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## THE DIAGNOSIS AND TREATMENT OF TICK BORNE DISEASES IN DOGS

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### EHRlichiosis

*Ehrlichia* species are a group of tick-transmitted, intracellular, gram-negative bacteria in the family *Rickettsiaceae*. Recent reclassification of the genera involving tick-transmitted rickettsial agents has resulted in the organisms causing clinical ehrlichioses in dogs to be placed in three genera *Ehrlichia*, *Anaplasma*, and *Neorickettsia*. Because of the closely related nature of the *Ehrlichia* and *Anaplasma*, and the similarity in the clinical presentation of disease, this material discusses these organisms as causative agents of canine Ehrlichiosis.

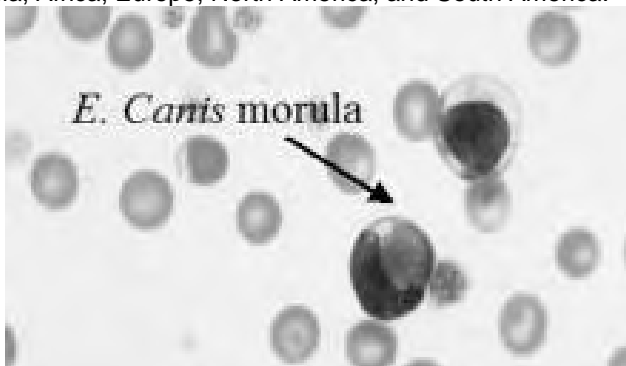
These infectious agents reside in one or more host blood cell types including granulocytes, monocytes, lymphocytes and platelets. However, each species has a fairly strong predilection for a specific cell type, thus categorizing most infections as either granulocytic or monocytic ehrlichioses. In addition, one known species of organism infects platelets (*Anaplasma platys*) and one species has a predilection for the endothelial cells of ruminant species (*E. ruminantium*).

Several different *Ehrlichia* species are known to infect dogs (*E. canis*, *E. ewingii*, *Anaplasma platys* (formerly *E. platys*), *Neorickettsia risticii* (formerly *E. risticii*), *E. chaffeensis*, and *A. phagocytophilum*, (formerly *E. equi*, the HGE agent and *E. phagocytophilum*)), and the clinical presentations may differ slightly, depending on the organism involved. Although any of these agents can be transmitted by blood transfusions from infected animals, most infections are tick-transmitted. Ticks are capable of harboring and transmitting the disease for several months after they are infected, making them important reservoirs. This review discusses the clinical findings and laboratory diagnosis of agents responsible for most clinical cases of canine ehrlichiosis, *E. canis*, *E. chaffeensis*, *E. ewingii*, *A. phagocytophilum* and *A. platys*.

### MONOCYTIC EHRlichioses

#### Etiology and Epidemiology

The monocytic form of canine ehrlichiosis is arguably the most common form. Canine monocytic ehrlichiosis (CME) may be caused by *E. canis* or *E. chaffeensis*, the causative agent of Human Monocytic Ehrlichiosis (HME). These intracellular rickettsial agents reside in the monocytes and lymphocytes of the infected host. CME has a worldwide distribution, and a significant seroprevalence in dogs from Asia, Africa, Europe, North America, and South America.



Transmission And Pathogenesis

*E. canis* is transmitted by the brown dog tick, *Rhipicephalus sanguineus*, and the primary vector for *E. chaffeensis* is the Lone Star tick, *Amblyomma americanum*. The organisms are transmitted through the saliva during a tick bite. They invade the monocytes and lymphocytes in the blood, liver, spleen, bone marrow, lymph nodes, lung, kidney, and central nervous system. Once inside the cells, the organisms form membrane-bound morulae that may contain from up to 50 or more bacteria.

### Clinical Findings

Natural infections with *E. canis* or *E. chaffeensis* cause diseases that can be clinically similar. Current serological assays cannot distinguish infections due to cross-reactive antigens. The clinical course of disease is well characterized for infections with *E. canis* and thus is detailed here. There are three phases of disease seen with CME: acute, subclinical, and chronic. Clinical findings usually occur 1 to 3 weeks after infection, and during the acute phase of the disease, are typically mild and consist of fever, depression, anorexia, weight loss, ocular and/or nasal discharge, and hemorrhage. The most consistent laboratory finding is thrombocytopenia but anemia and leukopenia may also occur. During the subclinical phase there are few if any clinical signs observed. Even so, many animals experience mild thrombocytopenia, hyperglobulinemia, and high antibody titer against *E. canis*. The chronic phase of the disease may be mild or severe. In mild cases, dogs remain infected but little evidence of illness is recognized. Animals are often febrile with outward signs of illness that may include weakness, depression, anorexia, weight loss, bleeding disorders and pale mucous membranes. Less frequent signs include ocular and nasal discharge, peripheral lymphadenopathy, edema, retinal lesions, ataxia, hepatomegaly, splenomegaly and possibly death. Laboratory findings include severe thrombocytopenia (> 80% of cases), nonregenerative anemia, and/or leukopenia, hyperglobulinemia, and elevated liver enzymes. The severity of disease varies with the pathogenicity of specific strains of the organism and individual differences in host defensive mechanisms (e.g., pups generally are affected more severely than adults).

### Diagnosis

It is rare to diagnosis canine monocytic ehrlichiosis by recognition of morulae in circulating mononuclear cells. The diagnosis is generally suspected based on clinical and routine laboratory findings and confirmed using serology. The serological assays most widely used are the indirect fluorescent antibody (IFA) test, which is available at most commercial laboratories, and the Snap<sup>7</sup> 3Dx (IDEXX Laboratories, Inc., Maine, USA) for clinic use. When compared to the IFA, the Snap<sup>7</sup> 3Dx had a 100% specificity and 80% sensitivity for diagnosing CME. The Snap<sup>7</sup> 3Dx assay, which uses recombinant analogs of the major outer membrane proteins (p30 and p30-1), has increased specificity and sensitivity over the older Snap<sup>7</sup> Canine Combo from IDEXX, which used whole-cells from the *E. canis* Oklahoma strain as antigens. Animals infected with either *E. canis* or *E. chaffeensis* will test positive using any of the currently available serological assays. The only way to distinguish between these two infectious agents is by in vitro cultivation or PCR analysis (available at the North Carolina State Univ. Tick-Borne Disease Testing Laboratory).



### Treatment And Prognosis

Tetracycline (20 mg/kg PO tid) or doxycycline (5-10 mg/kg PO bid) treatment for 3 weeks is generally effective in eliminating clinical signs. However, animals with very high titers (>1:10,000) can take over a year to seroconvert to a negative status. In some cases, titers (especially high titers) may persist indefinitely, suggesting that some animals remain persistently infected after treatment. Repeated therapy (or long term therapy) does not necessarily result in negative titers. Blood transfusions may be required in severe cases. Clinical improvement in response to therapy precedes the return of hematological parameters to normal, which may take months in severe cases. With treatment, the prognosis is excellent in acute cases and mildly affected chronic cases, but guarded in cases with severe pancytopenia and hypoplastic or aplastic bone marrow. Low dose tetracycline 7 mg/kg/day may be given orally as prophylaxis in dogs at high risk for reinfection.

### GRANULOCYtic EHRLICHIOSIS

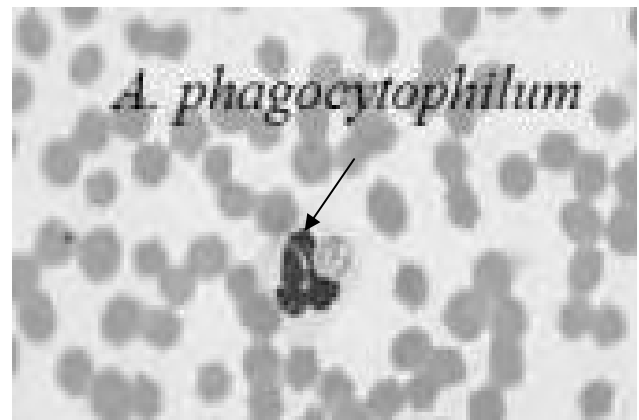
The granulocytic Ehrlichioses are caused by organisms that have a tropism for neutrophils. There are two main organisms that are known to infect dogs, *Ehrlichia ewingii*, and *Anaplasma phagocytophilum* (formerly *E. equi* and HGE agent). It has been reported in many states of the US and a particularly virulent strain of *A. phagocytophilum* has been reported in many dogs in Sweden. There are two clinically distinct disease syndromes seen with granulocytic ehrlichiosis. It is suspected that the two disease syndromes are associated with the two different organisms. Association of specific organisms to disease speculative but substantial evidence supports this conclusion.

**Clinical signs** for one form of the disease (caused by *E. ewingii*) include fever, malaise, lameness, and swollen joints secondary to polyarthritis. The disease mimics immune-mediated arthritis. The only tick species confirmed to be a vector for disease is *Amblyomma americanum*, but organism DNA has been identified using PCR analysis in ticks of the species *Rhipicephalus sanguineus* and *Dermacentor variabilis*. Laboratory findings include a mild nonregenerative anemia and thrombocytopenia in some cases. *Ehrlichia* morulae **are** often present in a small percent of circulating neutrophils. Joint fluid cytology reveals increased protein and neutrophils with a low percentage

containing morulae. A diagnosis depends on the recognition of morulae in neutrophils. No serological assays are available to diagnose infections with *E. ewingii*, but animals may test positive using *E. canis* assays due to cross-reacting

antibodies. PCR amplification and sequencing of the 16S rRNA gene have been used to confirm the diagnosis of *E. ewingii* infection. Tetracycline antibiotics are effective in treating this disorder (see recommendations for CME therapy).

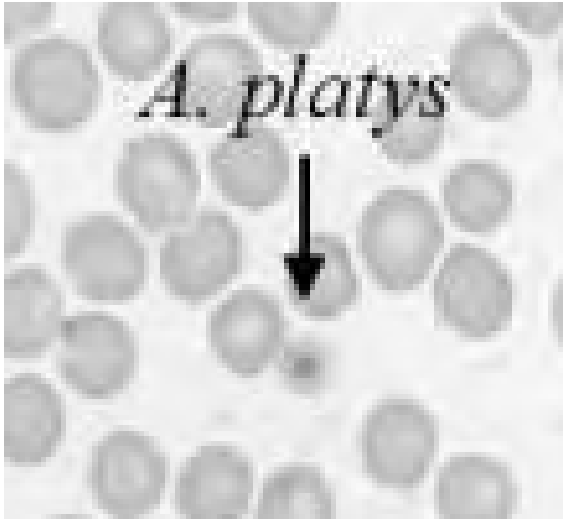
The second form of granulocytic ehrlichiosis is caused by *A. phagocytophilum*. This organisms is transmitted by the *Ixodes* tick, the same tick vector that transmits Lyme Disease. Thus, this disease is prevalent in humans and dogs in the Northeastern, US, Eastern US, and Upper Midwest. Co-infections with Lyme disease are often seen in areas where these two agents are endemic. Animals with this disease present primarily with signs similar to monocytic ehrlichiosis and hematological abnormalities such as moderate to severe nonregenerative anemia, lymphopenia and thrombocytopenia. However, unlike with monocytic ehrlichiosis, organisms can usually be found in low numbers of circulating neutrophils from infected animals. Serological assays are available to diagnose the disease (IFA). **However, it is important to note that animals infected with *A. phagocytophilum* will not test positive on assays designed to diagnose *E. canis* infections (SNAP 3Dx)**



### INFECTIOUS CYCLIC THROMBOCYTOPENIA

*Anaplasma platys* (formerly *Ehrlichia platys*) causes infectious cyclic thrombocytopenia in dogs. This agent is unique in that it is the only intracellular infectious agent described in man or animals to specifically infect platelets. The prepatent period is 1 to 2 weeks following experimental injection with infected blood. Cyclic parasitemias and concomitant thrombocytopenia occur at 1 to 2 week intervals. Parasitized platelets are easily found during the initial parasitemia, but subsequent parasitemias have decreasing percentages of parasitized platelets. Platelet counts usually remain below 20,000/ $\mu$ l for only 1 or 2 days, before rapidly increasing. Infected dogs usually do not exhibit evidence of illness, but mild fever may occur at the time of the initial parasitemia. Minimal or no evidence of hemorrhage is present in most cases, but epistaxis, petechia and ecchymosis of mucous membranes have been reported. Diagnosis of infection with this agent can be made by observing organisms within platelets. An IFA test for antibodies against *A. platys* has been developed (available at the diagnostic laboratory at Louisiana State University,

School of Veterinary Medicine), but it may also cross-reacts to some degree with other *Ehrlichia* organisms. The organism can be specifically identified using PCR technology, but this is not commercially available. Tetracycline antibiotics are effective in treating this infectious agent.

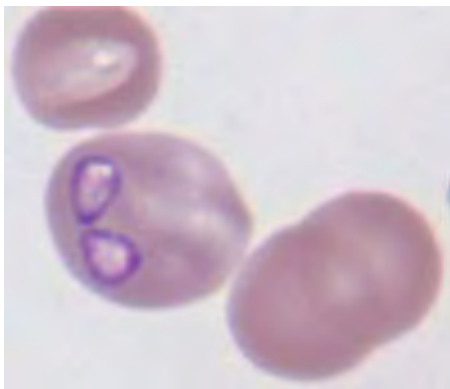


## BABESIOSIS

### *BABESIA CANIS*

#### Etiology And Epidemiology

*Babesia* species are intracellular protozoan parasites of RBCs that cause increased RBC destruction and anemia. Babesiosis occurs in dogs in many countries, including the United States. *Babesia canis* is a large (4-7 µm in length) pear-shaped parasite. Strains present in the U.S. generally cause mild or inapparent disease in adults (unless immunosuppressed), but severe disease in pups. South African strains can cause severe disease and death in adult dogs.



#### Transmission

*B. canis* is transmitted primarily by bites from infected ticks. Tick vectors in the US include the brown dog tick (*R. sanguineus*) and *Dermacentor* spp. Inoculation with contaminated blood may also result in transmission of the disease.

#### Clinical Findings

The severity of the disease varies with age of the animal and strain of *Babesia* involved. The course of disease may be acute and fulminating, subclinical or chronic. Clinical signs that may occur in dogs include lethargy, anorexia, pale mucous membranes, fever, emesis, amber to brown urine, splenomegaly, icterus, weight loss, rapid respiration and rapid heart rate. Animals with Babesiosis are usually anemic. The anemia results primarily from intravascular hemolysis although extravascular destruction of erythrocytes also occurs.

A regenerative response (reticulocytosis) is present in most cases. Mild to severe thrombocytopenia is often present, but hemorrhage is seldom apparent. Clinical chemistry profiles may demonstrate bilirubinemia and abnormalities related to anemic hypoxia, but profiles can be normal. Bilirubinuria is common, but prominent hemoglobinuria is rarely recognized in dogs in the U.S.

#### Diagnosis

A definitive diagnosis of *B. canis* infection is made by identification of the organisms in stained-blood films. Serological diagnosis can be made using Indirect fluorescent antibody (IFA) tests, but some cross-reactivity occurs between babesial species. High titers suggest current infection, but IFA tests may be negative in acutely infected animals, especially pups. If parasites are not recognized in the blood, it is difficult to differentiate babesiosis from autoimmune hemolytic anemia, because both disorders may be Coombs' test positive.

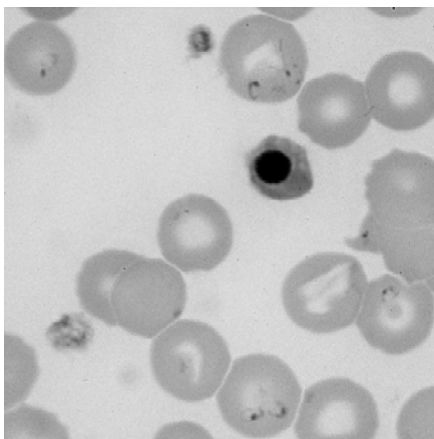
#### Treatment and Prognosis

Adult dogs with mild anemia and clinical signs do not require therapy, but can be reservoirs of infection for other animals. Imidocarb dipropionate (Imizol) (6.6 mg/kg SQ or IM, single injection, repeat dose in two weeks) along with supportive care (transfusions or IF fluid therapy) may be efficacious in treating this disease. Antibabesial drugs are potentially dangerous, and can cause neuromuscular signs and liver or kidney injury. Relapse following therapy can occur, but is more likely in dogs with *B. gibsoni* infections. Treated and untreated dogs often remain carriers of disease.

### *BABESIA GIBSONI*

#### Etiology and Epidemiology

*Babesia gibsoni* is considered to be a small *Babesia*, similar to *B. microti*, the etiological agent of human and rodent babesiosis. The organism is endemic in Africa, the Middle East and Asia. The first report in the US was in 1968, however, the infected Bull Terrier likely contracted the agent while in Malaysia. In 1979 the organism was isolated from a dog that lived in Connecticut and never traveled outside the US. Since that time, infected dogs have been identified in California, the Midwest (Oklahoma) and Southeastern US. Since 1998 there has been a rapid increase in the number of cases reported, predominantly in Pit Bull Terriers and American Staffordshire Terriers.



### Transmission and Pathogenesis

Known vectors of *B. gibsoni* infections outside the US include the ixodid ticks, *Haemaphysalis bispinosa* and *H. longicornis*. The brown dog tick *Rhipicephalus sanguineus* is the suspected vector in the US, but definitive transmission studies have not been done. Interestingly, inoculation with contaminated blood is believed to play a major role in maintaining this organism in the bull terrier population with transmission occurring on premises during tail docking, ear cropping, vaccinations between animals with single needles, and bite wounds. The vast majority of the reported cases in the US have either been in bull terriers or in animals that were attacked and bitten by bull terriers. Transplacental transmission is suspected to occur and may account for the high prevalence of this disease in Pit Bull and Staffordshire Terriers. Organisms have been detected in a dam and in 3 of her offspring at 3 days of age. Other methods of direct blood transmission include re-use of uncleaned instruments in tail docking or ear cropping procedures or the reuse of needles for vaccinations. Clinical infections have been seen in animals with a history of attack by Pit Bull Terriers. American Pit Bull Terriers and American Staffordshire Terriers can be subclinically infected carriers (55% PCR positive) MacIntire et al., JAVMA, 220:325-329, 2002. The incubation period for the development of clinical disease is 7 to 21 days. Dogs that survive the acute phase of the disease become chronic carriers and a reservoir for infection.

### Clinical Findings

Commonly reported clinical abnormalities in dogs include fever, lethargy, pale mucus membranes, lymphadenopathy, splenomegaly, regenerative anemia with intravascular hemolysis, hemoglobinuria, transient but profound neutropenia and thrombocytopenia with increased mean platelet volume. The thrombocytopenia can be severe (<50,000 cells /  $\mu$ l) and may develop before and last longer than the anemia or detectable parasitemia. In addition, persistent thrombo-cytopenia and anemia without a detectable parasitemia may result in a misdiagnosis of immune-mediated disease or ehrlichiosis. Mild anemia and thrombocytopenia with increased mean platelet volume may be seen in subclinically infected Pit Bull Terriers and Staffordshire Terriers. These findings in terriers living in endemic areas should alert the clinician to potential subclinical infection and prompt further testing.

### Diagnosis

The clinical diagnosis is often made by microscopic examination of a peripheral blood film. The small (1 -2.5  $\mu$ m) round to oval piroplasms are usually identifiable in erythrocytes of clinically infected animals. The organisms are detectable as early as 1 week post-infection and peak parasitemias are seen by 3 to 4 weeks. Peak parasitemias in most dogs range from 2% to 6% of erythrocytes infected, however, parasite numbers may in some cases be much higher. Many infected animals will be Coombs' test positive. Therefore, the diagnosis must be distinguished from IMHA. Specific species identification is accomplished by PCR analysis of infected, whole blood. PCR analysis is currently available through the North Carolina State University Tick-Borne Disease Testing Laboratory, or through the Department of Pathobiology at Auburn University. The parasitemia in subclinical carriers is too low to be detected microscopically and PCR analysis must be done to confirm a carrier state.

Serology using the IFA test demonstrates the presence of antibodies in serum directed against these organisms, but some cross-reactivity occurs between babesial species. Titers > 1:80 are considered significant, but most infected animals have > 1:320. Both false negatives and false positives can occur using the IFA test. Speciation can only be done using PCR analysis.

### Treatment and Prognosis

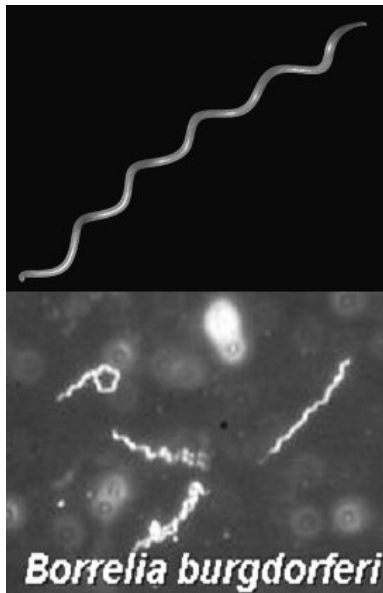
The small babesia such as *B. gibsoni* do not respond well to the typical anti-babesial drugs such as Imidocarb dipropionate. Although controlled studies have not been done, the current recommended treatment is azithromycin, 10mg/kg once a day for 10 days, and atovaquone 13.3 mg/kg once a day for 10 days. Using this treatment, approximately 50% of the infected animals will be PCR negative in 6 weeks. In addition, some animals may require supportive care with blood replacement products and/or fluid therapy. Again there is some question as to whether or not to treat with corticosteroids, although they may be used in cases where the anemia does not respond to anti-microbial therapy alone and eventually required corticosteroids to give clinical improvement.

### LYME BORRELIOSIS

#### Etiology and Epidemiology

Lyme Borreliosis is a commonly diagnosed, vector-borne disease in humans, dogs and cats, most often caused by infection with *Borrelia burgdorferi*. The organisms are small spirochetes measuring approximately 0.2 $\mu$ m x 30 $\mu$ m. They are visible using dark-field or phase microscopy. Although extracellular pathogens, these organisms do not survive free living in the environment and must be transmitted by a tick vectors. Borreliosis has been reported in all 48 states of the mainland US but most cases are from the Eastern coastal states, upper Midwest and Western coastal states. The distribution and prevalence of the disease coincides with the activity of the tick vectors.





### Transmission and Pathogenesis

*B. burgdorferi* can be transmitted by several species of Ixodes ticks (deer ticks). The species most commonly involved are *I. scapularis* in east and upper Midwest and *I. pacificus* in the West. These are the same ticks that transmit the granulocytic form of Ehrlichiosis (*A. phagocytophilum*) and *Anaplasma* sp. As with other tick-transmitted diseases, transmission to a susceptible host requires prolonged feeding of 1 to 3 days duration (most say 48 hours). The Ixodes ticks have a 2-year life cycle and remain infective in nature over wintering as infected nymphs, however, transovarial transmission in ticks is not thought to occur. It is suspected that nymphs are the primary source of infection to both humans and animals. Other tick species along with flies mosquitoes and fleas have been shown to be infected in nature, but are not believed to be important in disease transmission.

Following inoculation from an infected tick bite, *B. burgdorferi* disseminates by connective tissue migration. Pathogenesis of acute disease typically involves migration into joint capsules in closest proximity to the tick attachment, resulting in cytokine production and mono, or polyarthritis. Persistent infections are often established unless appropriate antibiotic therapy is instituted during the acute phase of infection.

### Clinical Findings

Not all animals infected with *B. burgdorferi* develop clinical disease. Evidence of clinical disease is low, suspected to be only 5-10% of infected dogs. Seropositivity may be as high as 75% in endemic areas, but this may be the result of cross reactivity of IFA or ELISA with nonpathogenic borrelia or antibodies resulting from previous vaccination. Acute polyarthritis is the most common clinical finding in dogs with Lyme Borreliosis. Major clinical signs are lameness, fever, regional lymphadenopathy (depending on the joints involved) and anorexia. These signs may spontaneously resolve in a few days, but may recur periodically. In experimental infections, Staubinger et al. 2000. J. Infect. Dis, 181:1069-1081, showed 75% of dogs had a 3-6 day episode of mono or polyarthritis of varied severity beginning at 2 mo. post-infection. Clinical and laboratory evidence of glomerulonephritis, neurological disease, or cardiac disease

can develop in chronic, persistent infections. The chronic form of the disease is often fatal, particularly if glomerulonephritis occurs. Antibiotic therapy greatly reduces, and often clears infection in dogs when treated during acute stages of disease. But occasionally infections may persist in animals, even when treated during the acute stages of the disease.

Hemogram, biochemical profiles and radiographic findings are usually normal during acute infections. Findings consistent with protein losing glomerulonephritis may be seen in chronic infections. The synovial fluid is often abnormal in acutely infected patients. The leukocyte count is elevated, ranging from 5,000 to 100,000 cells /  $\mu$ l (mean = 46,300 cells /  $\mu$ l). In acute disease, the cell types consist primarily of nondegenerate neutrophils (85% to 95%) and are usually found in multiple joints, particularly those nearest to the infected tick bites. In chronic disease a nonsuppurative inflammation may be seen in joint fluid.

### Cats

Despite seropositivity, natural disease has not been described as a distinct clinical entity. Cats may be more resistant to dogs with regard to development of clinical disease. Clinical disease has been experimentally induced by inoculation of organisms with infected ticks.

### Diagnosis

#### IFA and ELISA

Most investigators believe the disease is over diagnosed in both human and veterinary medicine. Elevated titers (usually >1:64 to 1:128 by most laboratories) signifies exposure to *Borrelia* sp. or related organisms, but does not necessarily mean that clinical signs in a patient are the result of infection. Animals in endemic areas often are seropositive and diagnosis of infection should be accompanied by history of tick exposure, consistent clinical signs and rapid response to appropriate antibiotic therapy.

Antibody titers develop by 4 to 6 weeks post-infection, and reach peak levels by 3 months. Titers usually precede clinical lameness. However, on occasion, false negative results from serological assays may occur during the early stages of the disease. High serum titers usually decrease after therapy. Even though high serum titers on IFA or ELISA usually decrease after effective therapy, they can still persist for a year or more. Titers that are increased after 6 months suggest persistent infection or re-exposure.

There are several problems associated with the IFA and ELISA tests. There is a lack of standardization among antigen preparations at various labs. In one study, matched sera sent to 10 commercial labs had only a 53% agreement (Green et al., 1991, J. Clin. Microbiol, 29:16-20). In addition, these assays use whole-cell antigen preparations resulting in cross-reactivity with related organisms, especially other nonpathogenic *Borrelia* spp. or *Leptospira* spp., as well as vaccinated animals. Vaccinated dogs have seroreactive for months to years after vaccination and vaccinated dogs cannot be distinguished from infected or naturally exposed animals using IFA or ELISA.

#### Western Immunoblot Assay

Western immunoblot can be used to distinguish infected from vaccinated animals, but analysis is difficult to interpret due to variations in reactivity at different times PI and differences in reactivity with different vaccines. In addition,

the assay is time consuming and is only available in certain commercial and research laboratories.

### **C6 Peptide Assay:**

The C6 used in the SNAP 3DX test is a synthetic peptide that is based on an invariable region of a variable surface protein of *B. burgdorferi*. This region was determined by Liang et al., 2000, J. Clin Microbiol., 38:4160-4166 to be the most immunogenic area of the protein, and luckily it was conserved among various strains of the organism. It was able to detect infection in 30% of 23 dogs as early as 3 weeks post-infection and all dogs by 1 to 2 weeks later. In 55 serum samples submitted by veterinarians from dogs suspected of Lyme disease, sensitivity and accuracy was equal to that of WB. Specificity was 100% when testing samples from 70 healthy dogs, 14 dogs with infections other than *B. burgdorferi*. Test sensitivity and specificity is now established to be 94% and 99.7%, respectively. In addition, serum samples from animals vaccinated with either of the three available Lyme vaccines, Recombitek, LymeVax, or GalaxyLyme, did not react with the C6 peptide using SNAP 3Dx test (O'Connor et al. Unpublished data). In this study dogs were given multiple doses of vaccine (0, 2, 33, 36, and 39 weeks) and none of the animals developed detectable antibodies to C6. This assay has been used in the field to do prevalence surveys in endemic areas to indicated the effectiveness of vaccination. In one study by Levy, SA, 2002, Vet. Ther. 3(4):420-424, Lyme Vax by Fort Dodge was used to vaccinate dogs prior to 6 months of age in an endemic area on Connecticut. Prevalence rate was 5% in vaccinated and 64% in unvaccinated dogs.

In addition, the C6 peptide is useful in monitoring response to therapy, particularly acutely infected animals. In one study by Philipp et al., 2001 J. Infect. Dis., dogs were treated for 30 days with ceftriaxone, starting on day 120 post inoculation. Antibody response to whole cell antigens (IFA and Western blot) only decreased slightly by 180 PI but always remained elevated even to 540 days PI. However, antibody response to C6 peptide declined rapidly by 180 PI (less than 2 months post TM), and down to baseline background level by about 6 months post TM. To accurately monitor therapy, IDEXX offers a Lyme C6 quantitative assay. Which converts OD reading of ELISA to antibody levels in µg/ml. There are a number of possible reasons for the rapid decline in antibody response, but some investigators feel that the C6 peptide does not elicit a good B cell memory response.

The Lyme portion of the 3Dx assay is calibrated to read positive for titers of approx 1:100 or more. Not all treated animals will drop below the sensitivity of the this assay, but many will and all will have markedly reduced levels if the disease is fairly acute. However, the same may not be true of chronically infected carrier animals. In people with chronic infections of 1 to 2 years duration or greater, there was a poor response to C6 reduction regardless of whether or not clinical signs resolved.

### **Treatment**

Early treatment with antimicrobials is critical in dogs with clinical Borreliosis. Treatment during the acute phase of the disease results in a reduction in antibody titers and organisms in tissues and prevention or cure of joint disease. Most treatment regimes are instituted for a minimum of 30 days. In acute cases, clinical improvement should occur in the first 24 to 48 hours. However, in some cases the organism may persist and relapse may occur after cessation of therapy. In addition, inflammatory conditions in the joint may become self-perpetuating even though the organism has been cleared.

Animals with chronic Borreliosis are less likely to show improvement or may have relapses even with prolonged therapy. First-line treatment of choice is doxycycline (10 mg/kg BID for 30 days). Inexpensive, lipid soluble and gets good concentrations in the joint. Newer erythromycin derivatives (azithromycin, 25mg/kg PO, SID, for 30 days) or third generation cephalosporins such as ceftriaxone (25mg/kg IV, SID, for 30 days) have been used for refractory cases in humans and animals and are believed to be more effective for treatment of chronic infections. Glucocorticoids should be avoided if at all possible, but has been given at anti-inflammatory doses for chronic arthritis that cannot be completely resolved with antibiotics. Immunosuppressive doses of corticosteroids should never be used since they increase the severity of clinical disease and/or cause the reoccurrence of clinical disease in subclinically infected dogs.

### **Zoonosis**

Dogs and cats are not considered a significant source of exposure to people because they do not secrete the organisms in any body fluids (not even urine) to any appreciable extent. Also, uninfected dogs housed with infected dogs for up To 1 year did not become infected or seroconvert (Appel et al., 1993m, J. Infect. Dis., 176:651-654). Dogs and cats are more a sentinel host, but not a reservoir for humans. The tick vectors needed for disease transmission don't survive well indoors and fed ticks won't reattach without molting. The greatest risk is introduction of partially fed ticks, which can quickly reattach.