



Vector-Borne Disease

Tick-Borne Diseases of the United States

Anaplasmosis

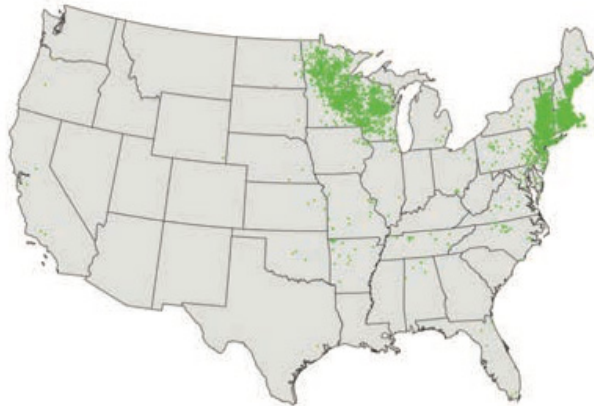


Figure 1: Geographic map of Anaplasmosis reported to CDC, U.S., 2016 (1).

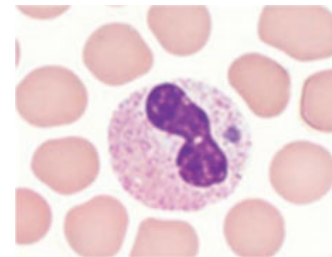


Figure 2: Morulae detected in a granulocyte on a peripheral blood smear, associated with *A. phagocytophilum* infection. Photo/Bobbi S. Pritt, Mayo Clinic (2).

Pathogen(s):	<i>Anaplasma phagocytophilum</i> (formerly Human Granulocytic Ehrlichiosis, HGE)
Location:	Upper Midwest and Northeast United States overlapping with the geographic distribution of Lyme disease and other Blacklegged tick (<i>Ixodes scapularis</i>) transmitted diseases.
Peak Infections:	June through August
Vector:	Blacklegged ticks (<i>Ixodes scapularis</i>)
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 symptom and the number and combination of symptoms varies greatly for each patient.
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 in during the first week of illness. Antibody based testing for rise in IgM (increase 2-3 days after illness) and IgG (typically up to 4-fold increase 7-10 days after illness). Samples should be taken within the first week of illness and a second sample should be taken 2-4 weeks later.
MDL Test Code(s):	441 <i>Ehrlichia chaffeensis</i> (HME) & <i>Anaplasma phagocytophilum</i> (HGE) by Real-Time PCR 439 <i>Anaplasma phagocytophilum</i> IgG/IgM by IFA
Treatment:	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 per dose Doxycycline (100 mg/dose max), twice per day, orally or IV for 10-14 days. *SEE NOTE ^{1,2} BELOW.
Comments:	Less severe and life-threatening compared to rickettsial diseases such as Rocky Mounted Spotted Fever or <i>E. chaffeensis</i> Ehrlichiosis. Due to the common tick vector, co-infection with <i>Anaplasma phagocytophilum</i> , <i>Burrelia burgdorferi</i> , <i>Babesia microti</i> 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



Figure 3: Geographic map of Ehrlichiosis reported to CDC, U.S., 2016 (1).

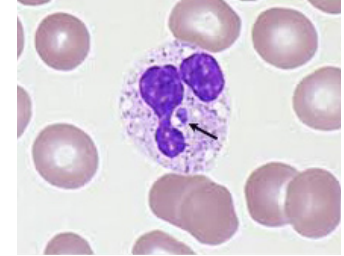


Figure 4: Morulae detected in a granulocyte on a peripheral blood smear, associated with Ehrlichia infection. Photo/ Peter Maslak and Lisa Southern, Memorial Sloan-Kettering Cancer Center (3).

Pathogen(s):

Ehrlichia chaffeensis, *Ehrlichia ewingii*, and *Ehrlichia muris euclairensis* (Human Monocytic Ehrlichiosis, HME)

Location:

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 euclairensis* 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* and the Blacklegged ticks (*Ixodes scapularis*) transmits *E. muris euclairensis*.

Incubation Period:

1 – 2 weeks

Signs & Symptoms:

The three species of Ehrlichia have similar clinical presentation of fever, chills, headache, 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:

Typically during the first week of clinical disease, thrombocytopenia, leukopenia (absolute), anemia (generally later in the illness), 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 in during the first week of illness. Antibody based testing for rise in IgM (increase 2-3 days after illness) and IgG (typically up to 4-fold increase 7-10 days after illness). Samples should be taken within the first week of illness and 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

456 Ehrlichia ewingii by Real-Time PCR

Future MDL Tests:

Ehrlichia muris euclairensis by Real-Time PCR

Ehrlichia chaffeensis (HME) IgG/IgM by IFA

Treatment:

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 there is evidence of clinical improvement. Minimum course of treatment is 5-7 days.

Children (weighing <100 lbs, 45.4 kg): 2.2 mg/kg per dose Doxycycline (100 mg/dose max), twice per day, orally or IV for at least 3 days after the fever subsides and until there is evidence of clinical improvement. Minimum course of treatment is 5-7 days.

***SEE NOTE 1,2 BELOW.**

Comments:

E. chaffeensis ehrlichiosis can cause fatal illness, whereas no deaths have been reported for *E. ewingii* or *E. muris euclairensis* ehrlichiosis. Cases of *E. chaffeensis* ehrlichiosis generally increases with age, however, case-fatality rates are highest among children aged <10 years and adults aged

Babesiosis



Figure 5: Geographic map of Babesiosis reported to CDC, U.S., 2016 (1).

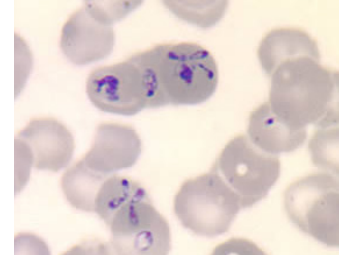


Figure 6: Babesia parasites in red blood cells on a stained blood smear. Photo/DPDx (4).

Pathogens:

Babesia microti, *Babesia duncani* (WA1), and *B. divergens*-like (MO1)

Location:

Upper Midwest (Wisconsin and Minnesota) and Northeast (New England, New York and New Jersey) of the United States overlapping with the geographic distribution of Lyme disease and other Blacklegged tick (*Ixodes scapularis*) transmitted diseases. Sporadic cases of infection caused by *B. duncani* (WA1) and *B. divergens*-like (MO1) have been detected in other U.S. regions, including the West Coast. Additionally, cases of blood transfusion-associated Babesiosis has been reported.

Peak Infections:

June through August

Vector:

Blacklegged ticks (*Ixodes scapularis*)

Incubation Period:

1-9+ weeks

Signs & Symptoms:

Wide range of signs and symptoms from asymptomatic to life threatening. Clinical manifestations, if any, usually develop within several weeks after exposure, but may develop or recur months later. S&S include fever, chills, headache, myalgia, arthralgia, gastrointestinal symptoms (nausea and anorexia with vomiting diarrhea being less common), dark urine, and rash (<10%). Less common include cough sore throat, emotional lability, depression, photophobia, and conjunctival injection. Mild splenomegaly, mild hepatomegaly, or jaundice may occur in some patients.

Severe cases can be associated with marked 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* (WA1) by Real-Time PCR

Future MDL Tests:

***Babesia duncani* (WA1) IgG/IgM by IFA**

***Babesia divergens*-like (MO1) by Real-Time PCR**

Treatment:

Adult combination therapy: Atovaquone 750 mg orally every 12 hrs PLUS Azithromycin 500-1000 mg orally on day 1, followed by 250-1000 mg (1000 mg/dose max) daily for 7-10 days OR

Clindamycin 300-600 mg IV every 6 hrs OR 600 mg orally every 8 hrs PLUS Quinine 650 mg orally every 6-8 hrs for 7-10 days (standard for severely ill patients).

***SEE NOTE 1 BELOW.**

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

Comments:

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

Borreliosis

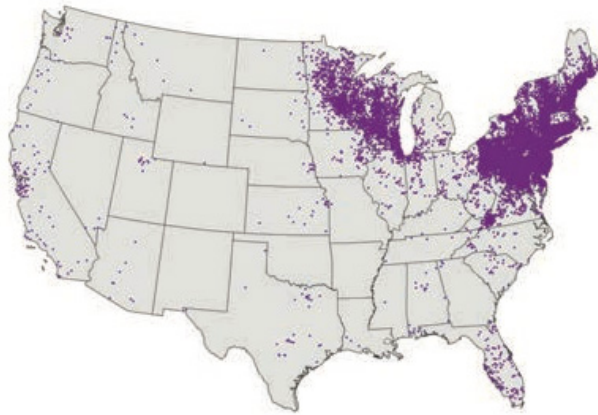


Figure 7: Geographic map of Lyme disease reported to CDC, U.S., 2016 (1).

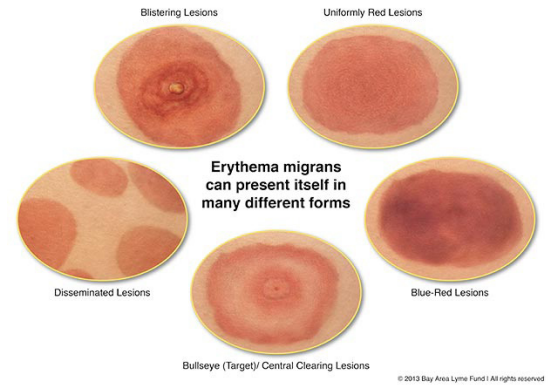


Figure 8: Various presentations of Erythema migrans rash (5).

Lyme Disease

Pathogens:

Borrelia burgdorferi and *Borrelia mayonii*

Location:

Lyme disease is most frequently reported in the Upper Midwest (Wisconsin and Minnesota) and the Northeast (New England, Delaware, Maryland, New Jersey, New York, Pennsylvania, and Virginia) of the United States accounting for 95% of the cases.

Peak Infections:

May through September, although cases have been reported year round.

Vector:

Blacklegged ticks (*Ixodes scapularis*) and Western Blacklegged Tick (*Ixodes pacificus*)

Incubation Period:

3 to 30 days

Signs & Symptoms:

Localized Early Stage: Erythema migrans (EM) a red ring-link or homogenous expanding rash present in 70-80% of patients. Flu-like symptoms with malaise, headache, fever, myalgia, arthralgia and lymphadenopathy. Early stages of illness serology may be insensitive.

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. 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**
- 449 *Borrelia mayonii* (United States) by Real-Time PCR**
- 417 Lyme disease C6 Peptide by ELISA**
- 440 Lyme disease IgG/IgM 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)**

Treatment:

Localized Early Stage Disease:

Adult therapy: Doxycycline 100 mg twice per day orally for 10-21 days OR Cefuroxime axetil 500 mg twice per day orally for 14-21 days OR Amoxicillin 500 mg three times per day orally for 14-21 days.

Children therapy: Amoxicillin 50 mg/kg per day orally, divided into 3 doses (500 mg per dose max) for 14-21 days OR Doxycycline 4 mg/kg per day orally, divided into 2 doses (100 mg per dose max) for 10-21 days OR Cefuroxime axetil 30 mg/kg per day 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 Disease:

Patients intolerant of amoxicillin, cefuroxime axetil, and doxycycline, macrolides azithromycin, clarithromycin, or erythromycin may be used although they have a lower efficacy and patients should be closely monitored to ensure symptoms resolve.

***SEE NOTE 1,2 BELOW.**

Comments:

More than 300,000 new cases 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 what is observed commonly with Lyme disease alone and with those patients who have a high-grade fever for more than 48 hr despite appropriate antibiotic therapy or who have unexplained leukopenia, thrombocytopenia or anemia. Co-infection should be considered in patients whose EM skin lesion has resolved but have persistent flu-like symptoms.

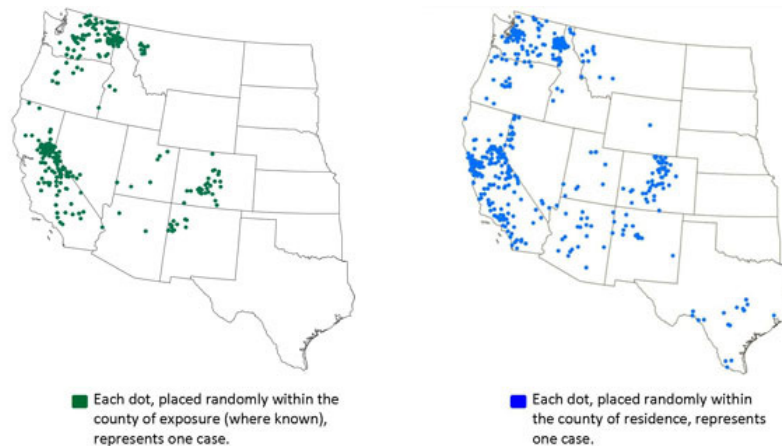
Tick-borne Relapsing Fever (TBRF): Western Soft Tick

Figure 9: Cases of Tick-borne Relapsing Fever, United States, 1990-2011 (6).

Pathogen(s):

Borrelia hermsii, and *Borrelia parkeri*, *Borrelia turicatae*

Location:

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

Peak Infections:

Summer and occasionally winter when fires warm cabin walls and activate resting ticks.

Vector:

Soft Bodied Tick (*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, headache, 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):

450 *Borrelia hermsii* by Real-Time PCR

451 *Borrelia parkeri* by Real-Time PCR

360 *Borrelia turicatae* by Real-Time PCR

Treatment:

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

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

***SEE NOTE 1 BELOW.**

Comments:

All patients should be observed during the first 2-4 hours of treatment for a Jarisch-Herxheimer reaction. Acute respiratory distress syndrome requiring intubation had occurred in several patients undergoing TBRF treatment.

Tick-borne Relapsing Fever (TBRF): Eastern Hard Tick

Pathogen(s):	<i>Borrelia miyamotoi</i>
Location:	A newer emerging TBRF that occurs mostly in the Upper Midwest, Northeast, and mid-Atlantic states, in places endemic for Lyme Disease. Most cases of TBRF occur in rodent infested cabins. TBRF may be associated with cave exposure in Texas.
Peak Infections:	July and August.
Vector:	May be spread by larval Blacklegged tick (<i>Ixodes scapularis</i>).
Incubation Period:	Days to weeks.
Signs & Symptoms:	Fever, chills, fatigue, severe headache, arthralgia, and myalgia. Uncommon S&S 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 <i>Borrelia miyamotoi</i> by Real-Time PCR
Treatment:	No comprehensive studies to evaluate treatment regimens. Published case series report successful treatment with antibiotics and dosages used for Lyme disease.

Southern Tick-Associated Rash Illness (STARI)

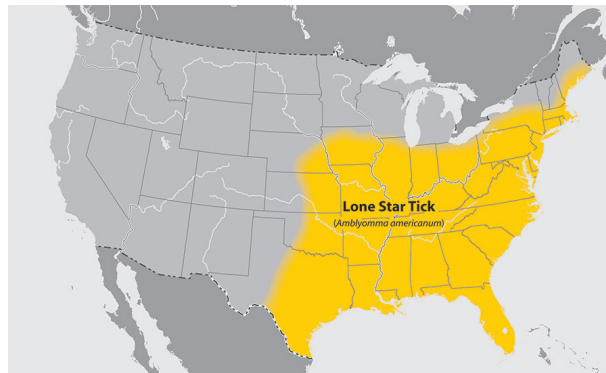


Figure 10: Geographic distribution of the Lone Star tick (*Amblyomma americanum*) (7).



Figure 11: Various presentations of Erythema migrans rash (8).

Pathogen(s):	<i>Borrelia lonestari</i> is the putative <i>Borrelia</i> species associated with STARI as discussed in the literature, however the definitive cause of STARI is currently unknown.
Location:	STARI is specifically associated with bites from the Lone Star tick (<i>Amblyomma americanum</i>), which has a range from central Texas and Oklahoma eastward across the southern states and along the Atlantic coast as far north as Maine.
Peak Infections:	June through August
Vector:	Lone Star tick (<i>Amblyomma americanum</i>)
Incubation Period:	1 – 2 weeks
Signs & Symptoms:	An expanding bull-eye rash (~3 inches in diameter) that develops around the site of the tick bite. Patients can also experience fatigue, headache, fever, joint and muscle pain within 30 days of the bite. Saliva from the Lone Star tick can be irritating, therefore redness and discomfort the bite site does not necessarily mean infection.
Laboratory findings:	Lyme disease testing is negative since the Lone Star tick does not carry and transmit <i>Borrelia burgdorferi</i> .
MDL Test Code(s):	440 <i>Borrelia lonestari</i> by Real-Time PCR
Treatment:	Unknown. However, because the signs and symptoms of STARI often resemble early Lyme disease, physicians will treat with Lyme disease oral antibiotics.

Rickettsiosis²

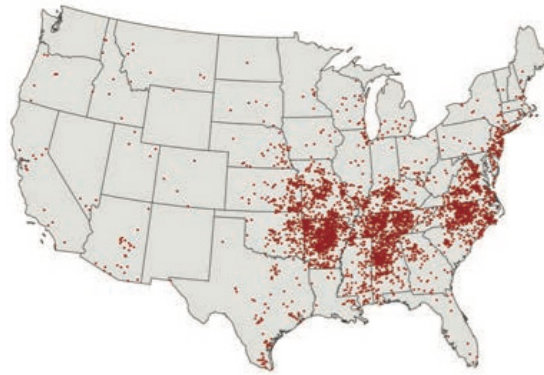


Figure 12: Geographic map of Spotted Fever Rickettsiosis (including Rocky Mountain Spotted Fever) reported to CDC, U.S., 2016 (1).

Spotted Fever Group Rickettsiosis



Figure 13: Early stage maculopapular rash. Photo/CDC (9).



Figure 14: Late stage petechial rash. Photo/CDC (9).

Rickettsia rickettsii (Rocky Mountain Spotted Fever, RMSF)

Pathogen(s):	<i>Rickettsia rickettsii</i>
Location:	RMSF cases have been reported throughout the United States. North Carolina, Oklahoma, Arkansas, Tennessee, and Missouri account for > 60% of the cases. Recently, certain areas of Arizona have had over 360 cases with 21 fatalities.
Peak Infections:	May-July with 90% of cases reported from April through September.
Vector:	American Dog Tick (<i>Dermacentor variabilis</i>) transmits RMSF in Eastern, Central, and Western U.S. Brown Dog Tick (<i>Rhipicephalus sanguineus</i>) transmits RMSF in Southwestern U.S. Rocky Mountain Wood Tick (<i>Dermacentor andersoni</i>) transmits RMSF in the Rocky Mountain states.
Incubation Period:	3-12 days
Signs & Symptoms:	Early S&S (1-4 days) include high fever, severe headache, malaise, Myalgia, Edema around eyes and on back of hands, gastrointestinal symptoms of nausea, vomiting and anorexia. Late S&S (≥5 days) include altered mental status, coma, cerebral edema, respiratory compromise or pulmonary edema and ARDS, necrosis requiring amputation, and multiorgan system damage for example 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 wrist, forearms, and ankles then spreading to the trunk and sometimes palms and soles. Late petechial rashes consist of red to purple spots, which are not seen until ≥6 days later after the onset of symptoms. Petechial rashes are considered progression to severe disease and 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 <i>Rickettsia</i> species (Rickettsiosis) by Real-Time PCR 447 <i>Rickettsia rickettsii</i> by Real-Time PCR
Treatment:	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. *SEE NOTE 1,2 BELOW.
Comments:	RMSF (5-10% fatality rate) can be rapidly fatal if not treated within the first 5 days of symptoms. 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

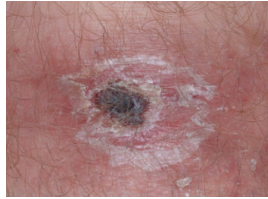


Figure 15: Eschar at site of tick bite. Photo/CDC (9).



Figure 16: Vesiculopapular rash. Photo/CDC (9).

Location:	<i>R. parkeri</i> rickettsiosis is transmitted by the Gulf Coast tick in the southeastern, mid-Atlantic states, and parts of southern Arizona.
Peak Infections:	July to September, but can occur April to October.
Vector:	Gulf Coast Tick (<i>Amblyomma maculatum</i>)
Incubation Period:	2-10 days
Signs & Symptoms:	<i>R. parkeri</i> rickettsiosis has overlapping S&S 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:	446 Rickettsia species (Rickettsiosis) by Real-Time PCR 448 Rickettsia parkeri by Real-Time PCR
Treatment:	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. *SEE NOTE ^{1,2} BELOW.
Comments:	RMSF antibody tests are available and often cross-react with <i>R. parkeri</i> .

Pacific Coast Tick Fever: Rickettsia philipii (364D)

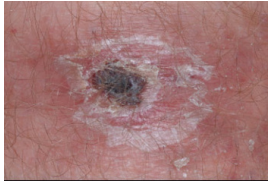


Figure 15: Eschar at site of tick bite. Photo/CDC (9).



Figure 16: Vesiculopapular rash. Photo/CDC (9).

Location:	<i>R. philipii</i> 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 (<i>Dermacentor occidentalis</i>) ranges from California to Oregon.
Incubation Period:	2-10 days
Signs & Symptoms:	<i>R. philipii</i> rickettsiosis has overlapping S&S 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 452 Rickettsia philipii (364D) by Real-Time PCR
Treatment:	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. *SEE NOTE ^{1,2} BELOW.
Comments:	RMSF antibody tests are available and may cross-react with <i>R. philipii</i> .

Tularemia



Figure 19: Geographic map of Tularemia reported to CDC, U.S., 2016 (1).



Figure 20: An ulcer caused by *Francisella tularensis*. (10).

Pathogen(s):	<i>Francisella tularensis</i> subspecies <i>tularensis</i> and <i>Francisella tularensis</i> subspecies <i>holarctica</i>
Location:	Endemic throughout the mainland United States. Most common in south central U.S., Pacific Northwest, and parts of Massachusetts, including Martha's Vineyard.
Peak Infections:	June through August
Vector:	Ticks that transmit tularemia include the Dog tick (<i>Dermacentor variabilis</i>), the Rocky Mountain Wood tick (<i>D. andersoni</i>) and Lone Star tick (<i>Amblyomma americanum</i>). The deer fly (<i>Chrysops</i> spp.) can also transmit tularemia. Tularemia is highly infections and can also be transmitted via handling infected animals, inhalation, and ingestions of undercooked meat or contaminated water.
Incubation Period:	3-5 days (range 1-21 days)
Signs & Symptoms:	Fever, headache, malaise, fatigue, anorexia, myalgia, chest discomfort, cough, sore throat, vomiting diarrhea, abdominal pain. Ulceroglandular S&S of localized lymphadenopathy, cutaneous ulcer at infection site (not always present). Oculoglandular S&S of photophobia, conjunctivitis, preauricular submandibular, or cervical lymphadenopathy. Oropharyngeal S&S of severe throat pain, exudative pharyngitis or tonsillitis, cervical, parotid and/or retropharyngeal lymphadenopathy. Typhoidal S&S of any combination of the general symptoms without localizing symptoms of other syndromes.
Laboratory findings:	May be normal or elevated: Leukocyte count and sedimentation rate, thrombocytopenia, hyponatremia, elevated hepatic transaminases, elevated creatine phosphokinase. May be present or not present: myoglobinuria and sterile pyuria.
MDL Test Code(s):	360 <i>Francisella tularensis</i> (subspecies <i>tularensis</i> & <i>holarctica</i>) by Real-Time PCR
Future MDL Tests:	<i>Francisella tularensis</i> IgG/IgM by ELISA
Treatment:	Adults: streptomycin 1 g IM twice daily (2 g per day max) for a minimum of 10 days OR Doxycycline 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 drug 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. *SEE NOTE 1 BELOW. 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 drug 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

- Location:** As of June 2018, a limited number of Bourbon virus disease cases have been identified in the Midwest and southern United States. The virus was first identified in 2014 from an infected patient from Bourbon County, Kansas.
- Peak Infections:** Not known
- Vector:** Lone Star Tick (*Amblyomma americanum*) is suspected but it is not fully understood.
- Incubation Period:** Specific ranges are unknown.
- Signs & Symptoms:** Fever, fatigue, anorexia, nausea, vomiting, and maculopapular rash. Some patients found to be infected with Bourbon virus have died during their acute illness.
- Laboratory findings:** Leukopenia and thrombocytopenia.
- Future MDL Tests:** **Bourbon virus by Real-Time PCR**
- Treatment:** There are no vaccines or medication to prevent or treat Bourbon virus infection. Supportive care is recommended.
- 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).

Colorado Tick Fever virus

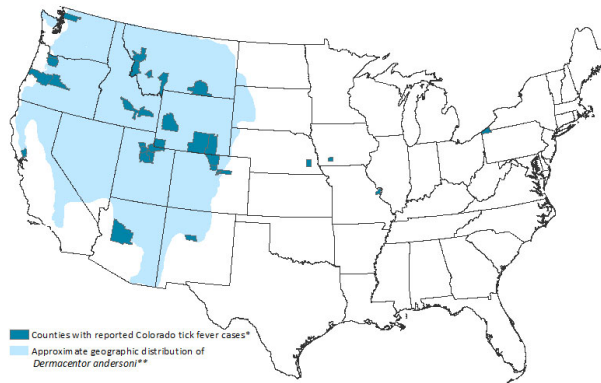


Figure 21: Geographic map of *Dermacentor andersoni* ticks for confirmed and probable Colorado Tick Fever (CTF) virus disease cases, United States, 2002–2012 (11).

- Location:** Colorado Tick Fever (CTF) caused by the Colorado tick fever virus geographic range includes 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 be transmitted via blood transfusions.
- Incubation Period:** 1–14 days.
- Signs & Symptoms:** Fever, chills, headache, 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 have affects on the central nervous system with symptoms of stiff neck and confusion. Some patients found to be infected with Bourbon virus have died during their acute illness.
- Laboratory findings:** Leukopenia and moderate thrombocytopenia.
- MDL Test Code(s):** **434 Colorado Tick Fever virus by Real-Time PCR**
- Treatment:** There are no vaccines or medication to prevent or treat Bourbon virus infection. Supportive care is recommended. Most people with mild disease recover completely. However, weakness and fatigue may last several weeks.
- 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. 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)

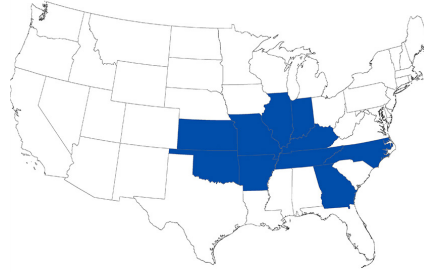


Figure 22: Geographic map of Heartland virus disease cases by state as of September 2018 (12).

Location:	As of September 2018, more than 40 cases of Heartland virus disease have been reported from Midwestern (Arkansas, Indiana, Illinois, Kansas, Missouri, and Oklahoma) and Southern states (Georgia, Kentucky, North Carolina, and Tennessee).
Peak Infections:	May through September
Vector:	Lone Star Tick (<i>Amblyomma americanum</i>)
Incubation Period:	Specific ranges are unknown, but most patients report a tick bite 2 weeks prior to illness.
Signs & Symptoms:	Most patients have fever, fatigue, decreased appetite, headache, nausea, diarrhea, and muscle or joint pain.
Laboratory findings:	Leukopenia, thrombocytopenia and mild to moderate elevation of liver transaminases.
MDL Test Code(s):	436 Heartland virus (Phlebovirus) by Real-Time PCR
Treatment:	There are no vaccines or medication 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 <i>Ehrlichia chaffeensis</i> and <i>E. ewingii</i> (Ehrlichiosis), <i>Francisella tularensis</i> (Tularemia), Heartland virus (Heartland virus disease), Bourbon virus (Bourbon virus disease) and Southern tick-associated rash illness (STARI).

Powassan virus

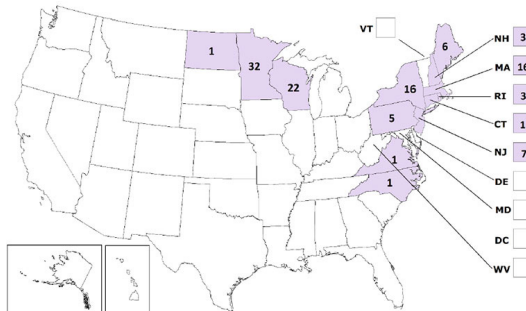


Figure 23: Geographic map of Powassan virus neuroinvasive disease cases reported by year, 2008-2017 (13).

Location:	Great Lakes region and Northeastern states
Peak Infections:	Late spring, early summer and mid-fall.
Vector:	Blacklegged ticks (<i>Ixodes scapularis</i>) and Groundhog Tick (<i>Ixodes cookei</i>)
Incubation Period:	1-4 weeks
Signs & Symptoms:	Many people who become infected do not have symptoms. S&S include fever, headache, vomiting, and generalized weakness. Usually progress to meningoencephalitis that may include meningeal signs, altered mental status, seizures, aphasia, paresis, movement disorders, or cranial nerve palsies.
Laboratory findings:	CSF findings include lymphocytic pleocytosis (neutrophils can predominate early), normal or mildly elevated protein, and normal glucose.
MDL Test Code(s):	282 Powassan virus IgG/IgM by ELISA
Future MDL Tests	Powassan virus by Real-Time PCR
Treatment:	There are no vaccines or medication 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 recurrent headaches, muscle wasting and memory problems. Approximately 10% of Powassan virus encephalitis cases are fatal. Due to the common Blacklegged tick (<i>Ixodes scapularis</i>) vector, co-infection with <i>Anaplasma phagocytophilum</i> , <i>Borrelia burgdorferi</i> , or <i>Babesia microti</i> is possible.

Tick Typing ¹

Lone Star Tick (*Amblyomma americanum*)

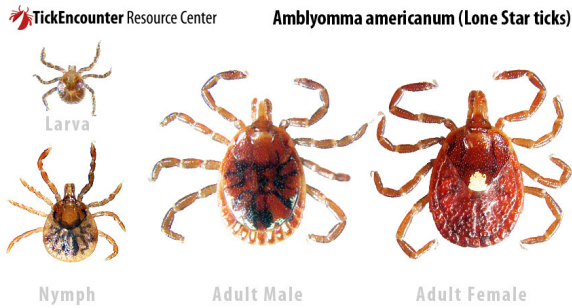


Figure 24: Lone Star tick (*Amblyomma americanum*). Photo/ TickEncounter Resource Center, University of Rhode Island (14).

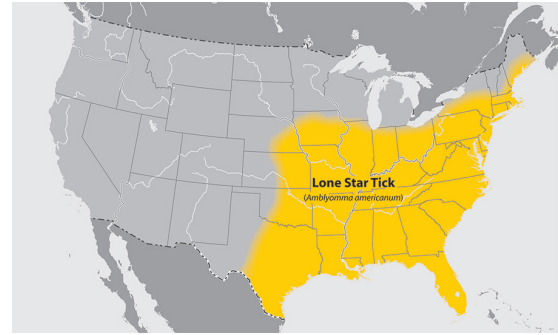


Figure 25: Geographic distribution of the Lone Star tick (*Amblyomma americanum*) (7).

Location: Eastern United States, more common 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, the nymphs and adult females most frequently bite humans. Greatest risk of being bitten occurs in early spring through late fall. Adult female ticks have a white dot or "lone star" on the back. There have been reports of allergic reactions associated with the consumption of red meat among persons bitten by the lone star tick.

Cayenne Tick (*Amblyomma cajennense*)

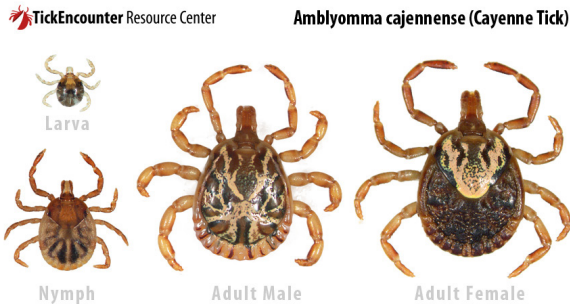


Figure 26: Cayenne Tick (*Amblyomma cajennense*). Photo/ TickEncounter Resource Center, University of Rhode Island (14).

Location: Southern Texas and occasionally Florida and coastal regions of the Gulf states.
Transmits: Spotted Fever Group *Rickettsia* species associated with Rickettsiosis.
Comments: This cold-sensitive tick feeds year round. The adult tick occasionally bites humans. Pain and tissue damage is common as a result from the feeding tick.

Gulf Coast Tick (*Amblyomma maculatum*)

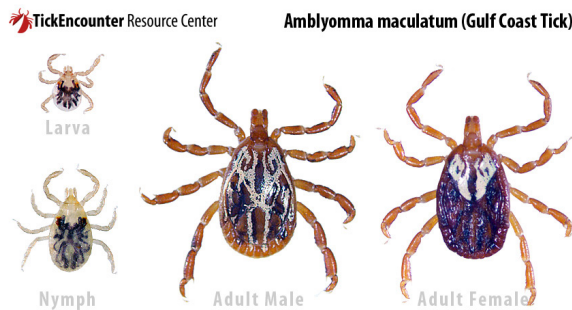


Figure 27: Gulf Coast Tick (*Amblyomma maculatum*). Photo/ TickEncounter Resource Center, University of Rhode Island (14).

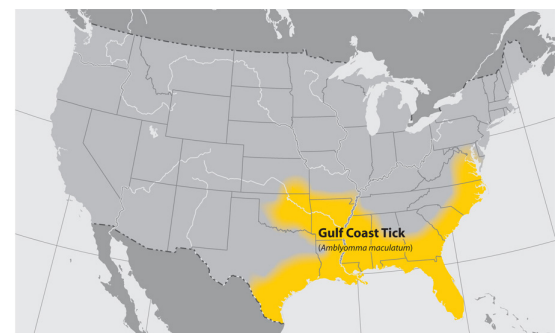


Figure 28: Geographic distribution of the Gulf Coast Tick (*Amblyomma maculatum*) (7).

Location: Southeastern and mid-Atlantic United States as well as southern Arizona.
Transmits: *Rickettsia parkeri* (Spotted Fever Rickettsiosis).
Comments: Adult ticks associated with *R. parkeri* transmission to humans.

Rocky Mountain Wood Tick (*Dermacentor andersoni*)

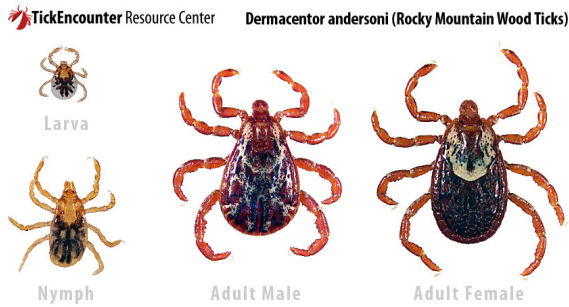


Figure 29: Rocky Mountain Wood Tick (*Dermacentor andersoni*). Photo/TickEncounter Resource Center, University of Rhode Island (14).



Figure 30: Geographic distribution of the Rocky Mountain Wood Tick (*Dermacentor andersoni*) (7).

Location: 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 associated with pathogen transmission to humans.

Pacific Coast Tick (*Dermacentor occidentalis*)

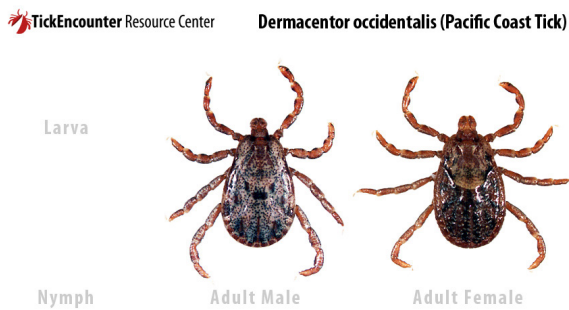


Figure 31: Pacific Coast Tick (*Dermacentor occidentalis*). Photo/TickEncounter Resource Center, University of Rhode Island (14).

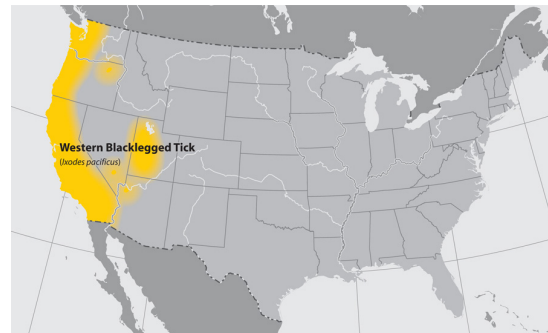


Figure 32: Geographic distribution of the Pacific Coast Tick (*Dermacentor occidentalis*) (7).

Location: 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*)

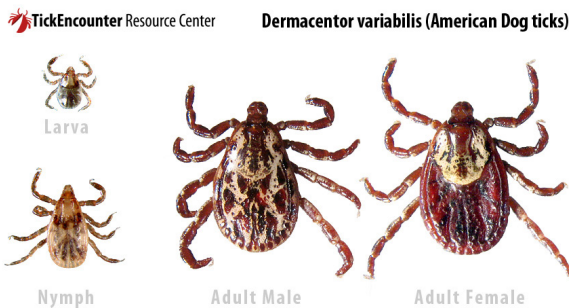


Figure 33: American Dog Ticks (*Dermacentor variabilis*). Photo/TickEncounter Resource Center, University of Rhode Island (14).



Figure 34: Geographic distribution of the American Dog Ticks (*Dermacentor variabilis*) (7).

Location: 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. Greatest risk of being bitten occurs during the spring and summer.

Asian Longhorned Tick (*Haemaphysalis longicornis*)³



Figure 35: Geographic distribution of the Lone Star tick (*Amblyomma americanum*) (7).

Location: Newly emerging invasive tick species found in 9 states between 2017 and 2018, which includes Connecticut, New York, New Jersey, Pennsylvania, Maryland, Virginia, West Virginia, North Carolina and Arkansas.

Transmits: *Rickettsia*, *Borrelia*, *Ehrlichia*, and *Anaplasma* although non have been reported thus far.

Comments: Due to egg laying rate, tick infestations can occur in which 100-1000 ticks could be found on an animal or human.

Groundhog Tick (*Ixodes cookei*)



Figure 37: Groundhog Tick (*Ixodes cookei*) Photo/ Steve Jacobs, PSU Entomology (16)

Location: Eastern United States

Transmits: Powassan virus (Powassan virus disease).

Comments: Also called woodchuck ticks. All life stages occasionally bite humans.

Western Blacklegged Tick (*Ixodes pacificus*)

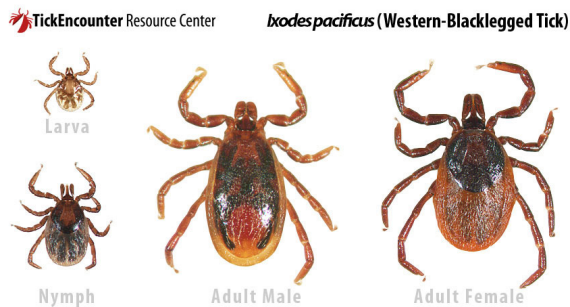


Figure 36: Western-Blacklegged Tick (*Ixodes pacificus*). Photo/ TickEncounter Resource Center, University of Rhode Island (14).

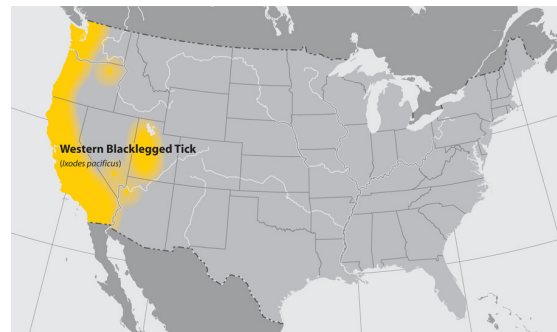


Figure 37: Geographic distribution of the Western-Blacklegged Tick (*Ixodes pacificus*) (7).

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*)

 TickEncounter Resource Center ***Ixodes scapularis* (Blacklegged ticks or Deer ticks)**



Figure 38: Blacklegged ticks or Deer ticks (*Ixodes scapularis*). Photo/TickEncounter Resource Center, University of Rhode Island (14).

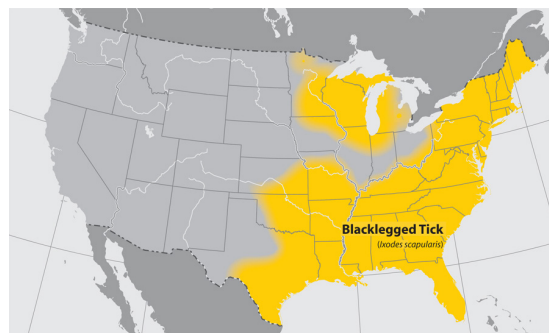


Figure 39: Geographic distribution of the Blacklegged ticks or Deer ticks (*Ixodes scapularis*) (7).

Location: Eastern United States

Transmits: *Borrelia burgdorferi* and *B. mayonii* (Lyme disease), *Anaplasma phagocytophilum* (anaplasmosis), *B. miyamotoi* (Relapsing fever), *Ehrlichia muris euclairensis* (Ehrlichiosis), *Babesia microti* (Babesiosis), and Powassan virus (Powassan virus disease).

Comments: All life stages bite humans, most commonly nymphs and adult females. Greatest risk of being bitten occurs in the spring, summer and fall in the Northeast, Upper Midwest and mid-Atlantic. Adult ticks may be found looking for a host during winter when temperatures are above freezing.

Soft Bodied Tick (*Ornithodoros spp.*)



Figure 40: Soft Bodied Tick (*Ornithodoros spp.*) (16).

Location: 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 the ticks emerge at night and feed briefly on the sleeping host, most times unaware they have been bitten. In Texas, tick bites have been associated with cave exposure.

Brown Dog Tick (*Rhipicephalus sanguineus*)

 TickEncounter Resource Center

***Rhipicephalus sanguineus* (Brown Dog Tick)**



Figure 41: Brown Dog Tick (*Rhipicephalus sanguineus*). Photo/TickEncounter Resource Center, University of Rhode Island (14).



Figure 42: Geographic distribution of the Brown Dog Tick (*Rhipicephalus sanguineus*) (7).

Location: Worldwide.

Transmits: *Rickettsia rickettsii* (Rocky Mountain Spotted Fever). 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. Greatest risk of being bitten occurs during the spring and summer.

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