Canine Vector-Borne Diseases: The Ehrlichias

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**Ehrlichia canis** (Canine Monocytic Ehrlichiosis)

**Vector:** *Rhipicephalus sanguineus*

**Distribution:**
- *Rhipicephalus sanguineus* (the brown dog tick) is found throughout the entire United States. It appears to prefer warmer climates; however, it can survive indoors throughout its entire life cycle, unlike other tick species.¹
- This is one of the few tick species with a world-wide distribution.

It is a vector for:

*Ehrlichia canis* and *Anaplasma platys* (*R. sanguineus* is the suspected vector for *A. platys* in the U.S., confirmed in Japan)²

Illness and clinical signs associated with *Rhipicephalus sanguineus* pathogens in dogs:

1) **Ehrlichia canis** is the causative agent of canine monocytotropic ehrlichiosis.³

-Clinical signs: The course of infection may present in three clinical phases: acute, subclinical, and chronic. The acute phase of infection typically manifests in transient illness that largely goes unrecognized. Many infected dogs recover spontaneously without medical attention. However, depending on the virulence of the strain and the health status of the dog, clinical signs might result in presentation to the veterinarian. Some clinical observations might include: fever, anorexia, lethargy, oculonasal discharge, and petechiation. In about 20% of cases, lymphadenomegaly and splenomegaly have been observed.³ If clinical signs during the acute phase of disease go undetected, the infection will progress into the subclinical phase of infection, where the patient will appear clinically healthy.⁴ Some animals will eventually progress to the chronic phase of infection wherein clinical signs reemerge. Again, the clinical presentation and severity of disease varies among patients. Signs can include weakness, anorexia, weight loss, fever, pallor lymphadenopathy, hepatomegaly, splenomegaly, retinal lesions, edema, nonseptic polyarthritis, and CNS disease. There is up to a 25% mortality rate in animals that develop chronic ehrlichiosis.

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Onset: The acute stage of the disease typically occurs 2 to 4 weeks after infection. As previously stated, this stage is transient and often goes undetected. Subsequently, if clinical signs resolve spontaneously the result will be the development of the subclinical phase of infection. The subclinical phase may persist for months or even years. Healthy, young dogs may be able to clear the infection at this phase on their own. However, E. canis can evade the host immune system. In as many as three or more years after initial infection, the chronic phase of the disease may develop. In cases where the chronic phase of disease does not occur, the agent may persist throughout the life of the animal.

Clinical pathology: During the acute phase of infection, common laboratories findings include thrombocytopenia, mild leukopenia and mild anemia (usually nonregenerative). During subclinical infection, otherwise clinically healthy dogs may have thrombocytopenia or mild nonregenerative anemia. The most common hematologic abnormality observed in chronic disease is thrombocytopenia. In severe cases, pancytopenia may develop as a result of severe, typically irreversible bone marrow damage. The prognosis for dogs with this form of the disease is grave. Other common laboratory abnormalities seen with chronic ehrlichiosis include granular lymphocytosis, elevated liver enzymes and hyperglobulinemia.

2) *Anaplasma platys* is the causative agent of canine infectious cyclic thrombocytopenia. It is the only infectious agent known to infect platelets.

Clinical signs: Minimal clinical signs appear in most naturally infected dogs. They may include fever, anorexia, petechiation or epistaxis. However, clinical signs associated with *A. platys* infections may be exacerbated by coinfection with other vector borne agents.

Onset: In experimentally infected animals parasitized platelets are noted as early as 8-15 days post infection.

Clinical pathology: Cyclic thrombocytopenic episodes that occur in 1-2 week intervals.

Diagnostic Tests:

Microscopic Evaluation: *E. canis*- The detection of morula in leukocytes is so infrequent that it is not a reliable means of diagnosis. Even in animals seen during the acute phase of infection, the detection of morula is difficult. Detection can be optimized by performing buffy coat smears of peripheral blood or by evaluating tissue aspirates taken from the spleen or lymph nodes which typically harbor the organism. *A. platys* morulae are often present in platelets of infected animals during thrombocytopenic episodes. The organisms are difficult to identify because of magenta granules normally present within the platelets. In contrast, *A. platys* morulae are dark purple to blue.

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Serology: Detection of antibodies to *E. canis* is the most reliable and frequently used method for confirming a diagnosis. Serum antibodies to *E. canis* can develop as soon as 7 days after infection but typically peak at 80 days post-infection in untreated animals. A negative antibody response in animals suspected to be acutely infected should be repeated in 2-3 weeks. As with other vector-borne infections, a positive serology by any method could indicate active infection, latent infection or previous exposure. The in-house ELISA assay is arguably the method most frequently used by most veterinarians since it is a point-of-care test. This assay is a qualitative assay so if quantification of antibody levels is desired, the IFA test can be used. IFA tests for *E. canis* are offered at most commercial diagnostic laboratories. This assay is highly sensitive in detecting antibodies to *E. canis*, but false positive reactions can occur due to cross-reactive antibodies and/or nonspecific binding. To confirm a diagnosis of monocytotrophic ehrlichiosis it is necessary to have a reciprocal titer of 80 and clinical or laboratory findings consistent with the disease.\(^6\)

A commercially available IFA test for *A. platys* is offered. Experimentally animals develop antibodies as early as 7 days post-inoculation.\(^7\) As with other IFA tests, false positives can occur. Animals infected with *A. platys* contain cross-reactive antibodies for *A. phagocytophilum*. It has been shown that animals experimentally infected with *A. platys* will test positive on the in-clinic ELISA test for *A. phagocytophilum* as early as 7 days post-inoculation.\(^7\)

PCR: Nucleic acid detection is rarely performed in the diagnosis of *E. canis* infection, but it can be used to differentiate between organisms of the genus *Ehrlichia*. As with *A. phagocytophilum*, dogs in the acute phase of clinical disease may be PCR positive, even prior to seroconversion. However, PCR analysis is not reliable in detecting subclinical, seropositive persistently infected carriers or animals in the chronic phase of the disease. PCR testing for *E. canis* is available at national and state diagnostic laboratories.

A PCR assay is commercially available to detect infections with *A. platys*.

**Treatment:**

- Early treatment of *Ehrlichia canis* is imperative. Doxycycline at a dose of 5 mg/kg BID, PO is currently the drug of choice. The standard length of therapy in naturally infected animals is 28 days.\(^6\) Usually, rapid remission of clinical signs occurs within 2-3 days after initiation of antimicrobial therapy in dogs with acute or mild chronic illness.\(^3\)

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severe chronic disease or those with aplastic anemia may not respond to antimicrobial therapy.

- A. platys may also be treated by tetracyclines or enrofloxacin at doses recommended for *E. canis*.

**Ehrlichia ewingii and Ehrlichia chaffeensis**

**Vector:** *Amblyomma americanum*

**Distribution:**

- *Amblyomma americanum* (the lone star tick) is found throughout the Eastern United States, from central and eastern Texas, north into Missouri, spreading east to the coast in a broad, sweeping belt.7

- A northern expansion of the tick is occurring. It is an “aggressive” tick species and feeds on multiple wild and domestic species, including dogs as well as humans.2

It is vector for:

- *Ehrlichia ewingii and Ehrlichia chaffeensis*

**Illness and clinical signs associated with *Amblyomma americanum* pathogens in dogs:**

1) **Ehrlichia ewingii** is the causative agent of canine granulocytotropic ehrlichiosis8

- Clinical Signs: Dogs present with polyarthritis and/or nonspecific clinical signs including fever, lethargy, anorexia, vomiting, or diarrhea
- Onset: Signs develop one to three weeks after the bite
- Clinical Pathology: Laboratory abnormalities include nonregenerative anemia, thrombocytopenia, lymphopenia, and eosinopenia.9

2) **Ehrlichia chaffeensis** is the causative agent of Human Monocytic Ehrlichiosis (HME) but also infects dogs.

- Clinical Signs: Clinical manifestations of this disease in dogs are not completely defined. Dogs may present with nonspecific clinical signs of anorexia, fever, lethargy or lymphadenopathy.3 Clinically, *E. chaffeensis* may be indistinguishable from infections of

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E. canis. However, adequate documentation in experimentally infected animals is limited and has only resulted in hematological abnormalities without evidence of clinical disease.

-Onset: The incubation period for this infection is not clearly defined but expected to be 1 to 3 weeks if similar to other related agents.

-Clinical Pathology: Thrombocytopenia has been documented in experimentally infected dogs.

Diagnostic Tests:

- Microscopic Evaluation of blood smear and/or synovial fluid: Morula: often observed for E. ewingii (in circulating neutrophils (Figure 1) and neutrophils in synovial fluid), Morula are rarely observed in circulating monocytes, lymphocytes or in lymph node aspirates in dogs acutely infected with E. canis. The same may be suspected of dogs infected with E. chaffeensis.

- Serology: It is most often used as an initial diagnostic assay to confirm infection in animals suspected of having a tick-borne disease. Unfortunately, there are currently no commercially available assays specifically designed to diagnose animals infected with either E. ewingii or E. chaffeensis. Dogs infected with E. chaffeensis will likely test positive using an IFA test or the in-clinic ELISA tests for E. canis. The IFA test and the in-clinic ELISAs are available at most commercial laboratories and from specific manufacturers, respectively.

- PCR analysis can confirm the presence of either pathogen in clinically ill patients. Most commercial laboratories can perform these assays on whole blood samples collected in EDTA.

Therapy:
Therapy with doxycycline continued for 3-4 weeks has proven efficacious in treating clinical disease in humans. Doxycycline typically causes rapid remission of clinical signs in dogs infected with E. ewingii. However, there is no well established protocol for dose or length of therapy at this time.

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