

March 2022

Tick-Borne Diseases: Crawling Across the United States

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Recommended Citation

Dennehy EM. Tick-Borne Diseases: Crawling Across the United States. *Lynchburg Journal of Medical Science*. 2022; 4(2).

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TICK-BORNE DISEASES: CRAWLING ACROSS THE UNITED STATES

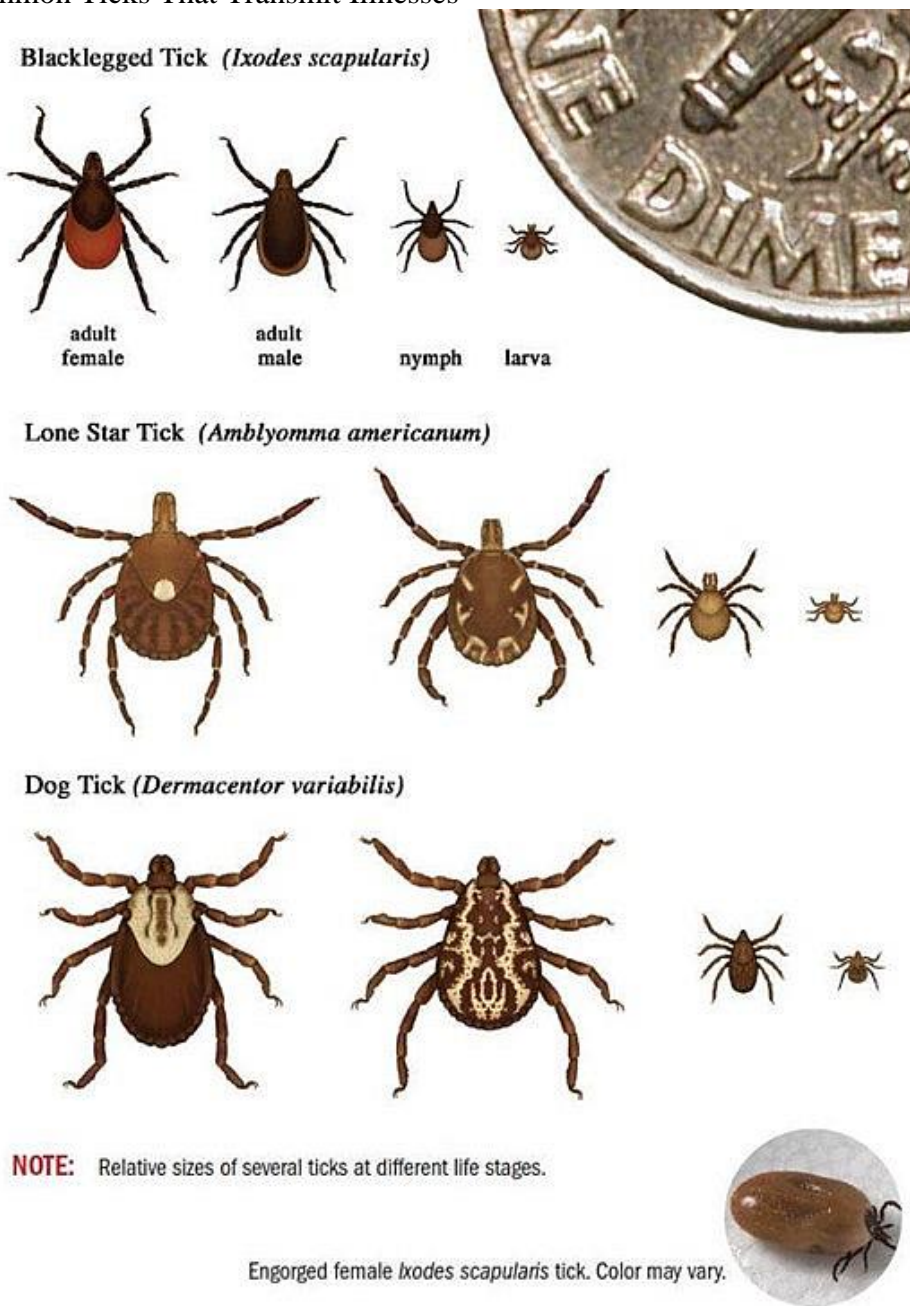
INTRODUCTION

Tick-borne disease in the United States has increased over the past decades, and roughly doubled over the past 15 years.¹ According to the Center for Disease Control (CDC), there were over 50,000 reportable tick-borne diseases in 2019. The actual account of tick-borne diseases may be higher due to empiric treatment or patients who remained untreated.² In the United States (US) there are six common tick-borne illnesses; anaplasmosis, babesiosis, ehrlichiosis, Lyme disease, Rocky Mountain spotted fever, and tularemia. There are also some less common diseases as well, including miyamotoi, and Powassan virus, among others.² There has been an increased geographic spread of different ticks, which has likely caused the increase of diagnosed tick-borne diseases.³ Having knowledge of the specific type of tick is helpful in narrowing the possible tick illness, as many of the non-specific symptoms overlap. Additionally, due to the severity of illness that some tick-borne diseases can cause, it has become increasingly necessary to identify tick-borne diseases in a timely manner.

COMMON TICKS FOUND IN THE UNITED STATES

Although not an inclusive list of ticks found in the US, the most common ticks that transmit illnesses are listed below (figure 1). Testing of patient-retrieved ticks for infections is not recommended.⁴

Figure 1 Common Ticks That Transmit Illnesses

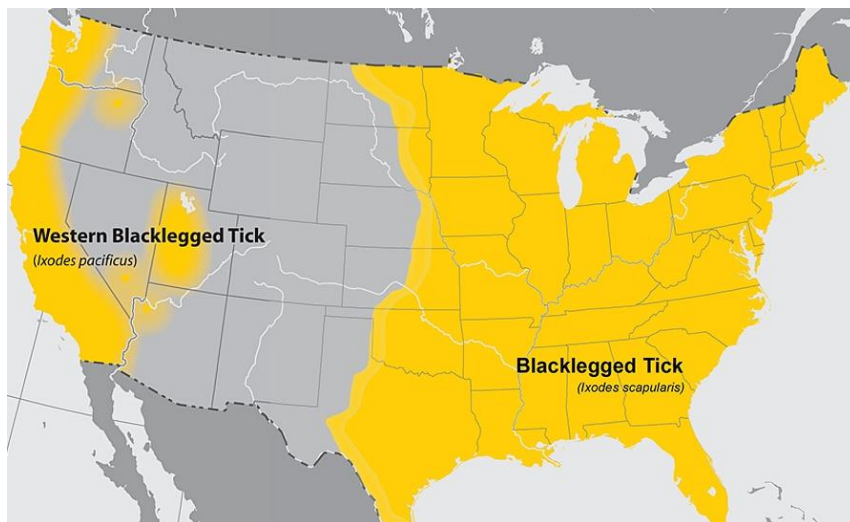


Content Source: Centers for Disease Control and Prevention, National Center for Emerging and Zoonotic Infectious Diseases (NCEZID), Division of Vector-Borne Diseases (DVBD)

Blacklegged Tick: *Ixodes scapularis*. Transmits: Lyme disease, anaplasmosis, miyamotoi, ehrlichiosis, babesiosis, and Powassan virus disease.² (figure 2) Commonly referred to as a deer tick, this tick is black or dark brown and is found widely distributed across the eastern US. Host-seeking nymphs were generally higher in the north compared to the south.⁵ Nymphs and adult females are most commonly found on people, the unengorged female has a red-orange body whereas the nymph has a lighter brown body. In comparing this tick to the other *Ixodes* species, the *Ixodes scapularis* is more likely to bite humans; therefore, the illnesses this tick can carry may be of greatest risk compared to the other ticks.⁶

Western blacklegged tick: *Ixodes pacificus*. Transmits: anaplasmosis, Lyme disease, and likely miyamotoi.² (figure 2) This tick is found in Pacific Coast states and transmits illnesses similar to the *Ixodes scapularis*. The female tick appears similar to the blacklegged tick, although the mouthparts and legs are paler in color.

Figure 2 Geographical Distribution of Blacklegged and Western Blacklegged Tick



Modified by Ellen Dennehy, PA-C, DMSc Fellow.
Content Source: Centers for Disease Control and Prevention, National Center for Emerging and Zoonotic Infectious Diseases (NCEZID), Division of Vector-Borne Diseases (DVBD)

Groundhog Tick or Woodchuck Tick: *Ixodes cookiei*. Transmits: Powassan virus.⁷

This tick is found mostly in Tennessee and North Carolina although the range may include eastern North America and is the second most common tick in Maine.⁸ This tick has pale brown legs, the adult male has a brown dorsal shield while the females have a reddish-tan marking behind the head. The nymphs are light tan in color.

Lone Star Tick: *Amblyomma americanum*. Transmits: ehrlichiosis, tularemia, Heartland virus disease, Bourbon virus disease, and Southern tick-associated rash illness (STARI).² (figure 3) The lone star tick is more common in the South but widely distributed across the eastern US. The adult females have a white marking in the middle of the back, while the males have white scattered stripes on the lateral edges of the body. This tick is fast-moving and will chase its intended target, which may include people in parking lots. The lone star ticks do not transmit Lyme disease, a chemical in the saliva has been found to destroy the responsible bacteria.⁹ There is a potential red meat allergy after people have been bitten by lone star ticks, known as alpha-gal syndrome.¹⁰ Although this syndrome is associated with lone star ticks in the US, other ticks have been suspected of causing this syndrome in other countries. It is possible that blacklegged ticks may also cause alpha-gal syndrome.¹⁰

Figure 3 Geographical Distribution of Lone Star Tick



Content Source: Centers for Disease Control and Prevention, National Center for Emerging and Zoonotic Infectious Diseases (NCEZID), Division of Vector-Borne Diseases (DVBD)

American Dog Tick: *Dermacentor variabilis*. Transmits: tularemia and Rocky

Mountain spotted fever² (figure 4) Found on the eastern Rocky Mountains and limited areas on the Pacific Coast, this oval flat tick is dark brown with the females having a pale white dorsal shield. The males may have a mottled appearance to the body.

Figure 4 Geographical Distribution of American Dog Tick



Content Source: Centers for Disease Control and Prevention, National Center for Emerging and Zoonotic Infectious Diseases (NCEZID), Division of Vector-Borne Diseases (DVBD)

Brown Dog Tick: *Rhipicephalus sanguineus*. Transmits: Rocky Mountain spotted fever.² (figure 5) Found throughout the US, dogs are the primary host for the reddish-brown tick.

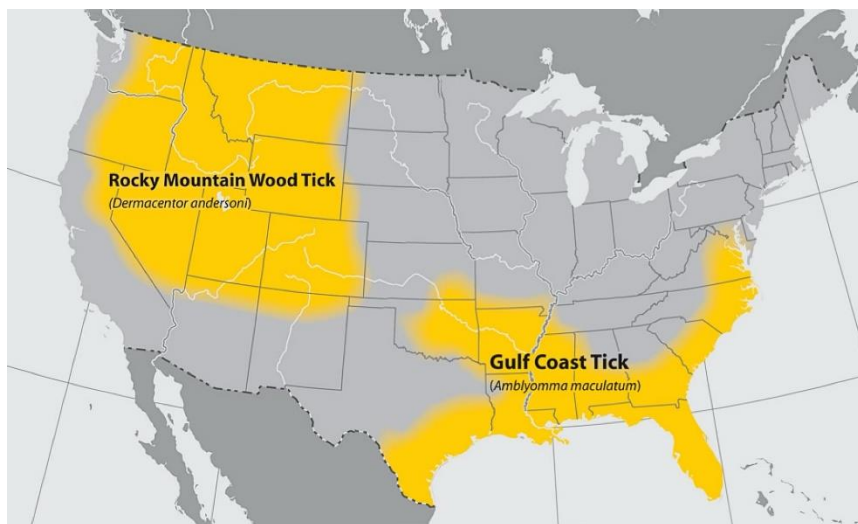
Figure 5 Geographical Distribution of Brown Dog Tick



Content Source: Centers for Disease Control and Prevention, National Center for Emerging and Zoonotic Infectious Diseases (NCEZID), Division of Vector-Borne Diseases (DVBD)

Rocky Mountain Wood Tick: *Dermacentor andersoni*. Transmits: Rocky Mountain spotted fever, Colorado tick fever, and tularemia. (figure 6) This oval-shaped tick is found in the Rocky Mountain states. It has a similar color as the American dog tick including the pale white dorsal shield on females. Adult ticks are primarily associated with biting humans.²

Figure 6 Geographical Distribution of Rocky Mountain Wood Tick and Gulf Coast Tick



Modified by Hannah Stewart. Content Source: Centers for Disease Control and Prevention, National Center for Emerging and Zoonotic Infectious Diseases (NCEZID), Division of Vector-Borne Diseases (DVBD)

Gulf Coast Tick: *Amblyomma maculatum*. Transmits: *Rickettsia parkeri*

Rickettsiosis and tularemia.² (figure 6) Found in Southeastern and mid-Atlantic states, the female of this brown tick has a small light-colored striped pattern directly behind the head.

Soft Ticks: *Ornithodoros* Species. Transmits: tick-borne relapsing fever.² There are several species of soft ticks, the head and mouthparts are hidden by the oval brown body with pale tan legs. Soft ticks usually burrow with rodents and feed briefly at night and may be found at higher elevations.¹¹

TICK-BORNE DISEASES

Many tick-borne diseases have similar presentations of constitutional symptoms such as fever, chills, malaise, headache, and myalgia. There can be a false negative with early serological testing.² Additionally, there are similarities of treatment, most are treated with doxycycline, which at the current regimen is indicated in children as well. There has not been evidence of causing staining to permanent teeth of children, even with multiple courses given before the age of eight.² Unless otherwise stated, doxycycline dosage is 100mg twice a day for adults (children 2.2 mg/kg per dosage twice a day).

Anaplasmosis

Anaplasmosis is a bacteria that is less likely to cause severe disease, except for those with advanced age, immunosuppression, comorbidities, and a delay in treatment.¹ The geographic distribution of anaplasmosis is similar to Lyme disease. There can be co-infections with Lyme disease, babesiosis, or Powassan virus, which may cause more severe illnesses.¹² Besides transmission through a tick bite, this may be associated with blood transfusions.^{1,12}

Transmission: *Ixodes scapularis* and *pacificus*¹² within 24 hours of attachment¹³

Symptoms: Incubation 5-14 days, constitutional, gastrointestinal (GI) symptoms, <10% rash

Laboratory: Mild anemia, thrombocytopenia, leukopenia, elevated hepatic transaminases¹²

Specific testing: Blood smear, polymerase chain reaction (PCR), indirect immunofluorescence antibody (IFA), immunohistochemical (IHC) staining on the skin, tissue, and bone marrow

Treatment: Do not delay if severe disease, doxycycline for 10-21 days or at least 3 days after defervescence.¹²

Babesiosis

Babesiosis is a protozoan infection that is most frequently reported in the northeastern and Midwestern US. Similar to malaria, babesiosis infects erythrocytes causing this disease to be transmitted through blood transfusions and congenital transmission.^{3,14} Babesiosis has caused the greatest number of transfusion-related fatalities caused by microbial infections reported to the United States Food and Drug Administration (FDA) from 2011-2015.¹⁴ In May 2020, the Red Cross implemented screening blood donations for babesiosis in 14 states that were considered endemic or contiguous to an endemic state.¹⁵ Due to the length of the incubation period, this diagnosis can be challenging. Although most patients do not require treatment, in hospitalized patients, congestive heart failure, myocarditis, acute respiratory distress syndrome, and disseminated intravascular coagulation can occur.¹⁴ It is not recommended to treat this illness with doxycycline.

Transmission: *Ixodes scapularis*

Symptoms: Incubation period is 1-9 weeks, constitutional, GI symptoms, upper respiratory symptoms, asymptomatic to fatal depending on risk factors, such as congestive heart failure, asplenia, or chronic obstructive pulmonary disease.¹⁴ Also signs could include mild splenomegaly, mild hepatomegaly, and jaundice.

Laboratory: Thrombocytopenia, hemolytic anemia, elevated serum creatinine and blood urea nitrogen (BUN), and mildly elevated hepatic transaminase²

Specific testing: Blood smear, PCR, IFA for IgG testing (may have false positive due to previous infections)¹

Treatment: 7-10 days of a combination of atovaquone (750mg twice a day) + azithromycin (first day 500-1000mg, subsequent days 250-1000mg, higher dosages for immunocompromised) or for severe illness, clindamycin (300mg -600mg IV every 6 hours, or 600mg orally every 8 hours) + quinine (650mg every 6-8 hours)¹⁶

Borrelia miyamotoi

Borrelia miyamotoi has been reported in the same areas as Lyme disease.² There is little known about this illness, although some evidence suggests it can be transmitted within 24 hours of tick attachment.¹³ Studies suggest that patients with *miyamotoi* will also have a positive C6 peptide enzyme-linked immunosorbent assay (ELISA) test for Lyme disease. Treatment is equivalent to that of Lyme disease, based on case reports, although no comprehensive studies have been completed at this time.

Transmission: Larval *Ixodes* species, more common in June/July

Symptoms: Incubation days to weeks, constitutional, uncommon symptoms dizziness, confusion, GI symptoms¹

Laboratory: Leukopenia, thrombocytopenia, elevated hepatic transaminase

Specific testing: Limited, PCR if available

Treatment: Suggested doxycycline 2-4 weeks^{3,17}

Colorado Tick Fever

The Colorado tick fever virus is found primarily in Colorado, Utah, Montana, and Wyoming. This virus can also be transmitted through blood transfusion and bone marrow donation; it is suggested to wait at least 6 months after recovery to be a donor.²

Symptoms may remit after 2-4 days, only to recur 1-3 days later in approximately 50% of patients.² A maculopapular or petechial rash is present in less than 20% of patients. It is uncommon to cause life-threatening symptoms.

Transmission: Rocky Mountain wood tick

Symptoms: Incubation 1-14 days, constitutional, prolonged weakness and fatigue in adults, photophobia, conjunctival injection, pharyngeal erythema, and lymphadenopathy²

Laboratory: Leukopenia, thrombocytopenia

Specific testing: Culture, PCR, IgM IFA (14-21 days after onset)

Treatment: Supportive care

Ehrlichiosis

There are three variations of ehrlichiosis. *Ehrlichia chaffeensis* can cause fatal disease, which can be transmitted by the lone star tick.¹ Oklahoma, Missouri, and Arkansas account for approximately a third of all *E. chaffeensis* cases.² *Ehrlichia ewingii* causes less severe illness and also is transmitted by the lone star tick. *Ehrlichia muris euclairensis* is transmitted by the *Ixodes scapularis* tick.

There is a sharp rise in IgG-specific antibody titers in the first week of illness. Antibody titers may be false negative in the first week of illness and IgM antibodies are less specific, causing possible false positives.

Due to the possible severity of symptoms, mostly in children under 10 and adults over 70, treatment should not be delayed while waiting on confirmatory testing.^{2,3}

Transmission: Lone star and Ixodes scapularis

Symptoms: Incubation 5-14 days, constitutional, GI symptoms, altered mental status, rash (30% adults, 60% children)¹⁸

Laboratory: Thrombocytopenia, leukopenia, anemia, hepatic transaminases elevations³

Specific testing: PCR (most sensitive in 1st week), IHC (skin, tissue, bone marrow)

Treatment: Doxycycline for 5-7 days, 3 days after defervescence or clinical improvement

Heartland Virus

Heartland virus has been reported over the past 10 years in the Midwest and Southern states¹⁹ Although the incubation period is unknown, most patients recall a tick bite within two weeks of illness.

Transmission: Lone star tick

Symptoms: Incubation unknown, constitutional, GI symptoms

Laboratory: Leukopenia, thrombocytopenia, hepatic transaminase elevations

Specific testing: Limited, Heartland virus RNA, IgM/IgG antibodies depending on location¹⁹

Treatment: Supportive care, although many recover fully, some require hospitalization.

Bourbon Virus

In the past five years, the Bourbon virus disease has been identified in the same geographical location as Heartland Virus, some of these patients have later died.^{2,3}

Transmission: Lone star tick

Symptoms: Incubation unknown, constitutional, nausea, vomiting

Laboratory: Leukopenia, thrombocytopenia

Specific testing: Limited at CDC or specialty labs

Treatment: Supportive care

Lyme disease

Lyme disease, from the *Borrelia burgdorferi* and *Borrelia mayonii* spirochete, which causes a bacterial infection, is the most common tick-borne illness, causing approximately 300,000 cases annually in the United States²⁰ and accounts for over 70% of tick-borne illnesses.⁵ It is most frequently reported in the northeastern United States and Upper Midwestern, although cases are now being reported in northern California, Oregon, and Washington.¹

After the initial phase, the disseminated phase may have multiple secondary annular rashes, rheumatologic, cardiac, and neurological manifestations.³

If the illness has been longer than one month, only the IgG test should be performed as the IgM test is not reliable.²¹ Serological testing should not be used to monitor treatment response, as there is an antibody persistence. Additionally other diseases, such as viral, bacterial, or autoimmune, can result in false-positive results.³

Treatment for early Lyme disease requires shorter antibiotic therapy. Alternative therapies include cefuroxime 500mg twice a day or amoxicillin 500mg three times a day, both for 14 days. In children, alternative treatment for 14-21 days includes amoxicillin 50mg/kg per

day divided into three dosages or cefuroxime 30mg/kg per day divided into two dosages. If patients cannot tolerate the preferred antibiotics, macrolides may be used, although they are considered less effective.² A possible temporary worsening of symptoms due to the antibiotic treatment of a spirochete infection, referred to as a Jarisch-Herxheimer reaction can happen after initiating treatment.²² Antibiotic prophylaxis with a one-day dosage of doxycycline 200mg is widely used; however, the efficacy depends on how endemic Lyme disease is in that area, causing recommendations to be conflicting.²³

Transmission: Ixodes scapularis and pacificus, attachment for over 24 hours¹³

Symptoms: Incubation 3-30 days, constitutional, arthralgia, erythema migrans (70-80%)

Laboratory: Elevated sedimentation rate, mildly elevated hepatic transaminases, microscopic hematuria or proteinuria²

Specific testing: 2 step testing recommended, ELISA, then Western blot^{1,3,21}

Treatment: Doxycycline for 10-21 days depending on the stage of disease, alternative recommendations are available

Powassan Virus Disease

Currently rare, Powassan virus disease has been diagnosed in the northeastern states and Great Lakes region with increasing cases in the past several years.² Although most patients are unable to recall the specific date of the tick bite,⁶ this disease can be transmitted quickly. In patients with encephalitis, there is a 10-15% mortality rate, and neurological deficits can persist among 50% of survivors.^{6,18}

Transmission: Ixodes species, within 15 minutes of attachment^{1,6,8,13}

Symptoms: Incubation 1-5 weeks, constitutional, vomiting, may progress to encephalitis, causing altered mental status, seizures, aphasia, paresis, and cranial nerve palsies⁸

Laboratory: CSF lymphocytic pleocytosis, mildly elevated protein, normal glucose²

Specific testing: Limited, viral RNA for CSF specimens, unknown sensitivity, antibodies may cross-react with other flaviviruses

Treatment: Supportive care, corticosteroids have been used with some success¹⁸

Rocky Mountain Spotted Fever

Rickettsia rickettsii is the bacteria that causes Rocky Mountain Spotted Fever, which has been reported in nearly every state within the United States.¹⁸ If it is not treated rapidly, it can be fatal, therefore suspected illness should be treated. Before current treatment was available, fatality rates were over 20%, compared to being currently <1% fatal if treated properly. Long-term complications can include hearing loss, blindness, and amputations due to gangrene.¹⁸ Failure to improve with treatment should lend suspicion to a different diagnosis.¹⁷

Late stages, beyond five days, include altered mental status, coma, respiratory distress, necrosis, and multi-organ failure. Early in the illness, there is a distal maculopapular rash, initially on wrists, forearms, and ankles that spreads to the trunk. The late rash is petechial and is considered a sign of progression to severe disease.¹⁸

Transmission: Rocky Mountain dog tick, American dog tick, brown dog tick, within 2 hours of tick attachment¹⁷

Symptoms: Incubation 3-12 days, constitutional, high fever, edema around eyes and back of hands, GI symptoms, the distal spreading rash appears usually in 2-5 days (90%)

Laboratory: Thrombocytopenia, elevated hepatic transaminases, and hyponatremia

Specific testing: IgG IFA, DNA using PCR for skin and serum, IHC tissue staining

Treatment: Doxycycline for 5-7 days minimum 3 days after defervescence or clinical improvement

Rickettsia Parkeri Rickettsiosis

Similar to Rocky Mountain Spotted Fever, the *Rickettsia parkeri* Rickettsiosis causes symptoms less severe and also has an inoculation eschar which is not common with RMSF.^{1,2}

Due to the similarities with RMSF, the antibody tests cross-react.

Transmission: Gulf Coast tick in southeastern and Mid-Atlantic States

Symptoms: Incubation 2-10 days, milder constitutional symptoms, inoculation eschar

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

Specific testing: DNA by PCR of eschar swab, whole blood, or biopsy, IgG IFA

Treatment: Doxycycline for 5-7 days, minimum 3 days after defervescence or clinical improvement

Southern Tick-Associated Rash Illness (STARI)

Southern tick-associated rash illness (STARI) is mostly found in southeastern and south-central United States. Symptoms are similar to Lyme disease although is not associated with arthritis, neurological, or chronic symptoms.²

Transmission: Lone star tick

Symptoms: Incubation: average 6 days, constitutional, rash similar to Lyme disease, although smaller sized erythema migrans

Laboratory: Typically normal

Specific testing: No reliable test is available

Treatment: Doxycycline, unknown if necessary¹⁸

Tickborne Relapsing Fever

Borrelia hermsii and *Borrelia turicatae* cause Tickborne Relapsing Fever (TBRF). This is most commonly found in western states during the summer months at higher elevations, transmitted by ticks or body lice.¹¹ Most cases are associated with sleeping in rodent-infested cabins in mountain states, such as California, Washington, and Colorado.¹¹

When initiating treatment, a Jarisch-Herxheimer reaction can happen, therefore patients should be observed, as some have required intubation for acute respiratory distress. Rarely does TBRF cause facial palsy.

Transmission: Soft tick within 30 seconds of tick attachment¹

Symptoms: Incubation average 7 days, constitutional, vomiting, arthralgia, 3 days of repeating febrile illness separated by afebrile periods of approximately 7 days

Laboratory: Increased white blood cells, thrombocytopenia, elevated ESR, elevated bilirubin, slightly elevated prolonged prothrombin time and partial thromboplastin time²

Specific testing: Blood smears are more accurate during febrile state, most accurate 10-14 days after onset

Treatment: Tetracycline or erythromycin 500mg four times a day for 10 days (children erythromycin 12.5mg/kg four times a day, up to 2g/day), ceftriaxone 2g per day if CNS involvement

Tularemia

Tularemia is caused by the highly virulent *Francisella tularensis* bacteria and has occurred in all states except Hawaii. Tularemia can be transmitted through tick bites, other animals, deer fly bites, inhalation, and ingestion. Most cases occur in southcentral United States.¹⁸

The route of inoculation can change the presentation of tularemia. The glandular presentation would include localized lymphadenopathy and a cutaneous ulcer at the infection site.¹ Oculoglandular signs and symptoms include photophobia, excessive lacrimation, conjunctivitis, preauricular, submandibular, and cervical lymphadenopathy.² Oropharyngeal signs and symptoms include sore throat, exudative pharyngitis or tonsillitis, and lymphadenopathy. Pneumonic signs and symptoms include a non-productive cough, substernal tightness, pleuritic chest pain, hilar adenopathy, infiltrate, or pleural effusion on chest x-ray.²

Gentamicin and ciprofloxacin are not FDA approved but have been used successfully to treat patients.

Transmission: Dog tick, wood tick, lone star tick

Symptoms: Incubation is usually 3-5 days (although it could be 21 days), constitutional, chest pain, cough, sore throat, GI symptoms

Laboratory: Leukocytosis, elevated ESR, thrombocytopenia, hyponatremia, elevated hepatic transaminases, and elevated creatine phosphokinase

Specific testing: Antibody titer to *F. tularensis* antigen or by direct immunofluorescence assay (DFA) or PCR)

Treatment: For severe illness give streptomycin 1gm IM twice a day or gentamicin 5mg/kg IM or IV daily (peak serum levels of at least 5mcg/mL) for a minimum of 10 days. For less severe illness, doxycycline for 14-21 days, or ciprofloxacin 400mg IV or 500mg twice a day for 10-14 days. In children with severe illness, streptomycin 15mg/kg IM twice a day (maximum of 2g per day) or gentamicin 2.5mg/kg IM or IV three times a day for a minimum of 10 days. Treatment for less severe illness would be ciprofloxacin 15mg/kg IV, or PO twice a day (maximum of 800mg/day) for 10 days.

CONCLUSION

Ticks are becoming more common, along with the diseases they can transmit to humans. Climate change including an overall increase of temperature, causing warmer winters and prolonged spring and autumn, may contribute to the increased range of ticks.⁸ Other environmental changes including rainfall patterns, change in land use, or reforestation of areas that introduce wildlife closer to humans may be adding to the increased tick-borne diseases in the United States.^{5,7} Migratory birds may also have introduced ticks to new areas.³

Although more common in rural areas, ticks are also present in urban locations.¹⁷ Keeping grass cut low, cleaning leaf litter near homes, and stacking wood off the ground will decrease exposure to ticks.³ Prevention of tick bites should be emphasized for patients, including being aware of where ticks live in the area, treating clothing and gear with permethrin, and using approved insect repellents. After returning indoors, people should check clothing for ticks, examine gear and pets, shower, and routinely do body tick checks. The risk of transmission of tick diseases increases with the attachment length of time.¹³

As healthcare providers are becoming more educated regarding tick-borne diseases, more diagnoses are documented, although a substantial number of tick-borne diseases may not be treated effectively.¹ Due to the possible vague constitutional symptoms, tick-borne diseases should be considered in patients who have a possible tick exposure, even if the patient does not recall a tick bite.⁴ Starting treatment may be indicated due to the severity of illnesses and comorbidities of the presenting patient.^{3,18} Additionally, ticks may carry multiple infections, adding to the complex illnesses and severity of diseases.^{3,17}

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Photograph of Blacklegged Tick (*Ixodes Scapularis*) by Ellen Dennehy, PA-C, DMSc Fellow



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