

Arthropod-Borne Diseases: The Camper's Uninvited Guests

GREGORY JUCKETT¹

¹West Virginia University School of Medicine, Morgantown, WV 26506

ABSTRACT Arthropod-borne diseases are a major problem whenever outdoor activities bring arthropods and people into contact. The arthropods discussed here include arachnids (ticks) and insects. Most arthropod bites and stings are minor, with the notable exception being bee-sting anaphylaxis. Ticks cause the most disease transmission. Key hard tick vectors include black-legged (*Ixodes*), dog (*Dermacentor*), and lone star (*Amblyomma*) ticks, which transmit Lyme and various rickettsial diseases. Insect repellents, permethrin sprays, and proper tick inspection reduce this risk significantly. Lyme disease and the milder southern-tick-associated rash illness (STARI) are characterized by the erythema migrans rash followed, in the case of Lyme disease, by early, disseminated, and late systemic symptoms. Treatment is with doxycycline or ceftriaxone. Indefinite treatment of "chronic Lyme disease" based on subjective symptoms is not beneficial. Rickettsial diseases include ehrlichiosis, anaplasmosis, and Rocky Mountain spotted fever, which are characterized by fever, headache, and possible rash and should be empirically treated with doxycycline while awaiting laboratory confirmation. Tularemia is a bacterial disease (*Francisella*) spread by ticks and rabbits and characterized by fever and adenopathy. Treatment is with gentamicin or streptomycin. Babesiosis is a protozoal disease, mimicking malaria, that causes a self-limited flu-like disease in healthy hosts but can be life threatening with immune compromise. Treatment is with atovaquone and azithromycin. Other tick-related conditions include viral diseases (Powassan, Colorado tick fever, heartland virus), tick-borne relapsing fever (*Borrelia*), and tick paralysis (toxin). Mosquitoes, lice, fleas, and mites are notable for their annoying bites but are increasingly significant disease vectors even in the United States.

INTRODUCTION

Arthropods are the invertebrate phylum that includes both the eight-legged arachnids (ticks, mites, and spiders) and the six-legged insects (mosquitoes, ants, bees, and wasps). Leisure-time activity frequently brings people in contact with these pests, so bites and stings are often part

of the price paid for outdoor fun. Most bites and stings are simply painful nuisances that resolve without treatment. Unfortunately, some arthropods, most notably ticks, pose the risk of transmitting serious infectious diseases such as Lyme disease (*Borrelia*) and rickettsial infections. This article will focus primarily on North American tick-borne diseases and syndromes. In the tropics, mosquitoes and other arthropods are a major source of disease transmission, but a few mosquito and other arthropod-borne North American diseases (e.g., babesiosis and West Nile disease) also merit discussion. Climate change and global transportation have the potential to change disease patterns, and many so-called tropical diseases are moving north or appearing in new areas.

A travel history is a vital, but often neglected, part of the medical interview. Most arthropod-borne illnesses are associated with the summer-time activities of camping and hiking. Certain geographic locations are well known "hot spots" for certain diseases (e.g., Nantucket Island for babesiosis). A tick bite history is often helpful, especially if an engorged tick (attached >24 hours) is found and if rash and fever are present. Because some ticks are quite small and easily overlooked, however, the absence of a tick bite history in no way excludes the presence of Lyme and other tick-borne diseases.

Received: 25 November 2014, **Accepted:** 6 February 2015,
Published: 31 July 2015

Editor: David Schlossberg, Philadelphia Health Department, Philadelphia, PA

Citation: Juckett G. 2015. Arthropod-borne diseases: the camper's uninvited guests. *Microbiol Spectrum* 3(4):IOL5-0001-2014. doi:10.1128/microbiolspec.IOL5-0001-2014.

Correspondence: Gregory Juckett, gjuckett@hsc.wvu.edu

© 2015 American Society for Microbiology. All rights reserved.

TICK SPECIES AND DISEASE OVERVIEW

There are two major types of tick: hard (family *Ixodidae*) and soft (family *Argasidae*). The hard ticks are the most medically important types and have a shield-like scutum with the head being visible from above. These are the familiar ticks in the underbrush that latch onto hikers. Soft ticks tend to be nest parasites with a leathery back which hides the head when viewed from above.

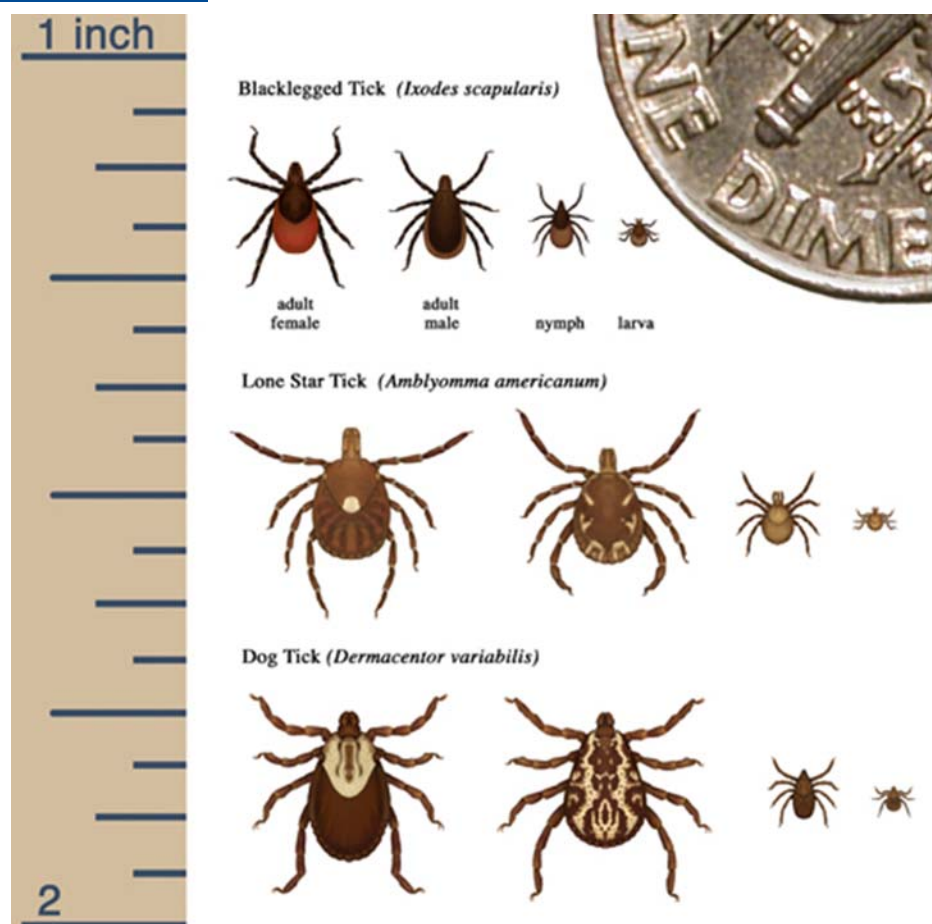
Common hard ticks in the United States include the tiny black-legged or deer ticks (*Ixodes scapularis*, *Ixodes pacificus*) which spread Lyme disease, anaplasmosis, and babesiosis. Powassan encephalitis in the northern United States has been associated with the woodchuck tick (*Ixodes cookei*) (Fig. 1).

The common American dog tick (*Dermacentor variabilis*) and the brown dog tick (*Rhipicephalus sanguineus*) spread Rocky Mountain spotted fever

(RMSF), ehrlichiosis, and tularemia. The similar Pacific coast tick (*Dermacentor occidentalis*) also transmits these diseases and has recently been linked to 364D rickettsiosis (*Rickettsia phillipi*) in California. The lone star tick (*Amblyomma americanum*) of the south-east transmits southern-tick-associated rash illness (STARI), a milder Lyme-like infection with a circular erythema migrans rash, headache, and fever. It is also the vector for ehrlichiosis and tularemia. Lone star tick bites may even provoke an alpha galactidase sensitivity in some of its victims, resulting in severe allergic reactions after red meat ingestion.

The major soft tick of medical importance in the United States is the pajaroella tick (*Ornithodoros coriaceus*) of the southwest, which is associated with localized pain and necrosis at the bite site. Tick-borne relapsing fever (*Borrelia hermsii*) is also associated with these western soft ticks.

FIGURE 1 Tick Identification “Relative sizes of several ticks at different life stages.” Courtesy of United States Centers for Disease Control and Prevention. [doi:10.1128/microbiolspec.IOL5-0001-2014.f1](https://doi.org/10.1128/microbiolspec.IOL5-0001-2014.f1)



PREVENTION OF TICK-BORNE DISEASES

Preventing tick bites should be a priority for all summer-time activities, especially where children are involved. Spraying outdoor clothing (pants, socks, shirts, sneakers, hats) with permethrin 0.5% spray is the most effective means of keeping ticks off. Permethrin treatment of socks and sneakers reduced tick bites by 75% in one study. Clothing should be sprayed outside until damp and allowed to dry before being worn. The spray remains effective even after multiple washings so a single treatment may be effective for months. Tucking pants into socks before hiking and performing a careful tick check after disrobing each evening should become routine summer-time habits in tick country. Exposed skin can be protected with diethyltoluamide (DEET)-containing repellents, preferably in the 20 to 35% range. DEET repellents are safe if concentrations are kept under 50%, and skin absorption can be further minimized by applying the repellents on top of sunscreen. Combination sunscreen/insect repellent products are not ideal since they wear off at different times. Sustained release repellents such as Ultrathon (35% DEET) can be effective for as long as 12 hours without swimming. Family pets often bring live ticks into the home unless they wear flea collars or get regular flea and tick treatment.

Most ticks crawl about for hours or days before attaching, so time is on the camper's side. A tick has to be engorged with blood, attached for over 24 hours (usually >36 hours), for it to transmit Lyme disease. If an attached tick is discovered, it should be grasped with forceps or a tick-removal device, as close to the skin as possible, and gently pulled off without twisting. It can then be flushed down the toilet. Using alcohol, heat, nail polish remover, or petroleum jelly on the tick may actually increase the risk of disease transmission.

LYME DISEASE

Lyme disease is the best known and probably the most feared tick-borne illness. It is by far the most common vector-borne illness in the United States, with over 27,200 cases reported in 2013. The vectors are the black-legged or deer ticks, *I. scapularis* and *I. pacifica*, the nymphs of which are the size of poppy seeds. Because deer tick nymphs are so tiny, there is often no reported history of tick bite. The disease is most frequently acquired in the north-eastern, coastal mid-Atlantic, upper Midwest, and Pacific-coast states (see Fig. 2), and it takes its name from the city of Lyme, CT, where it was first described in 1975. Much of the so-called Lyme disease of south-eastern states is probably STARI, a similar but

much milder, as yet unidentified infection spread by the lone star tick. Adult deer ticks live on deer or horses, while the nymphs are usually parasites of white-footed mice, which carry the Lyme bacteria. Humans and other mammals are only incidentally infected. Although there is controversy over how long the tick must be attached to transmit the infection, most experts believe this time period to be >24 hours.

Lyme disease is caused by the spirochete *Borrelia burgdorferi*, identified in 1981 by the entomologist Willy Burgdorfer. The disease has three stages: early localized infection, early disseminated infection, and late disseminated infection (Table 1). Most cases occur between May and October, reflecting the tick-bite season, with an average incubation of 1 week (potentially up to 1 month) before onset of the characteristic rash.

Stage 1 or early infection is manifested in 80% of cases by the appearance of erythema migrans, a circular expanding red rash at the site of the tick bite (Fig. 3). The rash starts as a red indurated patch or plaque that often, but not always, develops a bull's-eye pattern, with alternating red and pale bands. It usually enlarges over a 3-week period and then gradually fades away. There is no scaling or local tenderness. At this time, the patient often complains of flu-like symptoms with malaise, headache, and fever. Lyme testing may still be negative at this stage because antibodies have not yet developed.

Stage 2 is early disseminated Lyme disease, where *Borrelia* organisms spread via the circulation to affect distant sites. Headache, lymphadenopathy, and conjunctivitis may be evident, and recurrent erythema migrans-type rashes crop up in half the patients. Malaise and fatigue persist with migratory joint pains. The sudden onset of unilateral facial paralysis (Bell's palsy) or peripheral radiculoneuropathy should prompt immediate testing for Lyme disease. Cardiac involvement (<10%) may occur with myocarditis or atrioventricular block.

Stage 3 or late disseminated disease may produce disabling arthritis or additional neurological disorders such as encephalopathy, chronic pain, keratitis, and polyneuropathy. Bilateral knee (or other weight-bearing joint) arthritis is common. "Chronic Lyme disease" is a misnomer, and symptoms persisting after treatment should now be considered "post Lyme disease syndrome." Patients may be started on indefinite antibiotic treatments with no evidence of ongoing infection and no set end points. At least three double-blind, placebo-controlled trials demonstrated that additional antibiotic treatment for persistent subjective symptoms of appropriately treated patients poses substantial risks with little, if any, benefit. Most conventional infectious disease experts

Reported Cases of Lyme Disease—United States, 2013

One dot is placed randomly within the county of residence for each confirmed case. Though Lyme disease cases have been reported in nearly every state, cases are reported based on the county of residence, not necessarily the county of infection.

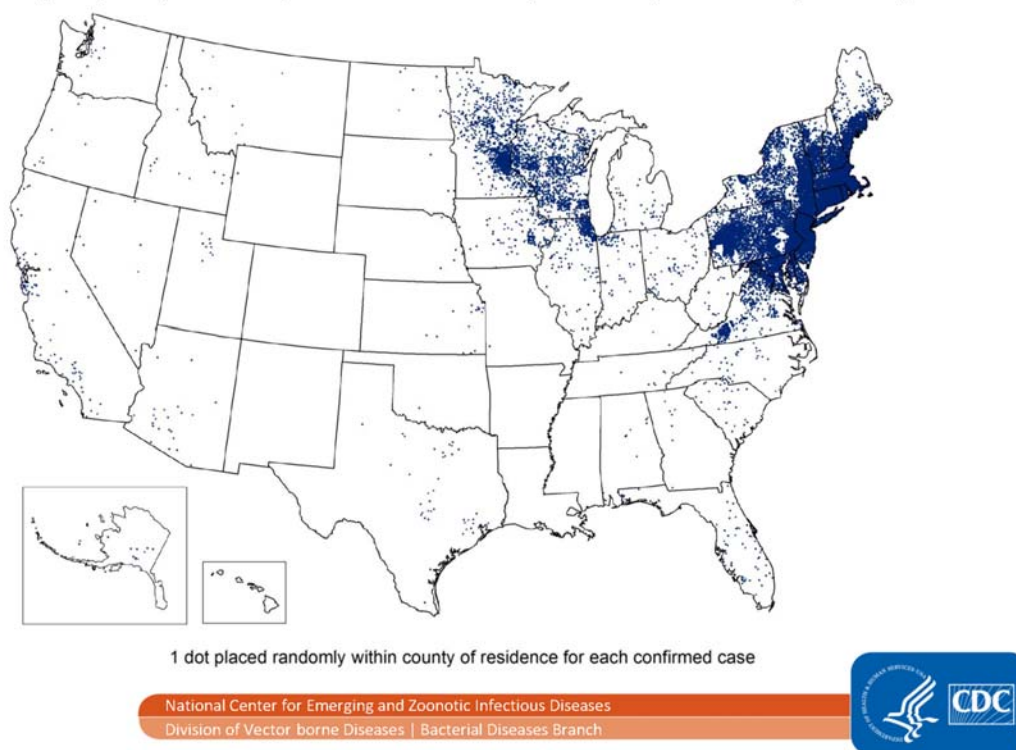


FIGURE 2 Map of Lyme disease distribution: “Reported cases of Lyme disease – 2013.”
Courtesy of United States Centers for Disease Control and Prevention. [doi:10.1128/microbiolspec.IOL5-0001-2014.f2](https://doi.org/10.1128/microbiolspec.IOL5-0001-2014.f2)

believe that even late-stage Lyme disease can be eradicated by 28 days of an appropriate antibiotic treatment.

Diagnosis of Lyme disease is made through a two-step serological testing program for antibodies. Initial screening is done through enzyme-linked immunosorbent assay testing for IgM and IgG Lyme antibodies, followed by more specific, confirmatory Western blot testing if the enzyme-linked immunosorbent assay test is positive or equivocal. Antibodies take 2 to 3 weeks to become detectable after disease transmission, so testing may be negative at the time the rash first appears. Antibiotic treatment of erythema migrans is recommended, but prompt treatment also diminishes the antibody response. PCR testing to detect *Borrelia* DNA is seldom recommended for routine cases. Urine tests for Lyme disease are unreliable, and the organism cannot be cultured. Lyme disease can be challenging to diagnose, because 20% of patients lack the characteristic rash, and similar symptoms occur with rheumatoid arthritis, lupus, fibromyalgia, chronic fatigue, and neurodegenerative disease.

Testing to exclude Lyme disease should be considered when these conditions fail to respond to therapy.

Treatment of early-stage Lyme disease and STARI is with doxycycline 100 mg twice daily for 14 days. Amoxicillin or cefuroxime are alternatives for pregnant women and children <9 years of age, in whom doxycycline is contraindicated. Oral therapy for patients with isolated Bell’s palsy, arthritis, or mild carditis should be continued until clinical improvement occurs (14 to 28 days). Later-stage Lyme disease with persistent arthritis, severe carditis or neurologic symptoms (meningitis, encephalitis) should be treated with parenteral penicillin G, ceftriaxone, or cefotaxime for 14 to 28 days.

Patients frequently ask for prophylactic Lyme disease treatment after removing an engorged tick. A single prophylactic dose of doxycycline 200 mg by mouth is reasonable if several criteria can be met: the engorged tick can be identified as *I. scapularis*, it has been attached for over a day, prophylaxis can be started within 72 hours of tick removal, local *Ixodes* tick infection

TABLE 1 Major clinical manifestations of Lyme disease^a

Stage 1: early localized infection
Erythema migrans rash
Headache
Arthralgias
Regional lymphadenopathy
Stage 2: early disseminated infection
Recurrent erythema migrans
Migratory bone and joint pain
Meningitis
Bell's palsy
Peripheral radiculoneuropathy
Atrioventricular block
Myocarditis/pancarditis
Conjunctivitis
Mild hepatitis
Hematuria/proteinuria
Malaise and fatigue
Stage 3: late infection
Acrodermatitis chronica atrophicans
Prolonged arthritis
Chronic neurological syndromes
Keratitis

^aAdapted from: Steere AC. 2001. Lyme disease. *New Engl J Med* 345:115–125; Wormser GP, Dattwyler RJ, Shapiro ED, Halperin JJ, Steere AC, Klemperer MS, Krause PJ, Bakken JS, Strle F, Stanek G, Bockenstedt L, Fish D, Dumler JS, Nadelman RB. 2006. The clinical assessment, treatment and prevention of Lyme disease, human granulocytic anaplasmosis, and babesiosis: clinical practice guidelines by the Infectious Diseases Society of America. *Clin Infect Dis* 43:1089–1134

rates are 20% or greater, and the patient can safely take doxycycline. Many physicians factor in the level of patient anxiety when deciding to prescribe prophylaxis.

Vaccination would be an ideal option in high-risk areas. A human Lyme disease vaccine (LYMErix) was approved in 1998 but withdrawn in 2002 due to poor sales and public concern about autoimmune side effects, although these were never substantiated. At present, the only Lyme disease vaccines available are for pet dogs.

Lyme disease treatment duration is currently mired in controversy, which results in a great deal of public confusion. Some Lyme practitioners believe there is a subset of patients who require ongoing antibiotic treatment that must be continued as long as symptoms persist. An entire Lyme disease industry, a form of alternative medicine, has emerged with unconventional labs and treatments. Some patients have died from the consequences of overtreatment. Many Lyme symptoms (fatigue, body aches, mood disorders) are subjective and have other associations. Thus, in the words of Feder et al. in a “Critical Appraisal of ‘Chronic Lyme Disease,’” chronic Lyme disease is the “latest in a series of syndromes . . . postulated in an attempt to attribute medically unexplained symptoms to particular infections.” Chronic

Lyme patients actually have “post Lyme disease syndrome” and most of these patients will improve in 6–12 months without any further treatment.

There is also controversy about possible Lyme transmission outside of the key U.S. hot spots. Current understanding of STARI in the U.S. South is that it presents with erythema chronicum migrans (ECM) rash, fever, and myalgia but lacks the long-term consequences (arthritis, neurologic disease) of true Lyme disease. The causative agent of STARI has yet to be identified. It must be recognized that many tick-borne infections have recently been discovered, and undoubtedly more will emerge with further research.

EHRlichiosis AND ANAPLASMOSIS

Some tick-borne infections attack human white blood cells. Ehrlichiosis, or human monocytic ehrlichiosis (HME), is a tick-borne disease spread by the rickettsial organism *Ehrlichia chaffeensis*. It is spread by the dog tick *Dermacentor variabilis* and the lone star tick *A. americanum*. Anaplasmosis, or human granulocytic anaplasmosis (HGA), is a similar disease caused by the rickettsia *Anaplasma phagocytophilum*, which

FIGURE 3 Erythema migrans “bull’s-eye” rash. Courtesy of CDC/James Gathany (CDC-PHIL ID#9875). doi:10.1128/microbiolspec.IOL5-0001-2014.f3



attacks human granulocytes instead of monocytes. It is transmitted by the same black-legged or deer *Ixodes* ticks which spread Lyme disease. The incubation period for both HGA and HME ranges from 2 days to 3 weeks. Both conditions present with fever, myalgia, headache, hepatosplenomegaly (with elevated liver function tests), thrombocytopenia, and leukopenia (Table 2). The leukopenia is a lymphopenia in HME and a neutropenia in HGA. Children with HME may have a generalized maculopapular or petechial rash (resembling that of RMSF), but the physical exam is usually normal for HME patients (without rash) and most HGA patients. However, peripheral neuropathies and unilateral facial paralysis (Bell's palsy) sometimes develop in HGA, just as in Lyme disease. Intracytoplasmic inclusions (morulae) can be identified in infected monocytes (HME) or neutrophils (HGA).

Diagnosis is difficult since it depends on a 4-fold or greater increase in antibody titers between acute- and convalescent-phase sera by indirect fluorescent antibody testing. An *E. chaffeensis* antibody titer of 1:64 or greater also confirms the diagnosis of HME.

The treatment for both conditions is oral doxycycline 100 mg twice daily continuing until patients are clinically improved and afebrile for 48 to 72 hours. Rifampin may be an alternative treatment.

ROCKY MOUNTAIN SPOTTED FEVER

RMSF is a severe vasculitic disease caused by *Rickettsia rickettsii*, one of the spotted fever rickettsiae. RMSF also

occurs in South America, where it is also known as Brazilian spotted fever (*febre maculosa*). Although first described in the Rocky Mountains, it is most common in the south-eastern states, where it is spread through the bites of infected dog ticks (*D. variabilis*), brown dog ticks (*R. sanguineus*), or lone star ticks (*A. americanum*). In the western United States, wood ticks (*Dermacentor andersoni*) are the vectors. Only 1% of vector ticks are infected, so most tick bites fail to result in illness. However, infected ticks can transmit disease within 6 to 10 hours of feeding. When infection does occur, symptoms usually start 7 days (1 to 14 days) after the bite. Two thirds of victims are children, and like most tick-borne diseases, it presents between April and September. Unfortunately, the classic RMSF symptom triad of fever, severe headache, and a centripetal, petechial rash along with a helpful history of tick bite is found in less than 18% of cases. Tick bites are only recalled in half to two thirds of cases. Centripetal spread means the rash starts on the extremities (ankles/feet, wrists/hands) and later spreads to the central body or trunk (Fig. 4). Red macules appear 2 to 3 days after the fever starts and quickly turn into petechial lesions. As with Lyme disease, up to 20% of patients lack the rash, so fever and headache alone warrant therapy.

The diagnosis of RMSF should be based on clinical suspicion of tick-borne illness in febrile patients, and empiric treatment should be started as soon as possible, not delaying for confirmation. Thrombocytopenia, leukopenia, and elevated liver function tests may be present, but none of these are specific for RMSF. Confirmation of the diagnosis requires serologic testing (a 4-fold increase in antibody titer between acute and convalescent serum samples), and this usually takes several weeks. A single titer of >1:128 also confirms the diagnosis. Skin biopsy can also be diagnostic. Serologic testing is performed by the CDC or state health departments.

Treatment is with doxycycline, which is continued for 48 to 72 hours after fever resolves. RMSF is an important exception to the rule about not using doxycycline in young children, since the benefits of using this drug far outweigh the risks. Failure to start treatment early enough may result in encephalitis, pulmonary edema, gastrointestinal bleeding, skin necrosis, and coagulopathy. Untreated RMSF has a 20 to 25% mortality rate, which falls to 5% with appropriate treatment (before the fifth day of illness). Because meningococcemia may mimic RMSF, it is common practice to initiate ceftriaxone with doxycycline in suspected cases.

TABLE 2 Comparison of HME and HGA symptoms^a

Sign, symptom, finding	% Patients with HME	% Patients with HGA
Fever	97	93
Myalgia	57	77
Headache	80	76
Malaise	82	94
Nausea	64	38
Arthralgia	41	46
Vomiting	33	26
Diarrhea	23	16
Rash	31	6
Stiff neck	3	21
Confusion	19	17
Leukopenia	62 (lymphopenia)	49 (neutropenia)
Thrombocytopenia	71	71
Elevated liver functions	83	71

^aAdapted from; Dumler JS, Madigan JE, Pusteria N, Bakken JS. 2007. Ehrlichioses in humans: epidemiology, clinical presentation, diagnosis, and treatment. *Clin Infect Dis* 45:S45–S51



FIGURE 4 Child's right hand and wrist displaying the characteristic spotted rash of Rocky Mountain spotted fever. Courtesy of CDC (CDC-PHIL ID #1962). [doi:10.1128/microbiolspec.IOL5-0001-2014.f4](https://doi.org/10.1128/microbiolspec.IOL5-0001-2014.f4)

TULAREMIA

Tularemia, or “rabbit fever,” is an uncommon zoonotic bacterial infection caused by *Francisella tularensis*. There are several subspecies of this Gram-negative coccobacillus, with *F. tularensis* subsp. *tularensis* (type A) being the most virulent and occurring in North America. Tick bites can spread this disease, but it can also be transmitted by contact with infected animals (usually rabbits or hares), animal bites, or the ingestion of infected uncooked meat. Wearing rubber gloves when skinning rabbits reduces the risk. Dog and wood ticks (*Dermacentor* spp.) and lone star ticks (*Amblyomma*) are the usual vectors, but fleas, mites, and even mosquitoes also transmit tularemia. The organism is highly infectious, and its incubation period is only 3 to 4 days (1- to 21-day range). Most cases occur in the south-central United States (Missouri, Arkansas, and Oklahoma).

Typically, tularemia presents as a febrile illness with adenopathy in someone who has had contact with rabbits or infected meat. There are six variations in clinical presentation (Table 3), depending on how the organism gains entry to the body. By far the most common presentation is ulceroglandular disease, where a painful papule at the tick bite site ulcerates and is followed by regional lymphadenitis (Fig. 5). Other presentations are glandular (adenopathy, but lacking the skin ulcer), oculoglandular (eye entry), oropharyngeal (oral exposure with sore throat), typhoidal (acute septicemia from various exposures including oral), and

pneumonic (inhalation). Simply mowing grass around a dead animal has resulted in pneumonic infection. The typhoidal and pneumonic forms have the highest mortality rates.

The diagnosis should be suspected clinically and antibiotics started prior to laboratory confirmation. History of tick bite or rabbit exposure in the setting of febrile illness with adenitis should raise concerns about tularemia. Diagnosis is confirmed by a 4-fold increase in antibody titer between acute and convalescent sera (obtained 2 weeks apart) or a titer of >1:160. Antibodies develop only after the second week of illness. Culture is difficult and poses a risk to lab workers (biosafety level 3 requirements). There is no risk of person-to-person transmission, but local health departments must be notified of any confirmed cases.

Aminoglycosides (gentamicin, streptomycin) or ciprofloxacin are the recommended treatments for tularemia. Gentamicin is often substituted for streptomycin because it is easier to obtain. A 7- to 10-day course, continuing

TABLE 3 Common forms of tularemia

Ulceroglandular (skin ulcer with adenopathy)	50%
Glandular (adenopathy without skin lesion)	9%
Oculoglandular (conjunctival nodules with adenopathy)	1%
Oropharyngeal (sore throat with adenopathy)	2%
Typhoidal (septicemia with possible meningitis)	8%
Pneumonic (inhalation, usually lab workers)	15%
Unclassified	15%



FIGURE 5 A tularemia lesion on the dorsal skin of the right hand. Courtesy of CDC/ Dr. Brachman (CDC PHIL ID # 2037). [doi:10.1128/microbiolspec.IOL5-0001-2014.f5](https://doi.org/10.1128/microbiolspec.IOL5-0001-2014.f5)

for at least 4 days after resolution of fever, is current practice. Although doxycycline appears effective, it has a higher rate of relapse. While a vaccine has been developed for high-risk groups, it is not commercially available. Tularemia is highly infectious, is easy to aerosolize, and has been studied as a potential bioterrorism agent.

BABESIOSIS

Babesia microti is a protozoan parasite that closely mimics malaria, causing a flu-like illness that may last for weeks. Although babesiosis was initially discovered in Europe, the first U.S. cases occurred on Nantucket Island in 1969, spread by the black-legged tick *I. scapularis*, the same tick that harbors Lyme disease. Blood transfusions also spread the infection, with *Babesia* being the most common disease transmitted in this manner. Southern New England and the northern Midwest are considered the highest-risk areas. The incubation period is 1 to 4 weeks after tick exposure and 1 to 9 weeks (up to 6 months) after transfusion of infected blood.

Most cases resemble a self-limited flu-like illness with fever/chills which can last several weeks. Although the disease may be nearly asymptomatic in healthy patients, immune-suppressed individuals (e.g., those using tumor necrosis factor alpha inhibitors, status post splenectomy) become very ill and may even die. As in malaria, there is a hemolytic anemia, lymphopenia, and thrombocytopenia. Giemsa-stained blood smears may demonstrate ring forms inside infected red blood cells that closely mimic those of *falciparum* malaria. The occasional finding of “Maltese cross” formations (tetrads of merozoites) within red cells confirms the diagnosis,

but repeated blood smears are needed since parasitemia is usually low (<1%) early in the illness (Fig. 6). PCR testing can detect *Babesia* DNA in blood, and indirect immunofluorescence assays detect *Babesia* Ig M within 2 weeks of symptom onset. A malaria-like summer or posttransfusion illness without a foreign travel history should point to babesiosis.

Treatment is usually with oral atovaquone and azithromycin for 7 to 10 days for mild to moderate disease. Severe disease is treated with intravenous clindamycin and oral quinine for 7 to 10 days. Immune-suppressed patients may require up to 6 weeks of therapy to prevent relapse. Quinine is avoided in pregnancy.

OTHER TICK SYNDROMES

Nonspecific fevers are common after tick bites, and several studies suggest that U.S. tick-borne infections are much more common than previously realized. In northwest Wisconsin, 27% of patients evaluated for fever without rash had evidence of tick-borne infection. A military study in Arkansas demonstrated that 15% of soldiers had laboratory evidence of antibodies to tick-borne diseases after training exercises. The bulk of these flu-like illnesses go unreported, because patients are often misdiagnosed or else fail to seek attention.

Powassan viral encephalitis is a rare but serious tick-borne infection found primarily in Minnesota, Wisconsin, and New England but is named after Powassan, Ontario, Canada, where it was first described. Encephalitis survivors frequently have severe neurologic sequelae, and there is no treatment. Vectors are the groundhog tick, *I. cookei*, and the black-legged tick, *I. scapularis*. Transmission of the virus may take place within 15 minutes of tick attachment, unlike most tick-borne illnesses, which require >24 hours.

Tick-borne relapsing fever is a *Borrelia* infection transmitted by long-lived soft ticks (*Ornithodoros* spp.) inhabiting rodent-infested cabins in Western states. *Borrelia hermsii*, *Borrelia turicatae*, and *Borrelia parkeri* have been implicated. *Ornithodoros* ticks attach for less than an hour while their victim is sleeping and are also thought to transmit infection quickly. Finding and removing the rodent nests that harbor the ticks is essential to preventing transmission.

Colorado tick fever is a viral disease (Colorado tick fever virus) transmitted by the Rocky Mountain wood tick, *D. andersoni*. Cases occur in Colorado, Utah, Montana, and Wyoming. Diagnosis, as in most of these tick-borne infections, is through serology. Supportive care is the only recommended treatment.

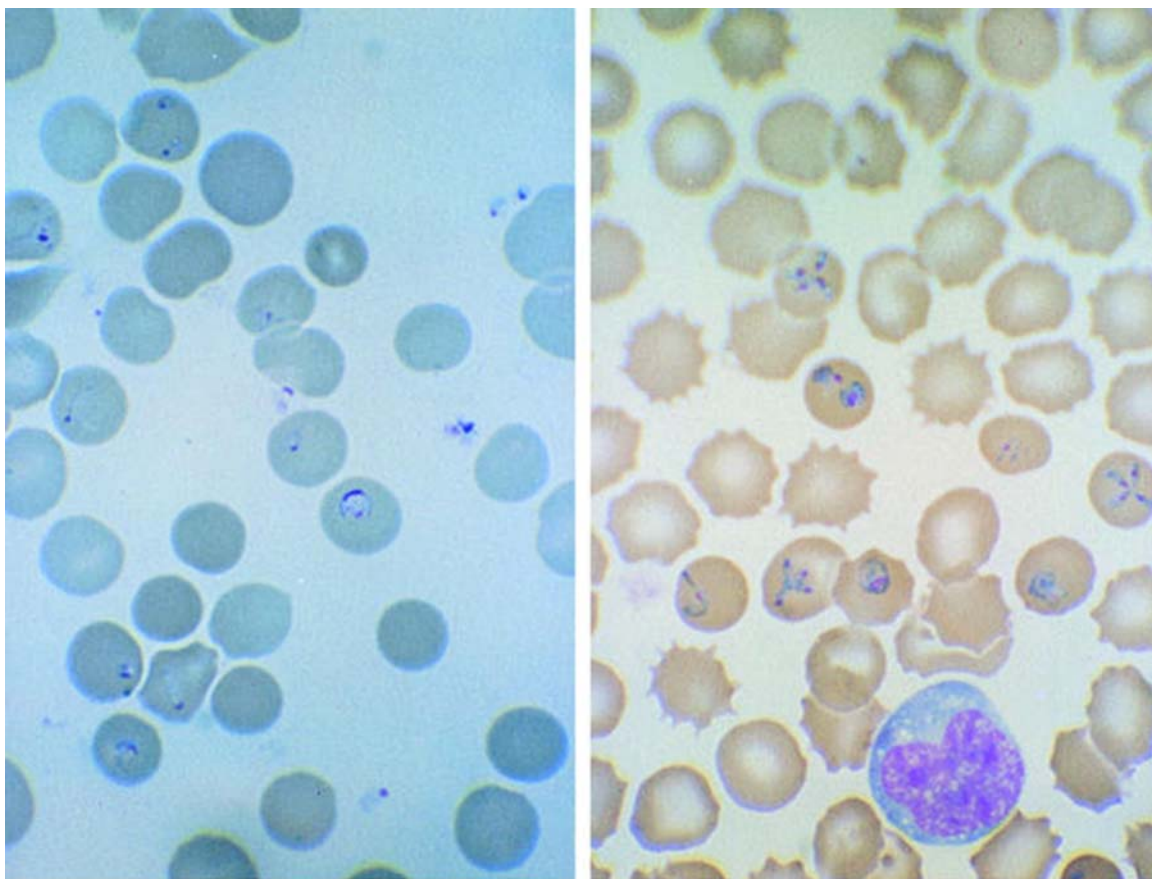


FIGURE 6 Babesia blood smear with ring forms and Maltese cross. (From Rogers W. 2011. *Plasmodium and Babesia*, p 2091-2112. In Versalovic J, Carroll K, Funke G, Jorgensen J, Landry M, Warnock D (ed), *Manual of Clinical Microbiology*, 10th Edition. ASM Press, Washington, DC.) [doi:10.1128/microbiolspec.IOL5-0001-2014.f6](https://doi.org/10.1128/microbiolspec.IOL5-0001-2014.f6)

New tick-borne diseases are constantly being discovered. *Borrelia miyamotoi*, a close relative *B. burgdorferi*, was recently discovered in Minnesota and appears to have the same vector and range as Lyme disease. It has a biphasic fever pattern but is responsive to doxycycline.

The heartland virus, a new potentially fatal phleboviral illness spread by the lone star tick, was identified in Missouri and Tennessee in 2012. Heartland symptoms include fever, headache, fatigue, nausea, diarrhea, leukopenia, and thrombocytopenia, but there are as yet no diagnostic tests available. Other newly discovered regional diseases include 364D rickettsiosis of California spread by the Pacific Coast tick, *D. occidentalis*, and *Rickettsia parkeri* of the Gulf Coast, spread by *Amblyomma maculatum*, the Gulf Coast tick. The cause of STARI in the southeast has yet to be discovered, although it is presumed to be another *Borrelia* species spread by the lone star tick.

Tick paralysis is an ascending paralysis with ataxia that occurs in children (usually under age 10) and pets when an embedded gravid female tick releases neurotoxins from her salivary glands. Symptoms do not start until the tick has been attached for several days. Five North American tick species, including black-legged (*Ixodes*), dog and wood (*Dermacentor* spp.), and lone star ticks (*Amblyomma*), may be responsible. This syndrome resembles the ascending paralysis of Guillain-Barre and is the opposite of the descending paralysis caused by botulism. Motor function quickly returns when the tick is removed. Unfortunately, engorged ticks hidden on the scalp or in an ear canal have resulted in respiratory paralysis and even death.

MOSQUITO-BORNE DISEASES

Mosquito-borne diseases used to be commonplace in the United States (Fig. 7). It is now feared that with



FIGURE 7 *Aedes aegypti* mosquito. Courtesy of CDC/James Gathany (CDC-PHIL ID #9181). [doi:10.1128/microbiolspec.IOL5-0001-2014.f7](https://doi.org/10.1128/microbiolspec.IOL5-0001-2014.f7)

climate change and world travel, they may once again gain prominence. In the United States these diseases are mostly arboviruses (arthropod-borne viruses), with the exception of tularemia, a bacterial disease, spread by both ticks and mosquitoes (Table 4). They cause flu-like symptoms and encephalitis in more severe cases.

West Nile virus from Africa appeared in the New York City area in 1999, taking only 5 years to cross the entire United States. Birds, also infected by mosquitoes, are the reservoir hosts for West Nile virus and helped spread the infection. Eighty percent of West Nile virus cases are subclinical, with symptoms in the remaining 20% consisting of fever, headache, arthralgia, and nausea. Serious neurologic disease (meningitis) occurs in less than 1%. More recently, starting in December 2013, another Eastern Hemisphere mosquito-borne virus, Chikungunya, emerged in the Caribbean and Central America, later spreading to Florida in 2014. This previously occurred with dengue or break bone fever, a similar illness that was once eradicated from the United States only to reemerge in Texas, Hawaii, and south

Florida. Both diseases cause fever and severe arthralgias, often with rash in the case of dengue. For all U.S. mosquito-borne infections, the emphasis is on prevention since the only treatment is supportive care.

LICE-BORNE DISEASES

Body lice are also capable of transmitting disease, but these are usually associated with poor hygiene and crowding rather than outdoor activities. Louse-borne relapsing fever, caused by *Borrelia recurrentis*, is rare in the United States. Typhus (epidemic louse-borne typhus) is caused by *Rickettsia prowazekii* and is also uncommon, although outbreaks have occasionally been associated with flying squirrels. The third louse-borne disease is trench fever, caused by *Bartonella quintana*. Body lice are responsible for all these infections, although *B. quintana* has also been found in head lice in Ethiopia.

FLEA-BORNE DISEASES

Bubonic plague (*Yersinia pestis*) is most associated with epidemics of Black Death in the Middle Ages, but isolated cases still occur in endemic areas of the American West. Most cases are associated with rodent flea exposure from picking up dead flea-infested rodents, such as squirrels or prairie dogs. Much more common is flea-borne or murine (endemic) typhus, spread by infected fleas carrying *Rickettsia typhi* or *Rickettsia felis*. Any flea-ridden mammal, wild or domestic, including dogs and cats, may be involved. Severe headache, fever, and rash mimic RMSF, and the symptoms quickly respond to doxycycline.

MITE-BORNE DISEASES

Mites are tiny eight-legged arthropods. The only significant mite-transmitted infection in the United States is

TABLE 4 Mosquito-borne infections in the United States

Disease	Agent	Vector
Western equine encephalitis	Alphavirus	<i>Culex tarsalis</i> (west of Mississippi), birds/horses
Eastern equine encephalitis	Alphavirus	<i>Culex</i> spp. and <i>Culiseta</i> (eastern U.S.), birds/horses
St. Louis encephalitis	Flavivirus	<i>Culex</i> spp.; elderly at risk
Dengue	Flavivirus, types 1–4	<i>Aedes aegypti</i> , <i>Aedes albopictus</i>
Chikungunya	Alphavirus	<i>A. aegypti</i> , <i>A. albopictus</i>
Venezuelan encephalitis	Alphavirus	<i>Culex</i> spp. rodents/birds/horses
Tularemia	Bacteria: <i>Francisella tularensis</i>	<i>Aedes cinereus</i> , deerflies, and ticks (<i>Ixodes</i> , <i>Dermacentor</i> , <i>Amblyomma</i>)
West Nile virus	Flavivirus	<i>Culex pipiens</i> and others
LaCrosse encephalitis (California serogroup)	Bunyavirus	<i>Aedes triseratus</i> , tree hole mosquito (Appalachia and Midwest); children at risk

rickettsialpox, caused by *Rickettsia akari*, from the Greek word *akari*, meaning “mite.” The pox in the name is because the associated papulovesicular rash closely resembles that of chickenpox. House mice infested with *Liponyssoides sanguineus* mites are the reservoir of infection. When mouse populations are suddenly reduced, mouse mites resort to attacking humans, causing an outbreak. Rickettsial pox is usually a mild, self-limited disease of urban rather than wilderness areas. The incubation period is 10 to 14 days. An eschar forms at the site of the mite bite, followed by fever, headache and a generalized rash with mild illness lasting a week or two. Doxycycline is the treatment of choice.

CHIGGERS

Mites are also a major source of skin irritation with outdoor activities. Chiggers, or “redbugs” (*Trombicula alfreddugesi*), are tiny larval trombiculid mites, which have six legs and which live in grassy areas. They attach themselves to hikers and crawl upward until they reach an area of constricting clothing such as a sock or belt line. Here they insert their stylosome, or biting mouth part, and inject digestive enzymes which provoke a severe allergic reaction, resulting in large red, itchy papules. Classically, these papules cluster along the clothing lines wherever the mites have fed. Contrary to popular opinion, chiggers do not burrow into human skin, although there is a tropical jigger flea (*Tunga penetrans*) which does so. The adult mites have eight legs and are harmless.

Hot showers and laundering of clothing will reduce the severity of chiggers but, once bitten, no treatment is very effective. Home remedies include Vick's VapoRub with added salt applied to the bites. Others use baking soda paste or applied heat from a hair dryer. Applying nail polish to the lesions to try to “suffocate” the chiggers is usually ineffective. It is important to minimize scratching to reduce the risk of secondary infection.

INSECT STINGS: INITIAL- AND LATE-PHASE HYPERSENSITIVITY REACTIONS

Bee stings classically produce a painful wheal at the sting site that spontaneously resolves within a few hours. Bees lose their barbed stingers and die soon afterward, whereas wasps (including yellow jackets) are able to sting repeatedly. Bee stingers are best removed by immediately scraping them off with a credit card, since pinching the venom sac may introduce more venom. Local application of ice and use of oral antihistamines can help reduce pain. In some patients the initial sting

reaction is followed >48 hours later by a localized allergic reaction with swelling, erythema, and heat developing around the sting site. This “late-phase hypersensitivity” reaction closely resembles cellulitis (but is more pruritic than tender) and should be treated with a short course of prednisone rather than antibiotics. Fortunately, localized reactions do not increase the risk of future bee sting anaphylaxis and do not require referral for desensitization. Generalized urticaria after a sting, however, indicate that the patient may be at increased risk for systemic sting reactions in the future. An epinephrine injection device (EpiPen) with referral for desensitization should be prescribed to prevent potential anaphylaxis.

PRACTICAL TIPS

- Suspect tick-borne disease with any summer or fall flu-like illness (headache, fever, arthralgias), whether or not any rash or history of tick bite is present.
- Most tick-borne bacterial infections are caused by *Borrelia* or *Rickettsia* infections, which respond to doxycycline. More than one infection may be present in any given patient. Start treatment empirically based on clinical suspicion since delaying treatment until diagnosis is confirmed worsens outcome.
- Tick bites can be prevented by spraying clothing in advance with permethrin 0.5% spray and using DEET repellents on exposed skin. Tucking pant legs into socks may also keep ticks out. Pets should be treated (flea/tick collars etc.) to prevent them from bringing ticks into the home.
- A thorough tick inspection after summer and fall outdoor activities is essential. Perform a complete body check (including hair) while in the shower. Discarded clothing may also contain ticks and should be laundered immediately.
- Proper tick removal involves grasping the tick with forceps and exerting gentle traction, without twisting, until it detaches. Avoid using heat, petroleum jelly, or alcohol, which may cause the tick to regurgitate. Do not crush the tick. Flushing ticks down the toilet is a safe means of disposal. In most instances, removing a tick within 24 hours of attachment will minimize the likelihood of disease transmission, although exceptions exist (e.g., RMSF).
- Carry an Epi-Pen kit if there is any history of generalized hives or anaphylaxis after bee or wasp stings.

RECOMMENDED READINGS

- Bratton RL, Whiteside JW, Hovan MJ, Engle RL, Edwards FD. 2008. Diagnosis and treatment of Lyme disease. *Mayo Clin Proc* 83:566–571.
- Clark RP, Hu LT. 2008. Prevention of Lyme disease and other tick-borne infections. *Infect Dis Clin North Am* 22:381–396, vii.
- Dana AN. 2009. Diagnosis and treatment of tick infestation and tick-borne diseases with cutaneous manifestations. *Dermatol Ther* 22:293–326.
- Dept. of Health and Human Services CDC. 2014. *Tickborne Diseases of the United States: A Reference Manual for Health Care Providers*, 2nd ed. <http://www.cdc.gov/lyme/resources/TickborneDiseases.pdf>.
- Feder HM, Johnson BJ, O'Connell S, Shapiro ED, Steere AC, Wormser GP, Agger WA, Artsob H, Auwaerter P, Dumler JS, Bakken JS, Bockenstedt LK, Green J, Dattwyler RJ, Munoz J, Nadelman RB, Schwartz I, Draper T, McSweeney E, Halperin JJ, Klemperer MS, Krause PJ, Mead P, Morshed M, Porwancher R, Radolf JD, Smith RP, Sood S, Weinstein A, Wong SJ, Zemel L, Group AHILD. 2007. A critical appraisal of "chronic Lyme disease." *N Engl J Med* 357:1422–1430.
- Harik NS. 2013. Tularemia: epidemiology, diagnosis, and treatment. *Pediatr Ann* 42:288–292.
- Jin H, Wei F, Liu Q, Qian J. 2012. Epidemiology and control of human granulocytic anaplasmosis: a systematic review. *Vector Borne Zoonotic Dis* 12:269–274.
- Juckett G. 2013. Arthropod bites. *Am Fam Physician* 88:841–847.
- Vannier E, Krause PJ. 2012. Human babesiosis. *N Engl J Med* 366:2397–2407.
- Woods CR. 2013. Rocky Mountain spotted fever in children. *Pediatr Clin North Am* 60:455–470.
- Wormser GP, Dattwyler RJ, Shapiro ED, Halperin JJ, Steere AC, Klemperer MS, Krause PJ, Bakken JS, Strle F, Stanek G, Bockenstedt L, Fish D, Dumler JS, Nadelman RB. 2006. The clinical assessment, treatment, and prevention of Lyme disease, human granulocytic anaplasmosis, and babesiosis: clinical practice guidelines by the Infectious Diseases Society of America. *Clin Infect Dis* 43:1089–1134.