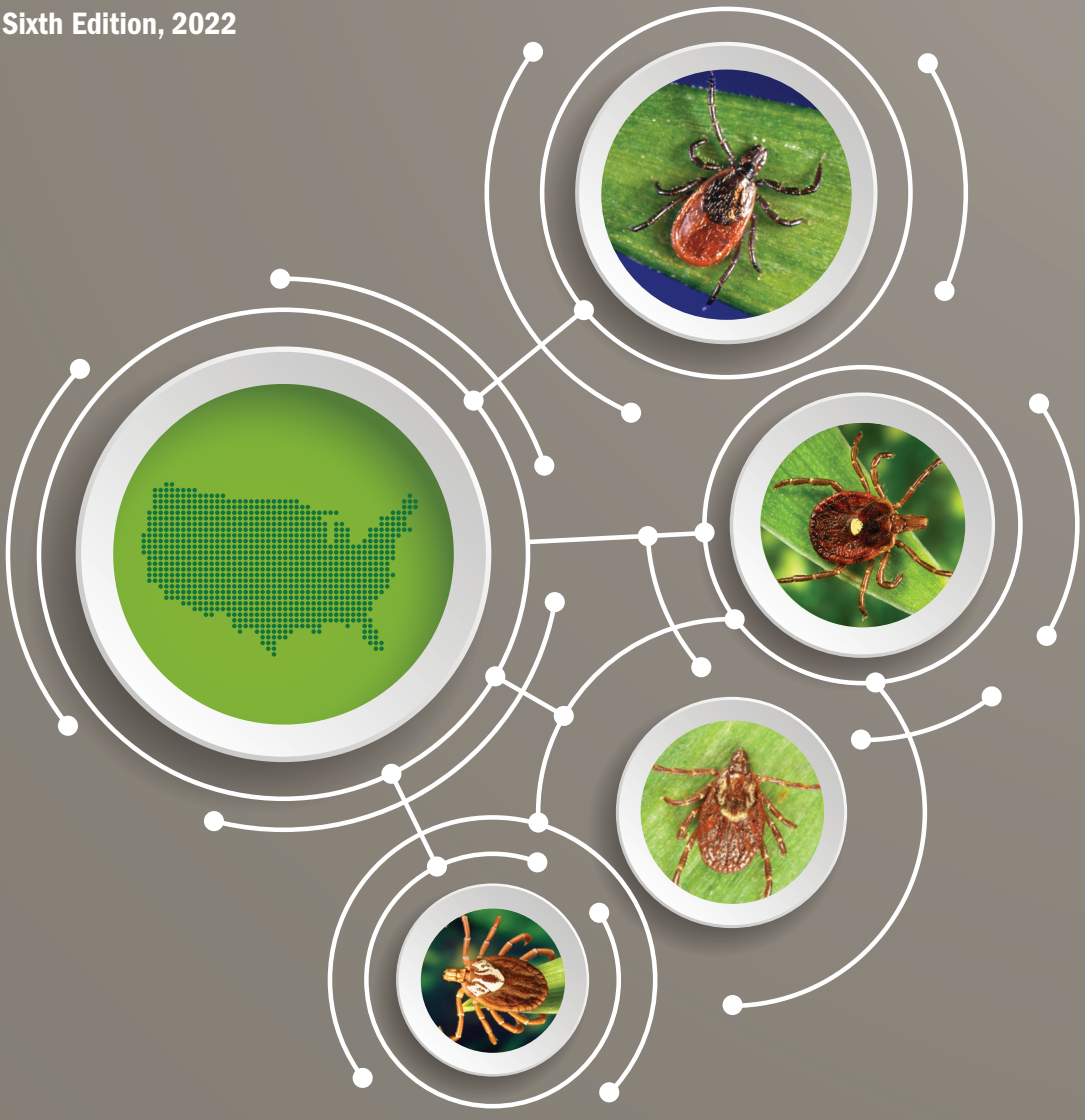
# TICKBORNE DISEASES OF THE UNITED STATES

## A Reference Manual for Healthcare Providers

Sixth Edition, 2022



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

# CONTENTS

# TICK ID

**BLACKLEGGED TICK** *Ixodes scapularis*

**WHERE FOUND** Widely distributed across the eastern United States.

**TRANSMITS** *Borrelia burgdorferi* and *B. mayonii* (which cause Lyme disease), *Anaplasma phagocytophilum* (anaplasmosis), *B. miyamotoi* disease (a form of relapsing fever), *Ehrlichia muris eauclairensis* (ehrlichiosis), *Babesia microti* (babesiosis), and Powassan virus (Powassan virus disease).

**COMMENTS** The greatest risk of being bitten exists in the spring, summer, and fall in the Northeast, Upper Midwest, and mid-Atlantic. However, adult ticks may be out searching for a host any time winter temperatures are above freezing. All life stages bite humans, but nymphs and adult females are most commonly found on people.

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**LONE STAR TICK** *Amblyomma americanum*

**WHERE FOUND** Widely distributed in the eastern United States, but more common in the South.

**TRANSMITS** *Ehrlichia chaffeensis* and *E. ewingii* (which cause human ehrlichiosis), *Francisella tularensis* (tularemia), Heartland virus (Heartland virus disease), Bourbon virus (Bourbon virus disease), and Southern tick-associated rash illness (STARI).

**COMMENTS** The greatest risk of being bitten exists in early spring through late fall. A very aggressive tick that bites humans. The adult female is distinguished by a white dot or "lone star" on her back. The nymph and adult females most frequently bite humans. Growing evidence suggests that alpha-gal syndrome (AGS) may be triggered by the bite of lone star ticks; however, other tick species have not been ruled out.

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**AMERICAN DOG TICK** *Dermacentor variabilis, D. similis*

**WHERE FOUND** *D. variabilis* is widely distributed east of the Rocky Mountains. Newly described *D. similis* is found west of the Rocky Mountains. More research is needed to understand the role of these species in disease transmission.

**TRANSMITS** *Francisella tularensis* (tularemia) and *Rickettsia rickettsii* (Rocky Mountain spotted fever).

**COMMENTS** The greatest risk of being bitten occurs during spring and summer. Adult females are most likely to bite humans.

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**BROWN DOG TICK** *Rhipicephalus sanguineus*

**WHERE FOUND** Worldwide.

**TRANSMITS** *Rickettsia rickettsii* (Rocky Mountain spotted fever). Primary vector for *R. rickettsii* transmission in the southwestern United States 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.

**GROUNDHOG TICK** *Ixodes cookei*

**WHERE FOUND** Throughout the eastern half of the United States.

**TRANSMITS** Powassan virus (Powassan virus 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. Photo courtesy of Steve Jacobs, PSU Entomology

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**GULF COAST TICK** *Amblyomma maculatum*

**WHERE FOUND** Distributed primarily in the southeastern United States, with focal populations in the northeastern, midwestern, and southwestern United States.

**TRANSMITS** *R. parkeri (R. 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.

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**ROCKY MOUNTAIN WOOD TICK** *Dermacentor andersoni*

**WHERE FOUND** Rocky Mountain states.

**TRANSMITS** *Rickettsia rickettsii* (Rocky Mountain spotted fever), Colorado tick fever virus (Colorado tick fever), and *Francisella tularensis* (tularemia).

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

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**SOFT TICK** *Ornithodoros* spp.

**WHERE FOUND** Throughout the western half of the United States, including Texas.

**TRANSMITS** *Borrelia hermsii, B. turicatae* (tickborne relapsing fever [TBRF]).

**COMMENTS** Humans typically come into contact with soft ticks in rustic cabins. The ticks emerge at night and feed briefly while people are sleeping. Most people are unaware that they have been bitten. In Texas, TBRF may be associated with cave exposure.

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

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**WESTERN BLACKLEGGED TICK** *Ixodes pacificus*

**WHERE FOUND** In the Pacific Coast states.

**TRANSMITS** *Anaplasma phagocytophilum* (anaplasmosis), *B. burgdorferi* (Lyme disease), and very likely *B. miyamotoi* (*Borrelia miyamotoi* disease, a form of relapsing fever).

**COMMENTS** Larvae and nymphs often feed on lizards, birds, and rodents, and adults more commonly feed on deer. Although all life stages bite humans, nymphs and adult females are more often reported on humans.

## TICKS THAT COMMONLY BITE HUMANS

### Blacklegged Tick (*Ixodes scapularis*)

Adult female

Adult male

Nymph

Larva




### Lone Star Tick (*Amblyomma americanum*)

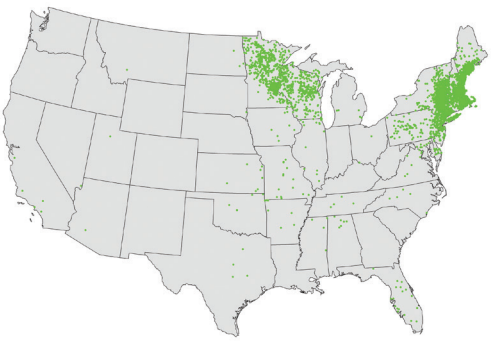
### American Dog Tick (*Dermacentor variabilis*)

**NOTE:** Relative sizes of several ticks at different life stages.

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

# OVERVIEW OF TICKBORNE DISEASES

## SELECTED TICKBORNE DISEASES REPORTED TO CDC, U.S., 2018



ANAPLASMOSIS

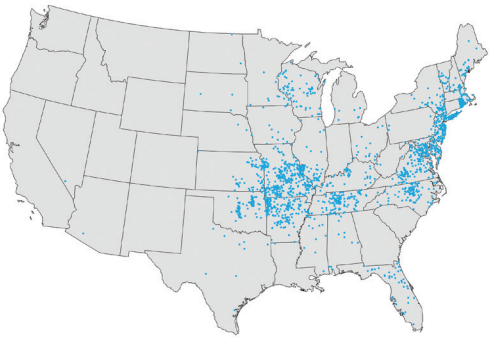
BABESIOSIS

**NOTE:** Each dot represents one case. Cases are reported from the infected person's county of residence (where known), not necessarily the place where they were infected. Maps do not include data if county of residence was not reported.

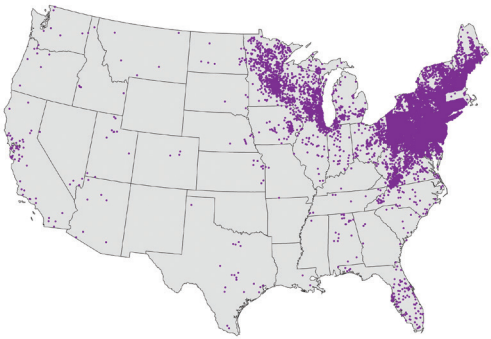
**NOTE:** In 2018, no cases of tickborne illness were reported from Hawaii. In 2018, Alaska reported 8 confirmed travel-related cases of Lyme disease.

**NOTE:** During 2018, babesiosis was reportable in Alabama, Arizona, Arkansas, California, Connecticut, Delaware, District of Columbia, Florida, Georgia, Illinois, Indiana, Iowa, Kansas, Kentucky, Louisiana, Maine, Maryland, Massachusetts, Michigan, Minnesota, Missouri, Montana, Nebraska, New Hampshire, New Jersey, New York, North Dakota, Ohio, Oregon, Rhode Island, South Carolina, South Dakota, Tennessee, Texas, Utah, Vermont, Virginia, Washington, West Virginia, Wisconsin, and Wyoming.

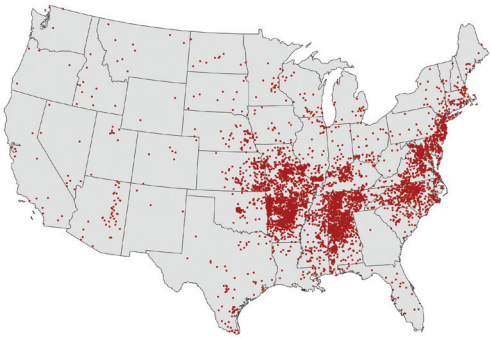
**FOR INFORMATION ABOUT REPORTING TICKBORNE DISEASE CASES OR QUESTIONS ABOUT TESTING, CONTACT YOUR STATE OR LOCAL HEALTH DEPARTMENT.**



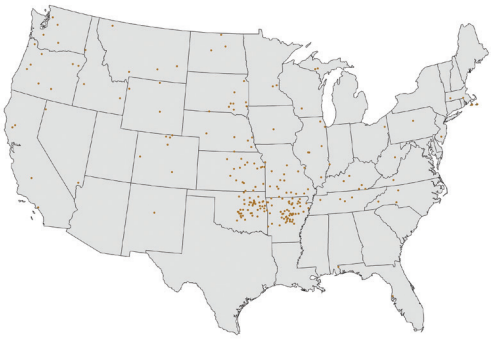
**EHRLICHIOSIS**



**LYME DISEASE**



**SPOTTED FEVER RICKETTSIOSIS (INCLUDING ROCKY MOUNTAIN SPOTTED FEVER)**



**TULAREMIA**

**NOTE:** Anaplasmosis and ehrlichiosis were not reportable in Colorado, Idaho, New Mexico, Alaska, and Hawaii in 2018.

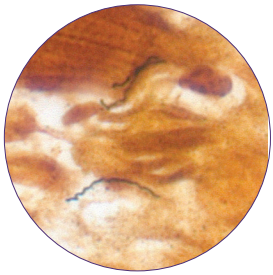
**NOTE:** Spotted fever rickettsiosis was not reportable in Alaska and Hawaii in 2018.

# LYME DISEASE

**AGENT:** *Borrelia burgdorferi, B. mayonii*

## WHERE FOUND

Lyme disease is most frequently reported from the upper midwestern, northeastern, and mid-Atlantic states where it is spread by *Ixodes scapularis* ticks. Some cases are also reported from northern California, Oregon, and Washington, where it is spread by *Ixodes pacificus* ticks. High-incidence states include Connecticut, Delaware, Maine, Maryland, Massachusetts, Minnesota, New Hampshire, New Jersey, New York, Pennsylvania, Rhode Island, Vermont, Virginia, Washington D.C., West Virginia, and Wisconsin. While these states account for the majority of cases, the geographic area of risk is expanding to include neighboring states.



## INCUBATION PERIOD

3–30 days

## SIGNS AND SYMPTOMS

*EARLY LOCALIZED (3 to 30 days after a tick bite)*

- Erythema migrans (EM)—Red annular or homogeneous rash at the site of tick bite; expands gradually over several days to >5 cm in diameter; central clearing may develop as the rash expands, resulting in a "target" or "bull's-eye" appearance; may feel warm to the touch but rarely itchy or painful. EM occurs in 70–80% of infected persons. The classic rash is not present in all cases; see examples on the following pages.
- Fever, chills, malaise, fatigue, headache, myalgia, arthralgia
- Lymphadenopathy

*DISSEMINATED (days to months after a tick bite)*

Untreated or unnoticed early Lyme disease will progress to disseminated disease for about 60% of patients, with diverse clinical manifestations. Most manifestations will appear in the first few weeks to months of infection, though rheumatologic manifestations may be particularly delayed.

*Dermatologic Manifestations*

- Multiple EM rashes, distant from site of tick bite

*Neurologic Manifestations*

- Cranial neuritis, most commonly Bell's palsy (facial paralysis, can be bilateral)
- Lymphocytic meningitis
- Painful radiculoneuritis involving one or multiple dermatomes
- Painful peripheral motor and sensory neuropathy (mononeuritis multiplex)
- Intracranial hypertension (rare)

*Cardiac Manifestations*

- Lyme carditis resulting in conduction abnormalities (e.g., atrioventricular node block; myopericarditis)
- Rarely, can be fatal

*Rheumatologic Manifestations*

- Oligoarticular arthritis: transient, migratory arthritis and effusion in one or multiple joints, often large joints; may cause Baker's cyst
- Migratory pain in tendons, bursae, muscle, and bones

### *LYME DISEASE OR STARI?*

An erythema migrans-like rash has also been described in humans following bites of the lone star tick. This condition has been named Southern Tick-Associated Rash Illness (STARI). Although the rash may be accompanied by systemic symptoms, disseminated or severe disease has not been reported. Because the cause of STARI is unknown, diagnostic blood tests are not available. 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.

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.

### GENERAL LABORATORY FINDINGS

- Elevated erythrocyte sedimentation rate
- Mildly elevated hepatic transaminases
- Microscopic hematuria or proteinuria

### LABORATORY DIAGNOSIS

1. For patients who present with an EM rash after being in an area where Lyme disease is common, Lyme disease should be diagnosed clinically (without diagnostic testing), as serologic tests may be negative during the first few weeks of infection before antibodies have developed.
2. Serologic tests are highly sensitive in patients with disseminated Lyme disease, and diagnosis relies on signs and symptoms supported by results of testing.
3. Two-step serologic testing is recommended using validated first- and second-tier tests according to a standard or modified two-test algorithm. IgM Western immunoblot results should only be considered if signs and symptoms have been present for less than 30 days.

### NOTES ON SEROLOGIC TESTS FOR LYME DISEASE

- For details, refer to the APHL guide for interpretation of serologic test results https://www.aphl.org/aboutAPHL/publications/Documents/ID-2021-Lyme-Disease-Serologic-Testing-Reporting.pdf
- While not necessary, acute and convalescent serologies may be useful for diagnosis in some cases, such as for patients with suspected re-infection.
- Serologic tests cannot be used to measure treatment response.
- Other conditions, including some tickborne infections and autoimmune diseases, can result in false positive test results.

**NOTE:** Coinfection with *Babesia microti* or *Anaplasma 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 should also be considered in patients whose erythema migrans skin lesion has resolved but who have persistent systemic symptoms.

## TREATMENT OF ERYTHEMA MIGRANS RASH

People treated with appropriate antibiotics in the early stages of Lyme disease usually recover rapidly and completely. Early diagnosis and proper antibiotic treatment of Lyme disease can help prevent late Lyme disease. Treatment regimens listed in the following table are for the erythema migrans rash, the most common manifestation of early Lyme disease. These regimens may need to be adjusted depending on a person's age, medical history, underlying health conditions, pregnancy status, or allergies. Consult an infectious disease specialist regarding individual patient treatment decisions. For treating other manifestations, see www.cdc.gov/Lyme/treatment/.

| AGE CATEGORY | DRUG | DOSAGE | MAXIMUM | DURATION (DAYS)* |
|---|---|---|---|---|
| Adults | Doxycycline OR | 100 mg, twice per day orally | N/A | 10–14 |
| | Amoxicillin OR | 500 mg, three times per day orally | N/A | 14 |
| | Cefuroxime | 500 mg, twice per day orally | N/A | 14 |
| Children | Doxycycline OR | 4.4 mg/kg per day orally, divided into 2 doses | 100 mg per dose | 10–14 |
| | Amoxicillin OR | 50 mg/kg per day orally, divided into 3 doses | 500 mg per dose | 14 |
| | Cefuroxime | 30 mg/kg per day orally, divided into 2 doses | 500 mg per dose | 14 |

* When different durations of antibiotics are shown to be effective for the treatment of Lyme disease, the shorter duration is preferred to minimize adverse effects, including infectious diarrhea and antimicrobial resistance.

**NOTE:** For people intolerant of amoxicillin, doxycycline, and cefuroxime, the macrolide azithromycin may be used, although it is less effective. People treated with azithromycin should be closely monitored to ensure that symptoms resolve.

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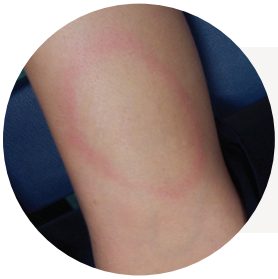
# LYME DISEASE

## ERYTHEMA MIGRANS RASHES

The erythema migrans (EM) rash occurs in 70-80% of patients with Lyme disease. EM rashes may have the classic appearance or may take alternate forms; solid lesions, blue-purple hues, and crusted or blistering lesions have all been documented.

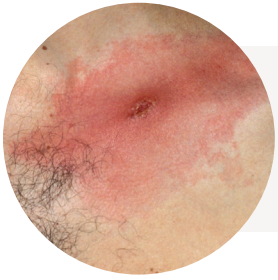


### CLASSIC EM—CIRCULAR RED RASH WITH CENTRAL CLEARING THAT SLOWLY EXPANDS

Photo courtesy of Taryn Holman.

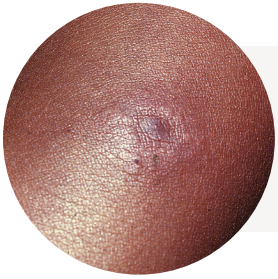
### BLUISH HUE WITHOUT CENTRAL CLEARING

Photo courtesy of Yevgeniy Balagula.



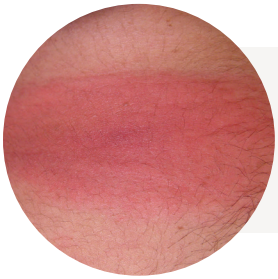
### EXPANDING LESION WITH CENTRAL CRUST ON CHEST

Photo courtesy of Bernard Cohen.



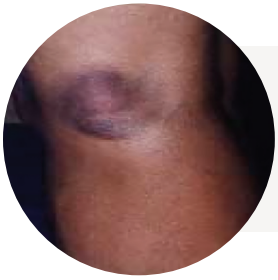
### EARLY, EXPANDING ERYTHEMA MIGRANS WITH NODULE

Reprinted from Bhate C, Schwartz RA. Lyme disease: Part I. Advances and perspective. *J Am Acad Dermatol.* 2011;64:619-36, with permission from Elsevier.



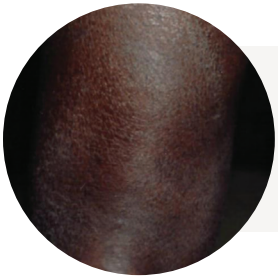
### RED, EXPANDING OVAL-SHAPED PLAQUE ON TRUNK

Photo courtesy of Alison Young.



### PURPLE LESION ON BACK OF KNEE

Photo courtesy of New York State Department of Health.

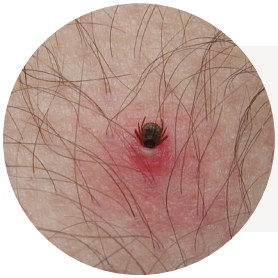


### FAINT EM ON BACK OF KNEE

Photo courtesy of Gary Wormser, New York Medical College.

### EARLY DISSEMINATED LYME DISEASE—MULTIPLE LESIONS WITH DUSKY CENTERS ON TRUNK

Photo courtesy of Bernard Cohen.



### TICK BITE WITH MILD ALLERGIC REACTION

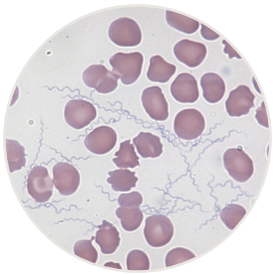
**Not erythema migrans.** Hypersensitivity reactions typically appear within the first 48 hours of tick attachment, are often itchy and are usually <5 cm in diameter. Localized tick bite reactions can occur following bites from any tick species.

Special thanks to DermAtlas for providing many photographs.

# TICKBORNE RELAPSING FEVER (TBRF)

## (SOFT TICK RELAPSING FEVER)

**AGENT:** *Borrelia hermsii, B. turicatae*



### WHERE FOUND

In the United States, TBRF usually occurs in mountainous areas of Western states, where it is associated with exposure to soft ticks in rustic cabins *(B. hermsii),* and in Texas, where it is most often associated with exposure to soft ticks in caves *(B. turicatae).*

### INCUBATION PERIOD

Approximately 7 days (range 4–21), with recurrent febrile episodes that last around 3 days and are separated by afebrile periods of approximately 7 days.

### SIGNS AND SYMPTOMS

TBRF most commonly presents with fever, headache, and myalgias. As with other borrelioses, neurologic involvement is possible, including meningoencephalitis, cranial neuritis and ocular manifestations. Acute respiratory distress syndrome is a rare complication.

- High fever with relapses
- Chills/rigors
- Sweats
- Headache
- Myalgia/arthralgia
- Dizziness
- Nausea/vomiting
- Facial palsy (rarely)

### GENERAL LABORATORY FINDINGS

- Leukocytosis
- Thrombocytopenia
- Mild hyperbilirubinemia
- Elevated erythrocyte sedimentation rate
- Slightly prolonged prothrombin time (PT) and partial thromboplastin time (PTT)

### LABORATORY DIAGNOSIS

Tests may include the following:

- Visualization of spirochetes by microscopy of peripheral blood obtained during a febrile episode prior to treatment.
- Molecular testing, such as PCR. Molecular tests should be performed as early as possible, ideally prior to treatment or soon after. PCR testing is more sensitive than microscopy.
- Serologic testing by immunofluorescence assay (IFA), enzyme immunoassay (EIA), or immunoblot.

**NOTE:** TBRF can be transmitted transplacentally and has been associated with pregnancy complications including spontaneous abortion, premature birth, and neonatal death.

**NOTE:** Serologic tests and some commercially available PCR tests cross-react with other *Borrelia* species, including *B. burgdorferi,* the cause of Lyme disease.

## TREATMENT

Treatment data for patients with TBRF are limited. Consider the following regimens for nonpregnant patients who do not have neurologic complications. In pregnant individuals or when neurologic involvement is present, initial parenteral therapy with a beta-lactam is advised; treatment should be continued for 10–14 days with close monitoring given the potential for severe complications.

| AGE CATEGORY | DRUG | DOSAGE | DURATION (DAYS) |
|---|---|---|---|
| Adults | Doxycycline, oral or intravenous (first-line) | 100 mg every 12 hours | 10 |
| | Azithromycin, oral | 500 mg daily | 10 |
| | Penicillin G, intravenous | 4,000,000 units every 6 hours | 10 |
| | Ceftriaxone, intravenous | 2 g daily | 10 |
| Children | Doxycycline, oral or intravenous (first-line) | 2.2 mg/kg per dose, every 12 hours, maximum 100 mg/dose | 10 |
| | Azithromycin, oral | 10 mg/kg daily, maximum 500 mg/day | 10 |
| | Penicillin G, intravenous | 50,000–100,000 units/kg every 6 hours, maximum 4,000,000 units/dose | 10 |
| | Ceftriaxone, intravenous | 50–75 mg/kg daily, maximum 2 g/day | 10 |

**NOTE:** When initiating antibiotic therapy, all patients should be observed during the first 4 hours of treatment for a Jarisch-Herxheimer reaction.

See http://www.cdc.gov/relapsing-fever/clinicians. for detailed treatment information.

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# HARD TICK RELAPSING FEVER

**AGENT:** *Borrelia miyamotoi*

## WHERE FOUND

Occurs in the upper midwestern, northeastern, and mid-Atlantic states, where it is transmitted by *Ixodes scapularis* ticks, and in Pacific coastal states, where it is transmitted by *I. pacificus* ticks. Unlike Lyme disease, which most commonly occurs in June and July, hard tick relapsing fever occurs most commonly in July and August.

## INCUBATION PERIOD

3 days to 6 weeks, exact range unknown

## SIGNS AND SYMPTOMS

Infection with *B. miyamotoi* most frequently presents as a self-resolving acute febrile illness, but the spectrum of illness varies from subclinical to severe. Severe manifestations (e.g., meningoencephalitis) appear to be more common in people with immunocompromising conditions. Symptoms may include:

- Fever
- Chills
- Relapsing fever (10-40% of cases)
- Fatigue
- Arthralgia/myalgia

## GENERAL LABORATORY FINDINGS

- Leukopenia
- Thrombocytopenia
- Elevated hepatic transaminases
- Proteinuria

## LABORATORY DIAGNOSIS

- Diagnosis relies on signs and symptoms coupled with:
  1. Polymerase chain reaction (PCR) assays that detect *B. miyamotoi* DNA in blood or cerebrospinal fluid; or
  2. Serologic assays

  Notably, serologic tests are most often negative during the acute presentation and are therefore of limited utility in diagnosis, though paired acute and convalescent tests can confirm a recent infection. Some serologic and PCR tests can cross-react with other *Borrelia* species, making travel and tick exposure history important to distinguish between these entities.

## TREATMENT

There are no randomized controlled trials that evaluate treatment regimens, but in published case series, patients were successfully treated with antimicrobial regimens effective for Lyme disease. A 2-week course of doxycycline or amoxicillin is appropriate for outpatient treatment of most patients, including young children. For persons with severe illness requiring hospitalization (e.g., meningoencephalitis), IV antibiotics such as ceftriaxone are appropriate initial therapy. When treating patients with immunocompromising conditions for suspected *B. miyamotoi* infection, consultation with an infectious disease specialist is advised.

*B. miyamotoi* symptoms typically improve within 24–72 hours following administration of appropriate antibiotics. The Jarisch-Herxheimer reaction has been described in a minority of treated patients

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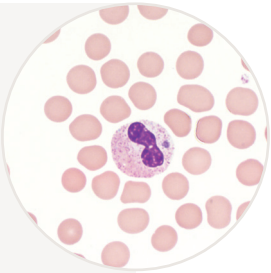
# ANAPLASMOSIS

**AGENT:** *Anaplasma phagocytophilum*



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

Severe and life-threatening illness is less common with anaplasmosis compared to other rickettsial diseases, such as Rocky Mountain spotted fever (RMSF) or *E. chaffeensis* ehrlichiosis. While the case-fatality rate among patients who seek care for the illness is <1%, predictors of a more severe course include advanced age, immunosuppression, comorbid medical conditions, and delay in diagnosis and treatment.

## WHERE FOUND

Anaplasmosis is most frequently reported from the Upper Midwest and northeastern United States in areas that correspond with the known geographic distribution of Lyme disease and other *Ixodes scapularis*-transmitted diseases. Due to the common vector, co-infection with *A. phagocytophilum* and *B. burgdorferi, Babesia microti,* or Powassan virus is possible; illness may be marked by a more severe course or incomplete response to treatment.

*A. phagocytophilum* is typically transmitted by the bite of an infected tick but may also be associated with blood product transfusions or organ transplant.

## INCUBATION PERIOD

5–14 days

## SIGNS AND SYMPTOMS

- Fever, chills, rigors
- Severe headache
- Malaise
- Myalgia
- Gastrointestinal symptoms (nausea, vomiting, diarrhea, anorexia)
- Rash (<10%)

*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.*

**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

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 DIAGNOSIS

- 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 tetracycline-class antibiotics.
- Demonstration of a four-fold rise in IgG-specific antibody titer by indirect immunofluorescence antibody (IFA) assay in paired serum samples. The first sample should be taken within the first 2 weeks of illness and the second should be taken 2 to 4 weeks later.
- Immunohistochemical (IHC) staining of organism from skin, tissue, or bone marrow biopsies.

**NOTE:** Antibody titers are frequently negative in the first 7–10 days of illness. Acute antibody results cannot independently be relied upon for confirmation.

**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.

## TREATMENT

Anaplasmosis, ehrlichiosis, and spotted fever group rickettsioses are treated 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 life-threatening allergy 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 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 multiple courses are given before the age of eight.

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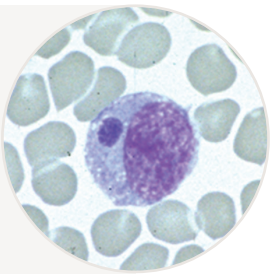
# EHRLICHIOSIS

**AGENTS:** *Ehrlichia chaffeensis, Ehrlichia ewingii, Ehrlichia muris eauclairensis*

*E. chaffeensis* can cause fatal illness, whereas no deaths have been reported for *E. ewingii* or *E. muris euclairensis* ehrlichiosis.

Incidence of *E. chaffeensis* enhrlichiosis generally increases with age, however, case-fatality rates are highest among children aged <10 years and adults aged ≥70 years.



## WHERE FOUND

Ehrlichiosis is most frequently reported from the southeastern and south-central United States, from the East Coast extending westward to Texas. The areas from which most 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*. In 2019, four states (Missouri, Arkansas, North Carolina, and New York) accounted for nearly half of all reported cases of *E. chaffeensis* ehrlichiosis. Since 2009, >115 cases of ehrlichiosis caused by *E. muris eauclairensis* have been identified in patients in the Upper Midwest. The tick responsible for transmitting this new subspecies of *Ehrlichia* is *Ixodes scapularis,* and the clinical presentation is generally similar to those associated with infections caused by *E. chaffeensis* and *E. ewingii.*

## INCUBATION PERIOD

5–14 days

## SIGNS AND SYMPTOMS

- Fever, chills
- Headache
- Malaise
- Muscle pain
- Gastrointestinal symptoms (nausea, vomiting, diarrhea, anorexia)
- Altered mental status
- 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.*

**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

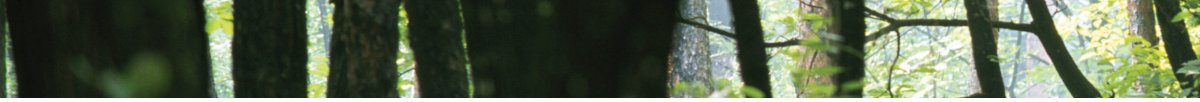
During the acute stage of illness, morulae can be detected in about 20% of patients. *E. chaffeensis* most commonly infects monocytes, whereas *E. ewingii* more commonly infects granulocytes. The target cell of *E. muris eauclairensis* has not yet been identified. Visualization of morulae during examination of blood smears is highly suggestive of a diagnosis; however, blood smear examination is insensitive and should never be relied upon solely to rule ehrlichiosis in or out.

## LABORATORY DIAGNOSIS

- 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 rise in IgG-specific antibody titer by indirect immunofluorescence antibody (IFA) assay in paired serum samples. The first sample should be taken within the first 2 weeks of illness, and the second should be taken 2 to 4 weeks later.
- Immunohistochemical (IHC) staining of organism from skin, tissue, or bone marrow biopsies.

**NOTE:** Antibody titers are frequently negative in the first 7–10 days of illness. Acute antibody results cannot independently be relied upon for confirmation.

**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.



## TREATMENT

Anaplasmosis, ehrlichiosis, and spotted fever group rickettsioses are treated 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 pregnancy or life-threatening allergy 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 multiple courses are given before the age of eight.

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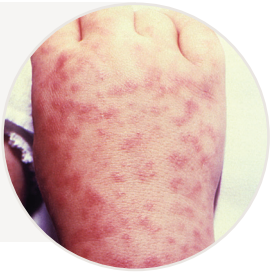
# ROCKY MOUNTAIN SPOTTED FEVER (RMSF)

**AGENT:** *Rickettsia rickettsii*

RMSF is most often transmitted by the American dog tick in the Eastern, Central, and Western United States; by the Rocky Mountain wood tick in the Rocky Mountain states; and by the brown dog tick in the Southwestern United States, along the U.S.-Mexico border. 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%.



## WHERE FOUND

Since 2010, cases of RMSF are reported as spotted fever rickettsiosis along with other spotted fevers like *Rickettsia parkeri* rickettsiosis in national surveillance. RMSF has become increasingly common in certain areas of Arizona over the last several years; between 2002–2021 more than 500 cases and 28 fatalities occurred.

## INCUBATION PERIOD

3–12 days

## SIGNS AND SYMPTOMS

*EARLY (1–4 DAYS)*

- High fever
- Severe headache
- Malaise
- Myalgia
- Edema around eyes and on the back of hands
- Gastrointestinal symptoms (nausea, vomiting, anorexia)

*LATE (5 DAYS AND BEYOND)*

- Altered mental status, coma, cerebral edema
- Respiratory compromise (pulmonary edema, ARDS)
- Necrosis, requiring amputation
- Multiorgan system damage (CNS, renal failure)

## RASH

- Typically appears 2–5 days after onset of symptoms; approximately 10% of RMSF patients never develop a rash.
- Decision to treat should not be based on presence of rash.

*Early Rash*

- Maculopapular: 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.

*Late Rash*

- Petechial: 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.

**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 more likely to prevent fatal outcome from RMSF if started within the first 5 days of symptoms.**

## GENERAL LABORATORY FINDINGS

- Thrombocytopenia
- Elevated hepatic transaminases
- Hyponatremia

**NOTE:** Laboratory values are often within normal limits in early illness.

## LABORATORY DIAGNOSIS

- Demonstration of a four-fold rise in IgG-specific antibody titer by indirect immunofluorescence antibody (IFA) assay in paired serum samples. The first sample should be taken within the first 2 weeks 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 PCR assay or in an acute phase whole blood specimen. Additionally, new pan-*Rickettsia* and *R. rickettsii*-specific PCR assays are available at some local and state health departments.
- Immunohistochemical (IHC) staining of organism from skin or tissue biopsy specimen.

**NOTE:** Antibody titers are frequently negative in the first 7–10 days of illness. Acute antibody results cannot be independently relied upon for confirmation

**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.

## TREATMENT

Anaplasmosis, ehrlichiosis, and spotted fever group rickettsioses are treated 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 life-threatening allergy 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 multiple courses are given before the age of eight.

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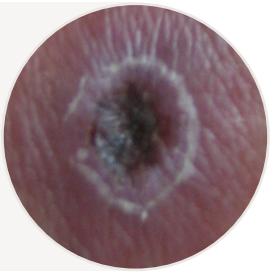
# *RICKETTSIA PARKERI* RICKETTSIOSIS

**AGENT:** *Rickettsia parkeri*

*R. parkeri* is closely related to *R. rickettsii,* the causative agent of Rocky Mountain spotted fever (RMSF). *R. parkeri* rickettsiosis and RMSF have similar signs and symptoms, including fever, headache, and rash, but also typically include the appearance of an inoculation eschar (seen at right) at the site of tick attachment. Eschar is not common in cases of RMSF.



## WHERE FOUND

*R. parkeri* rickettsiosis is transmitted by Gulf Coast ticks found primarily in the southeastern United States, with focal populations in the northeastern, midwestern, and southeastern United States.

## INCUBATION PERIOD

2–10 days

## SIGNS AND SYMPTOMS

*R. parkeri* rickettsiosis is characteristically less severe than RMSF and almost always associated with an inoculation eschar (ulcerated, necrotic lesion) at the site of tick attachment.

Several days after an eschar appears, the following can develop:

- Fever
- Headache
- Rash (sparse maculopapular or papulovesicular eruptions on the trunk and extremities)
- Muscle aches

**NOTE:** *R. parkeri* rickettsiosis can be difficult to distinguish from RMSF and other spotted fevers, especially during early stages of these diseases. Eschars are uncommonly identified in persons with RMSF.

## GENERAL LABORATORY FINDINGS

- Mildly elevated hepatic transaminases
- Mild leukopenia
- Mild thrombocytopenia, less common

**CONFIRMATION OF THE DIAGNOSIS IS BASED ON LABORATORY TESTING, BUT ANTIBIOTIC THERAPY SHOULD NOT BE DELAYED IN A PATIENT WITH A SUGGESTIVE CLINICAL PRESENTATION.**

## LABORATORY DIAGNOSIS

- Detection of rickettsial DNA by PCR in eschar swab, whole blood, or skin biopsy.
- Demonstration of a four-fold rise in IgG-specific antibody titer by indirect immunofluorescence antibody (IFA) assay in paired serum samples. The first sample should be taken within the first 2 weeks of illness and the second should be taken 2 to 4 weeks later.

**NOTE:** Species-level testing for *R. parkeri* is not commercially available. RMSF antibody tests are available commercially and often cross-react.

**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:** Acute antibody results cannot independently be relied upon for confirmation.

## TREATMENT

See Rocky Mountain spotted fever treatment on page 26.

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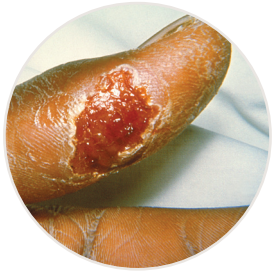
# TULAREMIA

**AGENT:** *Francisella tularensis*

Tularemia is caused by the highly infectious *F. tularensis* bacteria. It is spread through exposure to infected arthropods (including deer flies and several species of ticks), contact with infected carcasses or animals (such as rabbits, hares, and rodents), contaminated food or water, or inhalation of aerosols (such as by mowing over an infected rabbit carcass).

## WHERE FOUND

Tularemia has been reported in all states except Hawaii, but it is most common in the south-central United States, the Great Plains region, and parts of Massachusetts.



## INCUBATION PERIOD

3–5 days (range 1–21 days)

## SIGNS AND SYMPTOMS

The clinical presentation of tularemia depends on many factors, including the route of inoculation and subtype of *F. tularensis.* Tularemia can be serious or fatal without adequate treatment. Unusual and severe clinical manifestations have been described in patients with immunocompromising conditions.

- 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
- Vision impairment/loss
- Conjunctivitis
- Regional lymphadenopathy

### *OROPHARYNGEAL*

- Severe throat pain
- Exudative pharyngitis or tonsillitis
- Regional 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 the localizing symptoms of other syndromes
- May have infiltrates in chest radiograph in the absence of respiratory symptoms

## GENERAL LABORATORY FINDINGS

- Hyponatremia
- Leukocytosis
- Thrombocytopenia
- Elevated hepatic transaminases
- Elevated creatine kinase
- Elevated erythrocyte sedimentation rate
- Myoglobinuria
- Sterile pyuria

## LABORATORY DIAGNOSIS

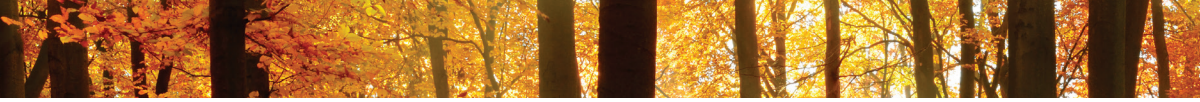
Isolation of *F. tularensis* in culture is optimal for diagnosis but can be challenging due to the slow-growing, fastidious nature of the organism. Appropriate specimens for culture include swabs or scrapings of ulcers, lymph node aspirates or biopsies, pharyngeal swabs, or respiratory specimens (e.g., pleural fluid), depending on the form of illness. Blood cultures are often negative.

Seroconversion from negative to positive IgM and/or IgG can also confirm the diagnosis when tularemia is suspected. Ideally, these are performed as paired acute and convalescent specimens, the latter collected 2–3 weeks after initial illness.

When available, other tests can be useful, including:

- Direct immunofluorescence assay (DFA)
- Immunohistochemical staining
- PCR assay

Clinicians who suspect tularemia should alert the laboratory to the possible need for special safety procedures to minimize risk of laboratory transmission.



## TREATMENT

These regimens may need to be adjusted depending on a person's age, medical history, underlying health conditions, pregnancy status, or allergies. Consult an infectious disease specialist regarding individual patient treatment decisions.

| AGE CATEGORY | DRUG | DOSAGE | MAXIMUM | DURATION (DAYS) |
|---|---|---|---|---|
| Adults | 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 500 mg PO twice daily | N/A | 10–14 |
| | Doxycycline | 100 mg IV or PO twice daily | N/A | 14–21 |
| Children | 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 | 800 mg per day | 10 |
| | Doxycycline | 2.2mg/kg IV or PO twice daily | 100mg IV or PO twice daily | 14–21 |

* Not a U.S. FDA-approved use but has been used successfully to treat patients with tularemia.
** Once-daily dosing could be considered in consultation with a pediatric infectious disease specialist and a pharmacist

**NOTE:** Gentamicin is preferred for treatment of severe tularemia. Dose should be adjusted for renal insufficiency.

**NOTE:** For tularemic meningitis, combination therapy should be considered in consultation with an infectious disease specialist.

See www.cdc.gov/tularemia/clinicians/ for detailed treatment information.

**Tularemia prophylaxis** is recommended in cases of laboratory exposure to infectious materials.

- Doxycycline (100 mg orally twice daily for 14 days) is generally recommended for prophylaxis in adults.
- Ciprofloxacin (500 mg orally twice daily) 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.

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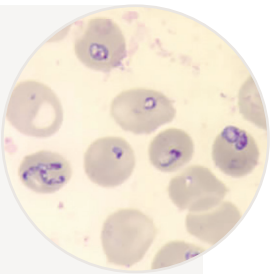
# BABESIOSIS

**AGENT:** *Babesia microti* and other *Babesia* species



Babesiosis is a disease caused by parasites that infect red blood cells. Most U.S. cases are caused by *B. microti,* which is transmitted mainly by *Ixodes scapularis* ticks, primarily in the Northeast and Upper Midwest and sporadically on the West Coast. Babesia parasites can also be transmitted via blood transfusion, perinatally, and via organ transplantation, anywhere, at any time of year. In 2019, the FDA licensed tests for the detection of Babesia species to utilize for screening of donors and recommended year-round regional testing for blood donations in areas endemic for babesiosis. Babesia infection can range from asymptomatic to life-threatening. Risk factors for severe babesiosis include a splenia, advanced age (age >50), and impaired immune function.

## WHERE FOUND

Babesiosis is most frequently reported from the Northeastern and Upper Midwestern United States in areas where *B. microti* is endemic; cases peak during spring and summer months. Sporadic cases of infection caused by novel Babesia agents have been detected in other U.S. regions, including the West Coast. Cases of babesiosis linked to *B. divergens*-like organisms have occurred in the Midwest region, Arkansas, Kentucky, Pennsylvania and Washington State. Cases linked to *B. duncani* have occurred on the West Coast of the United States. Transfusion-associated cases of babesiosis can occur anywhere in the country, at any time of year.

## INCUBATION PERIOD

1–4 weeks following tick bite; 1–9 weeks after contaminated blood transfusion (up to 24 weeks)

## SIGNS AND SYMPTOMS

*Not all infected persons are symptomatic or febrile (an estimated 25% of infected adults and 50% of children are asymptomatic). The clinical manifestations, if any, usually develop within several weeks after exposure, but may develop or recur months later (for example, in the context of surgical splenectomy).*

- Fever, chills, sweats
- Malaise, fatigue
- Myalgia, arthralgia, headache
- Gastrointestinal symptoms, such as anorexia and nausea (less common: abdominal pain, vomiting)
- Dark urine
- Less common: dry cough, sore throat, photophobia, 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.

## GENERAL LABORATORY FINDINGS

Findings consistent with hemolysis include:

- Hemolytic anemia with decreased haptoglobin, elevated lactate dehydrogenase (LDH) values, and reticulocytosis
- Thrombocytopenia
- Elevated creatinine and blood urea nitrogen (BUN) values
- Mildly elevated hepatic transaminase values
- Proteinuria

## 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
- 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 by experienced technicians, although multiple smears may need to be examined. 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 if applicable, perform serologic or molecular testing to get a species-level identification.

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

## TREATMENT

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 (e.g., >50 years of age or neonates).

The typical regimens for adults are provided in the table below. Note that some patients diagnosed with babesiosis may have concurrent Lyme disease, or anaplasmosis or may be infected with other pathogens transmitted by *Ixodes scapularis* in a region. For pediatric dosing and non-*B. microti* treatment recommendations please reference the *Clinical Practice Guidelines by the Infectious Diseases Society of America (IDSA): 2020 Guideline on Diagnosis and Management of Babesiosis.*

| AGE CATEGORY | DRUG | PATIENT CATEGORY | DOSAGE | DURATION (DAYS)* |
|---|---|---|---|---|
| Adults*** | (Preferred Regimen)<br>Azithromycin<br>+<br>Atovaquone (with a fatty meal)<br>Prescribe together | Non-hospitalized (mild to moderate disease) | Azithromycin 500 mg orally on day 1; on subsequent days, give 250 mg every 24 hours | 7–10 |
| | | | Atovaquone 750 mg orally every 12 hours | |
| | | Hospitalized (acute severe disease) | Azithromycin 500 mg IV every 24 hours until symptoms lessen, then transition to all oral step-down therapy | 7–10 |
| | | | Atovaquone 750 mg orally every 12 hours | |
| | | Hospitalized (step-down therapy) | Azithromycin 250-500 mg** orally every 24 hours | 7–10 |
| | | | Atovaquone 750 mg orally every 12 hours | |
| | (Alternative Regimen)****<br>Clindamycin<br>+<br>Quinine<br>Prescribe together | Non-hospitalized (mild to moderate disease) | Clindamycin 600 mg orally every 8 hours | 7–10 |
| | | | Quinine 650 mg orally every 8 hours | |
| | | Hospitalized (acute severe disease) | Clindamycin 600 mg IV every 6 hours until symptoms lessen, then transition to oral step-down therapy | 7–10 |
| | | | Quinine 650 mg orally every 8 hours | |
| | | Hospitalized (step-down therapy) | Clindamycin 600 mg orally every 8 hours | 7–10 |
| | | | Quinine 650 mg orally every 8 hours | |

* The duration of therapy may be greater than 10 days for patients that are immunocompromised; highly immunocompromised patients may benefit from 6+ weeks.

** In immunocompromised adults, consider azithromycin doses of 500-1000 mg daily.

*** Patients with high-grade parasitemia (>10%), severe hemolytic anemia, or severe pulmonary, renal, or hepatic compromise may benefit from exchange transfusion. Expert consultation is strongly advised.

****Patients who fail to improve while on therapy with the preferred regimen or who are unable to take the preferred regimen should be treated with clindamycin and quinine.

**NOTE:** Most persons without clinical manifestations of infection do not require treatment unless parasites are seen on thin blood smear for >30 days.

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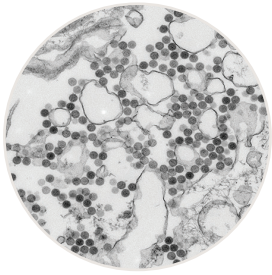
# HEARTLAND VIRUS DISEASE

**AGENT:** Heartland virus



### WHERE FOUND
As of 2017, more than 50 cases of Heartland virus disease have been reported from states in the Midwest and the South.

### INCUBATION PERIOD
Specific ranges are unknown; most patients report a tick bite in the 2 weeks prior to illness.

### SIGNS AND SYMPTOMS
- Fever
- Fatigue
- Decreased appetite
- Headache
- Arthralgia
- Myalgia
- Nausea
- Diarrhea

### GENERAL LABORATORY FINDINGS
- Leukopenia
- Thrombocytopenia
- Mild to moderate elevation of hepatic transaminases

### *BOURBON VIRUS DISEASE*
As of 2017, a limited number of Bourbon virus disease cases have been identified in the Midwest and southern United States. Some people who have been infected later died. Scientists continue to investigate possible symptoms caused by this new virus. Symptoms of people diagnosed with Bourbon virus disease included fever, tiredness, rash, headache, body aches, nausea, and vomiting. General laboratory findings included leukopenia and thrombocytopenia.

## LABORATORY DIAGNOSIS

Molecular and serologic testing for Heartland virus infection can be performed at CDC. There are no commercially available tests for Heartland virus infection in the United States. Please contact your state health department if you have a patient with an acute illness that may be compatible with Heartland virus disease.

## TREATMENT

Treatment of Heartland virus disease is supportive. Many patients diagnosed with the disease have required hospitalization. With supportive care, most people have fully recovered; however, a few older individuals with medical comorbidities have died.

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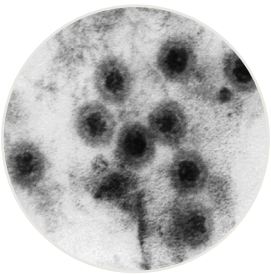
# COLORADO TICK FEVER (CTF)

**AGENT:** Colorado tick fever virus



## WHERE FOUND

The geographic range of Colorado tick fever virus includes the Western United States, primarily 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

Preliminary diagnosis of Colorado tick fever (CTF) is based on signs and symptoms, places and dates of travel, activities, and history of potential tick exposure. Acute samples should be tested by reverse-transcriptase polymerase chain reaction (RT-PCR) to detect viral RNA as antibody production is delayed until 14–21 days after onset of symptoms.

**NOTE:** CSF, cerebrospinal fluid; CNS, central nervous system

| TIMING OF SPECIMEN COLLECTION | SPECIMENS | PREFERRED TEST |
|---|---|---|
| <14 days after symptom onset | Serum (CSF if suspected CNS involvement) | RT-PCR for viral RNA |
| ≥14 days after symptom onset | Serum (CSF if suspected CNS involvement) | Antibody testing*; consider RT-PCR for samples from days 14–21 |

*If possible, acute and convalescent samples, collected at least 2 weeks apart, with the convalescent sample collected at least 3 weeks after symptom onset, should be obtained to look for seroconversion or a 4-fold rise in antibody titers typically using a plaque reduction neutralization test (PRNT).

**NOTE:** CTF testing is available at some commercial and state health department laboratories and at CDC. Contact your state or local health department for assistance with diagnostic testing. CTF cases are reportable to local public health authorities in certain states.

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# POWASSAN VIRUS DISEASE

**AGENT:** *Powassan virus*

## WHERE FOUND

Most cases have occurred primarily in northeastern states and the Great Lakes region. Less frequently, cases have been identified in Mid-Atlantic States.

## INCUBATION PERIOD

1–4 weeks

## SIGNS AND SYMPTOMS

- Fever, headache, vomiting, and generalized weakness
- Usually progresses to meningoencephalitis. 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

- Primarily through testing available at CDC and selected state health departments; limited commercial testing.
- Measurement of virus-specific IgM antibodies in serum or CSF. Cross-reaction with other flaviviruses (e.g., West Nile, dengue, or St. Louis encephalitis 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 this method should not be used to rule out the diagnosis, as antibodies are often present at the onset of neuroinvasive signs and symptoms. RT-PCR might be more appropriate for very acute samples or samples obtained from patients who are immunocompromised.

## TREATMENT

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

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# TICKBORNE DISEASES ABROAD

## AFRICAN TICK BITE FEVER (ATBF)

**AGENT:** *Rickettsia africae*

African tick bite fever (ATBF) is the most commonly diagnosed rickettsial disease among returning international travelers. ATBF is transmitted by *Amblyomma hebraeum* and *A. variegatum* ticks. Travel-associated cases of ATBF often occur in clusters with exposure during activities such as safari tours, game hunting, and bush hiking.

### WHERE FOUND

Sub-Saharan Africa, Caribbean (French West Indies), and Oceania

### INCUBATION PERIOD

Typically 5–7 days but may be as long as 10 days

### SIGNS AND SYMPTOMS

ATBF is typically a mild-to-moderate disease; no known deaths are attributable to infection with *R. africae*. ATBF is almost always associated with an inoculation eschar (see *R. parkeri* rickettsiosis) at the site of tick attachment. Multiple eschars are described in approximately 20–50% of patients with ATBF.

Several days after eschar(s) appear, the following can develop:

- Fever
- Headache
- Myalgia
- Regional lymphadenopathy
- Rash (generalized with maculopapular or vesicular eruptions)

### GENERAL LABORATORY FINDINGS

- Similar to other *Rickettsia,* see *R. parkeri* rickettsiosis.

### LABORATORY DIAGNOSIS

Confirmation of the diagnosis is based on laboratory testing, but antibiotic treatment should not be delayed pending laboratory confirmation.

- ATBF can be confirmed using IFA or detection of Rickettsial DNA by PCR of eschar swab, skin biopsy, or whole blood. See *R. parkeri* rickettsiosis.
- ATBF can be confirmed by comparing acute and convalescent (taken 4–6 weeks following illness onset) samples for evidence of seroconversion in IgG antibodies.

### TREATMENT

See RMSF treatment.

# LYME DISEASE (EUROPE AND ASIA)

**AGENTS:** *Borrelia afzelii, B. garinii, B. burgdorferi* sensu stricto, and *B. bavariensis* (previously considered a variant of *B. garinii)*

Outside North America, *Borrelia* spp. that cause Lyme disease are transmitted through the bite of infected *Ixodes ricinus* and *I. persulcatus* ticks

## WHERE FOUND

In Europe, Lyme disease is endemic from southern Scandinavia into the northern Mediterranean countries of Italy, Spain, Portugal, and Greece and east from the British Isles into central Russia. Incidence is highest in Central and Eastern European countries. In Asia, infected ticks occur from western Russia through Mongolia, northeastern China, and Japan; however, human infection appears to be uncommon in some of these areas.

## INCUBATION PERIOD

3–30 days

## SIGNS AND SYMPTOMS

Outside of North America, most infections are caused by *B. afzelii, B. garinii, B. burgdorferi* sensu stricto, and *B. bavariensis* (previously considered a variant of *B. garinii),* with each causing somewhat different clinical manifestations.

As in the United States, the erythema migrans (EM) rash is the most common early manifestation; later neurologic, cardiac, and rheumatologic disease may occur. In European Lyme disease, the EM rash may spread more slowly and is less commonly accompanied by systemic symptoms. Atrophic skin lesions (acrodermatitis chronica atrophicans) are a frequent late manifestation of infection with *B. afzelii.* In Lyme disease caused by *B. garinii,* some individuals may develop Bannwarth syndrome, a severe neuroborreliosis characterized by radiculopathy, neuropathy, and lymphocytic meningitis.

## LABORATORY CONFIRMATION

Antibodies to *Borrelia* species that cause Lyme disease outside the United States may not be reliably detected by all tests used in the United States. Providers who suspect internationally-acquired Lyme disease should use diagnostic tests that have been validated for these species.

## TREATMENT

See Lyme disease treatment.

## REFERENCES

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# TICKBORNE ENCEPHALITIS (TBE)

**AGENT:** Tick-borne encephalitis virus

TBE is transmitted through the bite of infected *Ixodes ricinus* and *I. persulcatus* ticks.

## WHERE FOUND

Endemic in focal areas of Europe and Asia, extending from western and northern Europe through to northern and eastern Asia. The highest disease incidence has been reported from the Baltic states, Slovenia, and Czech Republic. TBE may also be acquired by ingestion of unpasteurized dairy products from infected goats, sheep, or cows.

## INCUBATION PERIOD

8 days (range, 4–28 days)

## SIGNS AND SYMPTOMS

TBE disease often presents with mild illness but can cause neuroinvasive disease (i.e., aseptic meningitis, encephalitis). The course of illness can be monophasic or biphasic. If biphasic, the two phases are:

- First phase: nonspecific febrile illness with headache, myalgia, and fatigue. Usually lasts for several days and may be followed by an afebrile and relatively asymptomatic period.
- Second phase: central nervous system involvement. Findings depend on the specific presentation but might include meningeal signs, altered mental status, cognitive dysfunction, ataxia, rigidity, seizures, tremors, cranial nerve palsies, and limb paresis.

## LABORATORY CONFIRMATION

During the first phase of the illness, TBE virus or viral RNA can sometimes be detected in serum samples by virus isolation or RT-PCR. However, by the time neurologic symptoms are recognized, the virus or viral RNA is usually undetectable. Therefore, virus isolation and RT-PCR should not be used to rule out a diagnosis of TBE. Clinicians should contact their state or local health department or CDC's Division of Vector-Borne Diseases (970-221-6400) for assistance with diagnostic testing.

## TREATMENT

There is no specific antiviral treatment for TBE; therapy consists of supportive care and management of complications.

## PREVENTION

Inactivated TBE vaccine (manufactured as TICOVAC) is licensed and available in the United States. This vaccine is approved for use in people aged 1 years and older and is administered as a three-dose series.

TBE vaccine is recommended for persons who are moving or traveling to a TBE-endemic area and will have extensive exposure to ticks based on their planned outdoor activities and itinerary. In addition, TBE vaccine may be considered for persons traveling or moving to a TBE-endemic area who might engage in outdoor activities in areas ticks are likely to be found

# ADDITIONAL TRAVEL-ASSOCIATED TICKBORNE INFECTIONS

| DISEASES AND ETIOLOGIC AGENTS | GEOGRAPHIC LOCATION AND ADDITIONAL RISK FACTORS |
|---|---|
| Mediterranean spotted fever (also known as boutonneuse fever) | Europe (Mediterranean basin), Middle East, Indian subcontinent, and Africa. Caused by *Rickettsia conorii,* symptoms include fever, headache, muscle pain, eschar (usually single), and rash. It is typically a moderately severe illness, and can be fatal. |
| Crimean-Congo hemorrhagic fever<br>*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<br>*Omsk hemorrhagic fever virus* | Southwestern Russia. May also be acquired by direct contact with infected muskrats. |
| Kyasanur Forest disease | Southern India, Saudi Arabia (aka Alkhurma disease in Saudi Arabia). Typically associated with exposure while harvesting forest products. |

## 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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# TICK BITES/PREVENTION

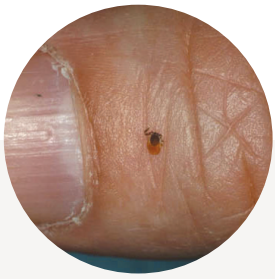
## TICK BITE PREVENTION

1. Know where to expect ticks. Ticks live in grassy, brushy, or wooded areas, or on animals. Spending time outside walking your dog, camping, gardening, or hunting could bring you in close contact with ticks. Many people get ticks in their own yard or neighborhood. Soft ticks that spread tickborne relapsing fever (TBRF) most often live in caves and rodent-infested rustic cabins.
2. Use Environmental Protection Agency (EPA)-registered insect repellents containing DEET, picaridin, IR3535, oil of lemon eucalyptus, para-menthane-diol, or 2-undecanone. Treat clothing and gear, such as boots, pants, socks, and tents with products containing 0.5% permethrin.
3. Treat dogs for ticks as recommended by a veterinarian.
4. 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.
5. Shower soon after being outdoors.

For more tips, see www.cdc.gov/lyme/prev/.

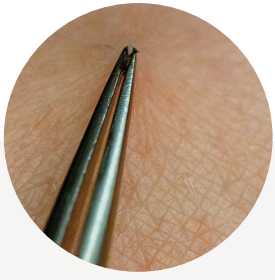
## TICK REMOVAL

1. Use fine-tipped tweezers to grasp the tick as close to the skin's surface as possible. The key is to remove the tick as soon as possible. Avoid 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 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 REMOVAL, STEP 1**
Photo courtesy of Mike Wren, NY State Department of Health



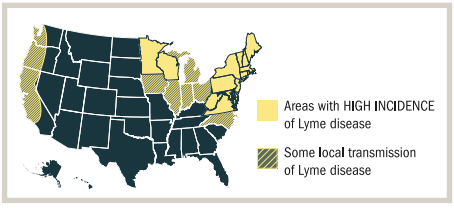
**TICK REMOVAL, STEP 2**
Photo courtesy of Mike Wren, NY State Department of Health

# LYME DISEASE PROPHYLAXIS AFTER TICK BITE

In areas that are highly endemic for Lyme disease, a single prophylactic dose of doxycycline (200 mg for adults or 4.4 mg/kg for children of any age weighing less than 45 kg) may be used to reduce the risk of acquiring Lyme disease after a high-risk tick bite.

Benefits of prophylaxis may outweigh risks when **all of the following circumstances are present:**

1. Where the tick bite occurred, are ticks likely to be infected with *Borrelia burgdorferi?*




2. Was the tick removed within the last 72 hours?

3. Was the tick's body engorged with blood (not flat)?


4. Was the tick an *Ixodes* (blacklegged) tick?


5. Is doxycycline safe for the patient? Considerations include allergy to doxycycline, pregnancy, and lactation.

**Antibiotic treatment following a tick bite is not recommended as a means to prevent anaplasmosis, babesiosis, ehrlichiosis, Rocky Mountain spotted fever, or other rickettsial diseases.** 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.

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Harms MG, et al. A single dose of doxycycline after an *Ixodes ricinus* tick bite to prevent Lyme borreliosis: An open-label randomized controlled trial. *J Infect.* 2021;82(1):98-104.

**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

Based on "Tickborne Diseases in Massachusetts: A Physician's Reference Manual," produced by collaboration between MDPH, Nancy Shadick, MD, MPH, and Nancy Maher, MPH of the RBB Arthritis and Musculoskeletal Diseases Clinical Research Center at Brigham and Women's Hospital and Dennis Hoak, MD, of Martha's Vineyard Hospital.

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