Heartland virus disease), Bourbon virus (Bourbon virus disease) and Southern tick-associated rash illness (STARI). |

**Powassan virus**

- Pathogen(s): Powassan virus
- Location: The Great Lakes region and northeastern United States.
- Peak Infections: Late spring, early summer, and mid-fall.
- Vector: Blacklegged tick (*Ixodes scapularis*) and Groundhog tick (*Ixodes cookei*).
- Incubation Period: 1-4 weeks
- Signs & Symptoms: Many people who become infected do not exhibit symptoms. In those who do, S&S include fever, headaches, vomiting, and generalized weakness. This usually progresses to meningoencephalitis and may include meningeal signs, altered mental status, seizures, aphasia, paresis, movement disorders, or cranial nerve palsies.
- Laboratory findings: Lymphocytic pleocytosis (neutrophils can predominate early), normal or mildly elevated protein, and normal glucose.
- Future MDL Tests: Powassan virus by Real-Time PCR  
  Powassan virus IgG/IgM by ELISA
- Treatment (1): There are no vaccines or medications to prevent or treat Powassan virus infection. Patients with severe Powassan virus disease often need to be hospitalized. Treatment may include respiratory support, IV fluids, and medication to reduce swelling in the brain.
- Comments: Approximately 50% of survivors have permanent neurological symptoms such as recurring headaches, muscle wasting, and memory problems. Approximately 10% of Powassan virus encephalitis cases are fatal. Due to the common blacklegged tick (*Ixodes scapularis*) vector, co-infection with *Anaplasma phagocytophilum*, *Borrelia burgdorferi*, or *Babesia microti* is possible.
**Tick Typing (1)**

**Lone Star Tick (Amblyomma americanum)**

*Figure 27: Lone Star Tick (Amblyomma americanum). Photo/TickEncounter Resource Center, University of Rhode Island (17).*

**Location:** The eastern United States, more commonly in the South  
**Transmits:** *Ehrlichia chaffeensis* and *E. ewingii* (ehrlichiosis), *Francisella tularensis* (Tularemia), Heartland virus (Heartland virus disease), Bourbon virus (Bourbon virus disease) and Southern tick-associated rash illness (STARI)  
**Comments:** A very aggressive tick. Nymphs and adult females most frequently bite humans. The greatest risk of being bitten occurs in early spring through late fall. Adult female ticks are distinguished by a white dot or “lone star” on the back. Some people bitten by the Lone Star tick have reported allergic reactions associated with consuming red meat.

**Cayenne Tick (Amblyomma mixtum formerly A. cajennense)**

*Figure 29: Cayenne Tick (Amblyomma cajennense). Photo/TickEncounter Resource Center, University of Rhode Island (17).*  
*Figure 30: Geographic distribution of the Cayenne Tick (Amblyomma mixtum) (10).*

**Location:** Southern Texas, and occasionally Florida and coastal regions of the Gulf states  
**Transmits:** Spotted fever group *Rickettsia* species associated with rickettsiosis  
**Comments:** *Amblyomma cajennense* has now been subdivided into six different species. *Amblyomma mixtum* is the species present in the United States listed above. This cold-sensitive tick feeds year-round. The adult tick occasionally bites humans, commonly resulting in pain and tissue damage.

**Gulf Coast Tick (Amblyomma maculatum)**

*Figure 31: Gulf Coast Tick (Amblyomma maculatum). Photo/TickEncounter Resource Center, University of Rhode Island (17).*  
*Figure 32: Geographic distribution of the Gulf Coast Tick (Amblyomma maculatum) (10).*

**Location:** Southeastern and mid-Atlantic United States, as well as southern Arizona  
**Transmits:** *Rickettsia parkeri* (spotted fever rickettsiosis)  
**Comments:** Adult ticks are associated with *R. parkeri* transmission to humans

**Rocky Mountain Wood Tick (Dermacentor andersoni)**

*Figure 33: Rocky Mountain Wood Tick (Dermacentor andersoni). Photo/TickEncounter Resource Center, University of Rhode Island (17).*  
*Figure 34: Geographic distribution of the Rocky Mountain Wood Tick (Dermacentor andersoni) (10).*

**Location:** The Rocky Mountain states at 4,000 to 10,000 feet above sea level  
**Transmits:** *Rickettsia rickettsii* (Rocky Mountain spotted fever), Colorado tick fever virus (Colorado tick fever), and *Francisella tularensis* (Tularemia)  
**Comments:** Adult ticks are associated with pathogen transmission to humans
Pacific Coast Tick (*Dermacentor occidentalis*)

![Pacific Coast Tick Image]

**Figure 35:** Pacific Coast Tick (*Dermacentor occidentalis*). Photo/TickEncounter Resource Center, University of Rhode Island (17).

**Location:** The Pacific Coast, mainly California and Oregon

**Transmits:** *Rickettsia philipii* (364D) (Pacific Coast tick fever or spotted fever rickettsiosis)

**Comments:** Most cases have been reported between July and September.

American Dog Tick (*Dermacentor variabilis*)

![American Dog Tick Image]

**Figure 37:** American Dog Ticks (*Dermacentor variabilis*). Photo/TickEncounter Resource Center, University of Rhode Island (17).

**Figure 38:** Geographic distribution of the American Dog Ticks (*Dermacentor variabilis*)(10).

**Location:** The eastern United States, east of the Rocky Mountains, and limited areas of the Pacific Coast

**Transmits:** *Francisella tularensis* (Tularemia) and *Rickettsia rickettsii* (Rocky Mountain spotted fever)

**Comments:** Adult females are most likely to bite humans. The greatest risk of being bitten occurs in the spring and summer.

Asian Longhorned Tick (*Haemaphysalis longicornis*) (18)

![Asian Longhorned Tick Image]

**Figure 39:** Asian Longhorned Tick (*Haemaphysalis longicornis*) (18)

**Figure 40:** Geographic distribution of the Asian Longhorned Tick (*Haemaphysalis longicornis*) (N = 45) - United States, August 2017–September 2018 (19).

**Location:** Found in 9 states between 2017 and 2018, including Connecticut, New York, New Jersey, Pennsylvania, Maryland, Virginia, West Virginia, North Carolina, and Arkansas

**Transmits:** *Rickettsia*, *Borrelia*, *Ehrlichia*, and *Anaplasma*, although none have been reported thus far

**Comments:** Newly-emerging invasive tick species. The rapid egg-laying rate can result in tick infestations of 100-1000 ticks on a single animal or human.

Groundhog Tick (*Ixodes cookei*)

![Groundhog Tick Image]

**Figure 41:** Groundhog Tick (*Ixodes cookei*) (20).

**Figure 42:** Geographic distribution of the Groundhog Tick (*Ixodes cookei*) (8).

**Location:** The eastern United States

**Transmits:** Powassan virus (Powassan virus disease)

**Comments:** Also known as woodchuck ticks. All life stages occasionally bite humans.
Western Blacklegged Tick (*Ixodes pacificus*)

*Figure 43:* Western-Blacklegged Tick (*Ixodes pacificus*). Photo/TickEncounter Resource Center, University of Rhode Island [17].

*Figure 44:* Geographic distribution of the Western-Blacklegged Tick (*Ixodes pacificus*) [10].

**Location:** Pacific Coast states

**Transmits:** *Anaplasma phagocytophilum* (anaplasmosis), *Borrelia burgdorferi* (Lyme disease), and *B. miyamotoi* (relapsing fever)

**Comments:** All life stages bite humans, most commonly nymphs and adult females.

Blacklegged Tick (*Ixodes scapularis*)

*Figure 45:* Blacklegged ticks or Deer ticks (*Ixodes scapularis*). Photo/TickEncounter Resource Center, University of Rhode Island [17].

*Figure 46:* Geographic distribution of the Blacklegged ticks or Deer ticks (*Ixodes scapularis*) [10].

**Location:** The eastern United States

**Transmits:** *Borrelia burgdorferi* and *B. mayonii* (Lyme disease), *Anaplasma phagocytophilum* (Anaplasmosis), *B. miyamotoi* (relapsing fever), *Ehrlichia muris eauclairensis* (ehrlichiosis), *Babesia microti* (babesiosis), and Powassan virus (Powassan virus disease).

**Comments:** All life stages bite humans, most commonly nymphs and adult females. The greatest risk of being bitten occurs in the spring, summer and fall in the Northeast, Upper Midwest and mid-Atlantic states. Adult ticks may also seek out hosts in winter, when temperatures are above freezing.

Soft Bodied Tick (*Ornithodoros spp.*)

*Figure 47:* Soft Bodied Tick (*Ornithodoros spp.*) [21].

*Figure 48:* Geographic distribution of the Soft Bodied Ticks (*Ornithodoros spp.*) [8].

**Location:** The western half of the United States, including Texas

**Transmits:** *Borrelia hermsii*, *B. parkeri*, and *B. turicata* (relapsing fever; see map of cases in the United States)

**Comments:** Humans typically come into contact with soft ticks in rustic cabins, where ticks emerge at night to feed briefly on sleeping hosts. Hosts may be unaware that they've been bitten. In Texas, tick bites have been associated with cave exposure.

Brown Dog Tick (*Rhipicephalus sanguineus*)

*Figure 49:* Brown Dog Tick (*Rhipicephalus sanguineus*). Photo/TickEncounter Resource Center, University of Rhode Island [17].

*Figure 50:* Geographic distribution of the Brown Dog Tick (*Rhipicephalus sanguineus*) [10].

**Location:** Worldwide

**Transmits:** *Rickettsia rickettsii* (Rocky Mountain spotted fever). It’s the primary vector for *R. rickettsia* transmission in the southwestern United States and along the U.S.-Mexico border

**Comments:** Adult females are most likely to bite humans. The greatest risk of being bitten occurs during the spring and summer.
Important Considerations:

The listed treatment regimens are CDC guidelines only and may need to be adjusted depending on a patient’s age, medical history, underlying health conditions, pregnancy status, or allergies. Consult an infectious disease specialist in severe cases, cases of pregnancy or life-threatening allergy.

Use doxycycline as first-line treatment for suspected anaplasmosis, ehrlichiosis and spotted fever group rickettsiosis in patients of all ages. The use of doxycycline to treat suspected anaplasmosis, ehrlichiosis and spotted fever group rickettsiosis in children is recommended by both the CDC and the American Academy of Pediatrics Committee on Infectious Diseases. Use of antibiotics other than doxycycline increases the risk of patient death. At the recommended dose and duration needed to treat anaplasmosis, ehrlichiosis and spotted fever group rickettsiosis, no evidence has been shown to cause staining of permanent teeth, even when multiple courses are given before the age of eight.

This summary of CDC Tick-borne Diseases of the United States: A Reference Manual for Healthcare Providers, 5th Edition, 2018 is provided as reference information only for clinicians who are clients of Medical Diagnostic Laboratories, L.L.C., (MDL) and is not intended to be further disseminated to patients or members of the public. This summary is not intended to substitute for the clinicians’ judgment or advice nor to diagnose, treat, cure or prevent any disease. This summary does not provide medical advice. Clinicians should review the CDC guidelines as well as any CDC updates to these guidelines.

REFERENCES:

20. Maine Medical Center Research Institute: Other ticks found in Maine [2019] Retrieved from http://www.ticksinmaine.com/ticks/other-ticks