TICKBORNE DISEASES OF THE UNITED STATES

A Reference Manual for Health Care Providers

Fourth Edition, 2017

U.S. Department of Health and Human Services
Centers for Disease Control and Prevention

Tick ID

BLACKLEGGED TICK
Ixodes scapularis

Where found: Widely distributed in the northeastern and upper midwestern United States.

Transmits: Lyme disease, anaplasmosis, babesiosis, and Powassan disease.

Comments: The greatest risk of being bitten exists in the spring, summer, and fall. However, adults may be out searching for a host any time winter temperatures are above freezing. Stages most likely to bite humans are nymphs and adult females.

LONE STAR TICK
Amblyomma americanum

Where found: Widely distributed in the southeastern and eastern United States.

Transmits: *Ehrlichia chaffeensis* and *Ehrlichia ewingii* (which cause human ehrlichiosis), tularemia, and STARI.

Comments: A very aggressive tick that bites humans. The adult female is distinguished by a white dot or "lone star" on her back. Lone star tick saliva can be irritating; redness and discomfort at a bite site does not necessarily indicate an infection. The nymph and adult females most frequently bite humans and transmit disease.

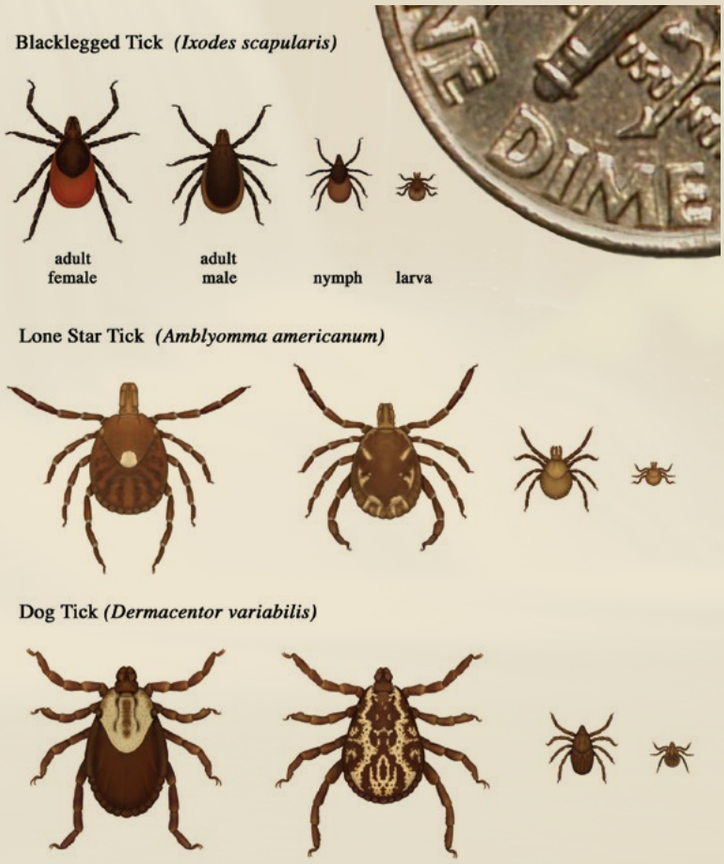
AMERICAN DOG TICK
Dermacentor variabilis

Where found: Widely distributed east of the Rocky Mountains. Also occurs in limited areas on the Pacific Coast.

Transmits: Tularemia and Rocky Mountain spotted fever.

Comments: The highest risk of being bitten occurs during spring and summer. Dog ticks are sometimes called wood ticks. Adult females are most likely to bite humans.

Engorged female *Ixodes scapularis* tick. Color may vary.



NOTE: *Illustrations are not to scale.*

Tick ID

BROWN DOG TICK
Rhipicephalus sanguineus

Where found: Worldwide.

Transmits: Rocky Mountain spotted fever (in the southwestern U.S. and along the U.S.-Mexico border).

Comments: Dogs are the primary host for the brown dog tick in each of its life stages, but the tick may also bite humans or other mammals.

Steve Jacobs, PSU Entomology

GROUNDHOG TICK
Ixodes cookei

Where found: Throughout the eastern half of the U.S. and Canada.

Transmits: Powassan disease.

Comments: Also called woodchuck ticks. All life stages feed on a variety of warm-blooded animals, including groundhogs, skunks, squirrels, raccoons, foxes, weasels, and occasionally people and domestic animals.

GULF COAST TICK
Amblyomma maculatum

Where found: Coastal areas of the U.S. along the Atlantic coast and the Gulf of Mexico.

Transmits: *Rickettsia parkeri* rickettsiosis, a form of spotted fever.

Comments: Larvae and nymphs feed on birds and small rodents, while adult ticks feed on deer and other wildlife. Adult ticks have been associated with transmission of *R. parkeri* to humans.

ROCKY MOUNTAIN WOOD TICK
Dermacentor andersoni

Where found: Rocky Mountain states and southwestern Canada from elevations of 4,000 to 10,500 feet.

Transmits: Rocky Mountain spotted fever, Colorado tick fever, and tularemia.

Comments: Adult ticks feed primarily on large mammals. Larvae and nymphs feed on small rodents. Adult ticks are primarily associated with pathogen transmission to humans.

O. hermsi tick, before and after feeding. Photo taken by Gary Hettrick RML, NIAID.

SOFT TICK
Ornithodoros spp.

Where found: Throughout the western half of the U.S. and southwestern Canada.

Transmits: Tick-borne relapsing fever *(Borrelia hermsii, B. parkerii,* or *B. turicatae)*

Comments: Humans typically come into contact with soft ticks when they sleep in rodent infested cabins. The ticks emerge at night and feed briefly while the person is sleeping. The bites are painless, and most people are unaware that they have been bitten.

WESTERN BLACKLEGGED TICK
Ixodes pacificus

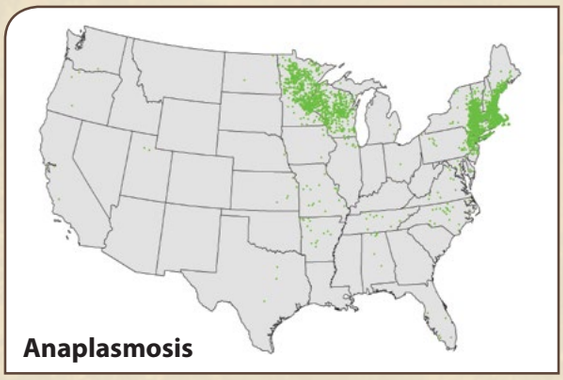
Where found: Along the Pacific coast of the U.S., particularly northern California.

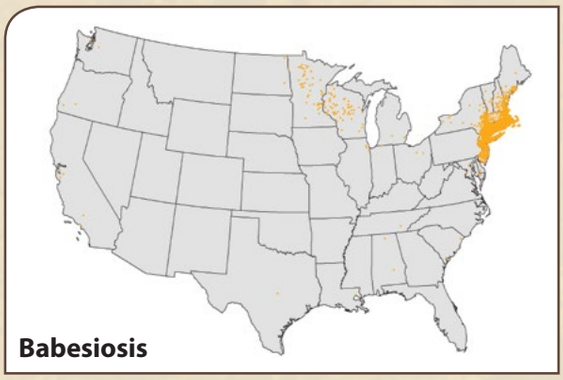
Transmits: Anaplasmosis and Lyme disease.

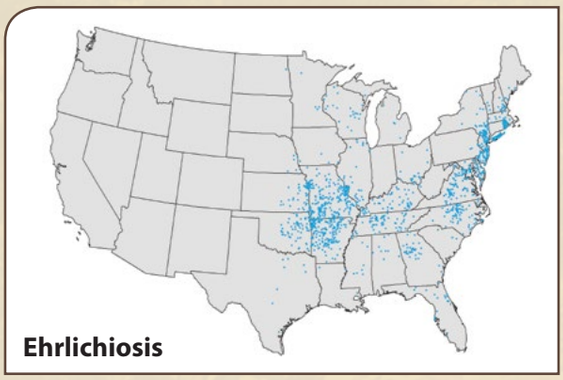
Comments: Nymphs often feed on lizards, as well as other small animals. As a result, rates of infection are usually low (~1%) in adults. Stages most likely to bite humans are nymphs and adult females.

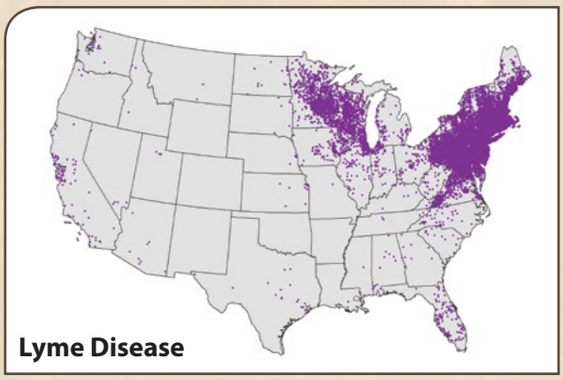
Overview of Tickborne Diseases

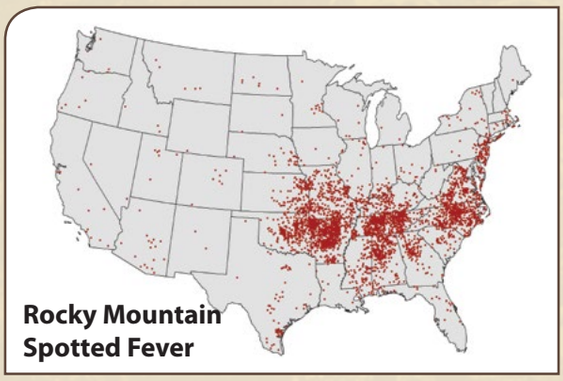
Selected Tickborne Diseases Reported to CDC, U.S., 2015

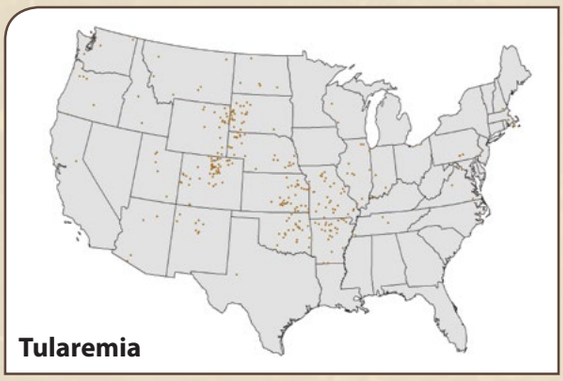












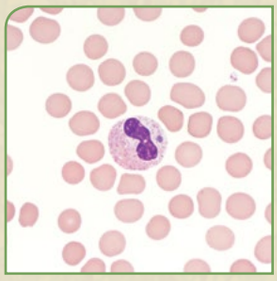
NOTE: *Each dot represents one case. Cases are reported from the infected person's county of* ***residence,*** *not necessarily the place where they were infected.*

NOTE: *During 2015, babesiosis was reportable in Alabama, Arkansas, California, Connecticut, Delaware, Illinois, Indiana, Louisiana, Kentucky, Maine, Maryland, Massachusetts, Michigan, Minnesota, Montana, Nebraska, New Hampshire, New Jersey, New York, North Dakota, Ohio, Oregon, Rhode Island, South Carolina, South Dakota, Tennessee, Texas, Utah, Vermont, Washington, West Virginia, Wisconsin, and Wyoming.*

NOTE: *In 2015, no cases of tickborne illness were reported from Hawaii. In 2015, Alaska reported 1 travel-related cases of Lyme disease and 2 cases of tularemia.*

Anaplasmosis

AGENT
Anaplasma phagocytophilum



WHERE FOUND

Anaplasmosis is most frequently reported from the upper midwest and northeastern U.S. in areas that correspond with the known geographic distribution of Lyme disease.

INCUBATION PERIOD: 1–2 weeks

SIGNS AND SYMPTOMS

- Fever, shaking, chills
- Severe headache
- Malaise
- Myalgia
- Gastrointestinal symptoms (nausea, vomiting, diarrhea, anorexia)
- Cough
- Rash (rare cases)

The Signs and Symptoms list presents symptoms commonly seen with anaplasmosis. However, it is important to note that few people will develop all symptoms and the number and combination of symptoms varies greatly from person to person.

Anaplasmosis and ehrlichiosis have similar clinical presentations, but they are transmitted by two different species of ticks and generally occur in different regions of the U.S.

Anaplasmosis was formerly known as Human Granulocytic Ehrlichiosis (HGE).

Confirmation of the diagnosis is based on laboratory testing, but antibiotic therapy should not be delayed in a patient with a suggestive clinical presentation.

GENERAL LABORATORY FINDINGS

Typically Observed During the First Week of Clinical Disease:

- Mild anemia
- Thrombocytopenia
- Leukopenia (characterized by relative and absolute lymphopenia and a left shift)
- Mild to moderate elevations in hepatic transaminases may occur in some patients.
- Visualization of morulae in the cytoplasm of granulocytes during examination of blood smears is highly suggestive of a diagnosis; however, blood smear examination is insensitive and should never be relied upon solely to rule anaplasmosis in or out.

LABORATORY CONFIRMATION

- **Detection of DNA by PCR of whole blood.** This method is most sensitive during the first week of illness; sensitivity may decrease after administration of antibiotics.
- **Demonstration of a four-fold change in IgG-specific antibody titer by indirect immunofluorescence antibody (IFA) assay in paired serum samples.** Antibodies to *A. phagocytophilum* are usually detectable within 7–10 days after illness onset. The reference standard serologic test looks for a four-fold change in antibody titers using IFA on paired samples. The first sample should be taken within the first week of illness and the second should be taken 2 to 4 weeks later.

NOTE: *IgM antibodies are less specific than IgG antibodies and are more likely to generate false positives. IgM results alone should not be used for laboratory diagnosis.*

NOTE: *Consider the possibility of coinfection with* Babesia microti *and/or* Borrelia burgdorferi.

NOTE: *Antibody titers are frequently negative in the first 7–10 days of illness, thus serologic tests may be falsely negative during this time period.*

Anaplasmosis

AGENT
Anaplasma phagocytophilum

Anaplasmosis, ehrlichiosis, and Rocky Mountain spotted fever are treated in the same manner with doxycycline. Clinical suspicion of any of these diseases is sufficient to begin treatment. Delay in treatment may result in severe illness and even death. The regimens listed below are 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 cases of documented pregnancy or life-threatening allergies to doxycycline.

AGE CATEGORY	DRUG	DOSAGE	MAXIMUM	DURATION (DAYS)
Adults	Doxycycline	100 mg twice per day, orally or IV	100 mg/dose	Patients with suspected anaplasmosis infection should be treated with doxycycline for 10-14 days to provide appropriate length of therapy for possible incubating co-infection with Lyme disease
Children weighing <100 lbs. (45.4 kg)	Doxycycline	2.2 mg/kg per dose twice per day, orally or IV	100 mg/dose	

NOTE: ***Use doxycycline as first-line treatment for suspected anaplasmosis in patients of all ages. The use of doxycycline to treat suspected anaplasmosis 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, no evidence has been shown to cause staining of permanent teeth, even when five courses are given before the age of eight.***

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Todd SR, Dahlgren FS, et al. No visible dental staining in children treated with doxycycline for suspected Rocky Mountain spotted fever. *J Pediatr,* Available online 17 March 2015, ISSN 0022-3476, http://dx.doi.org/10.1016/j.jpeds.2015.02.015

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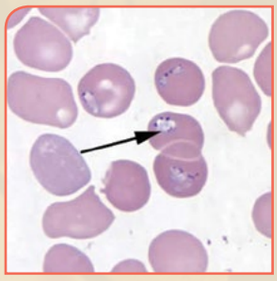
Babesiosis

AGENT
Babesia microti
and other *Babesia* species



WHERE FOUND

Babesiosis is most frequently reported from the northeastern and upper midwestern United States in areas where *Babesia microti* is endemic. Sporadic cases of infection caused by novel *Babesia* agents have been detected in other U.S. regions, including the West Coast. In addition, transfusion-associated cases of babesiosis can occur anywhere in the country.

INCUBATION PERIOD: 1–9+ weeks

SIGNS AND SYMPTOMS

- Fever, chills, sweats
- Malaise, fatigue
- Myalgia, arthralgia, headache
- Gastrointestinal symptoms, such as anorexia and nausea (less common: abdominal pain, vomiting)
- Dark urine
- Less common: cough, sore throat, emotional lability, depression, photophobia, conjunctival injection
- Mild splenomegaly, mild hepatomegaly, or jaundice may occur in some patients

NOTE: *Not all infected persons are symptomatic or febrile. The clinical manifestations, if any, usually develop within several weeks after the exposure but may develop or recur months later (for example, in the context of surgical splenectomy).*

Babesiosis is caused by parasites that infect red blood cells. Most U.S. cases are caused by *Babesia microti,* which is transmitted by *Ixodes scapularis* ticks, primarily in the Northeast and upper Midwest. *Babesia* parasites also can be transmitted via transfusion, anywhere, at any time of the year. As of February 2017, no *Babesia* tests have been licensed for screening blood donors. Congenital transmission also has been reported.

Babesia infection can range from asymptomatic to life threatening. Risk factors for severe babesiosis include asplenia, advanced age, and impaired immune function. 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.

GENERAL LABORATORY FINDINGS

- Decreased hematocrit due to hemolytic anemia
- Thrombocytopenia
- Elevated serum creatinine and blood urea nitrogen (BUN) values
- Mildly elevated hepatic transaminase values

LABORATORY DIAGNOSIS

- Identification of intraerythrocytic *Babesia* parasites by light-microscopic examination of a peripheral blood smear; or
- Positive *Babesia* (or *B. microti*) polymerase chain reaction (PCR) analysis; or
- Isolation of *Babesia* parasites from a whole blood specimen by animal inoculation (in a reference laboratory).

SUPPORTIVE LABORATORY CRITERIA

- Demonstration of a *Babesia*-specific antibody titer by indirect fluorescent antibody (IFA) testing for total immunoglobulin (Ig) or IgG.

NOTE: *If the diagnosis of babesiosis is being considered, manual (nonautomated) review of blood smears should be requested explicitly. In symptomatic patients with acute infection,* Babesia *parasites typically can be detected by blood-smear examination, although multiple smears may need to be examined. Sometimes it can be difficult to distinguish between* Babesia *and malaria parasites and even between parasites and artifacts (such as stain or platelet debris). Consider having a reference laboratory confirm the diagnosis and the species. In some settings, molecular techniques can be useful for detecting and differentiating among* Babesia *species.*

NOTE: *Antibody detection by serologic testing can provide supportive evidence for the diagnosis but does not reliably distinguish between active and prior infection.*

Treatment decisions and regimens should consider the patient's 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 age.

For ill patients, babesiosis usually is treated for at least 7–10 days with a combination of two medications—typically, either atovaquone PLUS azithromycin; OR clindamycin PLUS quinine (this combination is the standard of care for severely ill patients). The typical regimens for adults are provided in the table below.

AGE CATEGORY		DRUG	DOSAGE	MAXIMUM	DURATION (DAYS)
Adults	Prescribe together	Atovaquone	750 mg orally every 12 hours	N/A	7–10
		Azithromycin	On the first day, give a total dose in the range of 500–1000 mg orally; on subsequent days, give a total daily dose in the range of 250–1000 mg*	1000 mg per day	7–10
	OR				
	Prescribe together	Clindamycin**	300–600 mg IV every 6 hours OR 600 mg orally every 8 hours**	N/A	7–10
		Quinine**	650 mg orally every 6–8 hours	N/A	7–10

** The upper end of the range (600–1000 mg per day) has been used for adults who are immunocompromised.*

*** The standard of care for patients with severe babesiosis (e.g., with parasitemia levels ≥10% and/or organ-system dysfunction) is quinine plus clindamycin; typically, the clindamycin is administered intravenously. Such patients also might require or benefit from exchange transfusions, vasopressor therapy, mechanical ventilation, or dialysis.*

NOTE: *Most persons without clinical manifestations of infection do not require treatment. However, consider treating persons who have had demonstrable parasitemia for more than 3 months.*

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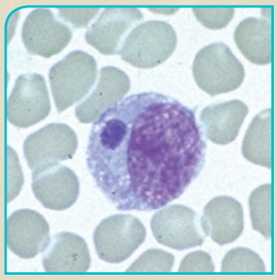
Ehrlichiosis

AGENTS
Ehrlichia chaffeensis, Ehrlichia ewingii, Ehrlichia muris-like (EML)



WHERE FOUND

Ehrlichiosis is most frequently reported from the southeastern and south-central U.S., from the eastern seaboard extending westward to Texas. The areas from which cases are reported correspond with the known geographic distribution of the lone star tick *(Amblyomma americanum),* which is associated with transmission of both *E. chaffeensis* and *E. ewingii.* Three states (Oklahoma, Missouri, Arkansas) account for 35% of all reported *E. chaffeensis* infections. Since 2009, >70 cases of ehrlichiosis caused by *Ehrlichia muris eauclarensis,* have been identified in patients in the upper Midwest. The tick responsible for transmitting this new subspecies is suspected to be *Ixodes scapularis* and the clinical presentation is generally similar to those associated with infections caused by *E. chaffeensis* and *E. ewingii.* No deaths have been reported.

INCUBATION PERIOD: 1–2 weeks

SIGNS AND SYMPTOMS

- Fever
- Headache
- Chills
- Malaise
- Muscle pain
- Gastrointestinal symptoms (nausea, vomiting, diarrhea, anorexia)
- Confusion
- Conjunctival injection
- Rash (more commonly reported among children)

The Signs and Symptoms list presents symptoms commonly seen with ehrlichiosis. However, it is important to note that few people will develop all symptoms and the number and combination of symptoms varies greatly from person to person.

Ehrlichiosis and anaplasmosis have a similar clinical presentation, but they are transmitted by two different species of ticks and generally occur in different regions of the U.S.

Confirmation of the diagnosis is based on laboratory testing, but antibiotic therapy should not be delayed in a patient with a suggestive clinical presentation.

GENERAL LABORATORY FINDINGS

Typically observed during the first week of clinical disease:

- Thrombocytopenia
- Leukopenia (absolute)
- Anemia (generally occurs later in illness than thrombocytopenia or leukopenia)
- Mild to moderate elevations in hepatic transaminases
- During the acute stage of illness, morulae can be detected in about 20% of patients. *E. chaffeensis* most commonly infects monocytes, whereas *E. ewingii* more commonly infects granulocytes.

LABORATORY CONFIRMATION

- **Detection of DNA by PCR of whole blood.** This method is most sensitive during the first week of illness and sensitivity can decrease after administration of tetracycline-class antibiotics.
- **Demonstration of a four-fold change in IgG-specific antibody titer by indirect immunofluorescence antibody (IFA) assay in paired serum samples.** Antibodies to *Ehrlichia* sp. are usually detectable within 7–10 days after illness onset. The reference standard serologic test looks for a four-fold change in antibody titers using IFA on paired samples. The first sample should be taken within the first week of illness and the second should be taken 2 to 4 weeks later.

NOTE: *IgM antibodies are less specific than IgG antibodies and are more likely to generate false positive results. IgM results alone should not be used for laboratory diagnosis.*

NOTE: *Antibody titers are frequently negative in the first 7–10 days of illness, thus serologic tests may be falsely negative during this time period.*

Ehrlichiosis

AGENTS
Ehrlichia chaffeensis, Ehrlichia ewingii, Ehrlichia muris-like (EML)

Anaplasmosis, ehrlichiosis, and Rocky Mountain spotted fever are treated in the same manner with doxycycline. Clinical suspicion of any of these diseases is sufficient to begin treatment. Delay in treatment may result in severe illness and death. The regimens listed below are 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 cases of documented pregnancy or life-threatening allergies to doxycycline.

AGE CATEGORY	DRUG	DOSAGE	MAXIMUM	DURATION (DAYS)
Adults	Doxycycline	100 mg twice per day, orally or IV	100 mg/dose	Patients should be treated 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)	Doxycycline	2.2 mg/kg per dose twice per day, orally or IV	100 mg/dose	

NOTE: ***Use doxycycline as first-line treatment for suspected ehrlichiosis in patients of all ages. The use of doxycycline to treat suspected ehrlichiosis 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 ehrlichiosis, no evidence has been shown to cause staining of permanent teeth, even when five courses are given before the age of eight.***

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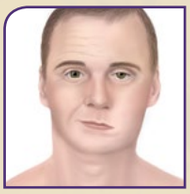
Lyme Disease

AGENT
Borrelia burgdorferi



WHERE FOUND

Lyme disease is most frequently reported from the upper midwestern and northeastern U.S. Some cases are also reported in northern California, Oregon, and Washington. In 2013, 95% of Lyme disease cases were reported from 14 states: Connecticut, Delaware, Maine, Maryland, Massachusetts, Minnesota, New Hampshire, New Jersey, New York, Pennsylvania, Rhode Island, Vermont, Virginia, and Wisconsin.

INCUBATION PERIOD: 3–30 days

SIGNS AND SYMPTOMS

Localized Stage†

- Erythema migrans (EM)—red ring-like or homogenous expanding rash; classic rash not present in all cases. See examples on following pages.
- Flu-like symptoms – malaise, headache, fever, myalgia, arthralgia
- Lymphadenopathy

*†During the **localized** (early) stage of illness, Lyme disease may be diagnosed clinically in patients who present with an EM rash. Serologic tests may be insensitive at this stage. During **disseminated** disease, however, serologic tests are usually positive.*

Disseminated Stage

- Multiple secondary annular rashes
- Flu-like symptoms
- Lymphadenopathy

Rheumatologic Manifestations

- Transient, migratory arthritis and effusion in one or multiple joints
- Migratory pain in tendons, bursae, muscle, and bones
- Baker's cyst
- If untreated, arthritis may recur in same or different joints

Cardiac Manifestations

- Conduction abnormalities, e.g. atrio-ventricular node block
- Myocarditis, pericarditis

Neurologic Manifestations

- Bell's palsy or other cranial neuropathy
- Meningitis
- Motor and sensory radiculoneuropathy, mononeuritis multiplex
- Subtle cognitive difficulties
- Encephalitis, encephalomyelitis, subtle encephalopathy, pseudotumor cerebri (all rare)

Additional Manifestations

- Conjunctivitis, keratitis, uveitis
- Mild hepatitis
- Splenomegaly

GENERAL 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.

LABORATORY DIAGNOSIS

- Demonstration of diagnostic IgM or IgG antibodies in serum. A two-tier testing protocol is recommended—EIA or IFA should be performed first; if positive or equivocal it is followed by a Western blot.
- Isolation of organism from a clinical specimen.
- In suspected Lyme meningitis, testing for intrathecal IgM or IgG antibodies may be helpful.

NOTES ON SEROLOGIC TESTS FOR LYME DISEASE

- Serologic tests are insensitive during the first few weeks of infection. During this stage, patients with an EM rash may be diagnosed clinically. While not necessary, acute and convalescent titers may be helpful in some cases.
- In persons with illness > 1 month, only IgG testing should be performed (not IgM). A positive IgM test alone is not sufficient to diagnose current disease.
- Due to antibody persistence, single positive serologic test results cannot distinguish between active and past infection.
- Serologic tests cannot be used to measure treatment response.
- Enzyme immunoassay (EIA) and immunofluorescence assay (IFA) tests have low specificity and may yield false-positive results. They may cross-react with antibodies to commensal or pathogenic spirochetes, some viral infections (e.g., varicella, Epstein-Barr virus), or certain autoimmune diseases (e.g., lupus).

LYME DISEASE OR STARI?

An erythema migrans-like rash has also been described in humans following bites of the lone star tick, *Amblyomma americanum*. This condition has been named Southern Tick-Associated Rash Illness (STARI). Although the rash may be accompanied by flu-like symptoms, long-term sequelae have not been reported. Because the cause of STARI is unknown, diagnostic blood tests are not available.

Lone star ticks can be found from central Texas and Oklahoma eastward across the southern states and along the Atlantic coast as far north as Maine.

It is not known whether antibiotic treatment is necessary or beneficial for patients with STARI. Nevertheless, because STARI resembles early Lyme disease, physicians often treat patients with the same antibiotics recommended for Lyme disease.

NOTE: *Coinfection with* B. microti *and/or* A. phagocytophilum *should be considered in patients who present with initial symptoms that are more severe than are commonly observed with Lyme disease alone, especially in those who have high-grade fever for more than 48 hours despite appropriate antibiotic therapy or who have unexplained leukopenia, thrombocytopenia, or anemia. Coinfection might also be considered in patients whose erythema migrans skin lesion has resolved but have persistent flu-like symptoms.*

Treatment regimens listed in the following table are for localized (early) Lyme disease. Treatment guidelines for patients with disseminated (late) Lyme disease are outlined in the reference below.[†]

These regimens are 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 for the most current treatment guidelines or for individual patient treatment decisions.

AGE CATEGORY	DRUG	DOSAGE	MAXIMUM	DURATION, DAYS (RANGE)
Adults	Doxycycline	100 mg, twice per day orally	N/A	14 (14–21)
	Cefuroxime axetil	500 mg, twice per day orally	N/A	14 (14–21)
	Amoxicillin	500 mg, three times per day orally	N/A	14 (14–21)
Children	Amoxicillin	50 mg/kg per day orally, divided into 3 doses	500 mg per dose	14 (14–21)
	Doxycycline	4 mg/kg per day orally, divided into 2 doses	100 mg per dose	14 (14–21)
	Cefuroxime axetil	30 mg/kg per day orally, divided into 2 doses	500 mg per dose	14 (14–21)

NOTE: *For patients intolerant of amoxicillin, doxycycline, and cefuroxime axetil, the macrolides azithromycin, clarithromycin, or erythromycin may be used, although they have a lower efficacy. Patients treated with macrolides should be closely observed to ensure resolution of clinical manifestations.*

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Lyme Disease

AGENT
Borrelia burgdorferi

The erythema migrans (EM) rash occurs in 70–80% of patients with Lyme disease. EM rashes expand slowly over a few days after which they may develop a "bull's-eye" appearance consisting of a red ring with central clearing. However, EM may take alternate forms—solid lesions, blue-purple hues, and crusted or blistering lesions have all been documented. The rash is not painful or pruritic, but it may be warm to the touch. If early localized Lyme disease is not treated, patients may develop multiple secondary circular rashes as spirochetes disseminate throughout the body.

Photo courtesy of Taryn Holman

Classic EM—Circular red rash with central clearing that slowly expands

Photo courtesy of Yevgeniy Balagula

Bluish hue without central clearing

Photo courtesy of Bernard Cohen

Red, expanding lesion with central crust

Photo courtesy of Alison Young

Red, oval-shaped plaque on trunk

Photo courtesy of Robin Stevenson

Red-blue lesion with central clearing on back of knee

Photo courtesy of Bernard Cohen

Early disseminated Lyme disease—multiple red lesions with dusky centers

Tick bite with mild allergic reaction. **Not an erythema migrans.** Allergic reactions typically appear within the first 48 hours of tick attachment and are usually <5 cm in diameter.

Special thanks to DermAtlas for providing the photographs.

Rocky Mountain Spotted Fever

AGENT
Rickettsia rickettsii

WHERE FOUND

Although Rocky Mountain spotted fever cases have been reported throughout most of the contiguous U.S., five states (North Carolina, Oklahoma, Arkansas, Tennessee, and Missouri) account for over 60% of RMSF cases.

Rocky Mountain spotted fever has become increasingly common in certain areas of Arizona over the last several years. Between 2003 and 2012 over 250 cases and 19 fatalities occurred. RMSF can be rapidly fatal if not treated within the first 5 days of symptoms. Before tetracycline antibiotics were available, case fatality rates ranged from 20–80%.

INCUBATION PERIOD: 2–14 days

SIGNS AND SYMPTOMS

- Fever, chills
- Severe headache
- Malaise
- Myalgia
- Gastrointestinal symptoms (nausea, vomiting, anorexia, abdominal pain, diarrhea, abdominal tenderness)
- Photophobia
- Focal neurologic deficits, including cranial or peripheral motor nerve paralysis or sudden transient deafness

Maculopapular Rash

- Typically appears 2–5 days after the onset of fever
- Small, flat, pink, non-itchy spots (macules) initially appear on the wrists, forearms, and ankles then spread to the trunk and sometimes palms and soles.
- Rash may not develop until late in the disease process, after treatment should have already begun. Approximately 10% of RMSF patients never develop a rash at all.
- Consider RMSF if other signs and symptoms support a diagnosis, even if a rash is not present.

Petechial Rash

- Red to purple spots (petechiae) are usually not seen until day 6 or later after onset of symptoms.
- Petechial rash is considered a sign of progression to severe disease. Every attempt should be made to begin treatment before petechiae develop.

NOTE: *Neurologic symptoms are typically not seen until later in the disease progression and may be prevented with early treatment.*

Confirmation of the diagnosis is based on laboratory testing, but antibiotic therapy should not be delayed in a patient with a suggestive clinical presentation. Antibiotics are less likely to prevent fatal outcome from RMSF if started after day 5 of symptoms.

GENERAL LABORATORY FINDINGS

- Thrombocytopenia
- Mildly elevated hepatic transaminase levels
- Hyponatremia

LABORATORY CONFIRMATION

- **Demonstration of a four-fold change in IgG-specific antibody titer by indirect immunofluorescence antibody (IFA) assay in paired serum samples.** Antibodies to *R rickettsii* are usually detectable within 7–10 days after illness onset. The reference standard serologic test looks for a four-fold change in antibody titers using IFA on paired samples. The first sample should be taken within the first week of illness and the second should be taken 2 to 4 weeks later.
- **Detection of DNA in a skin biopsy specimen of a rash lesion by polymerase chain reaction (PCR) assay or in an acute phase whole blood specimen, although this sample can be less sensitive.**
- **Immunohistochemical (IHC) staining of organism from skin or tissue biopsy specimen.**

NOTE: *IgM antibodies are less specific than IgG antibodies and are more likely to generate false positives. IgM results alone should not be used for laboratory diagnosis.*

NOTE: *Antibody titers are frequently negative in the first 7–10 days of illness, thus serologic tests may be falsely negative during this time period.*

Rocky Mountain Spotted Fever or *Rickettsia parkeri* rickettsiosis?

Rickettsia rickettsii and *R. parkeri* cause febrile illnesses that can be difficult to diagnosis in the early stages of infection.

RMSF is most often transmitted by American dog ticks in the eastern, central and Pacific costal U.S., by Rocky Mountain wood ticks in the Rocky Mountain states, and by brown dog ticks in the southwestern U.S. and Mexico. RMSF is a rapidly progressive illness which can be fatal if untreated.

Rickettsia parkeri rickettsiosis is transmitted by Gulf Coast ticks in the southeastern and mid-Atlantic states as well as parts of southern Arizona. *R. parkeri* rickettsiosis is characteristically less severe than RMSF and almost always associated with an inoculation eschar at the site of tick attachment. Both infections are treated effectively with doxycycline.

Rocky Mountain Spotted Fever

AGENT
Rickettsia rickettsii

Anaplasmosis, ehrlichiosis, and Rocky Mountain spotted fever are treated in the same manner with doxycycline.[†] Clinical suspicion of any of these diseases is sufficient to begin treatment. Delay in treatment may result in severe illness and even death. The regimens listed below are 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 cases of pregnancy or documented life-threatening allergies to doxycycline.

AGE CATEGORY	DRUG	DOSAGE	MAXIMUM	DURATION (DAYS)
Adults	Doxycycline	100 mg twice per day, orally or IV	100 mg/dose	Patients should be treated 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)	Doxycycline	2.2 mg/kg per dose twice per day, orally or IV	100 mg/dose	

NOTE: ***Use doxycycline as the first-line treatment for suspected RMSF in patients of all ages. The use of doxycycline to treat suspected RMSF 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 RMSF, no evidence has been shown to cause staining of permanent teeth, even when five courses are given before the age of eight.***

REFERENCES

[†]Centers for Disease Control and Prevention. Diagnosis and management of tickborne rickettsial diseases: Rocky Mountain spotted fever and other spotted fever group rickettsioses, ehrlichioses, and anaplasmosis—United States: a practical guide for health care and public health professionals. *MMWR* 2016; 65 (No.RR-2).

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Tularemia

AGENT
Francisella tularensis

WHERE FOUND

In the U.S., naturally occurring tularemia infections have been reported from all states except Hawaii. Ticks that transmit tularemia to humans include the dog tick *(Dermacentor variabilis),* the wood tick *(Dermacentor andersoni),* and the lone star tick *(Amblyomma americanum).* Other transmission routes include inhalation and direct inoculation.

INCUBATION PERIOD: 3–5 days (range 1–21 days)

SIGNS AND SYMPTOMS

- Fever, chills
- Headache
- Malaise, fatigue
- Anorexia
- Myalgia
- Chest discomfort, cough
- Sore throat
- Vomiting, diarrhea
- Abdominal pain

(Ulcero) Glandular

- Localized lymphadenopathy
- Cutaneous ulcer at infection site (not always present)

Oculoglandular

- Photophobia
- Excessive lacrimation
- Conjunctivitis
- Preauricular, submandibular and cervical lymphadenopathy

Oropharyngeal

- Severe throat pain
- Cervical, preparotid, and/or retropharyngeal lymphadenopathy

Pneumonic

- Non-productive cough
- Substernal tightness
- Pleuritic chest pain
- Hilar adenopathy, infiltrate, or pleural effusion may be present on chest X-ray

Typhoidal

- Characterized by any combination of the general symptoms (without localizing symptoms of other syndromes)

NOTE: *The clinical presentation of tularemia will depend on a number of factors, including the portal of entry.*

GENERAL LABORATORY FINDINGS

- Leukocyte count and sedimentation rate may be normal or elevated
- Thrombocytopenia
- Hyponatremia
- Elevated hepatic transaminases
- Elevated creatine phosphokinase
- Myoglobinuria
- Sterile pyuria

LABORATORY DIAGNOSIS

- Demonstration of a four-fold change in antibody titer in paired sera; or
- Isolation of organism from a clinical specimen; or
- Detection of organism by immunofluorescence assay (IFA) test or a single elevated serum antibody titer is supportive of the diagnosis; however, a single antibody titer should be confirmed by either one of the methods above.

The regimens listed below are 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 for the most current treatment guidelines or for individual patient treatment decisions.

AGE CATEGORY	DRUG	DOSAGE	MAXIMUM	DURATION (DAYS)
Adults	Streptomycin	1 g IM twice daily	2 g per day	Minimum 10
	Gentamicin*	5 mg/kg IM or IV daily (with desired peak serum levels of at least 5 mcg/mL)	Monitor serum drug levels	Minimum 10
	Ciprofloxacin*	400 mg IV or PO twice daily	N/A	10–14
	Doxycycline	100 mg IV or PO twice daily	N/A	14–21
Children	Streptomycin	15 mg/kg IM twice daily	2 g per day	Minimum 10
	Gentamicin*	2.5 mg/kg IM or IV 3 times daily	Monitor serum drug levels and consult a pediatric infectious disease specialist	Minimum 10
	Ciprofloxacin*	15 mg/kg IV or PO twice daily	1 g per day	10

*Not a U.S. FDA-approved use, but has been used successfully to treat patients with tularemia.

NOTE: *Gentamicin or streptomycin is preferred for treatment of severe tularemia. Doses of both streptomycin and gentamicin should be adjusted for renal insufficiency.*

NOTE: *Chloramphenicol may be added to streptomycin to treat meningitis.*

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Other Tickborne Diseases

Colorado Tick Fever (CTF)

Agent: Colorado tick fever virus

WHERE FOUND The geographic range of Colorado tick fever virus includes the western United States and southwestern Canada at elevations 4,000 to 10,000 feet. Cases occur primarily in Colorado, Utah, Montana, and Wyoming. Although rare, the virus can also be transmitted from person-to-person via blood transfusion.

INCUBATION PERIOD: 1–14 days

SIGNS AND SYMPTOMS

- Fever, chills, headache, myalgias, and lethargy
- ~50% of patients have a biphasic illness with symptoms remitting after 2 to 4 days, but then recurring 1 to 3 days later
- Conjunctival injection, pharyngeal erythema and lymphadenopathy may be present
- Maculopapular or petechial rash in <20% of patients
- Prolonged convalescence characterized by weakness and fatigue is common in adults
- Life-threatening complications and death are rare and usually associated with disseminated intravascular coagulation or meningoencephalitis in children

GENERAL LABORATORY FINDINGS

- Leukopenia
- Moderate thrombocytopenia

LABORATORY DIAGNOSIS

- Culture and RT-PCR during first 2 weeks of illness
- Serologic assays (e.g., IgM-capture EIA, indirect fluorescent antibody, and plaque-reduction neutralization) on convalescent samples. IgM antibodies usually do not appear until 14–21 days after illness onset.

TREATMENT

No specific antiviral treatment is available. Patients with suspected CTF should receive supportive care as appropriate. Patients with confirmed CTF should defer blood and bone marrow donation for at least 6 months after recovery.

REFERENCES

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Tickborne Relapsing Fever (TBRF)

Agent: *Borrelia hermsii* and other spp.

WHERE FOUND In the U.S., TBRF occurs most commonly in 14 western states: Arizona, California, Colorado, Idaho, Kansas, Montana, Nevada, New Mexico, Oklahoma, Oregon, Texas, Utah, Washington, and Wyoming. Most cases occur in the summer when people vacation and sleep in rodent-infested cabins. However, TBRF can also occur in the winter months when fires started to warm a cabin activate ticks resting in the walls and woodwork.

INCUBATION PERIOD: ~7 days, followed by recurring febrile episodes that last ~3 days and are separated by afebrile periods of ~7 days

SIGNS AND SYMPTOMS

- Headache
- Myalgia
- Chills
- Nausea, vomiting
- Arthralgia

COMMON FINDINGS ON ROUTINE LABORATORY TESTS

- Normal to increased white blood cell count with a left shift
- Mildly increased serum bilirubin
- Mild to moderate thrombocytopenia
- Elevated erthrocyte sedimentation rate
- Slightly prolonged prothrombin time (PT) and partial thromboplastin time (PTT)

LABORATORY DIAGNOSIS

- Observation of *Borrelia* spirochetes in smears of peripheral blood, bone marrow, or CSF
- Organisms are best detected in blood obtained while a person is febrile
- Serologic testing for TBRF is not standardized and results may vary by laboratory

TREATMENT

- Tetracycline 500 mg every 6 hours for 10 days is the preferred oral regimen for adults. If tetracyclines are contraindicated, an effective alternative is erythromycin 500 mg (or 12.5 mg/kg) every 6 hours for 10 days.
- For CNS involvement, ceftriaxone 2 g per day for 10–14 days is preferred.
- When initiating antibiotic therapy, all patients should be observed during the first 4 hours of treatment for a Jarisch-Herxheimer reaction.
- Acute respiratory distress syndrome requiring intubation has occurred in several patients undergoing TBRF treatment.

REFERENCES

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Other Tickborne Diseases

Powassan Disease

Agent: Powassan virus

WHERE FOUND Powassan virus infections have been recognized in the United States, Canada and Russia. In the United States, cases have been reported primarily from northeastern states and the Great Lakes region.

INCUBATION PERIOD: 1 to 4 weeks

SIGNS AND SYMPTOMS

- Fever, headache, vomiting, and generalized weakness
- Usually progresses to meningo-encephalitis. May include meningeal signs, altered mental status, seizures, aphasia, paresis, movement disorders, or cranial nerve palsies

GENERAL LABORATORY FINDINGS

- CSF findings include lymphocytic pleocytosis (neutrophils can predominate early), normal or mildly elevated protein, and normal glucose

LABORATORY DIAGNOSIS

- No commercially-available tests; testing available at CDC and selected state health departments.
- Measurement of virus-specific IgM antibodies in serum or cerebrospinal fluid (CSF). Cross-reaction with other flaviviruses (e.g., West Nile, dengue, or St. Louis viruses) can occur; plaque reduction neutralization tests should be performed to confirm the diagnosis.
- RT-PCR may detect viral RNA in acute CSF specimens or tissues but the sensitivity is unknown and this method should not be used to rule out the diagnosis.

TREATMENT

- No specific antiviral treatment for Powassan disease is available. Patients with suspected Powassan disease should receive supportive care as appropriate.

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Tickborne Diseases Abroad

Activities that increase risk for tick exposure worldwide include (but are not limited to): outdoor recreation such as camping, hiking, fishing, or bicycling; military training; outdoor occupations such as forestry; and collecting mushrooms, berries, or flowers in forested or agricultural areas.

DISEASE & ETIOLOGIC AGENT(S)	GEOGRAPHIC LOCATION AND ADDITIONAL RISK FACTORS
Lyme Disease *Borrelia afzelii, Borrelia garinii, B. burgdorferi* sensu stricto	Eastern and central Europe, northern Asia
Tick-Borne Encephalitis Tick-borne encephalitis virus	Temperate regions of Europe and northern Asia. May also be acquired by ingestion of unpasteurized dairy products from infected goats, sheep, or cows.
Spotted Fever Group Rickettsioses (includes tick typhuses) *R. akari, R. parkeri, R. africae, R. japonica, R. felis*, etc.	All continents except Antarctica. *R. africae* infection has been reported as a cause of fever in travelers returning from South Africa.
Crimean-Congo Hemorrhagic Fever CCHF virus	Asia, Africa, and Europe. May also be acquired by contact with infected blood or saliva or inhalation of infected aerosols.
Omsk Hemorrhagic Fever Omsk hemorrhagic fever virus	Southwestern Russia. May also be acquired by direct contact with infected muskrats.
Kyasanur Forest Disease Kyasanur forest disease virus	Southern India, Saudi Arabia (aka Alkhurma disease in Saudi Arabia). Typically associated with exposure while harvesting forest products.

NOTE: *Anaplasmosis, babesiosis, ehrlichiosis, tularemia, TBRF, and Powassan disease can also be acquired internationally. Please see disease-specific references for more information on worldwide distribution.*

REFERENCE

Goodman JL, Dennis DT, Sonenshine DE, editors. Tick-borne diseases of humans. Washington, DC: ASM Press; 2005.

Tick Bites/Prevention

Ticks are generally found near the ground, in brushy or wooded areas. They can't jump or fly. Instead, they climb tall grasses or shrubs and wait for a potential host to brush against them. When this happens, they climb onto the host and seek a site for attachment.

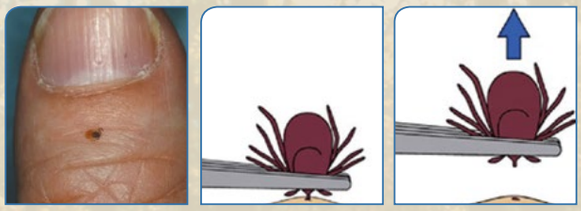
PREVENTION

1. Use repellent that contains 20 percent or more DEET, picaridin, or IR3535 on exposed skin for protection that lasts several hours. Use products that contain permethrin on clothing. Treat clothing and gear, such as boots, pants, socks and tents with products containing 0.5% permethrin. Additional repellent options are available. For more information, see http://cfpub.epa.gov/oppref/insect/.
2. Treat dogs and cats for ticks as recommended by a veterinarian.
3. Check for ticks daily, especially under the arms, in and around the ears, inside the belly button, behind the knees, between the legs, around the waist, and on the hairline and scalp.
4. Shower soon after being outdoors.
5. For tips on "tick-safe" landscaping, see www.cdc.gov/lyme/prev/in_the_yard.html.

TICK REMOVAL

1. Use fine-tipped tweezers to grasp the tick as close to the skin's surface as possible. You may use specialized tick removal tools, if you already have them. The key is to remove the tick as soon as possible. Avoid folklore remedies such as using nail polish, petroleum jelly, or heat to make the tick detach from the skin.
2. Pull upward with steady, even pressure. Don't twist or jerk the tick; this can cause the mouth-parts to break off and remain in the skin. If this happens, remove the mouth-parts with clean tweezers. If you are unable to remove the mouth parts easily, leave them alone and let the skin heal.
3. After removing the tick, thoroughly clean the bite area and your hands with rubbing alcohol, an iodine scrub, or soap and water.

Embedded tick



TICK BITE PROPHYLAXIS

The Infectious Disease Society of America (IDSA) does not generally recommend antimicrobial prophylaxis for prevention of **Lyme disease** after a recognized tick bite. However, in areas that are highly endemic for Lyme disease, a single dose of doxycycline may be offered to adult patients (200 mg) who are not pregnant and to children older than 8 years of age (4 mg/kg up to a maximum dose of 200 mg) when **all** of the following circumstances exist:

a. Doxycycline is not contraindicated.

b. The attached tick can be identified as an adult or nymphal *I. scapularis* tick.

c. The estimated time of attachment is ≥36 h based on the degree of engorgement of the tick with blood or likely time of exposure to the tick.

d. Prophylaxis can be started within 72 h of tick removal.

e. Lyme disease is common in the county or state where the patient lives or has recently traveled, (i.e., CT, DE, MA, MD, ME, MN, NH, NJ, NY, PA, RI, VA, VT, WI).

Antibiotic treatment following a tick bite is not recommended as a means to prevent **anaplasmosis, babesiosis, ehrlichiosis,** or **Rocky Mountain spotted fever.** There is no evidence this practice is effective, and it may simply delay onset of disease. Instead, persons who experience a tick bite should be alert for symptoms suggestive of tickborne illness and consult a physician if fever, rash, or other symptoms of concern develop.

Tularemia prophylaxis is recommended only in cases of laboratory exposure to infectious materials:

- Doxycycline (100 mg orally BID X 14 days) is generally recommended for prophylaxis in adults.
- Ciprofloxacin (500 mg orally BID) is not FDA-approved for prophylaxis of tularemia but has demonstrated efficacy in various studies, and may be an alternative for patients unable to take doxycycline.

For more information please contact:
Centers for Disease Control and Prevention
Division of Vector-Borne Diseases
3156 Rampart Road, Fort Collins, CO 80521
Telephone: 1-800-CDC-INFO (232-4636)/TTY: 1-888-232-63548
Contact: www.cdc.gov/cdc-info/
Web: www.cdc.gov/ticks

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