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Targeting Lyme disease

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LYME DISEASE (LD) is the most common vector-borne disease in the United States, with more than 20,000 confirmed cases reported annually.[1] Most reported cases (96%) in 2011 came from 13 states: Connecticut, Delaware, Maine, Maryland, Massachusetts, Minnesota, New Jersey, New Hampshire, New York, Pennsylvania, Vermont, Virginia, and Wisconsin.[1] However, an individual's state and county of residence doesn't accurately reflect the risk of LD because people, pets, and ticks travel. This article will discuss signs and symptoms of LD, review the controversies surrounding diagnosis and treatment, and provide prevention tips to share with patients.

A short history of LD

LD was named after the town of Lyme, Conn., when unusually high numbers of children were diagnosed with juvenile rheumatoid arthritis in the 1970s in Lyme and two neighboring communities. Researchers explored possible causes, such as airborne and waterborne microbes, until their focus shifted to deer ticks. Researchers knew that most of the children diagnosed with juvenile rheumatoid arthritis lived and played near wooded areas. Researchers also knew that the affected children's initial symptoms typically started during the summer, which is the height of tick season. Additionally, several of the affected children reported having a skin rash before developing arthritis, and many children reported having been bitten by a tick where the rash appeared.[2]

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It wasn't until 1981 that researchers identified the cause of LD and discovered the connection between the deer tick and the disease.

Transmission

LD is a bacterial infection that's transmitted to humans through the bite of an infected tick. In most cases, the tick must be attached to its host for 36 to 48 hours or longer before *Borrelia burgdorferi*, the spirochete that causes LD, can be transmitted.[3] The bacteria multiply at the site of the tick bite. Three to 32 days after the bite, they migrate from the site into surrounding skin. Bacteria also spread through the blood and lymphatic system to other organs or skin sites.[4]

The blacklegged tick (or deer tick, *Ixodes scapularis*) spreads LD in the northeastern, mid-Atlantic, and north-central United States. The western-blacklegged tick (*Ixodes pacificus*) spreads the disease on the Pacific coast (see *Looking at the blacklegged tick*). Adult ticks as well as immature ticks, called nymphs, can transmit LD. Nymphs are responsible for most cases of LD.[3]

LD can't be transmitted from person to person.[3] When caring for anyone suspected of or diagnosed with LD, follow standard precautions.[5] Pets, such as dogs and cats, can get LD, but no evidence indicates that pets can transmit LD to humans. However, pet owners must take precautions because pets can bring infected ticks into the yard and home, placing people at increased risk. Pet owners may want to consider the use of tick control products for their pets.[3]

Recognizing LD

Clinical manifestations of LD are divided into three phases: early localized disease, early disseminated disease, and late LD.[6] Signs and symptoms of LD often mimic other illnesses, especially in the late stages of the disease.

The most well-known sign of **early localized disease** is erythema migrans (EM), a rash that may be warm to the touch but is rarely painful or pruritic. EM typically expands slowly over days or weeks, often with a central clearing resulting in a target or bull's eye appearance.[6] EM is usually located at the site of the initial tick bite, most frequently in or near the belt line, axilla, inguinal area, or popliteal fossa.[6] If present, it appears between 3 and 30 days following the tick bite (see *Zeroing in on EM*).[7] According to the CDC, EM must be at least 5 cm (2 in) in diameter in order to be diagnostic for LD.[8]

Although EM is most commonly associated with LD, many patients present with an atypical rash or with no rash at all. Fewer than 50% of patients with LD recall having any type of rash.[9]

During **early disseminated disease** (days to weeks following infection), the patient may exhibit multiple EM lesions on other parts of the body.[7] Acute neurologic or cardiac involvement usually occurs during this stage. Cranial nerve VII (facial) dysfunction or Bell palsy is the most common neurologic sign associated with LD.[7] Other neurologic features of early disseminated LD may include lymphocytic meningitis, radiculopathy, peripheral neuropathy, and mononeuropathy multiplex.[6]

Manifestations of early disseminated disease also can include cardiac abnormalities. The patient may experience various degrees of atrioventricular block, sometimes with myopericarditis, which can cause dizziness.[6,7] If untreated, LD can lead to more serious cardiac complications, such as carditis and advanced heart block.[10]

Other manifestations of early, localized, or disseminated LD include flulike signs and symptoms such as fatigue, anorexia, fever, headache, myalgia, arthralgia, and regional lymphadenopathy.[6] Another indication of LD is extended flulike symptoms during off-season times, such as the summer months.[9] Those in highly tick-infested areas should be especially alert to these symptoms.

Late LD (months to a few years following the onset of infection) is most commonly characterized by intermittent or persistent arthritis in

Looking at the blacklegged tick

The blacklegged tick (or deer tick, *Ixodes scapularis*) spreads LD in the northeastern, mid-Atlantic, and north-central United States. Adult ticks are about the size of a sesame seed; nymphs are about the size of a poppy seed.[3]

Photo courtesy: Public Health Image Library

one or a few large joints, especially the knee.[6] Neurologic disorders including polyneuropathy are common.[7]

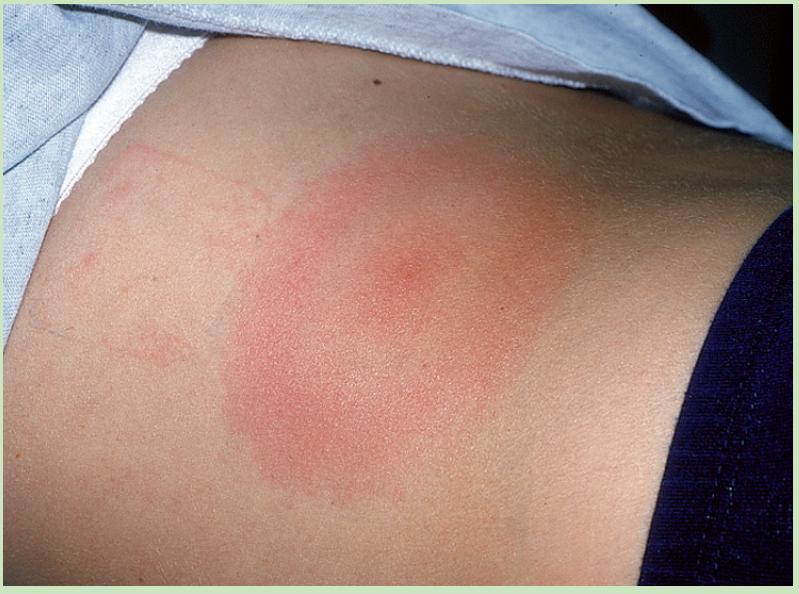
Diagnosing LD is controversial

The CDC recommends diagnosing LD based on the patient's signs and symptoms, possible exposure to infected blacklegged ticks, and lab tests.[11] Under current CDC guidelines, testing blood for evidence of antibodies to *B. burgdorferi* should occur in two steps, starting with an enzyme-linked immunosorbent assay (ELISA). If the ELISA is negative, no further testing is recommended. A positive ELISA result doesn't confirm the diagnosis by itself, so positive or equivocal findings warrant further testing with a more accurate test, most commonly the Western blot test. If the ELISA and the Western blot are both positive, the results are considered positive.[11] A positive Western blot test is considered evidence of infection with *B. burgdorferi*. If the Western blot is negative, testing is considered negative.[6]

However, the value of this approach is disputed by the International Lyme and Associated Diseases Society (ILADS), which maintains that no reliable method exists to diagnose LD.[9] ILADS maintains that the ELISA is unacceptably unreliable as the first step of a two-step screening process because it misses 35% of culture-proven LD. The ELISA also has several other flaws that can make it unreliable. The LD ELISA has a 65% sensitivity value, which falls significantly below the 95% sensitivity benchmark used for many other screening tests.[4] In addition, damaged immune systems, which often accompany LD, can lead to false-negative test results. When the body can't mount an adequate immune response, antibody production is low.[4] Furthermore, the efficacy of serologic testing decreases with time, which makes diagnosis even more difficult if the patient isn't tested soon after exposure.[4]

Zeroing in on EM

EM is the most well-known sign of early localized disease. Note the targetlike concentric rings with no scale.



Regarding the second step of the two-step process recommended by the CDC, ILADS maintains that 20% to 30% of patients with acute culture-proven LD remain seronegative on serial Western blot sampling.[9]

Because there is presently no definitive test for LD, ILADS maintains that clinical judgment can best determine which individuals should be treated and in what manner. ILADS recommends that laboratory results be used to support, rather than take the place of, the healthcare provider's judgment.[12]

When a diagnosis of LD is made, ILADS recommends testing for coinfections, which are infectious agents found within the tick gut that are also transmitted to the infected individual via the tick bite. Examples of common coinfections are bacterial strains from the genera *Ehrlichia*, *Babesia*, and *Bartonella*.[9]

According to the CDC, LD is a nationally notifiable disease.[13] However, reporting nationally notifiable diseases and conditions isn't required by federal law and varies slightly from state to state.[14] For information about which conditions are notifiable and whether LD is on the list, contact your local county health department or your state's health department.

Treating LD

Like the diagnosis of LD, treatment is also controversial, with competing views put forth by ILADS and the Infectious Diseases Society of America (IDSA). In 2006, IDSA published treatment guidelines in which many of the practices recommended in the ILADS guidelines are directly contraindicated or refuted. IDSA categorically rejects the idea that *B. burgdorferi* can persist inside the body after a regimen of appropriate antibiotics.[15]

IDSA and ILADS both recommend antibiotic treatment with doxycycline for nonpregnant and nonlactating adults and children 8 years of age or older for early-stage LD, but don't always agree on subsequent treatments. (See *Treatment recommendations* for a comparison of IDSA and ILADS guidelines.) The healthcare provider should weigh the benefits and risks of each approach when helping the patient make treatment decisions. Regardless of the

treatment plan, treatment will likely continue until the patient's condition improves and the improvement is maintained.[16]

No definitive test is available to indicate eradication of *B. burgdorferi*. Tests for LD detect antibodies to the bacteria. These antibodies may remain long after the infection is gone. If a patient's blood tests positive, it will likely continue to test positive for months or even years, even if the bacteria are no longer present.

Prevention is protection

In 1998, the FDA approved an LD vaccine for use in humans in the United States, but it was discontinued due to low demand.[17] Today, the best protection against LD is prevention.

Prevention begins with dressing appropriately for the outdoors in tick-laden environments. Appropriate dress includes wearing light-colored clothing to make ticks more visible and tucking pants into socks when going into areas that could harbor ticks.[4] Blacklegged ticks live in moist and humid environments, particularly in or near wooded or grassy areas. To avoid ticks, walk in the center of trails instead of walking through vegetation such as leaf litter or shrubs.[18]

Wear light-colored clothing and tuck pants into socks when going into areas that could harbor ticks.

Properly applying insect repellants containing 20% or more DEET before going outdoors may also help. Repellents containing DEET may be sprayed on exposed skin as well as clothes and offer protection that lasts for several hours. Products that contain permethrin can be used on clothing. Clothing and gear such as boots, pants, socks, and tents treated with permethrin remain protective through several washings.[16]

People should carefully examine themselves for ticks after coming in from the outdoors using a hand-held or full-length mirror to view all parts of the body. Teach patients how to properly remove any ticks they discover: Use fine-tipped tweezers to grasp the tick as close to the skin's surface as possible. Pull straight out with a steady movement until the tick releases. Once the tick has been removed, thoroughly clean the bite area and your hands with 70% isopropyl alcohol, an iodine scrub, or soap and water.[4]

Clothing and pets should also be closely examined for ticks. Placing clothes into a dryer on high heat kills ticks. Applying a tick repellent on dogs or a tick collar will assist in prevention.[18]

Knowledge is key

LD is the most common vector-borne disease in the United States, with more new cases reported annually than the number of new AIDS

Treatment recommendations

Two organizations, IDSA and ILADS, have different sets of guidelines for treating LD. The healthcare provider should weigh the benefits of these modalities against the risks when helping the patient make treatment decisions.

IDSA Guidelines[15,17]

- LD is easily treated with relatively short courses of appropriate oral antibiotics, including doxycycline or amoxicillin, or I.V. ceftriaxone when neurologic symptoms are present.
- Antibiotic prophylaxis is discouraged unless a series of stringent requirements is met including the likelihood of infected tick exposure, the length of time of tick attachment, and the length of time that has passed since tick removal.
- Patients with late-stage LD whose signs and symptoms haven't resolved after oral antibiotic use should be re-treated using the same antibiotics for an additional 3- to 4-week period.
- IDSA doesn't recognize the efficacy of long-term antibiotic use and believes that the risks associated with such treatments are too great.

ILADS Guidelines[12,19]

- Early-stage LD is treated with oral or I.V. doxycycline.
- In addition to the standard courses of oral or I.V. antibiotics, sequential treatments, combination antibiotic therapies, higher than normal dosages of antibiotics or longer than normal courses, pulsing of dosages, and integration of nonantibiotic drugs into the treatment regimen may be needed.
- Increased healthcare provider monitoring of patients utilizing such therapies is advised, as these treatment regimens are associated with increased risks to the patient, such as gastrointestinal distress, *Clostridium difficile* infection due to the killing of beneficial bacteria, development of resistant strains of bacteria, development of fungal infections, or suppression of the immune system.
- Withholding prophylaxis or providing inadequate prophylaxis to patients may lead to treatment delays and poor outcomes for many.

cases.[9] Despite the prevalence of this potentially debilitating infectious illness, controversy surrounds its diagnosis and treatment.

Nurses play an important role in reducing patient suffering by recognizing the signs and symptoms of LD and understanding how to address them. Nurses should stay current on LD research as well as attend staff-development programs when available. They should also educate the community on preventing LD through health fairs, seminars, pamphlets, and newsletters. Knowledge is the key to prevention and prompt treatment of LD, and nurses are in an optimal position to educate their patients and communities. ■

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