REVIEW ARTICLE

Lyme Disease: What the Wilderness Provider Needs to Know

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Lyme disease is a multisystem tickborne illness caused by the spirochete *Borrelia burgdorferi* and is the most common vectorborne disease in the United States. Prognosis after initiation of appropriate antibiotic therapy is typically good if treated early. Wilderness providers caring for patients who live in or travel to high-incidence Lyme disease areas should be aware of the basic biology, epidemiology, clinical manifestations, and treatment of Lyme disease.

Key words: Lyme disease, tickborne disease, Lyme carditis, *Borrelia burgdorferi*, *Ixodes scapularis*, tick

Introduction

Vectorborne diseases, including those spread by ticks, pose a growing risk to outdoor enthusiasts. The 2013 Outdoor Participation Report estimated that nearly 50% of US residents age 6 and older participated in outdoor recreational activity in 2012, accounting for more than 12 billion outdoor excursions.¹ Twelve percent of all US residents reported hiking, 13% reported camping, and 19% reported jogging or trail running.¹ Among hikers there was an average of 18 outings annually with a cumulative 603 million hiking outings in 2012.¹ In the next 30 years, person-days spent hiking, backpacking, and camping are all expected to increase, doubling in some areas of the country.²

Lyme disease is a multisystem illness caused by the spirochete *Borrelia burgdorferi*, which is transmitted through the bite of certain species of ticks. The risk of exposure is greatest at the confluence of wooded and grassy areas, where contact between humans and infected ticks can be common. Although infection can be cured quickly with early and appropriate antibiotic therapy, rare deaths in young adults with cardiac involvement have been reported.³ It is important

for wilderness medical providers to understand that risk for transmission of Lyme disease may parallel trends in outdoor recreational activities. Wilderness providers should understand spirochete and vector biology, prevention practices, and treatment strategies to prevent, diagnose, and treat patients with Lyme disease.

HISTORY

Lyme disease was first described by Steere et al⁴ in 1977 after an investigation of a cluster of arthritis cases in children living near Old Lyme, Connecticut, and in 1981 the causative spirochete *Borrelia burgdorferi* was discovered in nymphal *Ixodes scapularis* ticks.⁵ Although the discovery of Lyme disease as a clinical entity is relatively recent, evaluation of museum specimens of ticks collected in the early 1900s from the northeastern United States identified spirochete-specific DNA sequences by polymerase chain reaction (PCR).^{6,7} Since its discovery, the incidence and geographic distribution of reported Lyme disease cases has increased.⁸ The spread of Lyme disease is attributed to changing land-use patterns and deer densities in the Northeast and Midwest, in addition to improved Lyme disease detection and reporting practices.^{7–9}

CAUSATIVE AGENT

Borrelia burgdorferi, a member of the eubacterial phylum Spirochaetes, is a vigorously motile, 2-membrane, spiral-

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shaped bacterium that has limited metabolic capabilities.^{10,11} In Europe and Asia, there are 3 genospecies of *B burgdorferi* sensu lato that commonly cause human illness: *B burgdorferi* sensu stricto, *Borrelia garinii*, and *Borrelia afzelii*. In the United States, human infection is caused by *B burgdorferi* sensu stricto, hereafter referred to as simply *B burgdorferi*.

B burgdorferi has a small, linear chromosome containing at least 17 linear and circular plasmids.¹⁰ Gene sequencing has not identified any lipopolysaccharide, toxin, or secretion system virulence factors.^{10,11} Additionally, the spirochete has no genes for cellular biosynthetic reactions such as synthesis of amino acids, fatty acids, enzyme cofactors, or nucleotides, explaining why the organism is fastidious and difficult to culture in vitro.¹⁰

TRANSMISSION

Transmission of Lyme disease to humans occurs through a bite of certain species of infected *Ixodes* ticks. Ticks are arthropods, not insects, and are closely related to mites and spiders.¹² The vectors for Lyme disease in North America are *I scapularis* (the black-legged) tick in the Northeast and Midwest, and *Ixodes pacificus* (the western black-legged) tick along the Pacific coast.¹³ These ticks are flattened dorsoventrally and oval in shape with a capitulum or “false head” extending forward from the body (Figure 1). Distinguishing male from female ticks can be done based on scutum (the hard chitinous plate on the anterior dorsal surface of hard-bodied ticks) size and appearance, but is of little clinical value as both sexes can transmit Lyme disease.¹²

Humans are not part of the natural life cycle of the spirochete. Human infection only occurs when humans enter areas where ticks, infected reservoir hosts, and deer coexist at a level high enough to support a dynamic enzootic cycle (Figure 2). Larval ticks hatch in the spring from eggs laid the previous fall; they are uninfected as the spirochete is not transmitted transovarially.¹⁴ After several

days of maturation, the larval ticks climb up foliage and begin to “quest” for hosts (Figure 3), taking their first blood meal in the late summer, typically from small rodents, birds, and deer.¹² This blood meal lasts for approximately 3 days, after which the larva will drop to the ground to digest the meal.¹⁵ This is the first time that the ticks can become infected, most commonly from an infected rodent. It is important to note that although deer can provide the blood meal for the tick, deer are immune to infection and do not transmit the spirochete to the larva.

The larval ticks molt into nymphal ticks that quest again, searching for a blood meal; humans can be incidentally fed on during this time. If the nymph was infected as a larva, then the infected nymph can transmit the spirochete. Nymphal ticks typically feed during the late spring and early summer, with meals lasting approximately 5 days, after which the nymph disengages and falls to the ground.¹⁵ Although both nymph and adult ticks can transmit the spirochete, nymphs are believed to be the principal source of human infection owing to their greater abundance and smaller size, which makes detection more difficult.

The nymph molts to become an adult tick that feeds in the fall, most commonly on deer, although humans can also serve as blood meal sources. Again, the spirochete can be transmitted transstadially from nymph to adult. Adult female ticks consume more than male ticks, reaching more than 200 times their prefeed body weight.¹⁵ Adult ticks feed for approximately 1 week and then drop to the ground.^{13,15} If the adult tick feeds on humans, spirochetes can be transmitted. After feeding, adult female ticks can lay approximately 1000 to 10,000 eggs before dying.¹²

PATHOGENESIS

To maintain the enzootic cycle, spirochetes must be viable in both mammalian and tick hosts. There are

Figure 1. *Ixodes scapularis* life forms. Dime is provided for size reference (figure courtesy of CDC).

Figure 2. Lifecycle of the *Ixodes scapularis* tick (figure courtesy of CDC).

substantial differences in temperature and pH between mammals and ticks, requiring adaptation by the spirochete.

When the tick takes a blood meal from an infected host, spirochetes travel through the mouth and into the midgut of the tick. The spirochete lays dormant there until the following spring (if a nymph is infected) or fall (if an adult is infected).¹⁰ When the tick attaches for its next blood meal, the spirochetes multiply in the tick midgut and switch from expressing outer-surface protein A (OspA) to expressing outer-surface protein C (OspC).¹⁰ The spirochete then migrates from the midgut to the salivary glands; from there it can be injected into the host. Typically, a feeding period of at least 36 hours is required for the spirochete to make this journey.¹⁶ Consequently, risk of infection with *B burgdorferi* can be greatly reduced if the tick is removed within 24 hours of attachment. Adherence of

the tick is augmented by a cementlike substance secreted by the salivary glands of the feeding tick that glues the mouthparts onto the host.¹²

After leaving the tick, spirochetes disseminate locally at the site of the tick bite, initiating a robust innate immune response.¹⁵ If untreated, spirochetes can disseminate and infect other organ systems, including joints, heart, and nervous system tissue. Systemic clinical manifestations of infection are caused by the migration of spirochetes through host tissue, adhesion to host cells, and the subsequent immune response; the spirochete has no traditional virulence factors.^{11,15}

EPIDEMIOLOGY

There are approximately 30,000 confirmed and probable cases of Lyme disease reported annually to the Centers for Disease Control and Prevention (CDC); the actual

Figure 3. Adult *Ixodes scapularis* questing (figure courtesy of CDC).

number of annual infections is estimated to be 10-fold higher.^{8,17} Although cases have been reported by residents of all states, 95% of cases occur in high-incidence

states or districts in the Northeast (Connecticut, Delaware, Maine, Massachusetts, New Hampshire, New Jersey, New York, Pennsylvania, Rhode Island, Vermont), Mid-Atlantic (Maryland, Virginia), and upper Midwest (Minnesota, Wisconsin; [Figure 4](http://www.cdc.gov/lyme/stats/index.html); <http://www.cdc.gov/lyme/stats/index.html>).

The age distribution for infected patients is bimodal, with a slight male predominance (55% male); boys 5 to 9 years of age account for the largest proportion of Lyme disease cases reported from 2001 to 2010 (<http://www.cdc.gov/lyme/stats/chartstables/incidencebyagesex.html>). Illness onset in the United States is most likely to occur in June, July, or August (<http://www.cdc.gov/lyme/stats/chartstables/casesbymonth.html>).

CLINICAL MANIFESTATIONS

Lyme disease can be divided into 3 stages: early localized, early disseminated, and late disseminated. Wilderness medical providers will be most likely to encounter patients with early localized infection.

Reported Cases of Lyme Disease -- United States, 2013

1 dot placed randomly within county of residence for each confirmed case

Figure 4. Reported cases of Lyme disease in the United States by county of residence, 2012. One dot is placed randomly within the county of residence for each confirmed case (figure courtesy of CDC).

Figure 5. Erythema migrans lesion, left underarm (figure courtesy of CDC).

The hallmark of early localized disease is the erythema migrans (EM) rash; patients may also have constitutional symptoms such as fever and myalgia. The EM rash is typically described as a macular, erythematous, round or oval skin lesion that expands gradually over a period of days to reach a diameter of 5 to 20 cm (Figure 5).¹⁸ The EM rash is generally not painful or pruritic, but it may be

warm to the touch. It usually develops at the site of the infected tick bite, typically 7 to 14 days after tick detachment. Approximately 70% to 80% of patients with Lyme disease will present with an EM rash, and it is the most valuable clinical sign for the wilderness practitioner. In the appropriate clinical situation, the EM rash is the only sign of Lyme disease that is sufficiently distinct to allow clinical diagnosis in the absence of laboratory confirmation.¹⁹ Importantly, the usefulness of the EM rash is strongly dependent on the probability of the patient being exposed to an infected tick. As the potential for exposure to infected ticks decreases, so does the probability that an EM-like rash actually represents true infection; concomitantly the possibility of a false-positive diagnosis of Lyme disease based on EM increases.

Rashes that develop within 48 hours of tick bite are more likely a tick bite hypersensitivity reaction and do not necessarily represent transmission of the spirochete.¹⁸ One way to differentiate between EM and a local hypersensitivity reaction is to mark the rash and evaluate for 1 to 2 days before initiating antibiotic therapy; the EM lesion should continue to enlarge.¹⁹ Providers should be aware also of another condition, Southern tick-associated rash illness (STARI), which can mimic the EM rash associated with Lyme disease. STARI can occur after the bite of an *Amblyomma americanum*, or lone star tick, and can be accompanied by fever and other systemic symptoms. STARI is not caused by *B burgdorferi*, and it is unknown whether sequelae are common.^{20,21} No bacterial agent has yet been causally linked to STARI, suggesting the futility of antibiotics in this disease; however, in the absence of a means of distinguishing STARI from Lyme disease, some providers choose to treat STARI on the grounds that it might be Lyme disease.²¹ Readers are directed to a review on STARI for additional information.²¹

Figure 6. Degree of *Ixodes scapularis* nymph engorgement by duration of feed. A millimeter bar is provided for size reference (figure courtesy of CDC).

Table. Recommended therapy for patients with Lyme disease in austere environments^a

Indication	Treatment		Duration
Tick bite meeting prophylaxis indications ^b	Doxycycline, 200 mg in a single dose (4 mg/kg in children ≥ 8 years of age) or observation		—
Erythema migrans	Preferred dosage for adults: Amoxicillin, 500 mg 3 times per day orally Doxycycline, 100 mg twice per day orally Cefuroxime axetil 500 mg twice per day orally	Preferred dosage for children ^c : Amoxicillin, 50 mg/kg per day in 3 divided doses orally Doxycycline, 4 mg/kg per day in 2 divided doses orally Cefuroxime axetil, 30 mg/kg per day in 2 divided doses orally	14-day course
Suspected early disseminated disease (neurologic or cardiac manifestation)	Refer to medical provider for further evaluation		—
Suspected late disseminated disease (arthritis or neurologic manifestations)	Refer to medical provider for further evaluation		—

^a Adapted from tables in Wormser et al.¹⁹

^b A single dose of doxycycline may be offered to adult patients and to children ≥ 8 years of age when all of the following circumstances exist: 1) the attached tick can be reliably identified as an adult or nymphal *Ixodes scapularis* tick that is estimated to have been attached > 36 hours on the basis of the degree of engorgement of the tick with blood or of certainty about the time of exposure to the tick, 2) prophylaxis can be started within 72 hours after the time the tick was removed, 3) ecologic information indicates that the local rate of infection of these ticks with *Borrelia burgdorferi* is $\geq 20\%$, and 4) doxycycline is not contraindicated. For patients who do not meet these criteria, observation is recommended.

^c Maximum should be adult dosing recommendation.

Without early treatment, *B. burgdorferi* spirochetes can disseminate to infect joints and nerve and heart tissue, typically within several days to a month of development of the EM lesion. The most common early neurologic manifestation of Lyme disease is unilateral facial nerve palsy. This is characterized by unilateral, or rarely bilateral, facial nerve weakness, which can be preceded by sensations of numbness or tingling on the affected side and involves the forehead musculature.²² Additional early neurologic manifestations include radiculopathies, other cranial neuropathies, and mononeuropathy multiplex.^{19,22} Patients suspected of having a disseminated infection should be evaluated by an infectious diseases physician. Cardiac abnormalities can also manifest during this time. The most common manifestation of Lyme carditis is atrioventricular conduction blockade, which, if untreated, can result in death in rare instances.^{3,23–26} Symptoms include lightheadedness, palpitations, shortness of breath, chest pain, and syncope. Patients with suspected Lyme carditis should be evaluated as soon as possible by a physician, and an electrocardiogram should be obtained if indicated.

Late disseminated Lyme disease is characterized by rheumatologic and neurologic manifestations. Intermittent monoarticular or oligoarticular arthritis involving the knee, with effusions that are out of proportion to pain, is typical.¹⁹ Untreated, these episodes will typically resolve over weeks to months, often even without

antibiotic therapy.¹⁹ Clinical diagnosis of Lyme disease based solely on rheumatologic symptoms is unlikely to be of benefit to the wilderness provider as many acute and chronic ailments can be similar to Lyme arthritis. Late neurologic manifestations of Lyme disease, such as encephalomyelitis and peripheral neuropathy, are rare and will be the least likely clinical symptoms to be encountered by wilderness providers.¹⁹ Patients suspected of having late disseminated Lyme disease should be evaluated by a physician as soon as possible.

A small proportion of patients (10%–20%) treated for Lyme disease may have persistent symptoms including fatigue, pain, and joint and muscle aches.²⁷ This manifestation of Lyme disease presentation, described as posttreatment Lyme disease syndrome, currently has no known etiology. Prolonged courses of antibiotics have not shown any improvement in patients compared with those receiving placebo.^{28–30} Additionally, prolonged antibiotic therapy and incorrect diagnosis have been associated with complications, including death.^{31–36} Patients suspected of having posttreatment Lyme disease syndrome should be evaluated by an infectious diseases physician.

Readers are directed to existing reviews for additional information regarding clinical manifestations of Lyme disease.^{6,19}

DIAGNOSIS

Practitioners in wilderness or austere settings are unlikely to have immediate laboratory confirmation for suspected infection. Nevertheless, it is important to have a working knowledge of the recommended diagnostic testing for Lyme disease. There are a variety of laboratory tests developed to detect *B burgdorferi*, which can broadly be broken down into serologic tests that detect the body's immune response to the organism and tests that detect the organism directly.

Serologic tests are by far the most common means of confirming a clinical diagnosis of Lyme disease. Currently available serologic tests include whole-cell sonicate or C6 peptide enzyme immunoassays and Western blot to assess for immunoglobulin (Ig) M and IgG antibodies to specific spirochete antigens. A 2-tiered approach is recommended in which samples are first tested by enzyme immunoassays and then tested by Western blot only if positive or equivocal results are obtained (http://www.cdc.gov/lyme/healthcare/clinician_twotier.html). Physicians should recognize that the risk of false-positive laboratory results increase in patients with a low pretest probability of Lyme disease.³⁷ Additionally, the background serologic positivity rate can be substantial in patients living in endemic areas, particularly those in high-risk groups such as persons working outside in tick habitat.^{38,39} As IgM and IgG *Borrelia*-specific antibodies may persist for years in some patients, distinguishing newly acquired infections from past ones can be challenging when using serology alone, emphasizing the importance of only testing in appropriate clinical scenarios.

Direct tests include culture, detection of *B burgdorferi* DNA, and visualization of spirochetes in host tissue.⁴⁰ Although culture or visualization of spirochetes in tissue can demonstrate a causal association between patient symptomatology and Lyme disease, both of these methodologies are time-consuming, resource-intensive, and potentially invasive, and neither is recommended for routine diagnosis of Lyme disease in any of its stages.⁴¹ Polymerase chain reaction can be used to amplify and detect *B burgdorferi* nucleic acid and is useful as a diagnostic adjunct if acute neurologic Lyme disease or Lyme arthritis is suspected.¹⁹ Readers are directed to reviews of testing methods for additional information.⁴⁰

PREVENTION

Currently, the best method for preventing infection with Lyme disease or other tickborne diseases is avoiding the bite of infected ticks. Black-legged ticks typically live in moist and humid environments, particularly around the confluence of wooded and grassy areas. Ticks quest for

hosts on tall grass and brush, so avoidance of these areas reduces opportunities for exposure. Unfortunately, avoidance of these areas can be impractical for outdoor sport enthusiasts. Additional protection can be obtained by wearing clothing that covers the skin to prevent initial exposure (eg, long pants with complete covering of legs as opposed to shorts) and by applying repellents containing 20% *N,N*-diethyl-*m*-toluamide (DEET).⁴² Topical repellents can be applied to the skin in exposed areas, avoiding mucous membranes; these products may provide protection for several hours and should be used in accordance with manufacturer instructions. Clothing and gear (eg, boots, pants, socks, tents) can be treated with 0.5% permethrin to provide additional benefit. Permethrin-treated items remain protective through several washings. Permethrin should not be applied directly to the skin. A list of Environmental Protection Agency-registered repellents can be found at <http://cfpub.epa.gov/oppref/insect/>.⁴³ Wilderness providers and participants should defer to manufacturer instructions on the application and treatment of these products.

When outdoors in high-incidence Lyme disease areas, all persons should perform daily tick checks.⁴² All areas of the body should be examined daily, and a mirror used to examine difficult-to-view areas (eg, posterior scalp line, gluteal crease, posterior aspect of the scrotum).⁴⁴ Areas where ticks frequent include intertriginous areas such as the axilla or popliteal fossae, the periauricular area, in the umbilicus, and in head and body hair, as well as in the inguinal and gluteal creases. Parents should ensure that their children receive daily tick checks while in high-incidence areas. Tick checks should be a mandatory component of the daily routine for all participants in outdoor activities in high-incidence areas. Pets should also be examined daily as ticks on pets can move to the human owner.⁴⁵ Owners of pets are advised to use veterinarian-prescribed tick-collars or spot-on treatment for both the health of the pet and prevention of tick exposure to the pet owners.

The recommended method for removing a tick involves grasping the tick as close to the skin as possible using fine-tipped tweezers and removing the tick using gentle, outward pressure (http://www.cdc.gov/ticks/removing_a_tick.html).⁴⁶ Personal protective equipment consisting of nitrile or latex gloves should be worn if available. There is no increased risk of transmission of Lyme disease if the tick is accidentally crushed.⁴⁶ Attempts to encourage the tick to disengage, such as burning the tick with matches or cigarettes or applying a smothering substance like petroleum jelly, gasoline, or nail polish, is not recommended and can lead to patient morbidity. Monofilament fishing line has been

successfully used to remove ticks and might be useful if tweezers are not available.⁴⁷ If the tick is unable to be removed using recommended measures, more-invasive techniques may be required but should be performed in controlled settings.⁴⁸

Wilderness providers, and medical directors of wilderness programs, should consider ensuring participants in outdoor activities in high-incidence Lyme disease areas are educated to appropriate primary tick bite prevention methods and have supplies available to prevent infection.

Importantly, there may be copathogens carried by ticks with *B burgdorferi*, including rickettsia, bacteria, and viruses, that may be transmitted more rapidly than Lyme disease.^{13,19,49} This underscores the importance of frequent tick checks and their prompt and appropriate removal.

TREATMENT

Wilderness providers are most likely to encounter patients presenting immediately after a tick bite with early localized or early disseminated disease and need to be knowledgeable about treatment recommendations. Medical directors of outdoor programs with participants active in high-incidence Lyme disease areas should consider establishing treatment guidelines based on the Infectious Diseases Society's guidelines, tailored to the individual needs of the program.¹⁹

Patients with recently attached ticks are commonly encountered in wilderness medicine practice, particularly during spring and summer months. A tick can be found on a human immediately after successfully questing, as it travels on the human to a favorable feeding location, while feeding during its blood meal, or immediately after detachment.

Ticks that have not yet attached to the host are incapable of transmitting Lyme disease, so no antibiotic prophylaxis would be recommended if a tick were found at this stage. There is little risk of infection with recently (≤ 36 hours) attached ticks¹⁹ because, as discussed previously, *B burgdorferi* resides in the tick midgut and must travel to the salivary glands to enter the host. Additionally, not all competent *Ixodes* spp ticks will carry Lyme disease, even in high-incidence areas.

Routine prophylactic therapy is not recommended for all patients who experience a tick bite. Prophylaxis against Lyme disease should be given only if 1) the tick can be reliably identified as an *I scapularis* adult or nymph and is estimated to have been attached for > 36 hours by degree of engorgement (Figure 6), and 2) prophylaxis can be started within 72 hours of removal of the tick and 3) ecologic information suggests that the local rate of *I scapularis* tick infection is $\geq 20\%$.¹⁹ In

this setting, children 8 years of age or older and adults can be given a single dose of doxycycline (4 mg/kg up to 200 mg) orally and monitored for development of signs and symptoms of infections. Doxycycline is relatively contraindicated in pregnant women and in children younger than 8 years of age.¹⁹ In this case, patients should be monitored for signs and symptoms of infection and treated with an appropriate antibiotic course if signs or symptoms develop. No antibacterial prophylaxis is recommended otherwise in these two groups.¹⁹ Wilderness providers should consider having doxycycline available for prophylaxis if they practice in areas with $\geq 20\%$ tick infection rate.

Recommended antibiotic treatment regimens have been extensively documented by the Infectious Diseases Society of America.¹⁹ A summary of recommended regimens can be found in the Table. On clinical diagnosis of Lyme disease based on the presence of the characteristic EM rash in a high-incidence Lyme disease area, wilderness providers should provide early and appropriate antibiotic therapy. If early or late disseminated Lyme disease is suspected, prompt evaluation by a medical professional in a setting in which parenteral therapy is available should be considered. Any patient treated for Lyme disease in austere settings should be offered follow-up with a physician after returning from the backcountry.

Finally, although Lyme disease is the most common tickborne disease in the United States, there are many other pathogens carried by ticks.¹³ Patients should consider being evaluated by an infectious diseases physician if they develop signs or symptoms inconsistent with Lyme disease after a tick bite.

Conclusions

Lyme disease is the most common vectorborne disease in the United States. Human infection is a byproduct of a robust enzootic cycle dependent on pathogen, vector, and host biology. Although most cases resolve with appropriate and early antibiotic therapy, death has been reported. Wilderness medical providers, particularly those practicing in high-incidence Lyme disease areas, should be aware of recommended Lyme disease preventive measures, common clinical presentations, and established therapeutic regimens to ensure optimal patient care.

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