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, 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. 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. 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. atypticalis, Ehrlichia ewingii, Ehrlichia chaffeensis, Ehrlichia phagocytophila, and Ehrlichia equi, and human granulocytic Ehrlichia (HGE). The latter 3 species are most likely the same organism because they have been found to be closely related by DNA sequencing techniques. 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. Cats can be experimentally infected with E equi and E risticii after IV inoculation. Ehrlichia equi–infected cats were subclinically infected; 2 of 6 cats given E risticii–infected pony blood IV developed fever, anorexia, and diarrhea. 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 specification (eg, canis versus risticii) cannot be determined definitively because of serologic cross-reactivity among some ehrlichial species. 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.

3. What Is the Geographic Distribution of the Different Ehrlichial Species? 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 Rhizophelphus, 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).

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. If present, bleeding usually is manifested by dural 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. In addition to this classic presentation, uveitis, polymyositis, polyarthritides, and central nervous system signs including seizures, ataxia, vestibular deficits, and cerebellar dysfunction 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 polyarthritides more often than have the other species of Ehrlichia. In hu-
attributed to canine ehrlichiosis also have been described in signs to a single specific agent. Most clinical manifestations tibility. The evolving importance of coinfection with other positions to clinical disease have been reported; German to years without developing clinical signs. Breed predis-

is fulminant and often rapidly fatal. 

unknown why some animals harbor the agent for months but never show clinical signs (see question 17). It is

A diagnosis of ehrlichiosis usually is

Table 1. Geographic distribution of *Ehrlichia* spp.

<table>
<thead>
<tr>
<th><em>Ehrlichia</em> spp.</th>
<th>Geographical Distribution</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>E canis</em></td>
<td>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.</td>
</tr>
<tr>
<td><em>E chaffeensis</em></td>
<td>United States, primarily the southern region</td>
</tr>
<tr>
<td><em>E risticii</em> subsp. atypica</td>
<td>United States</td>
</tr>
<tr>
<td><em>E ewingii</em></td>
<td>United States, primarily the southern and lower mideastern regions, including Missouri</td>
</tr>
<tr>
<td><em>E equi</em></td>
<td>United States, primarily the West Coast (California), Wisconsin, Minnesota, and the northeast and north-central regions</td>
</tr>
<tr>
<td>Human granulocytic <em>Ehrlichia</em></td>
<td>United States, upper Midwest (Minnesota, Wisconsin) and northeast regions; Europe</td>
</tr>
<tr>
<td><em>E phagocytophila</em></td>
<td>United Kingdom, Africa, Asia, Europe (Sweden, Switzerland)</td>
</tr>
<tr>
<td><em>E platys</em></td>
<td>Southeastern United States, southern Europe (Greece, Italy, Israel, France), South America</td>
</tr>
</tbody>
</table>

*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.

<table>
<thead>
<tr>
<th><em>Ehrlichia</em> spp.</th>
<th>Tick Vector</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>E canis</em></td>
<td>Rhipicephalus sanguineus</td>
</tr>
<tr>
<td><em>E chaffeensis</em></td>
<td>Amblyomma americanum, Dermacentor variabilis</td>
</tr>
<tr>
<td><em>E risticii</em></td>
<td>Unknown</td>
</tr>
<tr>
<td><em>E ewingii</em></td>
<td>A americanum, Otobius megnini, Ixodes?</td>
</tr>
<tr>
<td><em>E equi</em></td>
<td>Ixodes pacificus, Ixodes scapularis</td>
</tr>
<tr>
<td>Human granulocytic <em>Ehrlichia</em> agent</td>
<td><em>E phagocytophila</em></td>
</tr>
<tr>
<td><em>E platys</em></td>
<td>R sanguineus</td>
</tr>
</tbody>
</table>

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.40–44 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.21–25,26

6. What Clinicothropologic 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 Granulalymphocytosis, which may be confused with well-differentiated lymphocytic leukemia, also has been reported.32 Nonregenerative anemia and thrombocytopenia are the most common hematologic abnormalities in cats. Hyperproteineemia has been reported in approximately 33% of affected dogs. Polycygal gammopathy is most common, but monoclonal gammopathies have been reported in both dogs and cats.26–45 Because of chronic infection the *Ehrlichia* spp. infection but remain seropositive (see question 15). Additionally, *E canis* antibodies cross-react with *E ewingii*,46 *E chaffeensis*,47 *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.44–46 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 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.57–12–25–28 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.59 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.60 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.61 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*.62 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. 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 reinfected 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, and the resolution of thrombocytopenia usually is indicative of a good response to therapy. After treatment, platelet counts begin to increase within 24–48 hours and are usually normal within 14 days. 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*. 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). 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.

**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. 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.

**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. 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. 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. 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. 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) 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, 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; (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; 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.

### 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 to cats or 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. 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.

### 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

1. ACVIM Forum, Seattle Convention Center, Seattle, WA, May 26, 2000
2. SNAP 3 Dx Assay, IDEXX Laboratories, Inc, One IDEXX Drive, Westbrook, ME

### Acknowledgments

The authors would like to thank the Infectious Disease Study Group members who gave oral input concerning this topic at the Study Group meeting held at 18th Annual ACVIM Forum in Seattle, WA, and to the following members who provided written review: Drs Helio Autran de Morais, Julie Levy, Meryl Littman, and Dennis Macy.

### References

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


Ehrlichia Consensus Statement


