

# CANINE AND FELINE ANAPLASMOSIS AND EHRLICHIOSIS

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## INTRODUCTION

Although tick-borne pathogens are of tremendous historical importance to both veterinary and human medicine, recent events emphasize an expanding role for newly discovered, as well as previously recognized tick-transmitted organisms, as a cause of animal and human suffering. One of the most important new developments related to anaplasmosis and ehrlichiosis is the realization that a given mammalian species can be infected simultaneously or sequentially by several *Ehrlichia* species.<sup>1</sup> As an example, both dogs and people can be infected with *Ehrlichia chaffeensis*, *Ehrlichia canis*, *Ehrlichia ewingii* and *Anaplasma phagocytophilum* (see reclassification below).

During the past decade observations related to ehrlichiosis in animals have contributed substantially to the rapid expansion of new knowledge related to human ehrlichiosis.<sup>2,3</sup> Increasingly, veterinarians in practice are being called upon to provide comparative medical information about ehrlichiosis in animals and to discuss the zoonotic risks that are attributable to members of the genus *Ehrlichia*. Without question, the increased spectrum of human and companion animal recreational activities continue to bring each of us, as well as our pets, into contact with competent tick vectors. Therefore, so as to decrease disease transmission, drug manufacturers should continue to search for effective acaricides and products with strong repellent characteristics, so as to prevent tick attachment. These preventive efforts must occur in conjunction with the development of enhanced diagnostic techniques and improved therapeutic management of tick-transmitted diseases.

## RECLASSIFICATION OF THE GENUS *EHRLICHIA*

Genetic analyses of 16S rRNA genes, heat shock and surface protein genes have resulted in a reclassification of the genera *Anaplasma*, *Ehrlichia*, *Cowdria*, *Neorickettsia* and *Wolbachia*.<sup>4</sup> As a result, the genus *Ehrlichia* is now comprised of: *Ehrlichia canis*, *Ehrlichia chaffeensis*, *Ehrlichia ewingii*, *Ehrlichia muris*, and *Ehrlichia ruminantium*. The genus *Anaplasma* is now comprised of: *Anaplasma phagocytophilum*, (previously *Ehrlichia equi*, *Ehrlichia phagocytophilia* or the human granulocytic ehrlichia, i.e. the HGE agent), *Anaplasma bovis*, and *Anaplasma platys*. *Ehrlichia risticii* has been transferred to the genus *Neorickettsia*, which includes: *Neorickettsia sennetsu*,

*Neorickettsia helminthoeca*, *Neorickettsia risticii* and the Salmon Fever agent.

Because of this reclassification, clinicians will have to reorganize the nomenclature that involves pathophysiology, diagnosis, treatment and preventive strategies related to these organisms. Although a currently cumbersome task, the recent reclassification will result in enhanced clarity, when considering similarities and differences among organisms in the same or different genera. The terms ehrlichiosis, anaplasmosis and neorickettsial infections continue to take on a new clinical meaning.

## **COMPARATIVE MEDICAL IMPORTANCE OF *ANAPLASMA* AND *EHRlichia* SPECIES INFECTIONS.**

Of comparative medical interest, cats, dogs, humans, as well as other domestic and wild animal species, can all be infected with the same *Ehrlichia* sp. For example, *E. chaffeensis* has been shown to infect dogs, goats, deer, and human beings.<sup>3, 5</sup> Similarly, *A. phagocytophilum* can be detected in blood samples from a wide range of wild and domestic animals and humans. With the recent application of new molecular diagnostic techniques, the study of vector-borne disease problems has been enhanced. This technology continues to result in substantial clarification of the role of established agents in the pathogenesis of previously undocumented disease sequelae. In many respects, the immunopathogenic consequences of tick-borne infections, such as ehrlichiosis, are nearly identical among infected animals, as well as human patients. The experimental characterization of the immunopathological response of a specific *Ehrlichia* sp. in animals has provided important insights as to the potential pathogenic consequences induced when the same organism infects human patients. Conversely, observations in human patients have contributed to the recognition of an increased spectrum of disease manifestations in animals, such as acute renal failure or acute respiratory distress syndrome (ARDS).

## **FELINE ANAPLASMOSIS AND EHRlichIOSIS**

In general, our knowledge of tick-borne diseases in cats is substantially less than our knowledge of the comparable disease in dogs or human patients.<sup>6, 7</sup> Recent molecular evidence indicates that cats can be infected with *A. phagocytophilum* and an *E. canis*-like organism.<sup>6, 8</sup> The infrequent diagnosis of ehrlichiosis in cats may be related to a number of factors including: a general under-recognition of tick-borne diseases in cats, decreased pathogenicity of tick-borne pathogens in cats as compared to other animals, or the more rapid removal of ticks from cats resulting in decreased opportunity for disease transmission. Most tick-transmitted pathogens require a 24 to 48 hour period of attachment to the host before there can be successful transmission of infectious organisms. Fastidious grooming may result in the early removal of most ticks from cats and thereby the prevention of disease transmission.

Although various *Ehrlichia*, *Anaplasma* and *Neorickettsia* species have been reported to cause disease in cows, sheep, dogs, horses and human beings, the role of any specific species as a pathogen in cats remains less clearly defined. The first evidence for naturally-occurring feline ehrlichiosis was provided by Charpetier and Groulade in France.<sup>8</sup> Feline ehrlichiosis was subsequently reported in 1989, by Buoro and colleagues, when they described intracytoplasmic inclusions in monocytes and lymphocytes derived from 3 cats in Kenya.<sup>9</sup> By both light and electron microscopy, the inclusions were morphologically similar to *Ehrlichia* sp. morulae, as observed on blood smears obtained from other animals. Subsequently, morulae were described in stained blood smears obtained from cats in the United States, France, Brazil and Sweden.<sup>10-13</sup> To date, no *Ehrlichia* species has been cultured from the blood of a cat, however, Bjoersdorff and colleagues amplified and sequenced 16S rDNA from an EDTA blood sample obtained from a 14-month-old shorthaired cat from Sweden that was 100% similar to canine and equine *A. phagocytophilum* strains from the same region.<sup>10</sup>

Recently, our research group has described *E. canis*-like infection in young cats from the southeastern United States, eastern Canada and France.<sup>6,14</sup> Based upon PCR amplification and DNA sequencing, the *Ehrlichia* DNA amplified from the blood of these cats was 100% similar to the comparable *E. canis* DNA sequences obtained from canine *E. canis* isolates. As no isolates were made from these cats, a more complete genetic characterization was not possible, therefore, we are currently describing these feline infections as *E. canis*-like. Antibodies could not be detected in these cats by IFA testing using *E. canis* antigens. Serum from all 3 cats in our study contained anti-nuclear antibodies.<sup>6</sup> The predominant disease manifestations were polyarthritis, accompanied by fever in 1 cat, bone marrow hypoplasia or dysplasia, accompanied by pancytopenia in a second cat and anemia and thrombocytopenia in the third cat. (Figure 2) In dogs, neutrophilic polyarthritis has been most frequently associated with *E. ewingii* infection. In this cat neutrophilic polyarthritis was confirmed by cytologic analysis of joint fluid at 1 and 3 years of age, suggesting the possibility of chronic *E. canis*-like infection. Previous serologic studies, have reported an association between thrombocytopenia, hyperglobulinemia and polyarthritis in cats that had *E. canis* antibodies.<sup>15,16</sup> Other nonspecific clinical abnormalities, including lethargy, anorexia, conjunctivitis, swelling in the ventral neck region and mild interstitial lung disease were reported in cats and can be observed in association with canine ehrlichiosis.<sup>17</sup>

In dogs and people with ehrlichiosis, bone marrow cytopathology can vary substantially, particularly in relation to the duration of infection prior to sampling.<sup>18,19</sup> The mechanisms by which ehrlichial organisms induce changes in the bone marrow, particularly hypoplasia or myelofibrosis, remain poorly understood. The extent to which

immunosuppression should be used concurrently with doxycycline in *E. canis* infected cats remains unclear, however ehrlichial infection should be considered as a differential diagnosis in cats with bone marrow hypoplasia, particularly when accompanied by dysplastic changes. When used concurrently, corticosteroids or other immunosuppressive drugs may interfere with the therapeutic effectiveness of doxycycline for the elimination of *E. canis* in cats. Therefore, when ever possible, treatment with only antibiotics (doxycycline) should be attempted.

To further define the spectrum of feline ehrlichiosis, PCR testing will be necessary, until such time as serologic testing is thoroughly validated in experimentally or naturally-infected cats. In addition, until *E. canis* has been isolated from cats and several isolates are available from disparate geographic regions for detailed comparative genetic study, the molecular evidence presented supporting *E. canis* infection in cats must be interpreted with caution. As tick exposure was not clearly established in these cats, it is possible that an *Ehrlichia* genotype, with complete or partial 16S rDNA homology with *E. canis* is capable of infecting cats and may have evolved with a different mode of transmission, as compared to tick transmission of *E. canis* to dogs.

PCR testing for *Anaplasma* and *Ehrlichia* species is available through the:  
Vector-borne Diseases Diagnostic Laboratory  
NCSU-CVM Rm 462A  
4700 Hillsborough Street  
Raleigh NC 27606

Phone: 919-513-8279

HYPERLINK "http://www.cvm.n" [www.cvm.ncsu.edu/docs/ticklab.html](http://www.cvm.ncsu.edu/docs/ticklab.html)

Recently, Lappin and colleagues have reported *A. phagocytophilum* infection, detected by PCR amplification and DNA sequencing in 4 young cats (less than 3 years of age) from the northeastern United States. Collectively, molecular results reported to date suggest that clinical disease might be expected more frequently in young cats. However, these results do not preclude infection in older cats or the possibility that PCR amplification of *Ehrlichia* or *Anaplasma* sp. DNA from the blood of an older cat might be a less sensitive diagnostic modality due to lower quantities of target DNA for PCR amplification. For the clinician, these observations emphasize the importance of obtaining blood samples for PCR testing prior to the initiation of antibiotic treatment. For the scientific community, there is a great need for feline isolates, which will allow for definitive genetic characterization and comparison to *Ehrlichia* and *Anaplasma* spp. isolates that have been obtained from other animals.

## **CANINE ANAPLASMOSIS AND EHRLICHIOSIS**

Canine ehrlichiosis is an infectious rickettsial disease of dogs, caused by *E. canis*,

*E. chaffeensis*, and *E. ewingii* and potentially *E. ruminantium*.<sup>17</sup> Investigators from South Africa have obtained molecular evidence (16S rDNA sequencing) that supports infection of dogs and people with an organism that is identical or closely related to *E. ruminantium* (previously *Cowdria ruminantium*).<sup>20</sup> The implications of this recent finding could prove to be of great importance, if *E. ruminantium*, the organism that causes Heartwater in cattle in Africa, was introduced into the United States by way of dog transport.

Although the clinicopathologic course of disease will vary depending upon the infecting *Ehrlichia* species, illness is typically characterized by an acute reduction in cellular blood elements, most often thrombocytopenia.<sup>17</sup> Historical synonyms for canine ehrlichiosis have included canine rickettsiosis, canine typhus, tropical canine pancytopenia, idiopathic hemorrhagic syndrome, canine hemorrhagic fever, and tracker dog disease. *Ehrlichia canis* was first recognized in Algeria in 1935, and first reported in the United States in 1963. The disease gained prominence due to devastating losses of military working dogs stationed in Vietnam. Canine ehrlichiosis, caused by *E. canis*, has been reported from tropical and subtropical regions throughout the world.<sup>21</sup> The distribution of *E. canis* infection is related to the geographic distribution of the vector tick, *Rhipicephalus sanguineus*, the brown dog tick, which spends all 3 stages of its life cycle on dogs. Canine ehrlichiosis, caused by *E. chaffeensis* and *E. ewingii*, have been diagnosed only within the United States. All 3 *Ehrlichia* spp. are encountered most frequently in dogs living in the southern states.<sup>1,5</sup> Based upon recent research, co-infection with multiple *Ehrlichia* species or *Ehrlichia* and *Anaplasma* spp. is not uncommon.

Canine infection occurs when salivary secretions from the tick contaminate the attachment site during ingestion of a blood meal. *Ehrlichia* spp. infection can also be introduced in susceptible dogs by way of blood transfusion. This has been accomplished with blood obtained from dogs chronically infected with *E. canis* up to 5 years in duration. This fact has obvious implications for canine blood donors in endemic regions. All 3 *Ehrlichia* spp. are capable of inducing chronic infections in dogs, whereas the extent to which *A. phagocytophilum* induces chronic infection in dogs is unknown. Experimentally-infected dogs have developed persistent *A. phagocytophilum* infection for months.

Ticks are thought to represent the primary reservoir for *E. canis*, whereas small mammals are the reservoir for *A. phagocytophilum*. Adult *R. sanguineus* are capable of transmitting *E. canis* for at least 155 days following detachment from the host. Ticks can obtain *E. canis* only if engorgement occurs during the acute phase of the disease in dogs. In contrast to *E. canis*, *Amblyomma americanum*, the Lone Star tick, is the most important vector for *E. chaffeensis* and *E. ewingii*. Deer serve as a major mammalian reservoir for both of these organisms and transmission to dogs or people is more likely in areas that

support a large deer population. In North America, *Ixodes scapularis* and *Ixodes pacificus* are responsible for the transmission of *A. phagocytophilum* and *Borrelia burgdorferi*.

Based upon experimental infection studies, canine ehrlichiosis has been divided into 3 phases: an acute, subclinical and chronic disease phase.<sup>22</sup> Although these 3 phases of disease can be utilized to infer some clinical utility, the onset and duration of infection is rarely known in the clinical setting. Clinical signs during the acute phase of disease are highly variable and can include: depression, anorexia, fever, severe loss of stamina, weight loss, ocular and nasal discharges, dyspnea, lymphadenopathy, and edema of the limbs or scrotum. Following experimental infection, acute phase clinical signs are transient and usually resolve in 1 to 2 weeks, even without appropriate treatment. Thrombocytopenia and leukopenia generally occur 10 to 20 days following infection. Despite moderate to severe thrombocytopenia, hemorrhages are rarely observed. A variety of central nervous system signs, including hyperesthesia, muscle twitching, and cranial nerve deficits, may occur due to inflammation and bleeding into the meninges. Clinical findings in the acute phase of ehrlichiosis can be identical to canine Rocky Mountain spotted fever or canine distemper.

Clinical manifestations, associated with the chronic phase of the disease, would be characterized as mild to absent in some dogs, while severe and life-threatening in other dogs. For example, it is not unusual in endemic areas to detect hematologic abnormalities due to chronic *E. canis* infection in clinically healthy dogs being evaluated for heartworm adulticide therapy. Undetected thrombocytopenia in these patients might potentiate the severity of pulmonary hemorrhage associated with thromboembolism. A combination of bleeding tendencies, pallor due to anemia, severe weight loss debilitation, abdominal tenderness, anterior uveitis, retinal hemorrhages, and neurological signs consistent with meningoencephalitis typify dogs that are chronically affected. Immunosuppression has been historically attributed to infection with *E. canis* in dogs, however, a recent experimental infection study did not induce detectable immunosuppression.<sup>23</sup> Secondary bacterial infections may be documented. Numerous patterns of hemorrhage may occur in dogs with ehrlichiosis. Epistaxis, once considered a hallmark of the disease, occurs infrequently in dogs in the United States and may be attributable to concurrent infection with a *Bartonella* species.<sup>24</sup>

In addition to clinical signs, which may be suggestive of ehrlichiosis, mild to severe laboratory abnormalities can contribute to the index of suspicion for the disease. Hematologic abnormalities, including pancytopenia, aplastic anemia, or thrombocytopenia, would be consistent with *E. canis* infection. Thrombocytopenia is the most consistent hematologic abnormality in both the acute and chronic stages of ehrlichiosis. However, some dogs will have normal or increased platelet counts. (Figure 5) Pancytopenia is documented in less than 25% of cases in retrospective clinical studies. Because *E. canis* causes defective platelet function, bleeding can be detected in dogs with normal or mildly

suppressed platelet counts. Lymphocytosis, which can be profound and mimic lymphocytic leukemia, has been observed in dogs with ehrlichiosis. Finding *E. canis* morula in peripheral blood smears or buffy coat smears is diagnostic; however, morula are found only during the first 2 weeks following infection and generally in very low numbers. Anemia, if present, will vary in degree of severity among affected dogs. Positive Coombs' tests suggest that immune-mediated damage, due to circulating anti-erythrocyte antibodies, can contribute to an acute hemolytic crisis in some dogs with ehrlichiosis. In this situation, a regenerative anemia may be encountered; however, a nonregenerative anemia is most frequently documented in chronically infected dogs. During the subclinical and chronic phases, bone marrow examination usually reveals a hypocellular marrow with varying degrees of suppression of the erythroid, myeloid, and megakaryocytic series. Hyperplasia of the bone marrow, especially megakaryocytic hyperplasia, occurs in the acute phase of the disease. Plasmacytosis is a frequently reported finding in the bone marrow.

Serum proteins are abnormal in approximately half of reported canine ehrlichiosis cases. Hyperglobulinemia is characterized by increased beta and/or gamma globulins. Serum protein electrophoresis may reveal a polyclonal or monoclonal gammopathy. A monoclonal gammopathy in association with severe bone marrow plasmacytosis could be easily misdiagnosed as a plasma cell myeloma. Hypoalbuminemia occurs in association with protein-losing nephropathy or a reciprocal decrease in albumin associated with progressive hyperglobulinemia. Less frequently encountered laboratory abnormalities include increased alanine aminotransferase, serum alkaline phosphatase, total bilirubin, azotemia, and proteinuria. *Ehrlichia canis* does appear to induce a protein-losing nephropathy, most likely related to immune complex glomerulonephritis.

Serologic diagnosis utilizing the indirect fluorescent antibody technique (IFA) is currently recommended for confirming a diagnosis of ehrlichiosis.<sup>25</sup> The IFA test for *E. canis* is sensitive and specific; however, based upon Western immunoblot (WI) analysis, low IFA titers are not diagnostic and may represent exposure to other infectious organisms. Current modalities that detect *E. canis* antibodies in serum samples obtained from dogs for diagnostic purposes, such as the microimmunofluorescent assay (IFA), do not facilitate differentiation of the infecting *Ehrlichia* species. There is substantial serologic cross reactivity between *E. canis* and *E. chaffeensis*, whereas *E. ewingii* infected dogs generally do not recognize *E. canis* antigens or do so at very low titers. Serologic cross-reactions to *E. canis* antigens have not been reported in association with *Rickettsia rickettsii*, *Babesia canis*, *A. platys*, or *A. phagocytophilia*. Due to extensive serologic cross reactivity, a positive *E. canis* IFA titer is indicative of infection with *E. canis*, *E. chaffeensis* or to a lesser extent *E. ewingii*. Dogs generally become seronegative within 3 to 9 months after effective treatment, although some dogs maintain persistent and stable titers for years. Although the clinical utility has not been clearly established, polymerase chain reaction (PCR) amplification can facilitate a molecular confirmation of the diagnosis of canine ehrlichiosis, determine of the infecting *Ehrlichia* species or help to confirm the therapeutic

elimination of infection. EDTA blood is required for PCR and should optimally be collected prior to or after cessation of antibiotics.

Tetracycline (22 mg/kg given every 8 hours) or doxycycline (5 mg/kg every 12 hours), administered daily for 4 weeks, represent the treatment of choice for canine and feline ehrlichiosis.<sup>26,27</sup> Oxytetracycline is also effective, but is nephrotoxic. Clinical improvement may be observed with penicillin, sulfonamides, enrofloxacin or imidocarb dipropionate but the therapeutic response is incomplete and therefore these antibiotics can not be recommended.<sup>28,29</sup> Dramatic clinical improvement generally occurs within 24 to 48 hours after initiation of a tetracycline derivative in dogs with acute phase or mild chronic phase disease. Hemorrhage, immunosuppression and concurrent infections with *Babesia* or *Bartonella* species may contribute to the death of chronically affected dogs, despite the initiation of tetracycline therapy. The duration of treatment of chronically affected dogs with severe pancytopenia or aplastic anemia is controversial. Despite clinical improvement and clearance of infection, bone marrow regeneration may require up to 120 days following treatment. Supportive therapy, including fluids, blood transfusion, vitamins, and anabolic steroids are required in some patients. Long-term tetracycline prophylaxis (6.6 mg/kg once daily), repositol oxytetracycline (200 mg IM twice weekly) or doxycycline have been utilized in military working dogs or dogs maintained in tick infested kennels to prevent ehrlichiosis. Following therapeutic elimination of the organism, dogs do not develop protective immunity and can be re-infected when re-introduced to a vector-competent tick. Experimentally, dogs have been re-infected by both homologous and heterologous challenge. Tick control is critically important, but does not assure prevention of the disease or elimination of re-infection. Although not well characterized, the long term prognosis following treatment for ehrlichiosis does not appear to be predictable.<sup>30</sup> The reasons for variability in post-treatment outcomes remains to be established through long term follow-up studies.

## **SIMULTANEOUS INFECTION WITH MULTIPLE VECTOR-TRANSMITTED PATHOGENS**

Recently, simultaneous infection with more than one tick-borne pathogen has been recognized with increasing frequency in human and canine patients. Obviously, simultaneous infection with more than one tick-transmitted pathogen has important diagnostic, therapeutic and prognostic implications for the individual patient. The pathophysiologic consequences of co-infection in dogs with various combinations of bacteria, rickettsia and protozoa have not been characterized clinically or experimentally. Although retrospective seroepidemiologic studies suggest that dogs may experience simultaneous infection with multiple tick-borne pathogens, microbiologic (culture) or molecular (PCR) evidence of simultaneous infection in dogs is currently limited. In nature, the risk of exposure to ticks, fleas, mosquitoes and biting flies is far greater for dogs than

for human beings. In addition, dogs can be infested with hundreds of ticks, and at times infestation may involve different tick species. Therefore, the unknown influences of concurrent infection with multiple tick-borne pathogens, including *Anaplasma*, *Ehrlichia*, *Rickettsia*, *Babesia* and *Bartonella* species, on factors such as pathophysiology, diagnosis, prognosis or therapeutic outcome could be more readily characterized in dogs. Of 27 dogs that were investigated in a kennel due to increased mortality, 25 were seroreactive to an *Ehrlichia* sp., 20 to a *Bartonella* sp., 17 to a *Babesia* sp. and 22 seroconverted to *R. rickettsii* antigen.<sup>1</sup> Based upon PCR analysis, several dogs were co-infected with multiple *Ehrlichia* species, as well as a *Bartonella*, *Babesia* or *Rickettsia* species. Prospective evaluation of sick dogs, managed in our teaching hospital, has yielded molecular evidence of co-infection with multiple tick-transmitted pathogens. Our recent experience indicates that dogs with heavy tick exposure can be infected at a high rate with multiple, potentially zoonotic, tick-borne pathogens.

## CAUSATION AND INFECTION WITH VECTOR-BORNE PATHOGENS

From an evolutionary perspective, it is obvious that vectors, vector-borne organisms, and animal and human hosts have developed a highly adapted form of interaction. In general, vectors need blood for nutrition. Bacterial, rickettsial and protozoal organisms need an intracellular environment to survive. Immunologically, most hosts appear to be able to support chronic infection with many vector-borne organisms for months to years without obvious deleterious effects. For these reasons, establishing causation associated with highly fastidious vector-transmitted pathogens will remain a challenge for the foreseeable future. As recent serologic and molecular evidence indicates that co-infection in dogs with *Ehrlichia*, *Babesia*, *Rickettsia* and *Bartonella* spp. may be more frequent than previously realized, the extent to which infection with *Bartonella*, for example, influences the pathophysiology of ehrlichiosis, a disease of much longer historical venue, deserves critical reappraisal. For example, infection with *Bartonella* in dogs concurrently infected with *Ehrlichia canis* may contribute to the tendency to develop epistaxis.<sup>24</sup> Historically, epistaxis has been attributed to ehrlichiosis, rather than bartonellosis.

## ZOONOTIC IMPLICATIONS OF EHRLICHIOSIS

Based upon isolation from patients, *E. canis*, *E. chaffeensis* and *E. ewingii* can all cause human ehrlichiosis. *Anaplasma phagocytophilum*, transmitted by *Ixodes scapularis*, *I. pacificus*, and *I. ricinus*, can also infect people and induce disease manifestations that are very similar to those caused by *Ehrlichia* spp.. However, the zoonotic role of dogs as a reservoir for human infection has not been clearly established for any *Ehrlichia* species. In South America, *E. canis* causes human monocytic ehrlichiosis and dogs are the probable reservoir host. It is probable that deer, rodents and other small mammals serve as the major reservoir for other *Ehrlichia* sp., with dogs playing only a minor role in the maintenance of

the organism in a given geographic location. Recently, the detection of *E. chaffeensis* DNA by PCR amplification provided the first documentation for natural infection of dogs residing in animal shelters or in a kennel in southeastern Virginia. Subsequently, we documented *E. chaffeensis* infection in dogs that was clinically and serologically indistinguishable from *E. canis* or *E. ewingii* infection.<sup>5</sup> Treatment with doxycycline resulted in therapeutic elimination of *E. canis*; however, based upon species-specific PCR amplification, *E. chaffeensis* DNA could be detected in all 3 dogs for up to 1 year following treatment, potentially due to frequent re-exposure and re-infection by *E. chaffeensis*-infected *Amblyomma americanum* ticks. The clinical or zoonotic implications of this observation await additional clarification.

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