Lyme Disease—Part I: Epidemiology and Etiology

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GOAL

To discuss the epidemiology and etiology of Lyme Disease (LD)

OBJECTIVES

Upon completion of this activity, dermatologists and general practitioners should be able to:

1. Describe the geographic distribution and incidence of LD.
2. Outline the epidemiology and etiology of LD.
3. Describe the life cycle of ticks infected with LD.

CME Test on page 367.

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Lyme disease (LD) is a tick-borne disease that typically presents with myalgia, fatigue, and a characteristic rash. LD occurs worldwide, and its incidence continues to increase. Prevention and early diagnosis based on increased understanding of disease transmission and pathomechanisms are crucial in stopping LD from progressing to its later stages. In this article, the first of a 2-part series on LD, we review epidemiologic and etiologic factors.

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Lyme disease (LD), a multisystem disease transmitted by the spirochete *Borrelia burgdorferi*, is the most common vector-borne disease in the United States. For surveillance purposes, the Centers for Disease Control and Prevention[1] defined LD by the presence of either an erythema migrans rash equal to or larger than 5 cm in diameter or at least one musculoskeletal, neurologic, or cardiac manifestation confirmed by laboratory testing.

Although LD has been identified and described in Europe since the early 20th century, it was not recognized as a distinct entity in the United States until the mid-1970s, when the incidence of childhood arthritis in Connecticut increased significantly.[2] Investigators of this anomaly described Lyme arthritis and its etiology. Generally presenting with myalgia, fatigue, and a characteristic rash

Main Vectors (Ticks), Main Sources of Blood Meals for Tick Nymphs, and Main Reservoirs of *Borrelia burgdorferi* by Location

Location	Vector (tick)	Preferred Blood Meal of Nymph	Reservoir
Northeast US	*Ixodes scapularis*	White-footed mouse* Any small vertebrae	White-footed mouse* Chipmunk Ground-feeding bird Dog
Western US	*Ixodes pacificus*	Lizard	Wood rat Kangaroo rat Deer mouse
Europe	*Ixodes ricinus*	Any small mammal, bird, or lizard	Vole Field mouse Wood mouse

*In the US region where Lyme disease is most endemic, the white-footed mouse is both the main source of blood meal for *Ixodes scapularis* and the main reservoir of *Borrelia burgdorferi*.

within the first month of transmission, LD can progress to arthritis, central nervous system manifestations, and cardiac abnormalities if left untreated. When LD is recognized and treated correctly, however, the prognosis for most patients is excellent. Moreover, individuals trying to avoid infection can take important preventive measures.

Epidemiology

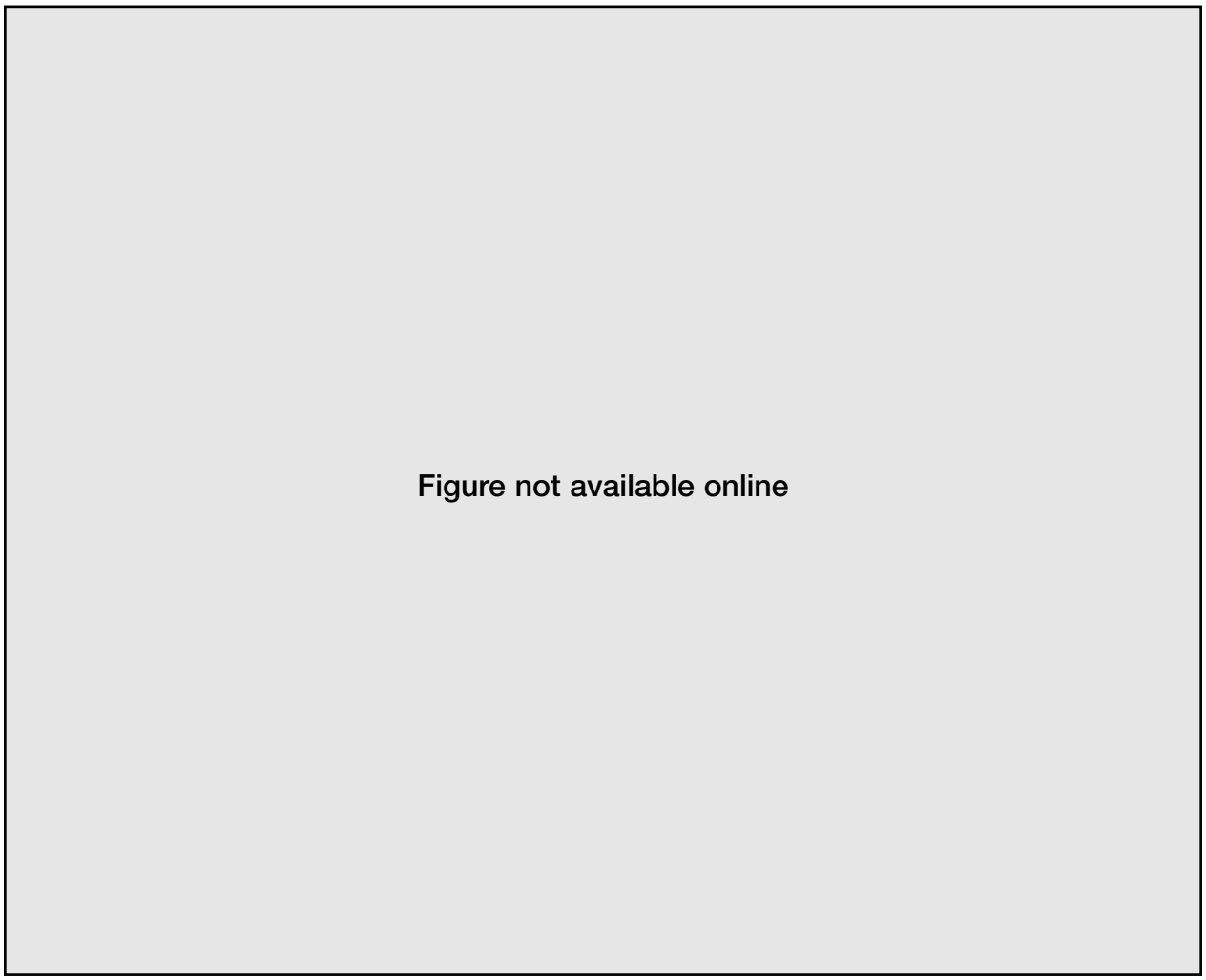
In the United States, more than 128,000 cases of LD were reported between 1982 and 2000[3]; more than 16,000 cases (6 cases/100,000) were reported in 1999.[4] In areas where LD is endemic, however, annual incidence ranges from 20 to 100 cases/100,000.[5] Data suggest that actual rates may be underrepresented and may be 10 times higher than those currently reported.[6] The number of cases reported each year continues to rise—a result of increased education and recognition; increased deer tick population; and increased time spent in rural areas, where exposure to ticks is significant.[6]

Although LD has been reported in 49 states (Montana being the exception), 92% of cases were from only 9 states (Connecticut, Rhode Island, New York, Pennsylvania, Delaware, New Jersey, Maryland, Massachusetts, Wisconsin).[4] In 1999, the incidence of LD in Connecticut was 98.0/100,000, the highest in the country.[4] Areas where LD is endemic are concentrated in the Northeast, the mid-Atlantic, and the upper Midwest, where the deer tick (*Ixodes scapularis*) is the vector (Table). LD also is endemic in a limited area of northern California; the vector is the western US black-legged tick (*Ixodes pacificus*). The sheep tick (*Ixodes ricinus*) is the vector in Scandinavia and central Europe.

People of all ages and races are susceptible to LD, but the age groups most commonly affected are 2- to 15-year-olds and 30- to 55-year-olds.[7] Men, accounting for 52.5% of reported cases, are slightly more commonly affected than women.[8] According to 1995 surveillance data, whites account for the large majority (95.8%) of reported cases in the United States.[9] Disease onset is most commonly reported in June (28.5%) and July (28.9%). Risk of acquiring LD is not linked to age, race, or gender but rather to amount, timing, and location of outdoor activity and use of preventive measures.

Etiology

Humans acquire LD from *Borrelia burgdorferi* transmitted through the saliva of infected feeding ticks. There is no evidence of human-to-human transmission of *B burgdorferi*. The *Borrelia burgdorferi sensu lato* complex consists of 10 genospecies, only 3 of which (*Borrelia burgdorferi sensu stricto, Borrelia garinii, and Borrelia afzelii*) are associated with disease in humans.[6] Other *Borrelia* species (eg, *Borrelia andersonii, Borrelia valaisiana, Borrelia japonica*) do



Three-stage (2-year) life cycle of the deer tick (*Ixodes scapularis*). Although both nymphs and adult ticks can transmit *Borrelia burgdorferi* to humans, nymphs are a more frequent source of infection. (Reprinted with permission from the American Lyme Disease Foundation, Inc., Somers, NY.)

not account for human disease. Either these species are not virulent, the ticks in which they live do not feed on humans, or both.[10]

Each *Borrelia* species responsible for human disease is associated with a unique clinical presentation. *B burgdorferi* is associated with arthritis, *B garinii* with neurologic manifestations, and *B afzelii* with cutaneous manifestations.[11] These 3 species and their clinical presentations are found only in Europe. *B burgdorferi sensu stricto* and its clinical presentation, are found only in the United States.[5]

Ticks can be infected with the *B burgdorferi* spirochete at any 1 of the 3 times the ticks feed during their 3-stage (2-year) life cycle (Figure). Maturation from one stage to the next (eggs to larvae, larvae to nymphs, nymphs to adults) depends on a blood meal from a host. The cycle begins in the spring, when adults lay thousands of eggs. These eggs hatch into larvae by late summer. Typically, in the eastern United States, the white-footed mouse (*Peromyscus leucopus*) or another small vertebrate is the first host for the larvae and the first potential source of infection with the spirochete.[6] (Humans also are potential hosts.[11]) These larvae, which remain dormant during autumn and winter, transform into nymphs the following spring. Then, in late summer or early autumn, nymphs mature into adults. Any vertebrate can become a host for adult ticks, but the usual host (and site for mating) is the white-tailed deer (*Odocoilus viginianus*).[6] Main reservoirs of the spirochete vary by region. In US areas where LD is endemic, white-footed mice, chipmunks, and dogs are both the main reservoirs and the main sources

of blood meals for larvae and nymphs.[11] As a result, the number of infected animals increases in these areas, and the source of infection for benign ticks expands. In areas where the incidence of LD is lower (eg, in the western United States), reservoirs are not the main sources of blood meals.

Nymphs are the most important vectors for transmission of the *B burgdorferi* spirochete to humans. Although adult ticks are more likely than nymphs to be infected with the spirochete, because adults have fed more and have been exposed to the source of infection longer, nymphs are much more likely than adult ticks to infect humans. Their small size allows nymphs to go undetected long enough for spirochete transmission to occur, and nymphs actively feed in the spring, when people are more likely to be outdoors and to be wearing less protective clothing.[6]

Several factors are significantly associated with the risk of transmission of the *B burgdorferi* spirochete from ticks to humans. Primarily, the proportion of infected ticks in a geographic area is correlated with the transmission rate; the incidence of infection in deer ticks is high in areas with a high incidence of LD in humans.[5] Also, exposure time (the time a tick spends feeding) is important. Few animals become infected after only 24 hours of exposure; most become infected after 48 hours.[12] The days needed for a tick to implant in its host and the time needed for *B burgdorferi* to travel from the tick's midgut to its salivary glands account for the time delay between initial exposure to tick and actual infection.[6] Not everyone who is bitten by an infected tick and who seroconverts displays clinical features.

Over the past several years, our knowledge of the epidemiology of LD has come into sharper focus. In addition, we have identified the organism and routes involved in LD transmission. Understanding the epidemiologic and etiologic factors in LD is key in clinical prevention and early diagnosis.

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