ACVIM Consensus Statement

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Consensus Statement on Ehrlichial Disease of Small Animals from the Infectious Disease Study Group of the ACVIM*

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The Infectious Disease Study Group of the American College of Veterinary Internal Medicine (ACVIM) held a Special Interest Group meeting at the 18th Annual ACVIM Forum in Seattle, WA,[a] to discuss controversies in the diagnosis and therapy of ehrlichiosis in dogs and cats. The Study Group chose this topic because of the large amount of new information generated in the last 10 years. One of the goals of this meeting was to develop a Consensus Statement that would represent the most current understanding of this disease in both dogs and cats. Consensus was difficult to achieve on some issues, but the Study Group did identify 20 issues on which there was general uniformity of opinion. The issues developed for this Consensus Statement were formulated by the members of the Study Group and were intended to reflect controversies in the veterinary literature. This document was reviewed and approved by the membership of the Infectious Disease Study Group on July 1, 2001.

1. What* Ehrlichia *spp. Infect Dogs? *Ehrlichia canis* was the 1st species found to infect dogs.[1,2] *E canis* infection results in a variety of acute and chronic clinical syndromes but also can be subclinical. *Ehrlichia platys* also has been recognized as a pathogen of dogs for over 20 years; infection results in thrombocytopenia but usually causes minimal clinical illness.[3] Since infection with these 2 *Ehrlichia* spp. was described, several other species have been shown to cause natural disease in the dog. These include *Ehrlichia risticii* var. *atypicalis*,[4,5] *Ehrlichia ewingii*,[6,7] *Ehrlichia chaffeensis*,[8,9] *Ehrlichia phagocytophila*,[10,11] *Ehrlichia equi*,[12,13] and human granulocytic *Ehrlichia* (HGE).[14] The latter 3 species are most likely the same organism because they have been found to be closely related by DNA sequencing techniques.[15,16] The prevalence of infection with specific ehrlichial species varies substantially among geographic regions (see question 3).

2. What* Ehrlichia *spp. Infect Cats? *Ehrlichia*-like bodies or morulae have been detected in neutrophils, eosinophils, and mononuclear cells of naturally exposed cats.[17–21] Cats can be experimentally infected with *E equi*[13] and *E risticii*[22] after IV inoculation. *Ehrlichia equi*–infected cats were subclinically infected[13]; 2 of 6 cats given *E risticii*–infected pony blood IV developed fever, anorexia, and diarrhea.[22] On the basis of a few seroprevalence studies utilizing primarily *E canis* and *E risticii* antigens, exposure appears to be common in the natural setting. Precise speciation (eg, *canis* versus *risticii*) cannot be determined definitively because of serologic cross-reactivity among some ehrlichial species.[23,24] Ehrlichial DNA has been amplified from the blood of cats utilizing polymerase chain reaction (PCR). On the basis of sequencing results, *E equi* (Sweden, Denmark, Ireland/United Kingdom, and Massachusetts) and *E canis* (Canada and North Carolina) appear to infect naturally exposed cats.[21,25–28]

3. What Is the Geographic Distribution of the Different Ehrlichial Species?[29] Ehrlichial species infect animals of most regions of the world. For some, geographic distribution has not been totally determined (see Table 1).

4. Are There Different Tick Vectors for the* Ehrlichia *spp. that Infect Dogs and Cats? Geographic distribution of ehrlichial species is likely related, at least in part, to the current distribution of vectors for these agents. As a general rule, *Ixodes* ticks are more likely to be vectors for the granulocytic forms of *Ehrlichia*, and the monocytic *Ehrlichia* spp. are more likely to be transmitted by *Rhipicephalus*, *Amblyomma*, or *Dermacentor* ticks. Several ticks are known, or at least strongly suspected, to be vectors for the transmission of specific ehrlichial infections in dogs (see Table 2).[29]

In addition, in the horse, *E risticii* has been transmitted by the ingestion of trematode stages that are found in intermediate hosts such as aquatic insects and snails. The *Ehrlichia*-infected metacercariae in these insects are transmitted after the ingestion of the insect and serve as efficient vectors of *E risticii*.[30–32]

5. What Are the Most Common Clinical Manifestations of Ehrlichiosis? Canine ehrlichiosis is a multisystemic disorder that now is known to be caused by a variety of ehrlichial species. The classic presentation is characterized by depression, lethargy, mild weight loss, and anorexia, with or without hemorrhagic tendencies.[29,33] If present, bleeding usually is manifested by dermal petechiae, ecchymoses, or both. Although bleeding can occur from any mucosal surface, epistaxis is most frequent. Hemorrhagic tendencies are most commonly associated with thrombocytopenia and thrombocytopathia.[29] In addition to this classic presentation, uveitis,[29] polymyositis,[34] polyarthritis,[35,36] and central nervous system signs including seizures, ataxia, vestibular deficits, and cerebellar dysfunction[37,38] have been attributed to infection with *Ehrlichia* spp. As a general rule, the granulocytic species of *Ehrlichia* (*E ewingii*, *E equi*, *E phagocytophila*, and HGE) have been associated with polyarthritis more often than have the other species of *Ehrlichia*. In hu-

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Table 1. Geographic distribution of *Ehrlichia* spp.

Ehrlichia spp.	Geographical Distribution
E canis	Worldwide; primarily tropical and temperate climates. Because of chronic infection, disease manifestations may develop years after tick transmission and after the dog has been moved to a nonendemic region where the disease might not be considered.
E chaffeensis	United States, primarily the southern region
E risticii	United States, Canada
E risticii subsp. *atypicalis*	United States
E ewingii	United States, primarily the southern and lower mideastern regions, including Missouri
E equi[a]	United States, primarily the West Coast (California), Wisconsin, Minnesota, and the northeast and north-central regions
Human granulocytic *Ehrlichia*	United States, upper Midwest (Minnesota, Wisconsin) and northeast regions; Europe
E phagocytophila[a]	United Kingdom, Africa, Asia, Europe (Sweden, Switzerland)
E platys	Southeastern United States, southern Europe (Greece, Italy, Israel, France), South America

[a] May all be geographic variants of the same species.

Table 2. Ticks known, or at least strongly suspected, to be vectors for the transmission of specific ehrlichial infections in dogs.[29]

Ehrlichia spp.	Tick Vector
E canis	*Rhipicephalus sanguineus*
E chaffeensis	*Amblyomma americanum, Dermacentor variabilis*
E risticii	Unknown
E ewingii	*A americanum, Otobius megnini, Ixodes*?
E equi	*Ixodes pacificus*
Human granulocytic *Ehrlichia* agent	*Ixodes scapularis*
E phagocytophila	*Ixodes ricinus*
E platys	*R sanguineus*?

mans, both adult respiratory distress syndrome and acute renal failure have been reported with monocytic and granulocytic *Ehrlichia* spp.; these syndromes also may occur in dogs.[39–41] Apparently, many dogs are exposed and seroconvert but never show clinical signs (see question 17). It is unknown why some animals harbor the agent for months to years without developing clinical signs. Breed predispositions to clinical disease have been reported; German Shepherd Dogs, for example, may have increased susceptibility. The evolving importance of coinfection with other tickborne diseases can make it difficult to attribute clinical signs to a single specific agent. Most clinical manifestations attributed to canine ehrlichiosis also have been described in cats.[17–21,23–26]

6. What Clinicopathologic Findings Should Alert the Clinician to the Possibility that an Animal May Have an Ehrlichial Infection? With canine ehrlichiosis, the most consistent CBC abnormalities are thrombocytopenia and mild nonregenerative anemia.[33] However, infected dogs may have normal platelet counts. Pancytopenia may be seen in the severe chronic phase of the disease and usually is the result of hypoplasia of all bone marrow precursor cells.[33] Granular lymphocytosis, which may be confused with well-differentiated lymphocytic leukemia, also has been reported.[42] Nonregenerative anemia and thrombocytopenia are the most common hematologic abnormalities in cats. Hyperproteinemia has been reported in approximately 33% of affected dogs. Polyclonal gammopathy is most common, but monoclonal gammopathies have been reported in both dogs and cats.[24,43]

7. How Should Serology Be Used for the Diagnosis of Canine Ehrlichiosis? A diagnosis of ehrlichiosis usually is based on the detection of serum antibodies by use of the indirect fluorescent antibody (IFA) test. In dogs experimentally infected with *E canis*, this test detects serum antibodies as early as 7 days after initial infection, but some dogs may not become seropositive until 28 days after infection. Clinical signs of disease can occur before the development of serum antibodies, and IFA test results can be negative in acutely infected dogs. If ehrlichiosis is strongly suspected in a seronegative dog, serologic testing should be repeated in 2–3 weeks to assess for seroconversion. There is variable serologic cross-reactivity among *E canis* and *E risticii*, *E platys*, and granulocytic *Ehrlichia* spp., and dogs infected with other species may be seronegative when assessed by IFA with *E canis* morulae. For example, over 100 dogs with clinical ehrlichiosis due to *E risticii* were seronegative to *E canis* antigens.[4,5]

Most laboratories report serum titers to reflect the quantity of antibodies present in a serum sample. However, titers do not correlate with the duration of infection or the severity of disease. Some laboratories use different ''cut-off'' values to differentiate positive and negative results. Because of differences in reporting among laboratories, the most appropriate cut-off titer is unknown at this time. It is the consensus of this group that titers $<1:80$ should be deemed suspect and that repeated serologic testing within 2–3 weeks, PCR confirmation, or Western immunoblotting should be considered. A recently marketed, point-of-care *E canis* antibody screening test[b] is calibrated to be positive at a titer of approximately 1:100 or greater. Clinical disease can be detected in some dogs before seroconversion, and failure to detect ehrlichial antibodies in acutely ill dogs does not exclude the diagnosis.

When clinical signs or clinicopathologic abnormalities consistent with ehrlichiosis are found in conjunction with positive ehrlichial serology, a clinical diagnosis of ehrlichiosis should be made and treatment instituted. However, because of latent infection, a positive antibody titer does not necessarily mean that the clinical manifestations are due to ehrlichiosis at the time of presentation. This is especially true in endemic areas where many healthy dogs have positive serum titers to *E canis*.[44] An unknown number of dogs may spontaneously resolve *Ehrlichia* spp. infection but remain seropositive (see question 15). Additionally, *E canis* antibodies cross-react with *E ewingii*,[45] *E chaffeensis*,[8] *Neorickettsia helminthoeca*,[46] and *Cowdria ruminantium*.[47]

Therefore, in regions where other rickettsial agents are endemic, a positive *E canis* titer should be considered evidence of infection with one or more of these other ehrlichial species or simply cross-reactivity with another rickettsial agent, as opposed to active disease due to *E canis.*

In some cases, serologic confirmation by Western immunoblotting may be indicated, but this test is not routinely available.[48,49] Western immunoblotting can be helpful in distinguishing between infection with *Ehrlichia* spp. that display serologic cross-reactivity in IFA such as *E canis* and *E ewingii* and *E canis* and *E chaffeensis.*[45]

If a dog does not respond to treatment for ehrlichiosis in the anticipated time frame, then another cause of the clinical abnormalities should be considered. Also, concurrent infections with other tick-transmitted agents may occur more frequently than we have realized in the past.[50] Therefore, testing for other tickborne agents such as *Babesia canis, Bartonella vinsonii,* or *Rickettsia rickettsii* may be indicated.

8. How Should Serology Be Used for the Diagnosis of Feline Ehrlichiosis? Definitive statements cannot be made at this time. Information on the *Ehrlichia* spp. infecting cats is not available, data from experimentally infected cats are lacking, and there is no standardization among laboratories currently providing *Ehrlichia* spp. serologic tests for use with cat sera. Most cats with suspected ehrlichiosis tested to date have been assessed by IFA utilizing *E canis* and *E risticii* morulae.[23,24] We recommend that cats with clinical findings referable to ehrlichiosis and seroreactivity with ehrlichial antigens be treated with anti-ehrlichial drugs (see question 10). Some cats with ehrlichiosis may have low or negative titers; 3 cats with *E canis* DNA were seronegative by IFA.[26]

9. How Should Blood Culture and PCR Be Used in the Diagnosis of Ehrlichiosis? Blood cultures may take up to 8 weeks to become positive, are expensive, and are not routinely available. For this reason, blood culture currently is considered a research tool.

PCR is a sensitive method for the detection of acute *E canis* and granulocytic ehrlichial infection in dogs.[51,52] PCR and DNA sequencing have been used to identify new species or to show that some *Ehrlichia* spp. such as HGE, *E phagocytophila* and *E equi* are closely related.[15,16] Primers can be designed to detect all sequenced *Ehrlichia* spp. or can be used to identify individual species.

There currently are several potential limitations to the use of PCR in the diagnosis of ehrlichiosis in clinical practice. Samples for testing must be sent to commercial laboratories, and current commercially available PCR assays are relatively expensive. Insufficient quality control can result in both false-positive and false-negative results. Whereas the specificity of PCR can be considerable on the basis of primer design, there currently is no standardization among laboratories, and comparison of results is difficult. PCR tests may yield positive results within 4–10 days of exposure to *E canis* in experimental studies.[53,54] Whereas PCR can become positive in experimentally infected dogs before seroconversion, sensitivity in naturally infected animals currently is unknown. In untreated animals, positive PCR results confirm infection by an ehrlichial species, whereas positive serologic test results only confirm exposure. It is unknown whether blood, bone marrow cells, or cells collected by splenic aspirate are optimal for testing. Performance of PCR assays on joint fluid, cerebrospinal fluid, and aqueous humor ultimately may prove beneficial in some cases. It is our consensus at this time that PCR should be used in conjunction with serology, not instead of it, for the initial diagnosis of ehrlichiosis in untreated animals. See question 14 for recommendations on the use of PCR in posttreatment monitoring.

10. What Are the Most Effective Treatments for Ehrlichiosis? Drugs that have been successful in the treatment of ehrlichiosis include tetracycline, chloramphenicol, imidocarb dipropionate, and amicarbalide.[29] Tetracycline and oxytetracycline have been considered the initial drugs of choice in the past[2] and still are effective, but doxycycline and minocycline now are used more frequently. Several different protocols have been used.[55–57] The consensus recommendation of the Study Group is to prescribe doxycycline at a dosage of 10 mg/kg PO q24h for 28 days. Dramatic clinical improvement generally occurs within 24–48 hours after the initiation of tetracycline therapy in dogs with acute-phase or mild chronic-phase disease. Platelet counts correspondingly increase during this time and usually are normal within 14 days of treatment. Tetracycline and doxycycline also have been used successfully in cats with presumed ehrlichiosis.[17–21,23–26] Although there is minimal information available at this time concerning the treatment of cats, the consensus recommendation of the Study Group is to prescribe doxycycline at a dosage of 10 mg/kg PO q24h for 28 days.

Enrofloxacin has been shown effective for the treatment of another rickettsial disease, Rocky Mountain spotted fever,[58] but it is ineffective against experimentally induced *E canis* infection.[57] For over 20 years, imidocarb dipropionate also has been shown to be an effective treatment of canine ehrlichiosis when administered at a dosage of 5 mg/kg IM twice, 2–3 weeks apart.[59] A recent evaluation of imidocarb dipropionate suggested that 2 doses of 5 mg/kg IM given 15 days apart were as effective as doxycycline in resolving clinical signs, but platelet counts were slower to normalize when compared to dogs treated with doxycycline.[60] Apparently, imidocarb also was effective in treating several cats with ehrlichiosis.

11. Is There a Difference in Response to Treatment among Different* Ehrlichia *spp.? To date, most studies have reported that doxycycline is effective against all ehrlichial species. Even the more recently recognized granulocytic species appear to be susceptible to the doxycycline regimen usually prescribed for the treatment of *E canis.*[61] The efficacy of newer antibiotics against ehrlichial infections still is compared to doxycycline as the standard therapy. There is some variability in the reported efficacy of imidocarb. In one report, the authors speculated that *E chaffeensis* infection of dogs may be more resistant to doxycycline therapy than *E canis* infection.[9] However, it is possible that the treated dogs did not have persistent immunity, were reexposed to *Amblyomma* ticks, or became rapidly reinfected, rather than failing to respond to doxycycline. Unlike *Rhipicephalus sanguineus,* which transmits *E canis* and generally is found in kennels or structures that house numerous dogs, *Amblyomma americanum* is a field tick

found in extremely high concentrations in areas with large deer populations. No immunity occurs after infection with *E canis* or *E chaffeensis*, and dogs reintroduced to tick-infested environments can become reinfected. Clinically, the efficacy of acaricides to control tick infestations in these 2 settings can differ substantially.

12. What Clinicopathologic Parameters Should Be Monitored during the Treatment of Canine Ehrlichiosis? Thrombocytopenia occurs in approximately 82% of *E canis*–infected dogs,[62] and the resolution of thrombocytopenia usually is indicative of a good response to therapy.[29] After treatment, platelet counts begin to increase within 24–48 hours and are usually normal within 14 days.[55,56] If platelet counts do not increase within 7 days of therapy, another mechanism for thrombocytopenia could be present, such as immune-mediated destruction or coinfection with *Babesia* or *Bartonella*.[29] Ineffective or incomplete responses with drugs like enrofloxacin have been reported (ie, an initial increase in the platelet count but recurrence of thrombocytopenia 14 days after treatment because of failure to eliminate the infection).[57] If platelet counts are used as a marker for improvement or cure, they should be reevaluated at least 4–8 weeks posttherapy. Gradual resolution of hyperglobulinemia over 6–9 months also suggests therapeutic elimination of the organism.[43]

13. How Should Serology Be Used for the Monitoring of Effective Treatment? After successful treatment in most dogs, antibody titers decline and generally become negative within 6–9 months of therapy. The duration of positive titers is in part dependent on how high the titers were at the beginning of treatment; higher titers usually take longer to become negative than low titers. Some laboratories (and the new point-of-care antibody screening test) provide only a positive or negative serum antibody result, and actual serum titers are unknown or unreported in these animals. If the laboratory reported the titer to a very high endpoint, the monitoring for a fall in titer from a very high concentration could be misleading, because there is a decreased accuracy with dilutions at high concentrations. Some dogs have a resolution of clinical and clinicopathologic abnormalities yet retain high titers to *E canis* for years.[63,64] It cannot always be determined in these dogs whether there is continued infection or merely persistence of antibodies. Thus, antibody detection by any methodology, including IFA, enzyme-linked immunosorbent assay, or Western immunoblotting, probably is not a very effective means of assessing response to treatment.[56,65]

14. How Should PCR Be Used for the Monitoring of Effective Treatment? PCR may ultimately prove useful in distinguishing successfully treated animals with persistently high IFA titers from unsuccessfully treated animals with persistent *E canis* infection.[53,66] It is the consensus of the group that if PCR is used to monitor treatment, the PCR assay should be repeated after antimicrobial therapy has been discontinued for 2 weeks. If PCR results are positive, an additional 4 weeks of treatment should be given with the PCR assay repeated after antimicrobial therapy has been discontinued for 2 weeks. If PCR results are positive after 2 treatment cycles, the use of an alternate anti-ehrlichial drug should be considered. If PCR results are negative, the test should be rechecked in 2 months; if still negative, therapeutic elimination is likely. However, the organism may be sequestered in other tissues, such as the spleen (see question 15).

15. Can Dogs with Ehrlichiosis Truly Be Cured or Cleared of the Infection? This is one of the more difficult questions to address because the ''gold standard'' to assess for organism clearance has not yet been determined in the dog. Experimental studies have shown that blood cultures and PCR of blood samples become negative with the resolution of clinical signs or thrombocytopenia, suggesting that the organism is cleared from the body.[55,57] However, in a recent study of 6 *E canis* experimentally infected dogs, 4 of 6 dogs were PCR positive on splenic aspirates 34 months after infection.[66] Of these 4 dogs, 2 were negative on PCR of blood samples. The other 2 dogs were PCR negative on all tissues. It is possible that the spleen is the last organ to harbor *E canis* during recovery or that the organism is sequestered in splenic macrophages to avoid immune elimination. However, it is also possible that ehrlichial DNA detected in the spleen could persist from dead organisms and does not represent active infection. It is our consensus that treated dogs have eliminated the organism if hyperglobulinemia and other clinical and laboratory abnormalities resolve progressively, even if a positive serum titer remains.

16. Can Dogs with Ehrlichiosis Be Reinfected? Dogs can become reinfected with *E canis* after a previously effective treatment, and recovery does not necessarily equate with permanent immunity.[56,67] Experimentally, dogs can be reinfected with homologous or heterologous strains of *E canis*. Reinfection is likely in environments with high tick density, and rigorous tick control measures or the prophylactic use of doxycycline (as used in military working dogs in tick-infested regions)[68] are important management considerations (see question 18).

17. Should Healthy Dogs Be Assessed Serologically for Ehrlichial Antibodies? Arguments for serologic screening in healthy dogs include the following: (1) the testing of large numbers of dogs over a wide geographic area would give more information concerning seroprevalence and identify endemic areas of ehrlichiosis; (2) seroprevalence studies would allow the dog to be used as a sentinel for ehrlichiosis in humans in the same geographic areas; (3) in multidog environments such as kennels and breeding operations, the testing of all dogs, especially new additions, might minimize the potential for development of the disease within the kennel or breeding operation; (4) the detection of subclinically infected dogs could promote more effective therapy, thereby reducing the chronic phase of illness; and (5) the testing and treating of subclinically infected dogs could reduce the reservoir of ehrlichial species in the environment.

Arguments against serologic screening in healthy dogs include the following: (1) healthy dogs presumably are a low incidence group, and false-positive test results in low incidence groups could result in the unnecessary treatment of uninfected dogs; (2) it is likely that most serologic screening of healthy dogs will be performed by the currently available point-of-care test,[a] which uses *E canis* antigen and will consistently detect infection with this species but will not detect other ehrlichial species that infect dogs;

(3) it is unclear whether treatment prevents the development of the chronic phase of infection (see question 14); (4) some immunocompetent dogs may be able to eliminate *E canis* infection without therapy[67]; (5) it is unknown how many dogs eliminate ehrlichial infection naturally; (6) it is impossible to determine which dogs will go on to develop chronic disease manifestations; (7) some dogs eliminate infection without treatment and, hence, the presence of serum antibodies only denotes exposure to an ehrlichial species and does not document current infection; (8) the treatment of healthy dogs is likely of minimal benefit because infected, treated dogs do not develop permanent immunity, and infected dogs generally are reexposed in their endemic environment; (9) other canid reservoir hosts exist in the environment, and the treatment of positive pet dogs is unlikely to have an impact on the prevalence of the organism in the environment; (10) although not proven at this time, the treatment of all seropositive dogs may increase the risk for the development of doxycycline resistance[69]; and (11) all drugs currently used for the treatment of ehrlichiosis have potential adverse effects and, if used extensively in animals that may never become clinically ill with ehrlichiosis, treatment may result in more problems than it prevents.

Because of the lack of data concerning the appropriateness of treating healthy animals, we currently recommend that, if a seropositive healthy animal is detected, the pros and cons of treatment (outlined above) be discussed with the owner and a decision made about which management course is best for the dog in question.

18. What Preventive Measures Should Be Used to Decrease Infection with Ehrlichial Organisms? Prevention in endemic areas can be accomplished by maintaining strict tick control programs for dogs and premises. If a kennel currently is known to be *Ehrlichia* negative, new additions to the kennel should be tested by IFA serology and, if positive, treated with a course of doxycycline before being housed with the other dogs. Additionally, a thorough check for the presence of ticks should be performed, and the dogs should be treated with acaricides. When frequenting an endemic area, treatment with doxycycline at 3 mg/kg PO q24h lessens the potential for infection but may ultimately result in antimicrobial resistance.[68,69]

19. Is There a Vaccine for Ehrlichiosis? At this time, no vaccine is available for the prevention of ehrlichiosis. Vaccination is an area of active interest, and several pharmaceutical companies currently are evaluating the feasibility and effectiveness of vaccines to protect against ehrlichiosis.

20. What Are the Public Health Considerations of Ehrlichiosis? There is no evidence of direct transmission of ehrlichial species from dogs or cats to people. However, the dog could act as a reservoir (carrier) for *E chaffeensis*, *E ewingii*, or *E equi* in endemic geographic regions, and cats have been shown to be infected by *E canis* and *E equi*. Consequently, animals carrying infected ticks could be a source of transmission to people. There has been only 1 report of a person becoming infected with an *E canis*–like agent.[70] Therefore, *E canis* appears to be of minimal zoonotic importance. The role, if any, of domestic animals in human ehrlichiosis is yet to be determined.

Wildlife hosts such as rodents probably are the maintenance reservoirs for *E chaffeensis* and *E equi*, with immature tick stages serving as vectors. Deer may become infected or involved in vector maintenance in the natural setting. Ticks should be removed with care and destroyed. In addition to tick exposure, some individuals may become infected by handling deer carcasses and contacting associated engorged ticks or infected blood.[71,72]

Summary

Within the past several decades, the number of *Ehrlichia* spp. recognized to infect cats, dogs, and human beings has expanded substantially. The recent application of advanced techniques in molecular biology has changed how ehrlichiosis is diagnosed and has provided new tools for the assessment of treatment. As these techniques are applied, the numerous questions that relate to the management of dogs and cats with ehrlichiosis ultimately will be answered. We hope this consensus statement will assist veterinarians in the management of their patients.

Footnotes

[a] ACVIM Forum, Seattle Convention Center, Seattle, WA, May 26, 2000

[b] SNAP 3 Dx Assay, IDEXX Laboratories, Inc, One IDEXX Drive, Westbrook, ME

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References

1. Donatien A, Lestoguard F. Existence en Algérie d'une Rickettsia du chien. Bull Soc Pathol Exot 1935;28:418–419.

2. Buhles WC Jr, Huxsoll DL, Ristic M. Tropical canine pancytopenia: Clinical, hematologic, and serologic response of dogs to *Ehrlichia canis* infection, tetracycline therapy, and challenge inoculation. J Infect Dis 1974;130:357–367.

3. Harvey JW, Simpson CF, Gaskin JM. Cyclic thrombocytopenia induced by a *Rickettsia*-like agent in dogs. J Infect Dis 1978;137:182–188.

4. Kakoma I, Hansen R, Liu L, et al. Serologically atypical canine ehrlichiosis associated with *Ehrlichia risticii* infection. J Am Vet Med Assoc 1991;199:1120.

5. Kakoma I, Hansen RD, Anderson BE, et al. Cultural, molecular, and immunological characterization of the etiologic agent for atypical canine ehrlichiosis. J Clin Microbiol 1994;32:170–175.

6. Anderson BE, Greene CE, Jones DC, et al. *Ehrlichia ewingii* sp. nov. the etiologic agent of canine granulocytic ehrlichiosis. Int J Syst Bacteriol 1992;42:299–302.

7. Stockham SL, Schmidt DA, Curtis KS. Evaluation of granulocytic ehrlichiosis in dogs of Missouri, including serologic status to *Ehrlichia canis*, *Ehrlichia equi*, and *Borrelia burgdorferi*. Am J Vet Res 1992;53:63–68.

8. Dawson JE, Ewing SA. Susceptibility of dogs to infection with

Ehrlichia chaffeensis, causative agent of human ehrlichiosis. Am J Vet Res 1992;53:1322–1327.

9. Breitschwerdt EB, Hegarty BC, Hancock SI. Sequential evaluation of dogs naturally infected with *Ehrlichia canis, Ehrlichia chaffeensis, Ehrlichia equi, Ehrlichia ewingii,* or *Bartonella vinsonii*. J Clin Microbiol 1998;36:2645–2651.

10. Johansson KE, Petterson M, Uhlen M, et al. Identification of the causative agent of granulocytic ehrlichiosis in Swedish dogs and horses by direct solid phase sequencing of PCR products. Res Vet Sci 1995;58:109–112.

11. Pusterla N, Huder J, Wolfensberger C, et al. Granulocytic ehrlichiosis in two dogs in Switzerland. J Clin Microbiol 1997;35:2307–2309.

12. Madewell BR, Gribble DH. Infection in two dogs with an agent resembling *E. equi.* J Am Vet Med Assoc 1982;180:512–514.

13. Lewis GE, Huxsoll DL, Risticii M, et al. Experimentally induced infection of dogs, cats, and nonhuman primates with *Ehrlichia equi*, etiologic agent of equine ehrlichiosis. J Am Vet Med Assoc 1975; 36:85–88.

14. Greig B, Asanovich KM, Armstrong PJ, et al. Geographic, clinical, serologic, and molecular evidence of granulocytic ehrlichiosis, a likely zoonotic disease in Minnesota and Wisconsin dogs. J Clin Microbiol 1996;34:44–48.

15. Bakken JS, Dumler JS, Chen SM, et al. Human granulocytic ehrlichiosis in the upper midwest United States: A new species emerging. JAMA 1994;272:212–218.

16. Chen SM, Dumler S, Bakken JS, et al. Identification of a granulocytotropic *Ehrlichia* species as the etiologic agent of human disease. J Clin Microbiol 1994;32:589–595.

17. Bouloy RP, Lappin MR, Holland CH, et al. Clinical ehrlichiosis in a cat. J Am Vet Med Assoc 1994;204:1475–1478.

18. Buoro IBJ, Atwell RB, Kiptoon J, et al. Feline anemia associated with *Ehrlichia*-like bodies in three domestic short-haired cats. Vet Rec 1989;125:434–436.

19. Charpentier F, Groulade P. Probable case of ehrlichiosis in a cat. Bull Acad Vet France 1986;59:287–290.

20. Beaufils JP, Marin-Granel J, Jumelle P. *Ehrlichia* infection in cats: A review of three cases. Pratique Medicale Chirurgicate de l'Animale de Compagnie 1995;30:397–402.

21. Bjoersdorff A, Svendenius L, Owens JH, et al. Feline granulocytic ehrlichiosis—A report of a new clinical entity and characterisation of the new infectious agent. J Small Anim Pract 1999;40:20–24.

22. Dawson JE, Abeygunawardena I, Holland CJ, et al. Susceptibility of cats to infection with *Ehrlichia risticii,* causative agent of equine monocytic ehrlichiosis. Am J Vet Res 1988;49:2096–2100.

23. Peavy GM, Holland CJ, Dulta SK, et al. Suspected ehrlichial infection in five cats from a household. J Am Vet Med Assoc 1997; 210:231–234.

24. Stubbs CJ, Holland CJ, Reif JS, et al. Feline ehrlichiosis; literature review and serologic survey. Compend Cont Educ Pract Vet 2000;22:307–317.

25. Lappin MR, Jensen WA, Brewer M, et al. *Ehrlichia equi* infection of 2 cats in Massachusetts. American Society of Rickettsiologists; August 2001.

26. Breitschwerdt E, Abrams-Ogg A, Hancock S, et al. Molecular evidence of *Ehrlichia canis* infection in cats from North America. Proceedings of the ACVIM Forum, Denver, CO, May 2001.

27. Shaw SE, Kenny MJ, Lerga AI, et al. A PCR-based survey of tick-borne infections in Danish cats and dogs. Proceedings of the 18th Conference of World Association for Advancement of Veterinary Parasitology, Stresa, Italy, August 2001.

28. Shaw SE, Kenny MJ, Lerga AI. PCR-based survey of tick-borne diseases in the UK/Ireland. European Society for Veterinary Internal Medicine, September 2001.

29. Neer TM. Canine monocytic and granulocytic ehrlichiosis. In: Greene CE, ed. Infectious Diseases of the Dog and Cat, 2nd ed. Philadelphia, PA: WB Saunders; 1998:139–147.

30. Pusterla N, Madigan JE, Chae JS, et al. Helminthic transmission and isolation of *Ehrlichia risticii*, the causative agent of potomac horse fever, by using trematode stages from freshwater stream snails. J Clin Microbiol 2000;38:1293–1297.

31. Reubel GH, Barlough JE, Madigan JE. Production and characterization of *Ehrlichia risticii*, the agent of potomac horse fever, from snails (Pleuroceridae: *Juga* spp.) in aquarium culture and genetic comparison to equine strains. J Clin Microbiol 1998;36:1501–1511.

32. Kanter M, Mott J, Ohashi N, et al. Analysis of 16SrRNA and 51-kilodalton antigen gene and transmission in mice of *Ehrlichia risticii* in virgulate trematodes from *Elimia livescens* snails in Ohio. J Clin Microbiol 2000;38:3349–3358.

33. Woody BJ, Hoskins JD. Ehrlichial diseases of dogs. Vet Clin North Am Small Anim Pract 1991;21:75–98.

34. Buoro IBJ, Kanui TI, Atwell RB, et al. Polymyositis associated with *Ehrlichia canis* infection in two dogs. J Small Anim Pract 1990; 31:624–627.

35. Stockham SL, Schmidt DA, Curtis KS. Evaluation of granulocytic ehrlichiosis in dogs of Missouri, including serologic status to *Ehrlichia canis, Ehrlichia equi* and *Borrelia burgdorferi*. Am J Vet Res 1992;53:63–68.

36. Stockham SL, Tyler JW, Schmidt DA, et al. Experimental transmission of granulocytic ehrlichial organisms in dogs. Vet Clin Pathol 1990;19:99–104.

37. Maretzki CH, Fisher DJ, Greene CE. Granulocytic ehrlichiosis and meningitis in a dog. J Am Vet Med Assoc 1994;205:1554–1556.

38. Meinkoth JA, Hoover JP, Cowell RL, et al. Ehrlichiosis in a dog with seizures and nonregenerative anemia. J Am Vet Med Assoc 1989;195:1754–1755.

39. Weaver RA, Virella G, Weaver A. Ehrlichiosis with severe pulmonary manifestations despite early treatment. South Med J 1999;92: 336–339.

40. Patel RG, Byrd MA. Near fatal acute respiratory distress syndrome in a patient with human ehrlichiosis. South Med J 1999;92: 333–335.

41. Modi KS, Dahl DC, Berkseth RO, et al. Human granulocytic ehrlichiosis presenting with acute renal failure and mimicking thrombotic thrombocytopenic purpura. Am J Nephrol 1999;19:677–681.

42. Weiser MG, Thrall MA, Fulton R, et al. Granular lymphocytosis and hyperproteinemia in dogs with chronic ehrlichiosis. J Am Anim Hosp Assoc 1991;27:84–88.

43. Breitschwerdt EB, Woody BJ, Zerbe CA, et al. Monoclonal gammopathy associated with naturally occurring canine ehrlichiosis. J Vet Intern Med 1987;1:2–9.

44. Hoskins JD, Breitschwerdt EB, Gaunt SD, et al. Antibodies to *Ehrlichia canis, Ehrlichia platys,* and spotted fever group rickettsiae in Louisiana dogs. J Vet Intern Med 1988;2:55–59.

45. Rikihisa Y, Ewing SA, Fox JC, et al. Analyses of *Ehrlichia canis* and a canine granulocytic *Ehrlichia* infection. J Clin Microbiol 1992;30:143–148.

46. Rikihisa Y. Cross-reacting antigens between *Neorickettsia helminthoeca* and *Ehrlichia* species, shown by immunofluorescence and Western immunoblotting. J Clin Microbiol 1991;29:2024–2029.

47. Kelly PJ, Matthewman LA, Mahan SM, et al. Serological evidence for antigenic relationships between *Ehrlichia canis* and *Cowdria ruminantium.* Res Vet Sci 1994;56:170–174.

48. Hegarty BC, Levy MG, Gager RF, et al. Immunoblot analysis of the immunoglobulin G response to *Ehrlichia canis* in dogs: An international survey. J Vet Diagn Invest 1997;9:32–38.

49. Matthewman LA, Kelly PJ, Mahan SM, et al. Western blot and indirect fluorescent anti-body testing for antibodies reactive with *Ehrlichia canis* in sera from apparently healthy dogs in Zimbabwe. J S Afr Vet Assoc 1993;64:111–115.

50. Kordick SK, Breitschwerdt EB, Hegarty BC, et al. Coinfection

with multiple tick-borne pathogens in a Walker Hound kennel in North Carolina. J Clin Microbiol 1999;37:2631–2638.

51. Engvall EO, Petterson B, Persson M, et al. A 165 r RNA-based PCR assay for detection and identification of granulocytic *Ehrlichia* species in dogs, horses, and cattle. J Clin Microbiol 1996;34:2170–2174.

52. McBride JW, Corstvet RE, Gaunt SD, et al. PCR detection of acute *Ehrlichia canis* infection in dogs. J Vet Diagn Invest 1996;8: 441–442.

53. Wen B, Rikihisa Y, Mott JM, et al. Comparison of nested PCR with immunofluorescent-antibody assay for detection of *Ehrlichia canis* infection in dogs treated with doxycycline. J Clin Microbiol 1997; 35:1852–1855.

54. Iqbal Z, Chaichansiriwithaya W, Rikihisa Y. Comparison of PCR with other tests for early diagnosis of canine ehrlichiosis. J Clin Microbiol 1994;32:1658–1662.

55. Igbal Z, Rikihisa Y. Reisolation of *Ehrlichia canis* from blood and tissues of dogs after doxycycline treatment. J Clin Microbiol 1994; 32:1644–1649.

56. Breitschwerdt EB, Hegarty BC, Hancock SI. Doxycycline hyclate treatment of experimental canine ehrlichiosis followed by challenge inoculation with two *Ehrlichia canis* strains. Antimicrob Agents Chemother 1998;42:362–368.

57. Neer TM, Eddlestone SM, Gaunt SD, et al. Efficacy of enrofloxacin for the treatment of experimentally induced *Ehrlichia canis* infection. J Vet Intern Med 1999;13:501–504.

58. Breitschwerdt EB, Davidson MG, Aucoin DP, et al. Efficacy of chloramphenicol, enrofloxacin, and tetracycline for treatment of experimental Rocky Mountain spotted fever in dogs. Antimicrob Agents Chemother 1991;35:2375–2381.

59. Matthewman LA, Kelly PJ. Brouqui P, et al. Further evidence for the efficacy of imidocarb dipropionate in the treatment of *Ehrlichia canis* infection. J S Afr Vet Assoc 1994;65:104–107.

60. Sainz A, Tesouro MA, Amusategui I, et al. Prospective comparative study of 3 treatment protocols using doxycycline or imidocarb dipropionate in dogs with naturally occurring ehrlichiosis. J Vet Intern Med 2000;14:134–139.

61. Klein MB, Nelson CM, Goodman JL. Antibiotic susceptibility of the newly cultivated agent of human granulocytic ehrlichiosis: Promising activity of quinolones and rifamycins. Antimicrob Agents Chemother 1997;41:76–79.

62. Troy GC, Forrester SD. Canine ehrlichiosis. In: Greene CE, ed. Infectious Diseases of the Dog and Cat. Philadelphia, PA: WB Saunders; 1990:404–418.

63. Bartsch RC, Greene RT. Post-therapy antibody titers in dogs with ehrlichiosis: Follow-up study on 68 patients treated primarily with tetracycline and/or doxycycline. J Vet Intern Med 1996;10:271–274.

64. Perille AL, Matus RE. Canine ehrlichiosis in six dogs with persistently increased antibody titers. J Vet Intern Med 1991;5:195–198.

65. Rikihisa Y, Ewing SA, Fox JC, et al. Western immunoblot analysis of *Ehrlichia chaffeensis, E. canis,* or *E. ewingii* infections in dogs and humans. J Clin Microbiol 1994;32:2107–2112.

66. Harrus S, Waner T, Aizenberg I, et al. Amplification of ehrlichial DNA from dogs 34 months after infection with *Ehrlichia canis.* J Clin Microbiol 1998;36:73–76.

67. Huxsoll DL. Canine ehrlichiosis (tropical canine pancytopenia): A review. Vet Parasitol 1976;2:49–60.

68. Davoust B, Boni M, Seignot J, Parzy D. Chemoprophylaxis with tetracycline for canine monocytic ehrlichiosis in Africa. Abstract 232C, EUWOG-ASR Joint Meeting, Marseille, France, June 14–16, 1999.

69. Goodman JL. Ehrlichiosis—Ticks, dogs, and doxycycline. N Engl J Med 1999;341:195–197.

70. Perez M, Rikihisa Y, Wen B. *Ehrlichia canis*–like agent from a man in Venezuela: Antigenic and genetic characterization. J Clin Microbiol 1996;34:2133–2139.

71. Bakken JS, Krueth JK, Lund T, et al. Exposure to deer blood may be a cause of human granulocytic ehrlichiosis. Clin Infect Dis 1996;23:198.

72. Telford SR. Risk for acquiring human granulocytic ehrlichiosis: Exposure to deer blood or deer ticks. Clin Infect Dis 1997;24:531.