In veterinary medicine, there can be little argument over the fact that infectious disease diagnosis, treatment, and prevention have been among the most fundamental, and important, elements of clinical practice for many years. In companion animal medicine, however, the most significant advances made in infectious disease management are relatively recent, dating back only 60 to 70 years. It wasn’t until the late 1940’s and early 1950’s, for example, that a national campaign to vaccinate dogs against rabies was implemented in the US…and with dramatic results. Prior to 1960, rabies in the US was predominantly found in domestic animals, especially dogs. Today, canine variant rabies has officially been eliminated in the US and human rabies infections acquired within the US have virtually ended. Worldwide, however, human deaths from rabies virus infection continue to be estimated at 55-60,000 each year…99% of those cases result from contact with infected dogs! The public health benefits derived from routine vaccination are obvious.

It must be highlighted, however, that our ability to diagnose infectious disease in companion animals has also had a significant impact on the level of health care veterinarians are able to provide. Recent advances in diagnostic technology have, quite likely, led to the use of the term “emerging infectious disease”, a common theme found among topics presented at major continuing education programs. Yet, one has to question whether the recent surge of infectious diseases documented in dogs and cats today (eg, canine influenza virus, anaplasmosis, feline cytauxzoonosis) are really “emerging”…or is it the diagnostic technology that has emerged, thereby enabling the clinician to assess the individual patient for an ever increasing spectrum of infectious agents.

Diagnostic Reality Check

Co-Infection. Conceptually, the decision whether or not to perform a particular diagnostic test on a particular patient is intuitive: if there is a test for a condition the patient may have…do the TEST. In fact, in veterinary medicine we have conventionally learned, and taught, infectious disease diagnostics within defined packages of information that include epidemiology, pathogenesis, clinical signs, and prevention. This is information found in virtually any textbook on infectious disease. To a large extent, it is this knowledge-base that guides diagnostic testing decisions in practice. However, individual patients, once infected, don’t limit their signs to those described in a textbook. A reasonable explanation for this is the fact that an infected, sick patient could have multiple infections simultaneously, ie, is co-infected…and, might manifest a novel range of clinical signs. Co-infection probably occurs much more frequently in both dogs (eg, A. phagocytophilum with B. burgdorferi or canine influenza virus with B. bronchiseptica) and in cats (eg, FIV or FeLV with calicivirus) than is realized. What’s more, the consequences of co-infection, potentially, could be significant…even life-threatening. Why, for example, do the clinical manifestations of canine influenza infection range from inapparent (subclinical) to death? One plausible explanation,

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1 Since 2000, there have been 23 documented human infections linked to rabies virus. Only 1 raccoon-variant rabies virus was found; bat-variant rabies was implicated in all other cases. (CDC, Rabies Surveillance Data in the US).
of course, is that other viruses, or bacteria, are involved in the same patient at the same time.

In veterinary medicine, access to diagnostic test “panels” for infectious disease is still in the early stages of development. The ability to evaluate an individual patient for multiple, simultaneous infections has several advantages in clinical practice. The 4Dx SNAP Test highlights this as an ELISA-based, point-of-care testing platform that enables the clinician to evaluate an individual patient for multiple infections quickly and to do so with a high degree of test sensitivity and specificity. This technology is advancing rapidly. And, in fact, enhanced testing capability has recently been introduced: The 4Dx PLUS SNAP Test.

While a “point-of-care” test result has obvious advantages, interpreting the meaning of the test result in the individual patient requires that the clinician understand not only the nature of the infection, but the nature of the antibody, or antigen, response throughout the course of the infection. The importance of using any “point-of-care” test platform requires understanding the meaning of a positive test result…as well as a negative test result…at various stages in the course of healthy patients as well as patients with clinical illness.

**Surveillance Testing.** In addition to co-infection, there is another aspect of diagnostic testing that has important application in practice: the concept of surveillance testing. Put another way, surveillance testing refers to routine screening of healthy-appearing, at risk patients for underlying infection. As Wellness Programs gain popularity in veterinary medicine, the role of surveillance testing for infectious disease takes on a fundamental role.

Current diagnostic testing technology enables the clinician to identify patients that are actively infected (subclinical), or have been exposed, to an infectious pathogen but do not manifest outward signs of clinical illness at the time of examination. It is not unusual, for example, when discussing canine Lyme disease with veterinarians who practice in the Northeastern US to hear comments to the effect that “I do treat ‘happy, healthy’ dogs that have a positive SNAP test for Lyme disease…and…and some of these dogs become ‘happier and healthier’ subsequent to treatment”. The unexpected clinical response in a seemingly normal dog with a positive test result is not entirely unusual and actually drives the decision by some veterinarians to treat all dogs that have a positive test for *B. burgdorferi* (C6) antibody.

However, incorporating surveillance testing into a wellness program goes beyond simply prescribing doxycycline for any dog with a positive 4Dx SNAP test result. A positive test result justifies further evaluation, both physical and laboratory, of the patient. In the case of the 4Dx SNAP test, a positive test result also provides insight on how well the client has managed flea-tick prevention at home.

The notes that follow provide insights into the practical aspects of interpreting 4Dx PLUS SNAP test results as well as recommended management strategies of patients with a positive, or negative, test result. It is important to note that new information continues to evolve as advanced technologies are used to study these infections.
CANINE EHRLICHIOSIS
The 10 Most Common Questions

1. There are many *Ehrlichiae* capable of infecting dogs…but we currently only test for one (*E. canis*)…which infections are most significant for dogs?

*E. canis* (officially called ‘canine monocytotropic ehrlichiosis’) is probably the most important. It’s certainly the most common infection in dogs in the US. However, infections with *E. chaffeensis*, *E. ewingi* (canine granulocytotropic ehrlichiosis), and *E. equi* are also known to infect dogs living in the US.

What compounds conventional diagnostic strategies is the fact commercial tests are simply not available (yet) for many of these infections. Furthermore, it’s becoming more apparent that individual dogs can be (and are) infected with multiple tick-borne pathogens simultaneously…such as *Anaplasma spp* and *Neorickettsia*.

2. What is the spectrum of clinical signs associated with ehrlichiosis?

The standard answer goes like this:

Incubation is 8 to 20 days.

**ACUTE** (2-4 weeks): signs may be mild to absent (at least to the owner) or may include lethargy, anorexia and possibly epistaxis. IF…the owner seeks medical attention, fever may be detected evidence of spontaneous bleeding. A laboratory profile may reveal thrombocytopenia, low albumin with elevated globulin (total protein may be elevated). THEN…they get better…whether or not they receive treatment.

**SUB-CLINICAL** (months to years [life?!]): any clinical signs that manifested in the ACUTE STAGE resolve…this is analogous to a “latent infection”. Any treatment administered will appear to have worked well…THEN…months to more than a year later, clinical signs associated with infection *may* redevelop…(we don’t know why some dogs never progress into the chronic stage of ehrlichiosis.

**CHRONIC** (months): This is where infections become complicated. Serious clinical signs may develop months to years following exposure and infection. Signs are highly variable. Usually, weight loss, decreased appetite, petechiation or ecchymoses, and epistaxis may develop. Peripheral edema (hypo-albuminemia) and even neurological signs (head tilt, paresis, seizures) may develop.

**LABORATORY CHANGES**: Thrombocytopenia and/or anemia appear in about 80% of dogs with ehrlichiosis. NOTE: platelet counts are only modestly reduced (ranges of 150,000 to 50,000 cells/µL are typical) and distinct from dogs with immune-mediated platelet destruction (3,000 to 5,000 cells/µL).
Hyperglobulinemia/hypoalbuminemia may be present (hence the peripheral edema). Granular lymphocytosis (counts between 5,000 and 17,000 lymphocytes/µL). Pancytopenia seems less common today. Less common are a variety of multisystemic signs, including peripheral limb edema, vasculitis (generalized), neurological signs ranging from head tilt (vestibular) to disorientation to meningitis and seizures. Hyperviscosity syndrome, retinal detachment, and a host of immune-complex disorders affecting joints and kidney may develop. Death is possible…despite aggressive treatment.

BUT…the variation in physical signs and laboratory values is significant. For example…the absence of thrombocytopenia does NOT exclude a diagnosis of ehrlichiosis. As such, it is not feasible to rely exclusively on clinical or laboratory findings to establish a diagnosis. Testing is important. The message here is not to limit testing to only those patients that have obvious physical signs that are distinctively associated with ehrlichiosis…”test outside the box”!

3. Is co-infection with other tick-borne agents significant with ehrlichiosis?

With increasing significance…YES. The more we look, the more we discover oc-infected dogs…and this is true in humans who are infected with tick-borne disease. AND…it’s the co-infected patient that makes it difficult to establish a diagnosis on the basis of clinical signs.

What’s still needed in veterinary medicine is a testing platform that will allow screening of individual patients for multiple tick-borne pathogens, simultaneously! And work is currently underway to achieve that.

4. Is there any breed, sex, or age predilection for development of ehrlichiosis?

There is no age or sex predilection for canine ehrlichiosis. However, there are reports suggesting German shepherds may be more susceptible to infection than other breeds. When clinical signs do develop, the clinical course seems to be more severe and prognosis poor. This is suggested to be associated with a breed-specific compromise in cell-mediated immunity.
5. Where is the geographic risk for infection (exposure) the greatest?

This map denotes exposures in dogs (2005 data) based on ELISA serology for *E. canis* antibody. IDEXX Laboratories has collected data based on ZIP Codes throughout the US. It’s clear from this data that ehrlichiosis occurs throughout the US with the occurrence being greatest in locations where the population density is greatest. The point being…for Ehrlichia spp. it may be appropriate to consider the fact there appears to be at least some risk of exposure to dogs throughout the US. Although there is clearly a greater risk in the Southern tier of States, canine ehrlichiosis has appeared in virtually all States.

6. How long does a tick have to feed in order to transmit the infection?

Interestingly…that is still not known! It’s an important fact since newly infected larval and nymph ticks can transmit the infection for 155 days, reservoir ticks can “overwinter” with their ehrlichia…becoming an early spring threat. Since most topical tick preventatives can take from 2 to 3 days to effective kill ticks, the time required to effectively transmit the organism is important!

7. How should the Snap Test for *E. canis* be interpreted in a sick patient vs. a healthy patient?

The SICK dog with a POSITIVE *E. canis* antibody test (blue-dot on the Snap 3Dx or 4Dx) should be treated (see below). NOTE: “SICK” is defined by either physical abnormalities or laboratory abnormalities consistent with ehrlichiosis. Following treatment, clinical and laboratory assessments need to made as necessary to document resolution of the clinical illness. NOTE: in dogs with ehrlichiosis, antibody concentrations do not fall subsequent to treatment…the SNAP test is not expected to revert to a negative status for several months (years?) following treatment.
NOTE: the Snap 3Dx or 4Dx do have an important role in assessment of the ‘healthy’ patient. Veterinarians are encouraged to utilize such ‘panels’ in conventional wellness programs. The HEALTHY “appearing” dog that has a POSITIVE *E. canis* antibody Snap Test result (*Surveillance Testing*) should be evaluated further: a thorough physical examination + a laboratory profile (CBC and Biochemistry profile at a minimum). *Interpretation:* Dogs with a POS test result that do NOT have physical or laboratory abnormalities...have been exposed to *Ehrlichia canis*; a POS test result alone does not define infection. Although treatment is not indicated and these dogs may never become ill, they have been exposed to ticks...NOTE: a positive test result in a healthy dog does define tick exposure and justifies reviewing the client on correct use/application of topical tick preventatives. Poor (or no) application technique/compliance when using tick preventatives is the most common reason tick infestations; not ‘resistance’ to the topical product.

Dogs with a NEGATIVE *E. canis* antibody test have not been exposed to the organism... a NEGATIVE dog, with clinical or laboratory signs, does not have *E. canis* exposure. However, it could be infected with a different type of tick-borne pathogen.

The dog with a NEGATIVE test result, in the absence of clinical or laboratory changes...is considered to be “not infected”.

8. **Treatment recommendations for a dog with a POSTIVE test result and clinical signs consistent with ehrlichiosis include:**

**Several options:**
- **Doxycycline,** 10 mg/kg, orally (rarely IV), q12-24h, for 28 days.
- Minocycline, 10 mg/kg, orally (rarely IV), q12h, for 28 days.
- Tetracycline, 22 mg/kg, orally, q8h, for 28 days.
- Chloramphenicol, 15-25 mg/kg, orally (or IV or SC), q8h, for 28 days.
- Imidocarb dipropionate, 5 mg/kg, IM, once, then repeat in 2-3 weeks.
- Amicarbalide, 5-6 mg/kg, IM, once, then repeat in 2-3 weeks.

Short term prednisolone (2-7 days) at 2 mg/kg, daily, may be indicated in severe or life-threatening cases.

It is NOT believed that combining parenteral with oral therapy provides any therapeutic advantage.

9. **Will the *E. canis* antibody test (3Dx or 4Dx SNAP Test) become negative following treatment?**

NO...(this is important) not for several weeks or even months. Unlike post-treatment testing patients for the Lyme C6 antibody, the titer of *E. canis* antibody does not fall
following treatment. THEREFORE...the 3Dx test result can remain positive for extended periods following treatment for ehrlichiosis.

10. What’s the prognosis for a dog with ehrlichiosis following treatment?

Physical signs, if present, may appear to resolve within 1-2 days. Resolution of thrombocytopenia is the most rapid laboratory response (7-10 days following treatment). It is recommended to recheck platelet counts monthly for up to 3 months following treatment to monitor possible relapse. Changes in serum proteins may require 6 to 12 months to resolve.

However, relapse is possible...as is re-infection. Infections may become chronic and resistant to treatment.

It has been suggested that resistant infections may be more common than previously realized...leading to recrudescence of clinical and laboratory abnormalities.


CANINE LYME BORRELIOSIS (Lyme Disease)...an update
On the Most Common Questions

1. Recent studies show a dramatic increase in human Lyme disease...has the geographic distribution of Canine Lyme disease changed?)
Typically, canine Lyme disease occurs with the highest prevalence in the same locations that human Lyme disease is most likely to be diagnosed...the Northeastern United States and the upper Midwest. Increased numbers of positive tests in dogs living in Texas suggest that risk of exposure may be significant, particularly around major metropolitan areas. What this author finds interesting are (unpublished) reports from veterinarians regarding the change in Lyme ‘positivity’ in geographic areas of the US that are clearly outside conventional regions of prevalence. For example: Western PA, Northern IL and Indiana, Southern Lower Michigan, Northern California (esp around Santa Rosa) and Eastern VA and NC. Furthermore, clinical cases being reported from these areas include dogs that have never lived or traveled outside of the community. Lyme disease does appear to be spreading...

Positive C6 Ab tests have been found in dogs living in virtually all States...the reason is not related to the presence of vector ticks...it’s related to the fact that dogs traveling with their owners can and do travel into high prevalence areas, where they have increased risk of exposure. Practicing in a non-endemic area (e.g. Denver CO) is no assurance that a dog presented to the practice will not be infected.

2. What clinical signs are characteristically associated with an active infection?

Experimentally, the time between infection and development of clinical signs ranges from 2 to 5 months following infection...but, signs are only expected to develop in 5%-10% of dogs infected. (much less in cats).

Systemic signs include fever, shifting leg lameness, joint swelling, enlarged lymph nodes, anorexia and lethargy....all of which are rapidly responsive to antimicrobial therapy.
**Arthritis.** Non-erosive polyarthritis is still reported as the MOST common clinical sign. Synovial fluid demonstrates suppurative polyarthritis (leukocytes: 2000 to 100,000 µL)

**Actue Renal Failure, aka “Lyme Nephropathy” (technically it’s not “Nephritis”).** Although uncommonly diagnosed, this acute, and frequently fatal, complication associated with *B. burgdorferi* infection is being reported with increasing frequency in dogs from Lyme endemic states...particularly the Northeastern US and, more recently, Northern California. Occasional cases are reported by veterinarians practicing in the upper Midwestern States...Minnesota and Wisconsin. Infections are most often reported in Labradors (Black?) and golden retrievers. The cause is still unknown.

**Meningitis.** Neuroborreliosis has been reported in humans; has been difficult to document in dogs.

**Other.** The erythema migrans (EM) ‘bulls-eye’ lesion at the site of tick attachment has been reported in about 80% of humans exposed to Lyme disease. Some dogs are known to manifest a faint EM-type lesion, but only transiently. The hair is a problem is identifying it. Additionally, rare reports of myocarditis (and death) and rheumatoid arthritis in dogs are cited.

**Routine Hematology/Biochemistry:** test results are typically normal. Proteinuria in dogs with protein-losing glomerular disease.

**3. Lyme Nephropathy...how does this manifest clinically, and how common is it?**

Although still regarded as uncommon, reports of Lyme nephropathy are characteristically that of an acute onset renal failure associated with both glomerular and tubular disease. It appears to be an immune-complex disease but is not associated with neutrophilic infiltration in the glomerulus. Most often reported in large breed dogs (especially Labradors and golden retrievers) residing in the Northeastern US. Sporadic cases from Minnesota and Wisconsin, as well as Northern California, have been noted. The prognosis is poor, despite aggressive and early treatment. Most dogs die shortly after clinical signs of acute renal failure become apparent. Recent studies at Cornell University (Dr. Richard Goldstein) suggest that the underlying lesion is likely associated with immune complex deposition in the kidneys of affected dogs.

**NOTE:** On going studies at Cornell University suggest there is NO correlation between prior vaccination and risk of developing Lyme nephropathy. (R. Goldstein, Personal communication).
4. Is there any breed, sex, or age predilection for infection?

No. However, it is cited that the severity of signs and propensity to develop signs is greatest in younger dogs vs. older dogs. Also, the onset of clinical signs is typically associated with a rise in antibody titer, suggesting a significant immune-mediated component to the clinical disease.

5. How long does a tick have to feed in order to transmit the infection?

Infection requires at least 48 hours of continuous tick attachment. Some have stipulated it could require up to 5 days for infected ticks to transmit the spirochete. This is important…reason…the topical tick preventatives can require from 2 to 3 days to effectively kill attached ticks. While tick death may not be particularly rapid, it is rapid enough to prevent transmission. This fact has been documented in some very well done challenge studies.

IT’S ALWAYS BETTER TO PREVENT LYME DISEASE THAN TREAT IT!

6. How should the SNAP Test for C6 antibody (canine Lyme disease) be interpreted in a sick patient vs. a healthy patient?

The C6 antibody test is an important and significant technological advancement in Lyme diagnosis in dogs…(the C6 antibody assay has been approved for use in humans and does correlate with infection in patients with an EM lesion).

In dogs, there is a strong correlation between infection and POSITIVE antibody test result (test specificity is 96%); a positive test generally denotes infection…it does NOT predict impending clinical disease. Test results may be positive as early as 2 weeks post infection.

A POSITIVE test result in a dog with compatible clinical signs obviously justifies immediate treatment (see below). NONE of the available Lyme disease vaccines will cause a FALSE POSITIVE test on the 3Dx or 4Dx SNAP testing platform.

A POSITIVE test result in a healthy appearing dog should be interpreted as an exposed and infected dog…a positive test result is NOT predictive of impending clinical disease. Despite confirmed infection, most dogs will never develop clinical signs. That said, discussions with veterinarians practicing in the Northeastern US suggest that most practices recommend treating a healthy dog with a POSITIVE C6 Ab test. Outside of Lyme endemic areas, there is a significantly greater tendency NOT to treat the healthy, POSITIVE dog. Instead, clients are informed of the ‘exposure/infection’ and advised that if lameness or myalgia develops, treatment should be initiated. NOTE: I have also had many comments from practitioners who indicate that treating the “happy and healthy” POSITIVE dog resulted in a “happier and healthier” dog… There are NO reliable laboratory changes (as seen on routine
CBC and biochemistry profile) supporting a diagnosis of Lyme disease in the healthy appearing dog with a POSITIVE test result.

A NEGATIVE test result indicates the patient is not infected at that time.

7. What’s does the “Quantitative C6 Antibody” test bring to the table and what are the indications for testing a patient?

The Quantitative C6 Antibody test is a ‘send-out’ test available only through IDEXX Laboratories. Because of the sensitivity/specificity of the C6 antibody test and it’s correlation with active infection, it has been suggested that determination of the C6 antibody concentration may be predictive of impending clinical illness…AND…can offer the clinician an opportunity to monitor a decline in antibody response subsequent to treatment. However…practitioners with years of experience managing cases of Lyme disease have suggested that a HIGH C6 Ab titer is less predictive than the initial data suggested.

One other aspect of performing the C6 test is that the Ab level, if high, will decrease within 4-6 months following treatment (regardless of the presence of clinical signs). This is usually a good sign that the patient was infected and, in fact, has responded (with a decline in spirochetes) to the treatment.

IF CLINICAL SIGNS ARE PRESENT…most dogs are expected to demonstrate good resolution within 2-3 days following treatment. Only occasionally will treatment result in a decline in antibody concentration such that the SNAP Test will become Negative. Don’t count on this happening.

A follow-up Quantitative C6 4 to 6 months post-treatment, will allow documenting a decline in antibody titer and, therefore, a serological response to treatment.

8. Treatment recommendations for a dog with a POSTIVE test result and clinical signs:

Doxycycline, 5 mg/kg, PO, q12h, for 30 days. (Recommended)
(ALT: Doxycycline @ 10 mg/kg, once daily for 30 days)
Amoxicillin, 20 mg/kg, PO, q8h, for 30 days.
Azithromycin, 25 mg/kg, PO, once daily, for 10-20 days.
Ceftriaxone, 25 mg/kg, IV or SC, once daily, for 14 to 30 days.
Chloramphenicol, 15-25 mg/kg, PO or SC, q8h, 14 to 30 days.

Drugs such as Chloramphenicol and Ceftriaxone are reserved for patients with neurologic or cardiac (arrhythmia) manifestations.
**Vaccination**...IS NOT PART OF THE TREATMENT REGIMEN! There is NO indication for vaccination as part of the therapy for canine Lyme disease. In fact, this may be the wrong thing to do! **NOTE:** Treatment is NOT expected to clear *B. burgdorferi*.

9. Here’s where it gets complicated...Prior to vaccination, a dog SHOULD be tested. BUT...if the test result is POSITIVE, should the dog receive a vaccine?

There is no known harm in doing so. But...studies performed at Cornell have shown a transient increase in the concentration (blood) of circulating immune complexes (CICs)...these are the complexes that can become “trapped” in the glomeruli...occurs in SNAP POSITIVE dogs vaccinated with a whole cell, killed Lyme vaccine. Administration of a recombinant Lyme vaccine to Lyme POSITIVE dogs resulted in a significantly less rise in CICs.

All that said, there is no known association with the rise in CICs and increased risk of renal disease/injury. But...is probably best to TEST before administering vaccine. If the test results are POSITIVE...it may be wise to treat these dogs prior administering vaccine.

10. ...and it gets ‘complexer’! Now...what happens if the patient was POSITIVE (healthy or clinical) *last year*, was treated, then comes back for the annual booster... is re-tested...and is still SNAP POSITIVE (healthy)?

This is where the conversation starts to ‘waffle’. Why is the dog still positive?

...one, the owner has done a great job of applying the topical tick preventative and the dog has been tick-free for a year. The SNAP test was positive due to residual, but low levels, of C6. Vaccinate the dog.

...two, the dog has been re-infected over the past year and although healthy, has an elevated C6 Ab level. Don’t vaccinate the dog...at least not until you’ve re-treated and only vaccinate after completion of the treatment period...or...you could do a Quantitative C6 (the SNAP does not indicate the level of Ab present) to know for sure where the titer is.

In either case, today, it seems prudent to re-vaccinate an “at risk” dog with the rLyme vaccine as a means of avoiding any risk that might be associated with CIC’s.

11. **Will the Lyme C6 antibody test (3Dx Snap Test) become negative following treatment?**

It might...clinical signs do tend to correlate with antibody titer. With treatment, the infected dog will experience a decline in the number of spirochetes...which, in turn results in a decline in measurable antibody concentration (C6)...which, in turn is
associated with resolution of physical signs. While most dogs will experience a significant decrease in antibody concentration with treatment (may take up to 6 months), only the occasional patient will see a decline in the antibody concentration such that the SNAP Test becomes NEGATIVE.

12. What’s the prognosis? FACT! Treatment is not likely (nor should it be expected) to clear spirochetes from the patient…rerudescence is possible…

The earlier treatment is started following the onset of clinical signs, the better. However, that’s not always possible. There is generally good resolution of clinical signs with 2-3 days following treatment. But, although it is customary to continue oral treatment for a 30 day period, relapse does occur (even in dogs isolated in tick-free environments) 8 to 12 months later. In clinical practice, distinguishing relapse from re-infection may be impossible.
13. Which vaccine is best: the recombinant or the killed, whole-cell (spirochete) vaccine?

Comparative studies have not been published. At this writing, one company sells a recombinant Lyme disease vaccine (Merial); 2 companies sell a killed, mono-valent whole-cell Lyme vaccine (Pfizer and BI); Merck Animal Health (formerly Intervet Schering-Plough) sells a bi-valent (OspA and OspC) vaccine. Both types of vaccine (recombinant and killed) induce an immune response to the outer surface protein A (OspA) of *Borrelia burgdorferi*. To date, there is no known advantage to the OspC fraction of the bi-valent vaccine.

The process whereby a recombinant vaccine is manufactured is significantly different than that of the killed, whole-cell vaccines. The recombinant vaccines contain OspA antigen only. The killed vaccines contain millions of dead spirochetes per dose and all of the associated, non-immunogenic proteins on the surface of the spirochete...some of which may be immuno-reactive in dogs. The only research report on the bi-valent OspA & OspC vaccine shows that it works as well as any other Lyme vaccine (all of which involve OspA antigen only). To date, the bivalent vaccine has not been demonstrated to induce a great degree of protection against challenge than that derived by existing vaccines (OspA killed or recombinant).

Natural immunity associated with Lyme disease is attributed to antibody produced against the up-regulated outer surface protein C (OspC) on spriochetes that enter the patient during feeding. Natural immunity is very short-lived (days) and considered to be insignificant.

The OspA antibody induced by either vaccine type (recombinant and killed) is ingested by the tick during feeding. The spirochete-antibody interaction takes place inside the tick midgut and prevents transmission.

**Vaccination is NOT part of the treatment for Lyme disease.** Vaccination is recommended only to prevent re-infection and, then, *only* after antibiotic treatment has been completed.


CANINE ANAPLASMOSIS
Anaplasma phagocytophilum infection
(or...more properly: canine granulocytotropic anaplasmosis, CGA)
(Granulocytic Anaplasmosis, or GA, is also used)

1. What is it?

It’s a tick-borne disease...recently recognized in the Northeast and upper
Midwestern US (especially Minnesota and Wisconsin) in dogs that presented with
clinical signs consistent with E. canis. Fever, lethargy, and loss of appetite are
predominantly reported clinical findings. Thrombocytopenia is the most common
laboratory change reported. Although these dogs appear similar to those infected
with E. canis, patients are expected to be NEGATIVE for E. canis antibody. In fact,
what we once thought was...Ehrlichia equi, is A. phagocytophilum.

Quite recently, E. equi was re-classified an anaplasma and is now correctly referred
to as Anaplasma phagocytophilum.

2. Why the emphasis on this organism and the infection it causes?

Two reasons: first, it ranks among the 3 most common tick-borne infections in dogs
in the US...with E. canis and Lyme disease. Second, it’s carried by the same Ixodes
scapularis known to transmit canine Lyme disease. Where there is Lyme disease,
there is (typically) anaplasmosis.

3. How is the infection characterized?

Very much like E. canis...although there is no known sex predilection, a breed
predisposition has been suggested (large breeds [Labradors and golden retrievers]
may dogs have greater risk. Physical signs include fever, lethargy, and anorexia.
Muscle pain is described in over half of the affected dogs. Muscle pain and
weakness are described. Joint pain is uncommon. Although mild to moderate
thrombocytopenia occurs in 80% of affected dogs, spontaneous bleeding disorders
are not described. Lameness is also reported. Laboratory changes look like
erlichiosis. Thrombocytopenia and lymphopenia predominate (80% of cases).
Hypoalbuminemia (and hyperglobulinemia) are relatively common. Dogs may have
a mild anemia.

In the few clinical studies that are published, affected dogs had a well-defined history
of spending considerable time outdoors (especially camping trips, hiking, hunting)
with the owner).
3. What does a “BLUE DOT” for *A. phagocytophilum* mean?

The IDEXX SNAP 4Dx test is the only rapid assay for *A. phagocytophilum* exposure on the market. The test platform should be assessed much in the same way that the *E. canis* antibody test is interpreted...ie, it does NOT confirm active infection...it denotes exposure.

This is an excellent example of how the SNAP test platform can be incorporated into a patient’s ‘wellness profile’. IF...the test result is NEGATIVE, exposure is very unlikely, the patient is not infected, and the client is likely to be providing adequate tick (and flea) control measures.

IF, on the other hand, the healthy-appearing patient has a POSITIVE test result, this denotes prior exposure, justifies the need to perform additional diagnostic (laboratory testing-especially hematology and platelet count) and clearly indicates that the client’s efforts in tick-control have been inadequate. Hence, the need to discuss what they are using and how they using it.

Dogs having any physical or laboratory abnormalities, should be treated for at least 2 weeks.

4. What the usual geographic distribution for this disease/exposure risk?

In addition to Lyme endemic areas (it’s transmitted via the *Ixodes* tick family), infections seem to be occurring in several locations throughout the US. Occurrence maps will be presented during the presentation.

5. How is anaplasmosis treated?

Doxycycline is the recommended treatment (5 mg/kg, orally, q12h, for at least 2 weeks...it’s common to treat for 28 days). Alternatively, 10 mg/kg of doxycycline can be administered orally ONCE daily as long as the patient is able to tolerate that dosing schedule. Resolution of the clinical signs and thrombocytopenia are expected quickly (as soon as 1 day, as long as 3 weeks). Also, rifampin and levofloxacin are reported to be effective. Chloramphenicol can be used in puppies to avoid the risk of doxycycline ‘labeling’ of enamel. I did find any reference to the use of imidocarb dipropionate to treat canine anaplasmosis.

Although experimental studies have suggested that treatment can be curative, clinical studies suggest this is not the case. Current publications suggest that a ‘carrier state’ is likely to develop following infection and treatment.

**NOTE**: there is a common theme here regarding treatment of these 3 tick-borne pathogens. That is, treatment is not likely to cure the patient. Obviously, tick-borne diseases are best PREVENTED...than TREATED.
6. **How is anaplasmosis prevented?**

There is currently no vaccine available for the prevention of canine anaplasmosis. AND…none is on the horizon. Today, proper use of a topical tick preventative is still the primary barrier to infection. NOTE: one of the key applications of the test to alert the clinician to the fact that *proper* selection and /or application of an effective topical tick preventative has not been adhered to. It’s an opportunity to review that information with the client.


*Updated January 2014*