Despite availability of a consensus statement and up-to-date canine vaccination guidelines (see Lyme Disease Vaccination Guidelines), the decision whether or not to vaccinate dogs against Lyme disease remains an ongoing debate among many veterinary professionals.

Today’s Veterinary Practice has gathered 3 experts to discuss this topic—Dr. Meryl Littman and Dr. Richard Goldstein evaluate the benefits and risks of vaccination, while Dr. Richard Ford outlines the current vaccination recommendations.

**FIRST DO NO HARM: LYME DISEASE VACCINATION MAY PRESENT MORE RISKS THAN BENEFITS**

Meryl P. Littman, VMD, Diplomate ACVIM

When veterinary clinicians decide whether to recommend a particular vaccine for a particular patient, risks and benefits are weighed. The “vaccinometer” tool, developed by Larry Glickman, was designed to help practitioners determine whether or not to recommend a vaccine.  

As we investigate Lyme disease vaccination, the questions posed by the vaccinometer help highlight many unanswered questions and potential risks related to this vaccine. With these concerns in mind, I choose “first do no harm.” In other words, if we use proper tick control, vaccination is unnecessary.

**Question:** What is the prevalence and risk of exposure/infection in your area (e.g., infectiousness)?

**Answer:** Risk of Lyme disease exposure/infection is high in my area, but proper tick control lowers the risk greatly. The CDC website shows that 95% of human Lyme disease is found in 12 endemic states in the Northeast, Mid-Atlantic, and Upper Midwest U.S. In some endemic areas, seroprevalence in healthy dogs is as high as 70% to 90%. In high-risk areas, risk of exposure can be lowered dramatically with adequate tick control, which also decreases the risk for other tick-borne diseases, such as anaplasmosis, babesiosis, bartonellosis, ehrlichiosis, and Rocky Mountain spotted fever.

**Question:** How great is the risk of severe disease once the dog is infected (e.g., pathogenicity and virulence)?

**Answer:** Risk of Lyme disease becoming severe is low, but possibly somewhat higher in retriever dogs. Less than 5% of seropositive (and seronegative) dogs had signs attributed to Lyme arthritis, which generally responds rapidly to antimicrobial therapy. Perhaps 10% to 15% of treated dogs remain non-clinical carriers. One study showed that 40% of dogs diagnosed with Lyme disease were misdiagnosed and had another condition instead. Adult beagles experimentally infected with Lyme disease via tick exposure became seropositive but remained nonclinical, and exposed puppies showed only self-limiting signs of arthritis, anorexia, and fever, which did not require treatment. Perhaps less than 2% of exposed dogs develop the more serious Lyme nephritis, an immune-mediated glomerulo-
nephritis, with high Lyme disease-specific antigen–antibody circulating immune complexes (ICs) and deposition in glomeruli, causing protein-losing nephropathy (PLN). This entity has not been duplicated in any experimental model, and is seen mostly in Labrador and golden retrievers. However, even in seropositive retrievers, Lyme nephritis is uncommon, and we do not understand why some dogs develop it while many do not, despite their high titers and high ICs. It appears that a genetic predisposition exists, and that inflammation from Lyme antigens, and possibly inflammation from other infectious and inflammatory conditions, may be an environmental trigger. A genetic podocytopathy identified in soft-coated wheaten terriers may predispose them to further glomerular damage; a similar condition may exist in affected retrievers.

In general, coinfections appear to result in more serious illness (eg, anaplasmosis/Lyme disease), which emphasizes the importance of tick control.

**Question:** How effective is the vaccine?

**Answer:** Not as effective as other vaccines we use.

Lyme vaccines appear to prevent seroconversion or illness in most (60%–86%) vaccines, but not consistently in all dogs, and not for a very long duration of immunity, thus annual (or even every 6 months) boosting has been recommended.

**Question:** How safe is the vaccine?

**Answer:** These vaccines are not as safe as other vaccines we use.

In the Banfield study of 1.2 million vaccinated dogs, the Lyme disease vaccine (monovalent bacterin), when used alone, produced more postvaccinal adverse events within 3 days than any other canine vaccine. Adverse events associated with Lyme disease vaccine were described as “moderate” by an AVMA council in 2002. All canine Lyme disease vaccines contain outer surface protein A (OspA), which attaches the spirochete to the tick’s midgut and is expressed on *Borrelia burgdorferi* while in the tick, and induces anti-OspA antibodies.

- OspA without adjuvant is a polyclonal B cell mitogen that induces pro-inflammatory cytokines, causes arthritis in rats, and causes a strong *T* helper 1 response in people with HLA-DR4 haplotype, immune-mediated arthritis, and high anti-OspA antibodies after natural infection.
- Lyme bacterin as well as OspA alone causes arthritis in hamsters and sensitization so that more severe arthritis is produced with boosters.
- Lyme bacterins were not developed for humans since various Lyme disease antigens appear to have a role in post Lyme disease immune-mediated diseases.
- In dogs with suspected Lyme nephritis, immunohistochemistry and elution studies have shown positive staining of glomerular immune complexes for a variety of Lyme antigens, including OspA and others, which are also found in Lyme disease vaccines. Remember, inflammation or deposition may be delayed for months after vaccination and not seem temporally related nor recognized as a problem associated with vaccination.

Original reports of Lyme nephritis suspect cases demonstrated that 30% had received Lyme disease vaccine, from 2 weeks to 15 months prior to illness. There is no experimental model for Lyme nephritis, which makes it impossible to study whether Lyme disease vaccine prevents, sensitizes, or aggravates it. However, since the most serious forms of Lyme disease are immune-mediated, I choose not to administer Lyme vaccine antigens that may elevate Lyme disease specific ICs (that increase after vaccination, as they should), which would circulate and need to be cleared (or deposited) for weeks to months after vaccination.

In addition, should we vaccinate retrievers (some of which are genetically predisposed dogs) that may develop Lyme nephritis or PLN? These patients are most likely the very ones we should NOT vaccinate lest we add more complexes or sensitize them for a more intense immune-mediated reaction when they are boosterized or exposed naturally.

**Question:** What is the potential for zoonotic spread to human contacts, and zoonotic spread to other dogs?

**Answer:** Potential for zoonotic transmission of Lyme disease is minimal.

*B burgdorferi* is transmitted via tick bites, and is not contagious from dogs to humans or dogs to dogs via excretions or blood transfusion. The reservoir hosts are wildlife, such as mice, small mammals, and birds. Seropositive dogs are sentinels that their human companions are at risk for exposure—not from dogs, but from ticks in the environment.

**In Summary**

The conclusions we can draw from the questions posed are:

- Tick control is important: it prevents pets from acquiring the numerous tick-borne infectious agents, and prevents ticks from feeding on sentinel dogs, thereby acquiring the agent and transmitting it to their next host.
- Most dogs exposed to *B burgdorferi* seroconvert, but are nonclinical and do not need antibiotics. While most dogs do not exhibit illness after vaccination against Lyme disease, neither do dogs that are naturally exposed.
- Dogs that have Lyme arthritis respond quickly to inexpensive/safe antibiotics.
- Lyme disease vaccines have lower efficacy, shorter duration of immunity, and cause more post vaccinal adverse events than other vaccines we use.
- Without an animal model for Lyme nephritis, we do not know if the Lyme disease vaccine prevents, sensitizes, or causes more immune complex deposition in kidneys, especially in genetically predisposed dogs.
- Accordingly, the subset of dogs that possibly need the most protection (eg, retrievers) from the serious (immune-mediated) forms of Lyme disease may be the very ones predisposed to complications.

**What the Future Holds**

Since immune-mediated disease triggered by Lyme antigens concerns many physicians, research is now directed at finding future vaccines that may incorporate tick proteins, which can be used to interfere with tick attachment, feeding, and/or transmission of disease. For instance, the tick salivary protein, SALP15, helps *B burgdorferi* infect its next host. This exciting new paradigm in vaccine development may help prevent tick-borne diseases, including Lyme disease.
WITH TICK CONTROL & VACCINATION IN ENDEMIC AREAS, LYME DISEASE IS PREVENTABLE
Richard E. Goldstein, DVM, Diplomate ACVIM & ECVIM

Lyme disease, its causative tick-borne agent—Borrelia burgdorferi, and Ixodes ticks are all on the rise. In August 2013, the Centers for Disease Control and Prevention (CDC) increased their estimate of the number of new human cases of Lyme disease from 30,000 to 300,000 annually.1

Tick removal and control is an important part of prevention of Lyme disease, but so is Lyme disease vaccination. No vaccine is completely without risk, but when weighing the risks versus the benefits, I believe the evidence strongly supports the following:

1. In endemic regions, Lyme disease negative dogs should be vaccinated. As part of a Lyme disease prevention protocol, dogs must be vaccinated in addition to tick removal and control. One infected tick that escapes those first 2 barriers can easily cause infection. There is no evidence of any deleterious effects due to vaccinating Lyme disease negative dogs.

2. In endemic regions, Lyme disease positive dogs with no clinical signs of disease should be vaccinated when risk of reinfec tion is high. There is no natural immunity due to previous infection, which likely results due to bacteria “hiding” themselves from the immune system, mainly in tissue, such as synovial membranes, and down-regulating immunogenic surface proteins.2 In a recent paper on infections in humans with recurrent signs, it appeared that humans can be re-infected over and over again, almost annually, causing severe clinical disease.3

3. In endemic regions, Lyme disease positive dogs with clinical signs should be vaccinated when risk of reinfec tion is high, and should receive antibiotic therapy, prior to or immediately following vaccination.

4. Lyme disease vaccination should be performed annually, with the currently available vaccines. In addition, tick control, even in vaccinated dogs, must be stressed to owners since very heavy exposure to Lyme disease may override vaccinal protection.

FACTS ON HUMAN VACCINATION
There is a race to bring a “new” human Lyme disease vaccine to market, with some vaccines already in advanced stages of development.4,5 A previous Lyme disease vaccine for humans had been approved for use in the U.S., but was removed from the market. The observation that this vaccine was unsuccessful due to lack of sales is often misused as an argument against canine Lyme disease vaccination. The University of Pennsylvania’s world renowned vaccinologist, Stanley Plotkin, described the human vaccine situation in 2011: A vaccine against Lyme disease was licensed in the United States in 1998 but was subsequently removed from the market because of lack of sales. I believe that the poor acceptance of the vaccine was based on tepid recommendations by the CDC, undocumented and probably nonexistent safety issues, and insufficient education of physicians... The fact that there is no vaccine for an infection causing 20,000 annual cases is an egregious failure of public health.4

FOUR SAFE & EFFECTIVE VACCINES
Compared to humans, dogs are lucky. There are currently 4 extremely safe, effective, and reliable vaccines6-8 (Table) on the market that have all been through the United States Drug Administration licensing requirements for safety, efficacy, purity, and potency.

All available canine Lyme disease vaccines produce borreliacidal antibodies in the dog in response to vaccinal outer surface protein A

CURRENT GUIDELINES: VACCINATION OF DOGS AGAINST LYME DISEASE
Although the controversy over whether or not to vaccinate dogs against Lyme disease continues, vaccination guidelines for dogs with known risk for exposure to Borrelia burgdorferi have been published (see Lyme Disease Vaccination Guidelines). Here is a summary of current recommendations:

1. The decision to vaccinate individual dogs is ultimately left to the discretion of the individual veterinarian and must take into consideration reasonable risk for exposure to vector ticks capable of transmitting B burgdorferi. The following protocol is recommended:

- Administer 1 dose not earlier than 12 weeks of age; administer second dose 2 to 4 weeks later.
- Administer 1 dose annually to dogs with sustained risk for exposure. Because this risk is seasonal (even in endemic areas), it is reasonable to recommend administering annual boosters in the spring. Comment: Two initial doses, 2 to 4 weeks apart, are considered critical to inducing a protective immune response; a single dose will not immunize. If the interval between the initial 2 doses exceeds 6 weeks, recommend administering the initial 2-dose series again.

2. Vaccination is not considered to be 100% effective in preventing infection or illness. Limiting tick exposure, through treatment of the dog’s environment, direct treatment of the dog, or both, must supplement any vaccination decision. Comment: Remind owners that tick control for the pet and its environment helps prevent Lyme disease and other vector-borne diseases (eg, ehrlichiosis, anaplasmosis, spotted-fever group).

3. Vaccination is not recommended for dogs residing outside of endemic states (or regions). Comment: Consider vaccinating individual dogs that travel into endemic areas of the U.S. and Canada and, subsequently, may be exposed to infected ticks. Administering prophylactic antibiotics during a period of possible exposure is not considered effective infection prevention.

Richard B. Ford, DVM, MS, Diplomate ACVIM & ACVPM (Hon), North Carolina State University
In addition to the evidence from the case study in guide dogs, I have evaluated or been a consultant on over 300 cases of dogs with Lyme nephritis; of these dogs, less than 10% were vaccinated. Moreover, I am not aware of a documented case in which a dog vaccinated against Lyme disease, but not infected with it, contracted Lyme nephritis. Ultimately, if we prevent Lyme disease, we prevent Lyme nephritis.

**Adverse Events**

It has been demonstrated experimentally that, upon vaccination of Lyme disease negative dogs, only a transient, relatively clinically insignificant rise in Lyme disease specific circulating immune complexes (CICs) occurs, and this rise lasts 8 weeks of less. When Lyme disease positive dogs were vaccinated, CICs rose, but this rise was most likely much lower than that seen with new infection, and could likely be mitigated with antibiotic therapy, prior to or immediately following vaccination of Lyme positive dogs.

The alternative—not vaccinating Lyme disease positive dogs and risking additional Lyme disease infections—is very likely more detrimental than the possible rare negative effects of vaccination.

In the next issue of Today’s Veterinary Practice, Dr. Richard Ford will provide an in-depth discussion on Lyme disease vaccination guidelines in the Vital Vaccination column.

**Table. Vaccines for Lyme Disease Vaccination**

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<thead>
<tr>
<th>Vaccine</th>
<th>Description</th>
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<tr>
<td>RECOMBITEK Lyme</td>
<td>Recombinant, nonadjuvanted</td>
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<tr>
<td>NoBIVAC Lyme</td>
<td>Whole-cell, bivalent bacterin (OspA, OspC)</td>
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<tr>
<td>RECOmBITEk Lyme</td>
<td>Plasma-derived, subunit vaccine (OspA)</td>
</tr>
<tr>
<td>LYMevax</td>
<td>Killed, adjuvanted</td>
</tr>
<tr>
<td>DURAMUNE Lyme</td>
<td>Whole-cell, bivalent bacterin (OspA, OspC)</td>
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(OspA). These antibodies work in the tick’s gut to bind the bacteria during the blood meal, sterilizing the gut of the tick and preventing transmission of bacteria into the dog.

OspC is the main immunogenic protein exhibited by *Borrelia* in the tick’s salivary glands and in the dog’s body during natural infection. Three of the current Lyme disease vaccines contain 2 strains of inactivated *Borrelia* isolates—1 OspA producing strain and 1 unique OspC producing strain, which perhaps adds an additional layer of protection.

**Efficacy of the Vaccine**

These vaccines are extremely safe and, in conjunction with tick removal and control, prevent *B. burgdorferi* infection and clinical Lyme disease, including Lyme nephritis.

The anecdotal evidence for this fact is overwhelming, but it has also been shown prospectively in multiple controlled studies in experimental infection and in the field. Following are just a few of many examples of such evidence in the field.

- Levy showed excellent field efficacy of canine Lyme disease vaccination in 2003.
- In 2010, Hebert and Eschner proved the efficacy of the Lyme disease prevention protocol, including vaccination in a large Rhode Island practice.
- In a population of guide dogs in New York, implementation of strict tick control and mandatory Lyme disease vaccination regimen reduced the number of Lyme nephritis cases from approximately 10/year to less than 1/year over 7 years.

**Combating Concerns About Vaccination**

There are still some who believe that Lyme disease is not a disease “worth” vaccinating against or the vaccine causes more harm than good. This is despite the:

- Extremely large number of clinical Lyme disease cases and nonclinical Lyme infections seen in small animal practice in endemic areas in the U.S., including the often fatal syndrome of Lyme nephritis
- Millions of dogs that receive Lyme disease vaccines annually with no data to suggest any resulting harm from the vaccine.

**Lyme Nephritis**

Concerns have also been raised that vaccination can contribute to clinical signs of Lyme disease or the syndrome known as Lyme nephritis. However, there is no evidence that Lyme nephritis is a vaccine-induced phenomenon or even commonly aggravated by vaccination.

**To View the References** for this article, go to todays veterinarypractice.com/resources.asp#resources.

**LYME DISEASE VACCINATION GUIDELINES**

2011 AAHA Canine Vaccination Guidelines

ACVIM Small Animal Consensus Statement on Lyme Disease in Dogs: Diagnosis, Treatment, and Prevention

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