

Borrelia burgdorferi infection and Lyme disease

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Summary

Infection with Borrelia burgdorferi, the Gram-negative spirochete bacterium that causes Lyme disease, is common in horses residing in regions endemic for Ixodes spp. ticks, and infection prevalence is likely on the rise as tick vectors undergo range expansion. While many horses will become infected with B. burgdorferi following a tick bite, the percentage of horses that will go on to develop Lyme disease is unknown. Documented syndromes attributed to *B. burgdorferi* include neuroborreliosis, cutaneous pseudolymphoma, and uveitis. Limited evidence exists to document stiffness, lameness, and malaise in horses as a result of *B. burgdorferi* infection, although these signs might be possible. Diagnosis of clinical Lyme disease in horses can be challenging. Ruling out other diseases which present with similar signs should be undertaken. A variety of serological tests exist to assess antibodies to B. burgdorferi in horses. These tests must be interpreted cautiously because a positive test result: (1) only indicates exposure, (2) does not prove that any clinical signs are due to B. burgdorferi infection, and (3) does not mean that the horse will experience disease in the future. Routine serological testing of healthy horses is not recommended, nor is the treatment of seropositive but otherwise clinically healthy horses.

In 2018 the American College of Veterinary Internal Medicine published "Borrelia burgdorferi and Lyme Disease in North American Horses: A Consensus Statement" to address some of the controversies regarding the clinical diagnosis, treatment, and prevention of *B. burgdorferi* infection and Lyme disease in horses. This expert review is available open access through ACVIM at: https://doi.org/10.1111/jvim.15042

Definition

Borrelia burgdorferi, a gram-negative motile spirochete, is believed to be the predominate cause of Lyme disease in North American horses.

Prevalence

Exposure and infection with *B. burgdorferi* is common in horses residing in regions endemic to *Ixodes* spp. ticks, the primary vector for transmission. Exposure prevalence is likely on the rise as the *Ixodes* spp. tick vectors are undergoing range expansion. Large mammalian hosts such as deer are important in maintaining the tick population while natural reservoirs of *B. burgdorferi* such as white-footed mice are important in infecting the ticks. While many horses will become infected with *B. burgdorferi* following a tick bite, the percentage of horses that will go on to develop Lyme disease is unknown.

Clinical signs

At this time, documented syndromes attributed to *B. burgdorferi* include neuroborreliosis (ataxia, atrophy, cranial nerve deficits, stiff neck, cutaneous hyperesthesia), cutaneous pseudolymphoma (dermal masses at the site of tick bite), and uveitis (blepharospasm, epiphora, yellow-green fibrinous aqueous flare). Limited proof exists for non-specific syndromes including lameness, poor performance, arthritis, and body soreness, but these signs might be possible as the organism preferentially resides in synovial membranes and close to blood vessels and nerves in connective tissue.

Lyme neuroborreliosis: *B. burgdorferi* infection of the central nervous system has been documented in both animals and humans. In horses, clinical signs of neuroborreliosis include: behavioral changes, hyperesthesia, ataxia, dysphagia, respiratory distress due to laryngeal dysfunction, cranial nerve deficits, muscle atrophy and neck stiffness. Cerebrospinal (CSF) fluid cytology is frequently abnormal with neutrophilic or lymphocytic pleocytosis. Antigen testing with PCR on CSF can confirm disease, however, this test has a very low sensitivity in humans and animals. A recent study by Johnson *et al* (2018) found the Lyme Multiplex assay performed on serum and/or cerebrospinal fluid (similar to how EPM is diagnosed) has a poor diagnostic accuracy in horses with neuroborreliosis. Neuroborreliosis, has been reported in horses with common variable immunodeficiency, and immune deficiencies may be a risk factor for development of severe disease following infection with *B. burgdorferi*.

Incubation period

It often takes 3 or more weeks following infection for antibodies to be detected by any of the currently available serologic assays.

Risk Factors

Horses residing in regions endemic to *Ixodes* spp. ticks, especially in environments conducive to tick habitation, including heavily wooded areas with dense, low-lying vegetation and ground cover.

Transmission

Vector transmission

- Infection with *B. burgdorferi* occurs following bite by infected *Ixodes* spp. tick
- Horizontal transmission (Horse-to-horse) does not occur
- Vertical transmission (mares to fetus) has not been documented

Diagnostic Sampling, Testing, and Handling

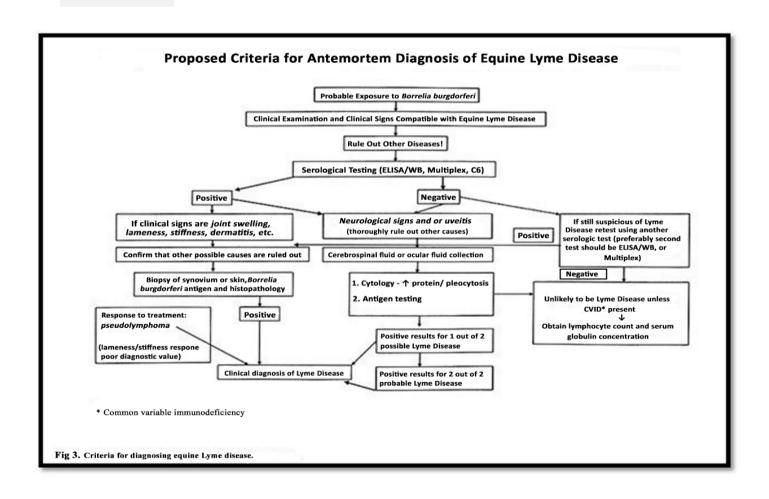
The diagnosis of Lyme disease in horses should be based on compatible clinical signs, evidence of exposure to *B. burgdorferi* (generally achieved through serology), and perhaps most importantly, ruling out all other possible causes. Several serologic assays are available for assessing exposure to *B. burgdorferi*, including ELISA, Western Blot, ELISA SNAP test, IFAT, and ELISA Multiplex assay. All detect antibody production against various organism surface antigens. The positive predictive value of disease is low for all antibody tests. Antigen detection assays (PCR, immunohistochemistry, silver staining, fluorescent in situ hybridization (FISH)) can be utilized when potentially infected tissues or samples such as skin biopsies, ocular fluid, cerebrospinal fluid, tissue samples or synovial

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samples are available. Horses with common variable immune deficiency may have Lyme disease and be seronegative. Although other borrelial organisms, including *B. miyamotoi*, *B. bissettii*, and *B. mayonii*, have been found in *Ixodes* ticks in parts of the United States, there are currently no reports of equine infection with any of the 3 organisms.

Key diagnostic concepts:

- <u>Serology alone only confirms exposure</u> to *B. burgdorferi* (or vaccination) and should not be viewed as a stand-alone test for Lyme disease, as exposure to the organism is very common in endemic areas, and many exposed horses will never show any clinical signs.
- Screening of normal horses and/or testing of horses without compelling clinical signs of disease (e.g., as part of a pre-purchase examination or routine screening) is <u>not routinely</u> recommended.
- None of the available seroassays are capable of differentiating exposure to *B. burgdorferi* from clinical Lyme disease.
- Magnitude of antibody titer has not been shown to correlate with likelihood of clinical disease.



Revised 2020; Reprinted with permission from: Divers TJ, Gardner RB, Madigan JE, Witonsky SG, Bertone JJ, Swineboard EL, Schutzer SE, Johnson AL. Borrelia burgdorferi Infection and Lyme Disease in North American Horses: A Consensus Statement. J Vet Intern Med 2018 32(2): 617-632.

Available open access at: https://doi.org/10.1111/jvim.15042

Carrier status

The potential for chronic B. burgdorferi infection in horses is not known. Many horses maintain positive titers for months to even years, with or without treatment. It is unknown whether persistently high titers are due to continued IgG production after organism clearance, persistent or chronic infection, or reinfection after treatment.

Treatment

Several options exist for treatment of horses with suspected Lyme disease, and a gold standard protocol has not yet been developed. Tetracycline antimicrobials are commonly administered for 7 to 30 days (oxytetracycline 6.6 mg/kg IV q24h; or doxycycline 10 mg/kg PO q12h; or minocycline 4 mg/kg PO q12h). It should be noted that tetracycline antimicrobials exert anti-inflammatory effects through their inhibition of matrix metalloproteases, which may contribute to improvement in clinical signs during treatment independently of any effects on B. burgdorferi. Accordingly, relapse of clinical signs following treatment should not necessary be interpreted as failure to clear the organism, as the improvement may have been due to the medication's anti-inflammatory properties alone.

Ceftiofur has also demonstrated in-vitro efficacy against B. burgdorferi, with MIC values falling within the range of expected serum and tissue concentrations following administration of ceftiofur crystalline-free acid (Excede®).

Titers should not be used alone to assess response to treatment or as deciding factors for prolonged therapy, as many treated horses maintain positive titers for months to even years.

Prognosis

The prognosis for *B. burgdorferi* infection is generally good as most exposed horses do not show clinical disease. The prognosis for neuroborreliosis and B. burgdorferi uveitis is guarded to poor.

Prevention

Tick control through environmental avoidance and diligent removal from horses remains the mainstay of preventing exposure and infection with B. burgdorferi.

- Tick repellants: Multiple spray and spot-on tick repellent products are available. These products may contain a combination of cypermethrin, permethrin, pyrethrins, or piperonyl butoxide, and demonstrate variable efficacies and durations of action.
- "Tickscaping": Environmental tick populations can be reduced by removal of leaves and woody debris, pasture mowing, and maintaining dry, well-lit paddocks whenever possible.

Vaccination While no Lyme vaccines are licensed for use in horses, there is reasonable evidence to suggest that vaccination with canine recombinant OspA vaccine or whole-cell vaccines are at least partially protective. Specific vaccination protocol and protective antibody levels have not been established.

Biosecurity

Equine B. burgdorferi infection is not contagious, and therefore, isolation and biosecurity measures are not necessary in infected horses.

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Zoonotic Potential No known zoonotic potential from horses to humans. Humans participating in outdoor activities in endemic regions are at risk for *B. burgdorferi* infection and Lyme disease if bitten by *Ixodes* spp. ticks.

Further reading

Borrelia burgdorferi Infection and Lyme Disease in North American Horses: A Consensus Statement.

Divers TJ, Gardner RB, Madigan JE, Witonsky SG, Bertone JJ, Swinebroad EL, Schutzer SE, Johnson AL. J Vet Intern Med. 2018 Mar;32(2):617-632.

Cerebrospinal fluid Lyme multiplex assay results are not diagnostic in horses with neuroborreliosis. Johnson AL, Johnstone LK, Stefanovski D. J Vet Intern Med. 2018 Mar;32(2):832-838.

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