

Lyme Disease in Dogs: Pathophysiology and Clinical Signs

IVMA CE Self-Study Offering
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AIM OF THIS ARTICLE

Lyme disease is one of the most common zoonotic tick-borne diseases worldwide. Although the disease is becoming an increasing problem in dogs, its clinical and diagnostic features remain as controversial in this species as they are in people with the disease.

This article—the first in a 2-part series—aims to review some key aspects of the epidemiology, pathogenesis, and clinical manifestations of Lyme disease in dogs.

LEARNING OBJECTIVES

Following completion of this continuing education article, you will be able to:

- Name the causative agent of Lyme disease
- Name Lyme disease vectors, hosts, and reservoirs
- Explain how Lyme disease is transmitted
- Explain how *Borrelia burgdorferi* increases its virulence to increase its chance of survival in the host
- Define which dogs are at greatest risk of developing Lyme disease

Epidemiology

Causative agent

The spirochete *Borrelia burgdorferi* is the primary etiological agent of Lyme disease in North America. The term used to collectively describe all genospecies of *B. burgdorferi* that cause Lyme disease is the *B. burgdorferi* sensu lato complex. These genospecies vary according to geographic region, and in North America, *B. burgdorferi* sensu stricto predominate.

The spirochetes cannot survive as free-living organisms in the environment and are transmitted between vertebrate reservoir hosts and tick vectors. Small mammals are the primary reservoir host for the spirochetes, whereas sheep, dogs, and humans are dead-end hosts. In North America, the most common vector is the deer tick *Ixodes scapularis*, also known as the blacklegged tick.

Vector

Ixodes scapularis is a three-host tick with a life cycle that is usually completed within two to three years, depending on climatic conditions and the supply of suitable hosts. Each tick stage attaches to a single host and feeds on its blood for several days before detaching and either molting to the next stage or producing eggs). Tick eggs are deposited in the spring. Larvae emerge approximately one month later, feed on small mammals such as rodents—the main reservoirs—in the summer, and then drop off the host onto the ground where they remain dormant over winter. Larvae molt into nymphs the following spring (year 2), and the nymphs then also feed on small mammals, as well as larger ones such as dogs and humans. Nymphs molt into adults in the fall, and the adults typically feed on larger mammals, such as deer and livestock, where they mate. Female ticks then leave their host by falling to the ground where they lay their eggs and later die.

The life cycle then repeats. Tick stages must take a blood meal to molt to the next developmental stage and produce eggs.

Immature larval and nymphal stages of *Ixodes scapularis* acquire spirochetes when they feed on infected rodents; the nymphs and adult ticks can then transmit the infection to vertebrate reservoir hosts. However, nymphs—because they are smaller than adults and therefore often go undetected for longer—are considered particularly important in transmission of infection to domestic animals and humans. Direct transmission of spirochetes between reservoir hosts is unlikely.

The distribution and density of tick vectors has changed over the years, with expansion from the main endemic areas across an increased geographic range. Movement of hosts can also affect tick numbers and result in establishment of tick populations in new areas. In addition, various environmental factors have contributed to an increase in the incidence of Lyme disease in animals and humans:

- Reduced deforestation
- Human encroachment on habitats that are favorable to ticks and their hosts
- Increased human outdoor activities
- Climatic changes that favor a wider distribution of tick vectors

Ticks are usually inactive in winter and, as temperatures rise, they become active and emerge onto vegetation to quest for a host to feed on. Peak tick season corresponds with rising temperatures and usually extends from spring through autumn. However, different tick life stages are active at different times of the year and these time periods can vary each year and in different locations. One UK study collected *Ixodes ricinus* ticks from vegetation in different sites in a park during the summer, and showed that the number of ticks was highest at temperatures between 70 °F and 78.8 °F, and decreased at temperatures higher and lower than this range. Ticks were also found to occur more frequently in lower humidity-environments (below 20.0% relative humidity). Lyme borreliosis is more commonly diagnosed during the summer, coinciding with peak tick activity.

Distribution of Lyme disease

In the past 20 years, the number of cases of Lyme disease in people have tripled. At the same time, the geographic ranges of *Ixodes scapularis* and *Ixodes pacificus* (which also commonly transmits Lyme disease to people and dogs) have increased, and these ticks have now been reported in half of all US counties.

Lyme disease is thus also becoming an increasing problem for dogs across North America. Typically, infection of dogs occurs more commonly in areas with endemic populations of ticks and where acaricide use is non-routine, but is rare in non-endemic areas without a travel history to an endemic area. In addition to increased tick numbers and *Borrelia* prevalence within the tick population, other factors contribute to the rising number of cases of Lyme disease; these include a greater awareness of the disease and improved diagnostic procedures.

Pathogenesis

It is typically believed that ticks must attach and feed for 24 to 48 hours before *B. burgdorferi* transmission occurs. However, spirochetal transmission has been shown to occur in less than 16 hours in animal studies, and the minimum attachment time for transmission of infection has never been definitively established.

To cycle between two different hosts, *B. burgdorferi* varies its gene expression. After a tick bite, *Borrelia* organisms in the tick do not immediately transmit to the vertebrate host. Instead, during the first 12 to 24 hours after biting the host, the organisms undergo a change in their outer surface to improve their chances of survival in the host; one important feature of this increased virulence is a switch in their outer surface proteins (Osp)—with upregulation of OspC and downregulation of OspA. OspC has been shown to be essential for spirochetal transmission through the tick and to establish infection in the host.

Spirochetes also produce another outer membrane protein known as variable major protein-like sequence (VlsE). This protein can change its amino acid sequence rapidly after infection of a host. However, the host is unable to rapidly generate specific antibodies against these quickly changing antigenic variants, and antibodies produced against previous VlsE variants therefore cannot neutralize the borrelial cell.

VlsE and its constant regions (including C6 peptide which is based on the invariable region 6 [IR6] of VlsE) is therefore used as a diagnostic tool to detect antibodies against *B. burgdorferi* in dogs and humans. Another important virulence factor is tick saliva protein 15 (Salp15) which binds to OspC on borreliae, enhances their transmission to the host, and provides initial protection from the host's immune system.

The exact mechanisms by which *B. burgdorferi* disseminates through the host remain poorly understood. One hypothesis is that the organism disseminates in the bloodstream and can survive in the blood. Another suggests that the immunological components of blood make it a hostile environment for borreliae, forcing the organisms to migrate through tissues and establish in collagen-rich tissues such as skin. Once they establish in these collagen-rich tissues, borreliae can proliferate and survive for years or disseminate to other locations, including joints, neural tissue, and the heart. Additionally, the extensive pathologies caused by borrelial infection are not considered to be a direct consequence of spirochetal activity, but are instead thought to arise from the host's strong inflammatory response to infection with even a small number of organisms.

Clinical features

Clinical Lyme disease is a less common outcome of infection in dogs than in humans, and only about 5% of dogs develop clinical signs of disease when exposed to *B. burgdorferi*.

Clinical disease usually presents acutely with nonspecific signs that include lethargy, anorexia, fever, depression, and lymphadenopathy, which may be overlooked, especially because they often disappear within a few days. Although erythema

migrans—a characteristic clinical feature of Lyme disease in humans—has not been reported in dogs, a small red lesion, approximately 1 cm diameter, may be present at the site of the tick bite. However, this also disappears within a few days after the tick is removed.

Another common acute presentation of Lyme disease in dogs is joint swelling and lameness, reported in 9% to 28% of seropositive dogs. This typically begins in the limb closest to the location of the tick bite, commonly improves and resolves within a few days, and may then occur in a different limb. If the infection goes undiagnosed and untreated, lameness may progress to chronic non-erosive polyarthritis.

The term “Lyme nephritis” has been attributed to a severe protein-losing, immune complex nephropathy with renal failure that has been described in dogs with advanced disease. This condition is progressive and often fatal. Although robust studies that document its prevalence are lacking, data estimate that Lyme nephritis develops in less than 2% of seropositive dogs in the United States.

Rare neurologic and cardiac manifestations have also been reported.

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