Canine Lyme disease, also called canine Lyme borreliosis, is among the most familiar tick (Ixodes species) transmitted infections known to occur in humans and dogs residing in North America.

Despite being the subject of review articles, research studies, scientific proceedings, and symposia, canine Lyme borreliosis continues to generate considerable controversy in clinical practice, particularly as it pertains to exposure risk, diagnosis, consequences of infection, and even prevention. This article addresses key controversies and current recommendations regarding management of dogs at risk for canine Lyme borreliosis.

**TRANSMISSION**

**Host & Reservoirs**
The host-associated bacteria—Borrelia burgdorferi, a spirochete—is maintained in a variety of wild animal reservoirs, ranging from rodents (principally the white-footed mouse), other small mammals (eg, chipmunks), and ground feeding birds (eg, American robin).

**Vector**
The black-legged tick, or deer tick, which parasitizes the mammalian and avian hosts, unwittingly serves as a vector of B burgdorferi to other mammals, including dogs and humans.

**Food Source**
White-tailed deer—often associated with Lyme disease—are not reservoirs for B burgdorferi. They are, instead, blood-feeding stations (and transport vehicles) for adult black-legged ticks. In recent years, increased deer tick populations are believed to be a result of similarly increased deer populations.

**PREVALENCE & DISTRIBUTION**

**Human Prevalence**
In August 2013, preliminary results from 3 complementary studies conducted through the Centers for Disease Control and Prevention (CDC) suggested that approximately 300,000 people in the U.S. are diagnosed with Lyme disease, 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.

**Canine Prevalence**
Canine Lyme borreliosis is not a reportable disease; therefore, precise estimates of disease prevalence are unavailable. However, compared with humans, dogs in endemic regions are at substantially greater risk for exposure to infected ticks. Surveillance reports of dogs with positive antibody test results suggest that up to 85% of dogs living in endemic areas are at risk for B burgdorferi infection.

**Geographic Distribution**
Today, risk extends beyond the traditional geographic boundaries defined—the New England states, Wisconsin, and Minnesota, with a relatively high number of infected dogs reported annually in northern California, Oregon, and parts of Washington State (Figure). Anecdotal reports from veterinarians practicing in western Pennsylvania, Ohio, Michigan, and central Illinois state that, over the past 5 years, risk for exposure to infected ticks is spreading. Results of surveillance studies in the U.S., Canada, and Europe designed to monitor the spread of infected ticks indicate that both climate change and migratory ground-feeding birds contribute to movement of infected ticks and increased risk for human and animal exposure. These stud-
ies highlight the importance of continued surveillance—through routine testing of dogs living in regions where the risk for exposure to Ixodes species ticks is high.

The concept of surveillance testing of healthy dogs for Lyme borreliosis, however, raises a series of important questions:

- What does a positive test result really mean?
- Does a dog infected with Lyme borreliosis derive long-lasting natural immunity to it?
- Should a dog with a positive test result, but no clinical signs be treated for Lyme borreliosis?
- Should a dog with a positive test result be vaccinated for Lyme disease?

These questions, and others, are addressed in the sections that follow.

**DIAGNOSIS OF LYME BORRELIOSIS**

In 2006, a consensus statement on Lyme disease in dogs, which addressed a series of questions on the diagnosis, treatment, and prevention of the disease, was published by the American College of Veterinary Internal Medicine. However, that document failed to provide a clear definition of what constitutes a diagnosis of canine Lyme borreliosis.

The recent introduction of laboratory-based and point-of-care testing technologies has added to the confusion over whether treatment is indicated when a serologic test result is positive in a dog.

**Serologic Testing**

In veterinary medicine, it must be emphasized that there is no single pathognomonic diagnostic test for canine Lyme borreliosis.

**Point-of-Care Tests.** For over 10 years, point-of-care tests (SNAP 4X and SNAP 4DX Plus, idexx.com) 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 with *B burgdorferi*, and is particularly valuable to screen dogs within areas where Lyme disease is emerging. None of the commercial Lyme disease vaccines cause false positive C6 test results. A positive test, however, cannot be used to predict the clinical outcome of an infected dog.

**Laboratory-Based Tests.** Because the majority of dogs infected with *B burgdorferi* have no clinical signs at time of testing, use of the laboratory-based, quantitative C6 assay (Lyme Quantitative C6 Antibody Test, idexx.com) has been proposed as a way to monitor response to treatment of non-clinical seropositive dogs (see TREATMENT). A second laboratory-based diagnostic test (AccuPlex4, antechdiagnostics.com), introduced in 2012, has the ability to detect 5 different antibody responses to *B burgdorferi* infection (OspA, OspC, Ospf, p39, and OspF). The test also reportedly differentiates between natural exposure and vaccination as well as distinguishing early from chronic infection. However, there are some limitations, which include inability to:

- Identify acute infection in dogs vaccinated with a whole-cell (inactivated) bacterin
- Reliably distinguish between dogs with a positive test result for chronic infection (OspF) and those that have been treated and re-infected
- Consistently and reliably detect vaccine-induced antibody (OspA); therefore, at this time, these results should not be considered when interpreting a report.

**Clinical & Laboratory Assessment**

Simply identifying antibodies to *B burgdorferi* in a dog does not constitute a clinical diagnosis of Lyme borreliosis. Before establishing a diagnosis of Lyme borreliosis, the clinician must:

1. Consider physical and laboratory findings (Table 1)
2. Determine whether the dog resides in, or has traveled to, a region inhabited by the Ixodes tick.

**Laboratory Assessment.** The laboratory assessment of any patient found to have serum antibodies against *B burgdorferi* should include:

- Hematology
- Serum biochemistry profile
- Urinalysis
- Urine protein:creatinine ratio (UP:UC), if proteinuria is deemed significant.
With uncomplicated Lyme borreliosis, hematologic and biochemical abnormalities are unlikely. However, seropositive dogs are at risk for co-infection with other vector-borne pathogens and may have underlying laboratory abnormalities (eg, thrombocytopenia, anemia, hypoalbuminemia).

Significant laboratory abnormalities, revealing serious un-derlying renal disease (see Lyme Nephropathy), can exist in the absence of expected physical abnormalities (eg, lameness).

**LYME NEPHROPATHY**
Lyme nephropathy is a rare, but often fatal, syndrome associated with *B burgdorferi* infection in dogs. This rapidly progressive renal disease is characterized by glomerulonephritis, tubular necrosis, and lymphocytic–plasmacytic interstitial nephritis.\(^1,2,3\)

Believed to be an immune-mediated disease, the pathogenesis of Lyme nephropathy remains unknown. The most commonly affected breeds include Labrador retrievers, golden retrievers, and Shetland sheepdogs; however, any breed or mixed-breed may be affected.

A critical factor in diagnosis of Lyme nephropathy is proteinuria, and assessing every seropositive patient for proteinuria (including a UP:Uc) is an important component of laboratory evaluation.

Studies have shown that approximately 30% of dogs with Lyme nephropathy manifest clinical signs of arthritis, and approximately 30% of affected dogs had been vaccinated for Lyme borreliosis.\(^1\)

**TREATMENT**
Diagnosis of Lyme borreliosis is based on the presence of all 3 following factors:
1. Positive serology results (C6, OspC, or OspF) +
2. Clinical and/or laboratory findings consistent with Lyme borreliosis (Table 1) +
3. A reasonable history of exposure to *Ixodes* species ticks.

**Therapy for Patients with:**
» Positive Serology
» Findings Consistent with Lyme Borreliosis
» History of *Ixodes* Species Tick Exposure

Treatment with an oral antimicrobial is indicated in any patient meeting the above criteria, and oral doxycycline is the preferred therapeutic approach to Lyme borreliosis (Table 2). Most authors agree that dogs exhibiting lameness and/or myalgia resulting from *B burgdorferi* infection will rapidly improve within 3 to 5 days.

However, due to the current difficulty in obtaining doxycycline and its high cost, 2 other antibiotics may be considered:
* Cefovecin (Convenia, zoetis.com): 8 mg/kg (single subcutaneous injection); maximum 2 treatments.
* Minocycline: 12 mg/kg Q 12 H or 25 mg/kg Q 24 H

An advantage of using these drugs is that they are effective against other tick-borne agents frequently carried by ticks, and patient co-infection with more than one agent is common, with signs mimicking Lyme borreliosis. The other alternative treatments listed in Table 2 are not effective against these other tick-borne agents.

It is important not to discontinue treatment earlier than recommended, even if clinical signs rapidly resolve. Also, although clinical signs may rapidly resolve with treatment, none of the antimicrobials outlined in Table 2 are known to clear *B burgdorferi* from tissue.

**Therapy for Patients with:**
» Positive Serology
» No Clinical Signs
» No Laboratory Abnormalities

Indications for treating the seropositive patient with no clinical signs or laboratory abnormalities are less clear than those for treating patients clearly affected by Lyme disease (see above). While treatment guidelines for healthy but antibody-positive dogs have not been published, anecdotally:
* Veterinarians in the northeastern U.S. tend to support empirical treatment with doxycycline—considered a relatively common approach to these patients
* In contrast, veterinarians practicing in nonendemic areas of the U.S. tend to avoid treatment unless clinical signs are present at time of testing.

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**TABLE 1. CLINICAL FINDINGS CONSISTENT WITH LYME BORRELIOSIS**

<table>
<thead>
<tr>
<th>Positive Antibody Test Result (C6, OspC, OspF)</th>
<th>Early</th>
<th>Late</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Physical Findings</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Articular swelling</td>
<td>• Dehydration</td>
<td>•</td>
</tr>
<tr>
<td>• Fever</td>
<td>• Peripheral edema</td>
<td>• Polydipsia</td>
</tr>
<tr>
<td>• Lymphadenomegaly</td>
<td>• Polyuria</td>
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<tr>
<td>• Malaise</td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Myalgia</td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Oligoarthropathy (nonerosive), with shifting leg lameness</td>
<td></td>
<td></td>
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<tr>
<td><strong>Laboratory Findings</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Neutrophilic inflammation noted on synovial cytology</td>
<td>• Anemia (nonregenerative)</td>
<td></td>
</tr>
<tr>
<td>•</td>
<td>• Azotemia</td>
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<tr>
<td></td>
<td>• Hypoalbuminemia</td>
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<tr>
<td></td>
<td>• Proteinuria</td>
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<tr>
<td></td>
<td>• Thrombocytopenia</td>
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</tbody>
</table>
Monitoring is often recommended for seropositive, healthy dogs that are (1) receiving antimicrobial therapy or (2) being observed for development of clinical signs because they did not receive treatment. However, difficulties arise because, for these uses:

- Monitoring is not defined and has no process outlined
- Intervals for monitoring have not been stipulated
- Lack of clinical signs makes it difficult to evaluate response to antimicrobial therapy.

**Response to Therapy.** One option for monitoring these dogs is to perform the laboratory-based quantitative C6 test. In addition to monitoring changes in C6 following antimicrobial treatment, a quantitative titer can also provide information on re-infection.

- Dogs with **pretreatment quantitative titer** ≥ 30 U/mL can be monitored for response to treatment by measuring reduction in C6 antibody concentration 6 months after treatment.

**PREVENTION**

Despite the fact that infection with *B burgdorferi* does not consistently cause clinical illness, canine Lyme borreliosis is a disease to prevent—not to treat. Prevention consists of 3 components:

1. **Limit Exposure to Ticks**

   Reducing or eliminating exposure to infected ticks is the core strategy to prevent canine Lyme borreliosis. Even in regions where tick exposure is considered minimal, appropriate administration of tick preventive is critical.

2. **Vaccinate At-Risk Dogs**

   In regions of the U.S. and Canada known to be endemic for ticks infected with *B burgdorferi*, vaccinate dogs in these areas annually. Vaccination is not routinely recommended for dogs living in nonendemic regions (eg, Colorado, Utah, New Mexico, western Canada). Instead, appropriate use of tick prevents reasonably manages any exposure risk.

**CANINE LYME DISEASE VACCINATION PROTOCOL**

**Initial Administration: Puppies & Adult Dogs**

- Conventional vaccination protocol involves administering 2 initial doses, 2 to 4 weeks apart.
- In puppies, the first dose can be administered at 12 weeks of age; however, in endemic areas, where risk of tick exposure is high, the first dose can be administered as early as 8 weeks of age.
- The second dose is administered 2 to 4 weeks later.

**Booster Administration: Adult Dogs**

- After the initial 2-dose series, annual boosters are recommended if the risk for exposure is sustained.
- Some authors recommend an early booster dose—administered 6 months following completion of the initial 2-dose series—for dogs living in known endemic regions.

**Dogs Overdue for Vaccination**

- Compared to most virus vaccines, the immunologic memory subsequent to Lyme disease vaccination is relatively short-lived.
- Therefore, the initial 2-dose series should be repeated if a dog with reasonable risk for exposure has not received a booster dose in over 2 years.

**LYME BORRELIOSIS IS A DISEASE TO PREVENT—NOT TO TREAT**

The reasons are clear:

- Cost of treatment and post treatment monitoring can be significant for the pet owner.
- Antimicrobial treatment, regardless of the drug used, is not expected to clear bacteria from tissue, and therapy is not entirely free of adverse consequences.
- Health consequences of long-term infection, particularly dogs subject to re-infection, are unknown.
- Natural immunity to *B burgdorferi* is short-lived and does not provide significant or sustained protection for pets re-exposed to infected ticks.

Dogs that experience reductions in antibody ≥ 50% have responded to treatment.

**Observe Nontreated Dogs.** Because laboratory-based antibody tests cannot predict clinical disease, conducting routine or quantitative serology is generally not useful in seropositive patients with no clinical signs or laboratory abnormalities.
LYME DISEASE VACCINE CONTROVERSY

This sidebar addresses 2 common concerns—both regarding safety—that contribute to the vaccine controversy.

1. Acute-Onset Adverse Reactions
Acute-onset adverse reactions (eg, angioedema) tend to occur most often in small breed dogs (<10 kg body weight) that receive multiple doses of vaccine at the same appointment.1,2

For small breed dogs, current vaccine guidelines1 recommend administering noncore vaccines, such as Lyme disease vaccine, 2 weeks (or longer) after administration of core vaccine(s). This practice may not be feasible, though, for young dogs at high risk for exposure within endemic regions.

Whole-cell bacterins may be more likely to cause acute reactions (associated with excipient proteins) compared with the recombinant vaccine.2,12-14 If young or small breed dogs must be vaccinated, the recombinant Lyme disease vaccine may minimize risk for acute adverse reaction, particularly when other vaccines are administered during the same appointment.

2. Renal Injury
Some speculate that Lyme disease vaccination contributes to renal injury (ie, Lyme nephropathy). The reasoning for this concern stems from Lyme nephropathy’s association with Lyme-specific circulating immune complexes (CICs), and the fact that Lyme disease vaccination can cause a transient increase in CICs.

However, to date, a link between vaccination and Lyme nephropathy has not been established, and additional studies are indicated. In addition, a number of points argue against the association between vaccination and renal injury:

- Hundreds of thousands of doses of Lyme disease vaccine are sold and administered to dogs throughout North America every year, yet cases of Lyme nephropathy are uncommon.
- 70% of dogs with confirmed Lyme nephropathy had never been vaccinated for Lyme disease.3
- In unvaccinated dogs, the rise in CICs following vaccination is transient (days), yet Lyme nephropathy appears to be a delayed manifestation of *B burgdorferi* infection.
- The role of co-infections (*Anaplasma* species) in the pathogenesis of Lyme nephropathy has been raised.

All vaccines immunize by stimulating antibody to the OspA antigen—ingested by ticks while they feed (on the dog), binding to spirochetes in tick mid-guts and preventing transmission of *B burgdorferi*. Currently, two types of Lyme disease vaccine are available:

- Inactivated (killed) whole-cell bacterins
- Recombinant, plasmid-derived OspA vaccine.

Based on results of *in vitro* studies, some products (whole-cell bacterins) claim provision of expanded protection due to the addition of OspC antigen. However, OspC antibody has not yet demonstrated *in vivo* protection against infection when independent from the OspA antibody.

3. Avoid At-Risk Regions
Encourage owners to avoid traveling with their dogs to regions inhabited by the *Ixodes* tick. However, if dogs must travel to, or reside within or in the periphery of, Lyme endemic regions, especially during period of increased tick activity (spring/summer/fall) highly recommend application of a tick preventive as well as vaccination.

SUMMARY

- Serologic testing for antibody to *B burgdorferi* is an established, valuable tool for identification of infected dogs.
- Routine, or surveillance, testing of healthy dogs living in areas of the U.S. and Canada adjacent to known endemic areas are key in assessment of emerging infection risk.
- Canine Lyme borreliosis is a disease to prevent—not treat.
- Implementation of preventive measures in dogs considered at risk for exposure to *Ixodes* species is justified by the inability of:

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Serologic tests to predict clinical outcomes in infected dogs
• Antimicrobial treatment to clear *B. burgdorferi* from the tissues of infected dogs.
• Ideally, preventive measures include early and compliant vaccination and year-round tick control for all residing in endemic regions.
• Serologic surveillance testing of healthy dogs, combined with vaccination and tick control, offer the most comprehensive approach to reduce risk for infection and disease caused by *B. burgdorferi*.

CDC = Centers for Disease Control and Prevention; CIC = circulating immune complexes; IFA = immunofluorescence assay; UP:UC = protein:creatinine ratio

References
4. Available at www.capcvet.org; search “Parasite Prevalence Maps.”