Clinical

Urgent Care Diagnosis and Management of Tick-Borne Diseases

Urgent message: As the incidence of tick bites increases, it is imperative for urgent care physicians to be able to recognize various species of ticks and the symptoms of tick-borne illnesses and to know what to do when a patient presents with a tick bite.

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Introduction

yme disease is the most common tick-borne infection in the United States (**Figure 1**) and Europe. With a total Lof 279,509 cases reported between 2003 and 2012, it is currently the seventh most common reportable disease in the United States. B. afzelii and B. garinii are the causative spirochetes in Asia and Europe. In the United States, however, Lyme disease is caused by the bite of an *Ixodes* tick carrying the spirochete *Borrelia burgdorferi*, so the discussion here is limited to B. burgdorferi.

Lyme disease was first brought to medical attention when a cluster of what was thought to be juvenile rheumatoid arthritis cases occurred in Lyme, Connecticut; since then, the number of both suspected and confirmed cases has grown progressively each year, with 13 states (Figure 2) accounting for 95% of all reported cases: Connecticut, Delaware, Maine, Maryland, Massachusetts, Minnesota, New Hampshire, New Jersey, New York, Pennsylvania, Vermont, Virginia, and Wisconsin.²

Lyme disease is transmitted by different *Ixodes* species. In the eastern and north central regions of North America, most cases are caused by *I. scapularis*, whereas most

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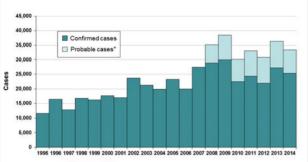
cases in the western regions are caused by *I. pacificus*.

Life Cycle of *Ixodes scapularis* and Transmission to Humans

Stage 1: Larvae

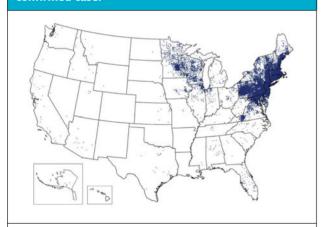
The larvae of *I. scapularis* are six-legged hatchlings usually found in the early summer that are generally uninfected. After they are released, they search for their first blood





(From Lyme disease graphs. Atlanta, GA: Centers for Disease Control and Prevention [updated 2015 November 5; cited 2015 August 27]. Available from: http://www.cdc.gov/lyme/stats/graphs.html.

Figure 2. Reported cases of Lyme disease in the United States in 2014. The map shows 1 dot placed randomly within the county of residence for each confirmed case.



(From Data and statistics. Atlanta, GA: Centers for Disease Control and Prevention [updated 2015 March 4; cited 2015 October 27]. Available from: http://www.cdc.gov/lyme/stats/.

meal from birds and from mice and other small rodents. It is usually this first blood meal that transfers the *B. burgdor-feri* spirochete. Once fed, the larvae detach from their host, molt, and reemerge as nymphs the following spring.

Stage 2: Nymphs

Nymphs find a host to feed on and, in the process, transfer the spirochete to the host. Through this process, small rodents become infected and ensure the transfer of infection to future larvae. Nymph activity starts in mid-May and usually peaks in June. By late July, nymph activity is at its most minimal. Once fed, nymphs molt to adults in the fall.

Figure 3. Female nymph-stage blacklegged tick, Ixodes scapularis Say.



(Photograph courtesy of Michael Patnaude, University of Florida, with permission. Retrieved 2015 September 1 from http://entomology.ifas.ufl.edu/creatures/urban/medical/deer_tick.htm.)

Figure 4. Male nymph-stage blacklegged tick, *Ixodes* scapularis Sav.



(Photograph courtesy of Michael Patnaude, University of Florida, with permission. Retrieved 2015 September 1 from http://entomology.ifas.ufl.edu/creatures/urban/medical/deer_tick.htm.)

Stage 3: Adults

Adults feed during warm days; their preferred host is the white-tailed deer. Ticks seek warm-bodied hosts that emit carbon dioxide and will latch onto any organism that fits this description. In the spring, after a blood meal, the female (**Figure 3**) lays her eggs and the process repeats itself. The adult female tick may feed for 5 to 7 days, but the male tick (**Figure 4**) feeds only sparingly, if at all.

Because female ticks lay and their eggs in woodlands, people may be at higher risk because of their occupations (forestry, hunters, etc.) or because of their recreational activities (camping, hiking). In highly endemic areas, people might be high risk in their own backyards, especially where grassy lands meet woodlands.

Transmission of Lyme disease to humans has been found primarily to be through nymphs as vectors. Although most people would notice adult ticks attached to them, most nymphs are smaller than 2 mm, allowing them to go undetected for the 2 days necessary to transfer B. burgdorferi to their hosts.

Evaluation of Tick Bites: Pertinent Medical History Questions

Most patients with an actual tick bite understandably find the whole experience very stressful and frightening. As public awareness of Lyme disease and incidental situational exposure to ticks increases, urgent care physicians must know what time-sensitive questions to ask and how to act on the answers:

- Was the tick species of the *Ixodes* family? This is a very important question to ask because not every tick that bites is of the Ixodes family, and neither is every tick a carrier of B. burgdorferi. A study was conducted on 3766 specimens submitted and identified by physicians as ticks between 1988 and 1990. Of these, 36.5% were beetles, most often spider beetles; 11.6% were mites; 10.4% were true bugs, mostly bedbugs; 12% were lice (crabs, or pubic lice—head and body); and 7.9% were spiders.² Valid identification of the insect in question can reduce unnecessary testing and treatment, alleviating the fears of the patient. Adult ticks are usually 3 mm in size, with males being any color from dark brown to black. Female *Ixodes* ticks typically are orange to red in color and have a dark brown oval spot called a scutum on their back. Another tick commonly misidentified as Ixodes is Dermacentor variabilis, the American dog tick, which is much larger than Ixodes.
- Was the tick a larval, nymphal, or adult tick? As previously mentioned, nymphs are much more likely than adult ticks to escape detection because of their small size, allowing them to remian attached for the duration necessary to transmit B. burgdorferi. Ixodes nymphs are approximately the size of poppy seeds and have a round body. D. variabilis nymphs are much larger and rarely bite human beings.
- Was the tick attached? If so, for how long? Lyme disease is transmitted during the tick feeding process; this requires a firm attachment to the human body. Ticks found in clothing or walking along the surface of the body cannot transmit the disease. Attachment duration is another important factor for evaluating disease risk. A study was conducted in which rabbits were exposed to spirochete-infected Ixodes ticks for various numbers

- of hours. Rabbits exposed to ticks for shorter periods than 48 hours were not infected.4
- Was the tick engorged? When ticks feed and become engorged with blood, they release their spirochete-laden saliva into the wound, thus transferring B. burgdorferi into their host.

Tick Removal

The removal of an attached tick should be approached with the proper technique, with the goal of removing the insect intact, including all parts of the mouth. Different lay techniques have included burning the tick with a match, covering it with petroleum jelly or nail polish in attempts to suffocate it, and pulling it out directly. Some of these methods carry the risk of infection by releasing infectious secretions onto already pierced skin, thereby increasing the chances of spirochete transmission.

To properly remove a tick, use a small utensil such as tweezers or forceps. Firmly grasp the tick as close as possible to the surface of the patient's skin. Pull upward instead of twisting or squeezing. If there are remnants of the mouthpiece, leave them alone; they usually spontaneously fall out. Thoroughly clean the area with a disinfectant, such as alcohol or Betadine. If the patient has a clear and precise timeline indicating that a nonengorged tick was attached for less than 48 hours, give the patient clear instructions on monitoring the site for the development of erythema migrans (EM), teaching the patient how to distinguish between EM and a postbite reactive rash.

Clinical Manifestation of Lyme disease

Lyme disease can be categorized into three distinct stages.

Early Localized Disease

EM usually appears at the site of the tick bite; it is the most common localized reaction to Lyme disease, occurring in 70% to 80% of patients with tick bites.⁵ It is extremely relevant clinically because it is the only manifestation of Lyme disease in the United States that is sufficiently distinctive to allow clinical diagnosis in the absence of laboratory confirmation.⁶

EM is considered an early manifestation because it presents anywhere from 3 to 30 days (average, 7-14 days) after tick detachment.⁶ It is important to for physicians to be able to distinguish EM from tick-bite reactions that may occur in reaction to the antigens being injected into the skin. Hypersensitivity reactions occur

Figure 5. Erythema migrans is an erythematous rash that occurs in 70% to 80% of patients with Lyme disease



(From James Gathany via the U.S. Centers for Disease Control and Prevention. Retrieved 2015 October 27 from http://phil.cdc.gov/phil/details.asp?pid=9875.)

while the tick is still attached to the skin and usually encompass an area of 5 cm at most, are pruritic, and start to fade in 24 to 48 hours. In contrast, EM tends to affect a larger area initially and continue expanding (Figure 5). In some instances when it is difficult to distinguish EM from hypersensitivity, it can be helpful to use a skin marker to outline the rash's border and then observe the rash for 48 hours before initiating therapy.

Primary EM varies in appearance among patients. Although the typical red rash with a central clearing, also called a bull's-eye rash, is common, sometimes EM rashes are homogenously red. In other situations, especially on the lower extremities, the lesion may be purpuric with vesicles or pustules present. When there is more than one EM rash, the secondary lesions are thought to be hematogenous dissemination from the primary rash.⁶

Early Disseminated Disease

Neurologic symptoms are necessary for Lyme to be considered disseminated, and in some situations, they may be the first manifestations of the disease. They include cranial nerve palsies, with cranial nerve VII (the facial nerve) being the most typically affected; Lyme disease is one of the few causes of bilateral cranial nerve palsies. Also noted are peripheral neuropathy, radiculopathy, and even lymphocytic meningitis. The most common presenting group of neurologic anomalies is a triad of meningitis, a motor or sensory radiculoneuropathy, and a cranial neuropathy.

Late Disseminated Lyme

Arthritic disease, either monoarticular or polyarticular, is a frequent physical sign of late Lyme disease, with the knee being the most common joint involved. The arthritis symptoms may be frequent or intermittent and tend to appear months after the initial tick contact. Lyme encephalopathy is the neurologic manifestation of late disease, and in its specificity, it is completely different from the neurologic findings in early disease.

Approach to Serologic Testing

Serologic testing for Lyme disease should be performed in all individuals who meet *all* of the following criteria:

- Residence in or travel to an endemic area
- At risk for tick exposure (e.g., landscapers, horticulturists)
- Symptoms consistent with any stage of Lyme disease

Testing is contraindicated under the following criteria:

- In screening the general public
- In asymptomatic people living in endemic areas
- In people with vague, nonspecific symptoms (e.g., fever, malaise, arthralgia)
- In people with EM; the early disease symptom of EM qualifies for automatic treatment without the need for testing

A two-tiered approach is recommended for testing for B. burgdorferi antibodies. The patient undergoes an initial sensitive enzyme-linked immunosorbent assay (ELISA); if test results are positive, a more specific Western blot test is conducted on the same sample. If the ELISA results negative, there is need for further testing. This approach is recommended because the ELISA can easily produce false positive results because of the presence of other diseases such as syphilis, systemic lupus erythematosus, rheuma-



(From the U.S. Centers for Disease Control and Prevention. Retrieved 2015 September 1 from https://commons.wikimedia.org/wiki/File:Amblyomma_americanum_tick.jpg.)

toid arthritis, and even bacterial infections. The ELISA can distinguish between early disease (immunoglobulin M bands) and late disease (immunoglobulin G bands). The Western blot works by the detection of antibodies to specific parts of *B. burgdorferi* and is therefore more specific. It is important to know that seropositivity alone does not make a diagnosis of active Lyme disease, because antibodies may still be present even up to 20 years after full treatment and resolution of the disease.³

Therapeutic Management of Lyme Disease

Early Disease (Erythema Migrans)

In the absence of neurologic findings, doxycycline (100 mg twice a day) is the recommended treatment for adult patients with early localized or early disseminated Lyme disease. If there is an allergy to penicillin, if the patient is pregnant, or if the patient is younger than age 8 years, amoxicillin (500 mg three times a day) or cefuroxime (500 mg twice a day for 14 days) may be used. Although treatment duration has always been 21 days, trials have proven that doxycycline for 14 days is just as effective.

In disseminated disease with facial palsy but without any other neurologic findings, a 21-day regimen of doxycycline remains the first choice. It is imperative to explain to the patient that the antibiotics are not necessarily to treat the facial palsy but to prevent further neurologic complications. Any other neurologic findings require intravenous treatment and are beyond the scope of urgent care.

Jarisch-Herxheimer Reaction

In a small minority of patients, there may be a worsening of symptoms within the first 24 hours of antibiotic treatment. This is known as a Jarisch-Herxheimer reaction; it is a systemic response to the release of antigens by dying spirochetes. A patient might call to report feeling worse than before treatment. Conservative management (increased hydration, rest, nonsteroidal anti-inflammatory medications, etc.), along with reassurance, can help the patient through this phase.

Differential Diagnosis

Southern Tick-Associated Rash Illness

STARI, or southern tick-associated rash illness, is associated with the lone star tick (Amblyomma americanum) and the spirochete *B. lonestari*. STARI presents as a rash similar to EM with flu-like symptoms, but when patients with it are tested, there is no serologic evidence of B. burgdorferi. Another factor that differentiates STARI from Lyme disease is the rash; although both have erythematic rings with central clearing, STARI rashes have the development of papules at the very point of the tick bite. A. americanum is also physically different from *I. scapularis*; it can be distinguished by the solitary white spot or "star" found on the back of the female tick (Figure 6). At present, there is no specific serologic test for STARI. Most patients with STARI experience significant symptom relief with the doxycycline regimen used in Lyme disease. Although the name suggests that the disease occurs strictly in Southern U.S. states, cases of STARI have been found as far away as Maine.

Human Monocytic Ehrlichiosis

Human monocytic ehrlichiosis is another disease transmitted by the vector *A. americanum*, but carrying the bacteria *Ehrlichia chaffeensis*. Although there are different species of *Ehrlichia, chaffeensis* is the most common one found in human infections. Symptoms are usually nonspecific and may include malaise, fever, chills, and myalgia. Diagnosis is made by polymerase chain reaction, and treatment is with doxycycline (100 mg daily)—or with rifampin in children and pregnant women—for 7 to 10 days.

Babesiosis

Babesiosis is a flu-like infection that is tick-borne and caused by protozoa, most commonly *Babesia microti*. It is a disease that is spread by tick bites and transfusion of *Babesia*-infected blood. Because the *Ixodes* tick is vector for both *B. burgdorferi* and *B. microti*, babesiosis is a

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reasonable differential diagnosis for patients with Lyme disease. Although symptoms may include arthralgia, malaise, and myalgia, there is no rash associated with this disease. Diagnosis is made via polymerase chain reaction, which is more sensitive and specific than microscopic evaluation of red blood cell smears. Treatment is a regimen of 7 to 10 days of a combination of atovaquone with azithromycin or of quinine and clindamycin.

Conclusion

As the incidence and awareness of Lyme disease increases, urgent care physicians are usually the first providers to see patients with the disease who are seeking fast and efficient care for tick exposure. Thus, it is prudent for urgent care providers to have a firm understanding of Lyme disease and an appropriate treatment plan.

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