Discussion of Lyme Disease in Dogs

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Introduction

Lyme disease is often considered a controversial topic in both human and veterinary medicine. The syndrome was first described less than forty years ago, and the scientific community's understanding of the illness is still growing. Early in my career, veterinarians took nearly all of their knowledge of Lyme disease from the human literature. We assumed that most of it would apply in dogs. However, we have since learned that dogs respond to Lyme very differently than people. We have also learned that even the strain of organism that usually affects dogs is different than the one that typically affects people!

Lyme disease gets its name from Lyme, Connecticut, where a cluster of cases was identified in 1975. It begins with an infection by a tick-borne bacterial spirochete, called *Borrelia burgdorferi*. There have been thirty naturally occurring strains identified. Although all the strains are carried by the *Ixodes scapularis* tick (a.k.a. "deer tick" or "black-legged tick"), the unique strains tend to be adapted to causing infection in specific host species. That may be a part of why Lyme disease can behave so differently in people, dogs, horses, mice, or other species.

When discussing this illness, it is important to make a distinction between infection with *Borrelia burgdorferi* and the clinical syndrome that we call Lyme disease. The disease itself is not directly caused by the germ itself, but by an interaction between the bacteria and the dog's immune system. After being exposed to the bacteria, the body makes antibodies against proteins on the surface of the organism. These antibodies can attach to more than one bacterium, and each bacterium can have more than one antibody attached to it. These chains of bacteria and antibodies form large clumps, called antigen-antibody complexes. These complexes get stuck in small blood vessels and lead to inflammation. That inflammation is what we know as *Lyme disease*.

Indications of Lyme Disease

There appears to be considerable variability between individual dogs when it comes to symptoms of Lyme disease. Most dogs who test positive for *Borrelia burgdorferi* do not have clinically noticeable disease. There are some experimental studies that indicate that a high percentage of infected dogs develop microscopic changes to their joints and inflammation of the nerves and blood vessels near the tick bite. However, the actual clinical significance of these changes is debated among experts. The most commonly encountered symptoms of Lyme disease in "real world" dogs are swollen joints, muscle aches, general soreness, and/or fever. Sometimes these symptoms wax and wane, vary in severity, and switch legs. The most commonly affected joints are the carpus (wrist) and tarsus (hock/ankle). There have been sporadic reports of effects on the retina, nervous system, or heart muscle.

Veterinarians who practice in Lyme-endemic areas also describe a scary form of the illness, called **Lyme nephritis**. Affected dogs present with sudden-onset kidney disease characterized by protein

loss in the urine. These patients usually have significant permanent kidney damage by the time they are taken to the veterinarian. Because of the nature of the damage, there is often little that can be done to prolong the life of these dogs for more than a few weeks or months. The condition seems to be the worst in Labrador Retrievers, but is also over-represented in Golden Retrievers and retriever crosses.

Protein loss in the urine is so bad because it indicates damage to the glomerulus, a fine meshwork of cells that form microscopic filters within the kidneys. Proteins are large molecules that should not fit through the small openings of the glomerulus. However, if antigen-antibody complexes get caught in the filter, the resulting inflammation seems to blast holes in the meshwork that allow the proteins to slip through. I like to describe the situation as a child's plastic sieve at the beach. It should let sand through the holes, but not pennies. If you were to make a hole large enough to push pennies through, and then kept pushing the pennies through, the hole would get larger and larger. So, the proteins in the urine are not only a symptom of a serious problem, but they also do further irreversible damage to the filter. After a while, the filter will no longer be able to keep enough proteins inside the body and the blood protein levels will begin to drop, eventually leading to muscle wasting and fluid accumulation in body cavities – if the patient has not died of kidney failure first.

There is some debate among experts if Lyme disease is really the culprit for these cases. Diagnosing the actual cause of glomerulonephritis requires a kidney biopsy, something that is rarely done in general practice, especially on a sick dog. Even then, whether or not the condition has been caused directly by the Lyme antigen-antibody complexes is difficult to determine for certain. Many kinds of chronic infection and tumors can induce an immune response that leads to glomerulonephritis due to antigen-antibody complexes. Other causes of protein-losing glomerular disease include auto-immune diseases, pancreatitis, Cushing's syndrome, and hereditary kidney problems, including amyloidosis. A dog testing positive for antibodies to *Borrelia burgdorferi* could still have any of these other underlying conditions as the true cause of the illness. It is also possible the presence of Lyme makes another underlying condition worse.

That being said, most practicing veterinarians believe there is some contribution from *Borrelia* infection that leads to Lyme nephritis. I have seen about fifteen dogs die from this condition, more than two-thirds of which were Labrador Retrievers. Every one of them had shown some mild symptoms for at least four days, just never bad enough for the owners to make an appointment. They all took a "watch and see" approach to mild soreness, reduced appetite, or intermittent limping. Then on day five or six, the dog became really, really sick. By then, heroic medical interventions were required and all of them eventually succumbed to the disease. *Any dog who is sick or sore, even mildly, for more than three days should be taken to a veterinarian for evaluation*.

Regardless of the presence or absence of other contributing factors, protein-losing glomerular disease is such an important issue that the American College of Veterinary Internal Medicine (ACVIM) consensus statement on Lyme disease recommends that all dogs living in endemic areas be tested for *Borellia burgdorferi* exposure annually and that Lyme positive dogs have their urine checked for protein. Lyme-positive dogs with high levels of urine protein should be treated aggressively. However, the experts did not reach a consensus on how often asymptomatic Lyme-positive dogs should have their urine retested. Many veterinarians recommend checking urine protein every six months for the rest of the dog's life. The full ACVIM consensus statement can be found at www.acvim.org/Publications/JVIM/Consensus-Statements.

Discussion of Lyme Disease Testing/Treatment

Another area that did not garner consensus among the ACVIM experts was whether or not to treat dogs who test positive for antibodies to *Borellia burgdorferi*, yet have no symptoms or urine protein. Two-thirds did not recommend routine treatment of these patients. However, there have been no carefully controlled clinical trials testing the long-term outcomes of treated and untreated asymptomatic dogs. Until the science catches up, it remains up to the judgement of each practicing veterinarian, in consultation with each dog's owner.

Some veterinarians use a quantitative antibody test to help determine whether or not an asymptomatic dog should be treated. The levels of antibodies against the *Borrelia*'s C6 surface antigen are an indication of bacterial load in a dog's body. The antibody level drops several months after infections are successfully treated. However, there are many dogs with high levels who never get sick, and some dogs develop symptoms even with low C6 antibody levels. Therefore, by itself, a quantitative C6 antibody test is not particularly helpful in determining which dogs to treat.

For what it is worth, I currently do treat asymptomatic dogs who were negative last year and test positive this year. However, I do not treat chronically positive dogs without symptoms or proteinuria. I use the C6 antibody level only after treatment to establish a new baseline level. Since treated dogs often remain positive on screening tests, monitoring the quantitative level of antibodies helps me determine whether or not a dog is exposed again in the future. I will readily admit that this strategy has changed several times during my career and that I sometimes break my own rules when circumstance, owner preference, or gut-feeling suggests it.

One area where the ACVIM consensus statement is unambiguous is on year-round, high-quality tick control. One hundred percent of the experts on panel agreed that "because ticks can become active even during the winter if temperature increases above 40°F (4°C), year-round tick prevention is advocated." Each situation is different, so it is important to consult a veterinarian when deciding upon tick prevention products for your pets.

In my practice, we have seen a considerable drop in the number of Lyme disease patients since the introduction of oral tick prevention. In real world usage, the isoxazoline class of oral tick control products has been more effective at preventing *Borrelia* than topical products. In fact, Nexgard is the first tick control product in history to be approved for a disease prevention claim by the U.S. Food and Drug Administration (FDA). The approved indications include the phrase "NexGard is indicated for the prevention of Borrelia burgdorferi infections." I cannot say that I remember a single dog getting the disease while on year-round NexGard purchased through a legitimate veterinary source. (There are real problems with counterfeit product online, so be very careful!) Even without comparable labeling, other isoxazolines would be expected to be similarly effective when used appropriately.

Recommendations

Obviously, reducing exposure to *Ixodes scapularis* ticks is the best way to reduce the risk of Lyme disease. The U.S. Centers for Disease Control and Prevention (CDC) recommends taking the following steps in your yard: "Remove leaf litter. Clear tall grasses and brush around homes and at the edge of lawns. Place a 3-ft wide barrier of wood chips or gravel between lawns and wooded areas to restrict tick migration into recreational areas. Mow the lawn frequently. Stack wood neatly and in a dry

area (discourages rodents). Keep playground equipment, decks, and patios away from yard edges and trees. Discourage unwelcome animals (such as deer, raccoons, and stray dogs) from entering your yard by constructing fences. Remove old furniture, mattresses, or trash from the yard that may give ticks a place to hide." (www.cdc.gov/ticks/avoid/in_the_yard.html)

If a dog remains in low-risk environments and is given effective tick control all year, it is highly unlikely to ever come down with Lyme disease. However, real life is rarely that neat and tidy. Doses get forgotten or vomited up. Housedogs occasionally go for a hike with their families. Rodents sometimes bring ticks inside. For that reason, many veterinarians and pet owners turn to vaccination as a "back-up plan" to the other methods of prevention. Perhaps more than any other type of canine vaccine, there is considerable variability in the type of products available to inoculate against *Borrelia burgorferi*.

Vaccine Information

The first Lyme vaccine was made by Fort Dodge, a company that no longer exists. It was a whole-cell bacterin vaccine, meaning that it was basically the entire bacterium ground up and put into a jar. To get the immune system to recognize the ground up bacteria, chemical additives, called adjuvants, were added to the vaccine. Fairly or unfairly, it developed a reputation for being a reactive vaccine that was prone to causing side effects. When that particular product was the only Lyme vaccine on the market, I used to discourage its use. Sometimes, I still run across "never vaccinate against Lyme" statements in materials provided by breeders. I often wonder if those are the result of bad experiences with adjuvanted whole-cell bacterin vaccines.

Although they are generally more purified than the original Fort Dodge version, there are still several whole-cell bacterin vaccines on the market. They tend to be the least expensive products, so they are the ones more likely to be found at vaccine clinics and low-cost veterinary practices. The newer types of Lyme vaccine are genetically engineered to limit the number of proteins being injected into the dog. Some of them have chemical adjuvants, some have plant-based adjuvants, and some have no adjuvants at all. If you are considering vaccinating a dog against *Borrelia burgdorferi*, you should ask your veterinarian which product he or she uses and why.

The vaccine that I strongly prefer does not use any adjuvant. It uses a live canarypox virus as a vector to get the immune system's attention. Canarypox is so specific to canaries that even other birds aren't affected by it, much less dogs. The canarypox has been modified to present the dog's immune system with a single *Borrelia* protein, called Osp-A. The Osp-A protein is used by the bacterium to move from the tick's digestive tract into the dog's blood stream. If a tick attaches to a dog with anti-Osp-A antibodies, the first sip of blood will bind all the Lyme disease causing bacteria inside the tick. You read that right; this single-protein, non-adjuvanted vaccine works inside the tick, not inside the dog! In fact, because the Osp-A protein is not expressed on the bacteria's surface once it is inside of a dog's body, there is no risk for the vaccine to contribute to the formation of antigen-antibody complexes. If there is a pre-existing *Borrelia* infection, it would still be perfectly safe to use this type of vaccine. Because it uses only a single *Borrelia* protein, it is also often safe to use in dogs with a history of adverse events with other types of Lyme vaccine.

All the Lyme vaccines are very time sensitive. While viral vaccines more easily elicit long-term immunity, the body "remembers" bacterial diseases for much shorter periods of time. Think about how children can only get chickenpox one time, but can get Strep throat over and over. The most recent

American Animal Hospital Association (AAHA) vaccine guidelines recommend restarting with a series of two Lyme vaccines anytime a dog is overdue. There is also good evidence that puppies mount much stronger immunity if they are given a booster six months after receiving the initial series of two inoculations. If there is enough of a concern about Lyme disease to be vaccinating your dog, be sure to follow the recommended booster intervals carefully.

Conclusion

This overview of Lyme disease and its prevention is based on the most recent science available. As I mentioned at the outset, the veterinary profession is still learning more about this complicated disease. In addition, new prevention strategies are emerging all the time. It is important to establish a good working relationship with a knowledgeable veterinarian. Each combination of dog, lifestyle, and geography will be a little different, so be sure to discuss all of these topics with your own trusted veterinarian.

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