Borrelia burgdorferi infection in horses is common in some areas of North America, yet the incidence of clinical disease has not been determined which makes Lyme disease in the horse controversial. Progress is being made, case-by-case, in defining the several clinical presentations of Lyme disease in adult horses. Current serologic tests are very sensitive and specific for detecting either previous or concurrent infection or exposure but may not distinguish between those. Treatment protocols are available for Lyme disease in the horse, however, their ability to eliminate the organism remains questionable. Currently, minocycline is being tried in some presumed Lyme cases as a possibly improved alternative to doxycycline and oxytetracycline. Vaccination, like many aspects of Lyme disease, remains controversial, although the canine-approved vaccines have the potential to prevent infection based upon vaccine studies in ponies and other animals.

The mid-Atlantic and northeastern states have a high seroprevalence for Borrelia in the equine population, as do areas of Minnesota and Wisconsin extending into southern Canada. Infected horses are also reported in some regions of California and are fairly common in Virginia (certainly as far south as Charlottesville!). The geographic areas with horse and human infections appear to be spreading. In one New England survey, 45% of horses had Borrelia antibodies. A Wisconsin study found that 118 of 190 horses were serologically positive. The Borrelia organism lives in the tick’s gastrointestinal tract and is transferred to animals during blood meals. Generally, 24 to 48 hours of attachment are required to transfer the organism successfully from the tick to the mammalian host. This time may be needed for the organism to downregulate an outer membrane protein (OspA), which may be important to maintaining survival in the mammalian host. Simultaneously, other outer surface proteins (e.g., OspC, OspE, OspF) that are normally in low concentration in the tick gastrointestinal tract are upregulated. This is particularly true for OspC (found in the tick salivary gland), which enhances complement resistance and other methods of immune evasion in the mammalian host. These changes in expression of surface proteins may be triggered by the blood meal. Other proteins, such as the C6 peptide found in a dominant invariable region of the variable major protein-like gene VisE, permit antigenic variation, ensuring survival in the host. B. burgdorferi may also survive in the host by residing in collagen and connective tissue, likely via low molecular weight decorin-binding proteins, thus having no requirement for iron. After experimental infection of ponies, the organism appears to reside mostly in skin near the tick bite, as well as in connective tissue and muscle and around nerves and blood vessels near synovial membranes. Persistent infection, especially following antibiotic treatment, has been very controversial in humans and most studies do not support a syndrome of chronic infection/chronic Lyme disease in properly treated patients. However, a recent article provided evidence that both cysts (round bodies) and biofilm-like colonies exist and may cause chronic disease in humans.
A wide variety of clinical signs have been attributed to *Borrelia* infection in horses, but cause and effect have been difficult to document in most cases. Because of both the high prevalence of antibodies against *Borrelia* in horses in some regions of the U.S. and the difficulty in proving clinical disease in most cases, Lyme disease is undoubtedly the most controversial equine disease in those areas. The clinical signs most often attributed to equine Lyme disease include stiffness and lameness in more than one limb, muscle tenderness, hyperesthesia, lethargy, and behavioral changes. Unlike human Lyme disease, joint effusion has been minimal in most Lyme-suspect horses. Muscle wasting and pain over the thoracolumbar area have been present in a few horses with high serum titers and some of these horses have had neurologic signs. In one report, two horses were diagnosed with Lyme neuroborreliosis and both had chronic, necro suppurrative-to-nonsuppurative, perivascular-to-diffuse meningo radiculoneuritis on necropsy examination. Hyperesthesia, lumbar pain and muscle wasting were the initial clinical findings followed by ataxia of all four limbs, facial nerve paralysis and finally head tremors with depression in one horse. On necropsy, spirochetes were identified by Steiner silver impregnation in both cases, predominantly in the affected dura mater of brain and spinal cord. *Borrelia burgdorferi sensu stricto* was identified by polymerase chain reaction, with the highest spirochetal burdens in tissues with inflammation, including the spinal cord, muscle, and joint capsules. In another report, a horse with severe neck stiffness that progressed to ataxia had lymphohistiocytic meningitis and *B. burgdorferi* DNA in the cerebrospinal fluid (CSF). That horse originally responded to doxycycline treatment but relapsed after discontinuing the treatment. Another case was a Thoroughbred hunter that presented for lameness and ataxia and had lymphocytic pleocytosis and was PCR positive for *Borrelia* on CSF analysis. The horse initially responded well to doxycycline but had some deterioration when treatment was discontinued. The author has examined two other suspect Lyme horses with ataxia and severe lymphocytic infiltration and thickening of the meninges. Based upon these few cases, it may be that ataxia and lumbar muscle wasting caused by lymphohistiocytic meningitis and radiculoneuritis, with occasional fasciculations and neck stiffness, are common characteristics of neuroborreliosis in the horse. CSF would likely show a lymphocytic pleocytosis and, although uncommon in humans with neuroborreliosis, some horses have CSF that is PCR positive for *B. burgdorferi*. Bilateral uveitis was recently reported in 2 horses associated with *Borrelia* infection of the eye. *Borrelia* was found on cytologic examination and confirmed by PCR in the vitreous in both horses. No organisms were observed in the aqueous although one aqueous sample was PCR positive. *Borrelia* was also observed with silver stain in the inflamed uveal tissue. In addition to the uveitis, a chronic, multifocal, lymphohistiocytic gangglioradiculitis and neuritis with presumptive neuronal degeneration in the spinal nerves was found in one of the horses with uveitis. Another report describes a horse with Lyme pseudolymphoma (multiple lymphohistiocytic cutaneous nodules). The horse responded completely to doxycycline treatment, as might be expected for a cutaneous form of borreliosis.

The diagnosis of exposure to *Borrelia* can usually be determined by serology. Enzyme-linked immunosorbent assay (ELISA) testing and Western Blot testing have been the most commonly used screening tests for detection of antibodies indicating exposure. The C6 SNAP test (IDEXX Laboratories, Westbrook, Maine), which is based on antibody to a peptide that reproduces the sequence of the invariant region 6 (an immunodominant, conserved region), has
good correlation of results with the ELISA in horses; specificity is better than sensitivity. Vaccination should not cause the C6 SNAP test to be positive. A multiplex antibody bead test for OspA, OspC and OspF quantitative antibody detection has recently been introduced for the serodiagnosis of equine Lyme disease. The concept is that high levels of OspA suggest vaccination, elevated OspC indicates recent infection (antibody against this antigen typically increases with early infection and then declines after several months), and OspF elevations suggest either chronic infection or more long-lasting antibodies. Since the introduction of the Multiplex assay, a larger number of unvaccinated horses are found to be OspA antibody positive; importance of this is unknown! Clinical diagnosis is difficult and should be based upon the following parameters: exposure to and infection with *Borrelia* (geographic location and serologic testing), probability of the clinical signs being due to *Borrelia* infection based upon knowledge of most common anatomical locations for the organism to reside in the horse (synovial membranes, skin, meninges, nerves, vitreous), reported clinical syndromes, laboratory testing by PCR and/or histopathology (usually a lymphoplasmacytic or histiocytic inflammation) and most importantly ruling out other diseases!

The two most frequently used drugs for treatment of Lyme disease in horses are intravenous (IV) tetracycline and oral (PO) doxycycline or minocycline. Minocycline is preferred over doxycycline. Minocycline has better oral bioavailability than doxycycline in the horse and it attains higher concentration in CSF and aqueous fluids because it is more lyophilic and less protein bound than doxycycline. Minocycline (4 mg/kg PO q12h) may eventually replace doxycycline as preferred treatment for Lyme disease in the horse. Doxycycline protocols as used in human Lyme disease may not be as successful in the horse because of the low bioavailability of doxycycline in the horse and the likelihood of more long-standing infections in horses than in humans prior to treatment. Proper duration of treatment is unknown. The use of metronidazole for the unproven and controversial cystic borreliosis lacks sufficient clinical information in either humans or domestic animals.

Prevention of *Borrelia* infection has centered around the use of the canine Lyme vaccines and tick sprays. Canine Lyme vaccines appear to be safe and those that maintain high OspA antibody would be expected to provide protection. Dose and frequency of vaccination are unproven. Ultra Boss® by Merck is an equine-approved product for tick prevention.

**ANAPLASMA PHAGOCYTOPHILIA**

*Anaplasma phagocytophilia* is a common and geographically expanding tick-borne disease in horses. Several strains are known, associated with individual small mammals who serve as reservoir host. Clinical signs are mostly fever, jaundice, petechiations, leg edema, and depression often with mild ataxia. In rare cases, myopathy and recumbency may occur. Diagnosis is by clinical signs, PCR during the febrile stage, finding inclusion bodies in neutrophils in early febrile period, and response to therapy. Serology is only mildly helpful in confirming the disease; approximately 30% are positive on snap test towards the end of the febrile stage. The incubation period after tick bite is approximately 5 days with clinical signs occurring on days 5-12, and may remain infected for 4 weeks or more if not treated. Intravenous tetracycline is the treatment of choice; minocycline and doxycycline are second choice antibiotics. Steroids improve clinical signs but may prolong infection. Even without treatment recovery is nearly 100%. Immunity is thought to be approximately two years.
**TICK-BORNE ENCEPHALITIS VIRUS**

Powassan virus a member of the Flavivirus genus is known to infect man and animals in Canada and spread by Ixodes ticks. The virus has been inoculated intracerebrally into horses. In horses, eight days after inoculation, prominent neurological signs occurred and lesions were those of nonsuppurative encephalomyelitis, neuronal necrosis, and focal parenchymal necrosis. The virus could not be re-isolated from horse brains. Clinical importance of this infectious agent in horses is unclear.


**Bartonella henselae**

Horses in the southeastern United States are naturally infected with *B. henselae*, *B. vinsonii* subsp. *berkhofii* genotypes I and III, and a bacteria most similar to *candidatus Bartonella volans*. Antibodies were not detectable by indirect fluorescent antibody assay (IFA) testing in bacteremic foals or horses, and prolonged enrichment culture for periods up to 21 days were necessary to document bacteremia in most horses. *Bartonella* was found in both healthy and sick horses/foals and an association of infection with disease was not clear. Further investigation into the pathogenic potential of *Bartonella* spp. infection in horses is warranted.


Recently *Bartonella henselae* was reported in associated with severe suppurative cholangiohepatitis in a foal. The foal responded well to treatment with minocycline which supported the association between the infection and disease.


**EHRlichia SPP. ORGANISMS**

From horses in south central U.S., 8.75% (21/240) of randomly acquired samples and 24.7% (18/73) of the serum samples from tick-infested horses were seropositive for *Ehrlichia* spp., but species-specific ELISA and PCR failed to confirm exposure to or infection with any known *Ehrlichia* spp; *E. canis*, *E. chaffeensis*, *E. ewingii*, and an *E. ruminantium*-like organism. Horses are likely infected with other *Ehrlichia* organisms but clinical importance is unknown.
PIROPLASMOSIS

Piroplasmosis is a tick-borne disease caused by either Babesia caballi or Theileria equi (B. equi). The infection and disease was thought to have been eradicated from the U.S. in 1988 but has resurfaced. Amblyoma cajennense and Dermacentor anocentor appear to be the most common vectors for transmission in the U.S. Theileria equi has been the causative agent in the recent U.S. piroplasmosis (theileriosis) outbreaks. Babesia caballi and Theileria equi affects all equid species, including horses, donkeys, mules. These intraerythrocytic organisms can cause hemolytic anemia and associated systemic illness (fever, hepatopathy, leg edema, etc.). Theileria equi infects both erythrocytes and mononuclear cells. Many infected horses are asymptomatic but with stress or steroid administration those horses may develop fulminant disease. Asymptomatic horses have such low number of erythrocytes infected that the organism is generally not observed on blood examination; this is unlike in clinical cases where 5% or more of erythrocytes are infected. T. equi can be eliminated from some infected horses with appropriate dosing of imidocarb dipropionate.