In August 2013, preliminary results from 3 complementary studies conducted through the Centers for Disease Control and Prevention (CDC) suggest that approximately 300,000 people in the U.S. are diagnosed with Lyme disease each year, a significant increase from 2012 estimates of 30,000 reported cases. Of reported cases, 96% occurred in 13 states, particularly the northeastern U.S. and Upper Midwest; this distribution did not change from 2012 to 2013.1

What’s more, cases of human Lyme disease are not only occurring with increasing frequency in known endemic States, but the number of confirmed cases is expanding into States, and regions within States, that have not previously documented the infection.

In veterinary medicine, there can be little argument over the fact that a dog’s risk of exposure to ticks, and to tick-borne diseases, dramatically exceeds that in people. Because tick-borne diseases are not reportable in dogs in the US, precise estimates of prevalence are not available. Published estimates suggest that up to 85% of dogs living in Lyme endemic States are antibody positive (and likely to be infected) for Lyme disease. Today, it must be assumed that many dogs are infected with one, or more, tick-borne diseases, yet remain undetected.

As the number of infected ticks expands beyond geographic limits of the upper Midwest and Northeastern US, an increasing number of veterinarians who are not accustomed to managing patients with a tick-borne infection will be challenged to address fundamental questions, such as:

- When is testing indicated?
- What is the significance of a POSITIVE SNAP test in a healthy dog?
- What are the indications for a Quantitative C6 test (canine Lyme disease)?
- Should all dogs with a POSITIVE test result be treated?
- Should routine vaccination (canine Lyme disease) be implemented?
- Should dogs with a POSITIVE test (canine Lyme disease) be vaccinated?

The objective of this presentation, and the paper that accompanies it, is to review these issues and to address current controversies concerning the diagnosis and management of dogs at risk for tick-borne disease.

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1 www.cdc.gov/lyme/stats/humanCases.html.
Diagnostic Reality Check

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. Recent advances in diagnostic technology have, quite likely, led to the use of the term “emerging infectious diseases”, a common theme found among topics presented at major continuing education programs today. Yet, one has to question whether the recent surge of infectious diseases documented in dogs and cats today (eg, canine influenza viruses, ehrlichiosis, 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.

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 with defined packages of information (ie, textbook chapters) that address epidemiology, pathogenesis, clinical signs, and prevention of a defined infection. To a large extent, it is this knowledge-base that guides diagnostic testing decisions in practice. What’s missing, however, is the fact that individual patients, once infected, don’t limit their clinical 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 is likely to occur much more frequently in dogs (eg, A. phagocytophilum and B. burgdorferi or canine influenza virus and B. bronchiseptica) and in cats (eg, FIV or FeLV and calicivirus) than is realized. What’s more, the consequences of co-infection can 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, of course, is that other viruses, or bacteria, are involved in the same patient at the same time.

In veterinary medicine, the ability to assess an individual patient for multiple infections has several advantages. The 4Dx Plus SNAP Test highlights the impact of a sensitive/specific, point-of-care testing platform that enables the clinician to evaluate an individual patient for multiple infections and to do so during the appointment.

While a “point-of-care” test result has obvious advantages, interpreting the meaning of the POSITIVE vs. NEGATIVE 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.

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 patients that are considered to be at-risk for exposure. As Wellness
Programs gain popularity in veterinary medicine, the role of surveillance testing for infectious disease takes on a fundamental role.

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 unique insight on how well the client has managed tick prevention.

**Canine Lyme Disease**

Today, the decision to implement routine, surveillance testing for Lyme disease in dogs living in States adjacent to the Lyme-endemic States is critical. The risk for infection with *Borrelia burgdorferi*, the spirochetal agent responsible for Lyme disease, is clearly expanding...States such as Iowa, Illinois, Indiana, Ohio, and Michigan seem to be among the latest targets for infection risk as infected ticks expand their reach. The reason for the changing edemicity of Lyme disease has been linked to both climate change and, most importantly, movement of infectious ticks on birds, particularly ground-feeding passerines (eg, sparrows, wrens, robins).

**Point-of-Care Testing.** For over 10 years, point-of-care tests (SNAP 4x and SNAP 4Dx Plus) have been available to detect antibodies to the highly conserved C₆ peptide of B burgdorferi. With high sensitivity and specificity, this rapid assay is an excellent surveillance tool for identifying dogs that are infected, not simply “exposed”, with B burgdorferi, and has become a valuable for screening dogs that reside within areas where exposure risk is emerging.

**Surveillance Testing of Healthy-Appearing Dogs.** Given that most dogs with a positive test result for C₆ antibody are not clinically ill at the time of testing, despite the likelihood of being infected, highlights the importance of surveillance testing of healthy dogs, particularly in regions of the US where new infections are beginning to emerge. Surveillance testing is the only means of assessing risk within a defined population of dogs.

Healthy-appearing, antibody-positive dogs may, however, have significant underlying laboratory changes. An appropriate laboratory profile in the antibody-positive patient includes the following:

- hematology (complete blood count including assessment of platelets)
- biochemistry profile
- urinalysis
- urine protein:creatinine ratio (UP:UC) in patients with significant proteinuria.
- quantitative C₆ assay
Significant proteinuria is a critical diagnostic factor in dogs affected with Lyme nephropathy, a rare syndrome associated with *B. burgdorferi* infection. The syndrome is characterized by rapidly progressive renal failure, glomerulonephritis, tubular necrosis, and lymphocytic-plasmacytic interstitial nephritis.

**Treatment options** for dogs diagnosed with Lyme disease are outlined below. Generally, treatment is indicated when the individual patient meets the following criteria:

- Positive Serology (SNAP Test), and
- Clinical findings consistent with Lyme borreliosis (especially, acute-onset lameness and/or myalgia), and
- A history of *Ixodes* spp tick exposure.

<table>
<thead>
<tr>
<th>ANTIMICROBIALS</th>
<th>DOSAGE</th>
<th>RECOMMENDED TREATMENT PERIOD</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>PREFERRED TREATMENT</strong></td>
<td></td>
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</tr>
<tr>
<td>Doxycycline</td>
<td>10 mg/kg PO q24h (or, 5 mg/kg PO q12h)</td>
<td>4–6 weeks (1-month minimum)</td>
</tr>
<tr>
<td><strong>ALTERNATIVE TREATMENTS</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Minocycline</td>
<td>25 mg/kg PO q24h</td>
<td>4–6 weeks (1-month minimum)</td>
</tr>
<tr>
<td>Cefovecin</td>
<td>8 mg/kg SQ</td>
<td>2 doses@14 day interval</td>
</tr>
<tr>
<td>Amoxicillin</td>
<td>20 mg/kg PO Q 8 H</td>
<td>1 month (minimum)</td>
</tr>
<tr>
<td>Azithromycin</td>
<td>25 mg/kg PO Q 24 H</td>
<td>1 month (minimum)</td>
</tr>
</tbody>
</table>

Dogs manifesting lameness/myalgia associated with *B. burgdorferi* infection are expected to experience resolution of clinical signs within 3 to 5 days following the onset of treatment. Dogs with laboratory evidence of significant proteinuria and renal disease should be aggressively treated in accordance with recommendations outlined in the current Lyme Consensus Statement (see REFERENCE #1).

**Vaccination:** Natural immunity following *B. burgdorferi* infection is especially short-lived (less than 2 months, see REFERENCE #8) and is not considered to induce long-term protection. Vaccination, particularly in combination with an oral or topical tick preventative, can provide significant protection (1 year) in dogs exposed to infected ticks.

The AAHA Canine Vaccination Task Force categorizes Lyme disease vaccines as non-core (optional) in dogs. However, veterinarians practicing in endemic regions of the US commonly include Lyme disease vaccine as core (ie, all dogs seen in the practice will be vaccinated). The decision to recommend Lyme disease vaccination in practice is left to the discretion of the individual clinician, but should be based on known exposure risk, include travel into endemic areas, as determined through surveillance.
testing within the practice or through published surveillance maps (see REFERENCE #3).

It is important to understand that vaccination does not interfere with C₆ peptide antibody (SNAP Test). However, other commercial Lyme disease test platforms may detect vaccine-induced antibody to the Outer Surface Protein C (also called OspC) in dogs recently vaccinated with a whole-cell (killed) vaccine thereby leading to a false-positive test result.

There are no contraindications to administering Lyme disease vaccine to a healthy dog that has a positive SNAP test result for Lyme disease. Doing so is indicated to prevent reinfection.

**Ehrlichiosis**

*E. canis* (officially called ‘canine monocytotropic ehrlichiosis’) is among the most common tick-borne infections found in dogs in North America. However, *E. chaffeensis*, and *E. ewingii* (canine granulocytotropic ehrlichiosis), have been recognized as important pathogens as well. (More on this during the presentation).

**A POSITIVE result** indicates the presence of antibody to *E. canis* and/or *E. ewingii* (4Dx PLUS) and denotes either current infection (in the presence of clinical signs or laboratory abnormalities) or, simply, prior exposure to Ehrlichiae.

NOTE: *Ehrlichia* antibody is known to persist in dogs for several months (or longer) following treatment…ever wonder WHY?

**Treatment**: Dogs with clinical signs or laboratory abnormalities consistent with ehrlichiosis are justifiably treated with oral doxycycline (@ 5 mg/kg twice daily; or, 10 mg/kg once daily) for 3 to 4 weeks. Alternatively, the antiprotozoal injection imidocarb dipropionate (*IMIZOL*, Merck Animal Health) can be administered parenterally (5.0 mg/kg IM or SQ; 2 doses recommended 2 weeks apart). **NOTE**: not to be confused with IMAZOL (a topical antifungal)!

However, a POSTIVE test result in a healthy-appearing dog (surveillance testing) justifies performing a thorough physical examination and submitting a CBC, biochemistry profile, and platelet count. (NOTE: healthy-appearing dogs can have thrombocytopenia, hyperglobulinemia, anemia, etc.) **ALSO**…review home care for tick prevention. IF…physical examination and laboratory test results are within normal, treatment is unlikely to be needed…ie, the patient has experienced prior exposure (an may have mounted an effective immune response against ehrlichia. If abnormal physical findings (eg, petechiae, limb edema) or laboratory findings (slight to moderate thrombocytopenia, hypoalbuminemia, hyperglobulinemia, anemia, etc) are present, the patient should be treated as outlined above.

NOTE: dogs having received prior treatment for ehrlichiosis may remain SNAP Positive for several months.
A NEGATIVE result indicates no prior exposure (and no infection). The SNAP test is highly sensitive (ie, FALSE NEGATIVE test results are unlikely). Rarely, one might encounter the infected patient (with ticks ‘in-tow’) that has not yet seroconverted. Interestingly, it is still not known how long it takes a tick to actually transmit *Ehrlichia*. 

Action: No treatment is indicated. Review tick-prevention with the client (products used and application technique)… is an opportunity to reinforce client’s efforts to manage ticks (and fleas).

**Anaplasmosis**

In the clinical setting, Anaplasma infection in dogs may be most important from the perspective that transmission (esp. *A. phagocytophilum*) tends to follow the *Ixodes* tick…New England, upper Midwest, Northern California. Consequently, these are the same geographic locations where co-infection with *B. burgdorferi* is most likely found. Furthermore, the significance of a POSITIVE test may be most important from the standpoint of co-infection.

A POSITIVE result indicates the presence of antibody to either *A. phagocytophilum* or *A. platys* and, like *Ehrlichia* antibody, suggests prior exposure or, in the presence of defining clinical signs or laboratory abnormalities, active infection. Geographically, *A. platys* infection is most likely to occur among dogs residing in the Gulf Coast states. Like *E. canis* antibody positive dogs, the test may remain POSITIVE for several months following treatment, suggesting the development of a carrier state.

**Treatment**: Management consideration of any dog with a POSITIVE test result for anaplasma tends to follow the same recommendations for ehrlichia. The only exception being that the treatment period with doxycycline is generally limited to 10 days rather than 3 to 4 weeks. The ability of parenteral imidocarb dipropionate to clear dogs of anaplasmosis is unknown.

A NEGATIVE result indicates the patient is not actively infected and has no prior exposure. Treatment is not indicated.

Updated: August 2015
ADDITIONAL RESOURCES


