Anaplasmosis

<u>Tests available</u>: Serology via IDEXX Snap® 4DXPlus and PCR for *Anaplasma* spp.

Neutrophilic canine anaplasmosis causing an acute febrile illness with thrombocytopenia, neutropenia and anemia is attributed to *Anaplasma phagocytophilum*, whereas **thrombocytotropic anaplasmosis**, characterized by cyclic thrombocytopenia, is caused by *A.platys*. Commercial serology methods do not differentiate between neutrophilic and thrombocytotropic anaplasmosis and clinicians generally rely on presumed endemic regions to ascertain causation: *A.phagocytophilum* in northern regions and *A. platys* in southern regions. The degree to which these assumptions influence treatment and outcomes are unknown, but new research tools may facilitate clarification.

<u>Disease</u> (Dogs with the following are reasonable candidates for testing)

- History of tick attachment.
- thrombocytopenia, leukopenia, and anemia.
- fever, myalgia, lethargy

<u>Disease:</u>

A.phagocytophilum transmitted by the black legged deer tick (*Ixodes scapularis)* infects host neutrophils and results in an acute febrile disease in dogs presenting with thrombocytopenia, leukopenia, and anemia. Cats also can be infected with *A.phagocytophilum*.

Ref. Eberts MD, DVM, Diniz PPVP, Beall MJ, Stillman BA, Chandrashekar R, Breitschwerdt EB. Typical and Atypical Manifestations of *Anaplasma phagocytophilum* Infection in Dogs. JAAHA 2011;47.

Ref . Lappin MR, Breitschwerdt EB, Jensen WA, et al. Molecular and serological evidence of *Anaplasma phagocytophilum* infection of cats in North America. J Am Vet Med Assoc 2004. In press.

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

A. platys, transmitted by the brown dog tick (*Rhipicephalus sanguineus*), is an obligate intracellular rickettsial organism that infects platelets. *A. platys* is considered a pathogen of low virulence, often in association with other infections or diseases. Most dogs infected with *A. platys* are healthy, but experience a cyclic thrombocytopenia. 20% of dogs tested from the Caribbean island of Grenada were infected with *A. platys* and 25% with *E. canis* supporting frequent transmission of these organisms in regions in which *R. sanguineus* is the only known tick species.[16] Strain differences in pathogenecity has been suggested to explain more severe disease displayed by European *A. platys* infected dogs.

Ref. French TW, Harvey JW. Serologic diagnosis of infectious cyclic thrombocytopenia in dogs using an indirect fluorescent antibody test Am J Vet Res. 1983;44(12):2407-11.

Ref. Harrus S, Aroch I, Lavy E, Bark H. Clinical manifestations of infectious canine cyclic thrombocytopenia. Vet Rec. 1997;141:247-50.

Ref. Gaunt S, Beall M, Stillman B, Lorentzen L, Diniz P, Chandrashekar R, Breitschwerdt E. Experimental infection and co-infection of dogs with *Anaplasma platys* and *Ehrlichia canis*: hematologic, serologic and molecular findings. Parasit Vectors. 2010;3:33.

<u>Testing</u>: **Serology** (IFA) using cell grown *A.phagocytophilum* antigen is available through commercial laboratories. IFA is not available for *A.platys* as unless antigen slides can be prepared from blood of infected animals. With the advent of ELISA based in-house kits (IDEXX Snap® 4DXPlus) designed to detect antibodies to *E.canis*, *A.phagocytophilum* and *Borrelia burgdorferi*, serosurveys have determined that some synthetically derived peptides are not species specific and that the *A.phagocytophilum* peptide will react with *A.platys*-infected dog serum. An assumption was made by veterinarians that the infecting species could be presumed to be *A.phagocytophilum* in northern endemic regions while in southern regions, *A.platys* infection should be considered most likely when dog sera

reacted with the *Anaplasma* peptide. Newly designed peptides may be capable of differentiating these species to a degree that the geographic regions require redefining.
PCR testing for *Anaplasma* species using *16S* rRNA, *GroEL* or *p44* gene targets can be utilized to detect *Anaplasma* DNA in whole blood of infected animals (available through the Vector-borne Diseases Diagnostic Laboratory).

Treatment: 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 anaplasmosis. Oxytetracycline is also effective, but is nephrotoxic.

Insights gained through VBDDL associated research.

A treatment study in dogs naturally-infected with *A.phagocytophilum* showed: Although clinical observations of selected cases, as well as preliminary data from an experimental study, have suggested that doxycycline may not clear the infection in all treated dogs, our results suggest that doxycycline at a dose of 5 mg/kg twice a day for 28 days is effective in controlling *A. phagocytophilum* infection and in reversing clinical signs in dogs in selected areas of the USA.
ACVIM 2009 Abstract: Efficacy of doxycycline treatment in dogs naturally infected with *Anaplasma phagocytophilum*. Diniz, PPVP; Correa, MT; Chandrashekar, R; Beall, M; Breitschwerdt, EB.

Serological analysis using a multi analyte research tool that enables the differentiation of *A.phagocytophilum* from *A.platys* was presented in poster format at the 2013 American Society of Rickettsiology Conference and showed that

- *A.phagocytophilum* is most prevalent in a population of dogs in the Northeast and MidAtlantic states while *A.platys* is most prevalent in the Caribbean and Southern states as would be predicted.
- Interestingly, *A.platys* is found at a higher seroprevalence in the Northeast and Canada than the overall percent seroprevalence.
- Seroreactivity to both species analytes (16/25 sera 64%) were found in an area along the Atlantic coast from NC up to the area around Philadelphia indicating a possible area of overlapping vectors and potential co-infections.

***A.platys* in other species:** Individual cases that have been referred to and tested using the array of serological and molecular methods offered by the VBDDL have resulted in the detection of *Anaplasma* spp in novel hosts.

- In 2012, an American Domestic Shorthair cat from North Carolina presented for a chronic hyperglobulinemia of 11 months duration. Two separate collection dates of EDTA whole blood amplified ***A. platys*** 16S rDNA, GroEL, and p44 genes, demonstrating molecular evidence of infection with *A.platys,* along with *Mycoplasma* and *Bartonella* spp. To our knowledge this is only the second cat in which *A. platys* infection has been documented. Published article: Qurollo BA, Maggi RG, Zegre-Cannon C, Breitschwerdt EB. Splenic plasmacytosis and monoclonal gammopathy in a cat infected with *Anaplasma platys*, *Bartonella henselae*, *Bartonella koehlerae* and '*Candidatus* Mycoplasma haemominutum'.
- A veterinarian experiencing migraine headaches, seizures and other neurological and neurocognitive abnormalities was tested for vector-borne pathogens. ***Anaplasma platys***, *Bartonella henselae* and *Candidatus* Mycoplasma haematoparvum DNA was amplified and sequenced from the woman's blood, serum or blood culture samples. Despite symptomatic improvement, six months of doxycycline most likely failed to eliminate the

B. henselae infection, whereas *A. platys* and *Candidatus* M. haematoparvum DNA was no longer amplified from post-treatment samples. Published article: Maggi RG, Mascarelli PE, Havenga LN, Naidoo V, Breitschwerdt EB. Co-infection with *Anaplasma platys*, *Bartonella henselae* and *Candidatus* Mycoplasma haematoparvum in a veterinarian. Parasites & Vectors 2013, 6:103.