



From the Health and Genetics Committee

Please read this article for important updates on these issues:

- *Vector-borne diseases are common*
- *Heartworm preventatives may not be completely effective against some strains in some areas of our country*
- *Some researchers believe there could be a connection between vector-borne Bartonella and hemangiosarcoma*
- *Golden Retrievers receiving tick prevention had less lymphoma*
- *Important considerations when traveling with your dog, i.e. to the next National Specialty*
- *It's not just that fleas and ticks get killed, it's also how quickly.*

Fleas, Ticks, and Mosquitoes: Recognized Vectors of Disease

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I graduated from veterinary school at Texas A&M in 1981. At that time, heartworm preventatives were recommended in areas of the south where mosquitoes were present throughout the year. Fleas were a major problem and were mostly associated with flea bite allergies or contributing to anemia in heavily infested puppies. We did not recognize them as important vectors of human and canine diseases. Ticks were known to transmit Rocky Mountain Spotted Fever and *Ehrlichiosis* but we thought these diseases were rare. Lyme disease had been described a few years previously and ticks were implicated in its transmission, but back then it was considered localized to a few areas of the United States [1, 2]. Also, the number of options for treating and preventing fleas and ticks was very limited.

The situation is entirely different now.

This article is designed to emphasize new developments in canine diseases transmitted by fleas, ticks and mosquitoes. It also includes useful references, often with online links, for those who want to learn more about these new developments. Hopefully, it will stimulate discussions with your Golden Retriever's attending veterinarian, who should always be the primary source of information on the health of your Golden Retriever.

Vector-borne infections in dogs today

Today, we know that vector-borne **exposures** and **infections** of dogs **are common**. Importantly, exposure means that the dog came into contact with the vector-borne organism. Infection means that the vector-borne organism became established within the dog and usually replicated there. In most cases of exposure and/or infection, the dog will develop an immune response which results in antibodies which can be detected by antibody tests which indicate exposure. That immune response may or may not result in elimination of the

vector-borne organism. If the vector-borne organism is still present in the blood sample, protein or DNA from that organism can sometimes be detected by other tests which indicate exposure and infection. However, in some but not all situations, an infected dog will develop a clinically recognized vector-borne **disease**. A disease is a condition that interferes with normal health. Understanding these differences is very important because most of our data on the spread of vector-borne organisms in dogs come from reports of positive tests from reference laboratories and do not necessarily reflect clinically recognized disease. For some vector-borne infections, whether treatment should or should not be given to a healthy dog is a source of major controversy. In addition, the drugs that are best for treating different infections are often different. These are all topics which each owner should discuss with their dog's veterinarian.

As mentioned above, we now know that vector-borne exposure and infections are common in dogs. For example, in a recent study of healthy North Carolina dogs, **82% had evidence of exposure to, or infection with, at least one organism** that can cause a vector-borne disease [3]. For many of the infections, the frequency and geographic range is increasing [4]. For example, the agent causing Lyme Disease, which is carried by ticks, is now more common in the United States than any of the intestinal worms. Controlling the vectors which spread vector-borne diseases is a simple way to prevent vector-borne infections before they happen. Fleas, ticks and mosquitoes can also transmit several important diseases to humans so controlling them is important for people too [5, 6]. The number of known organisms that can cause vector-borne diseases in dogs also continues to increase [7].

Heartworm disease

Heartworm disease is caused by the worm, *Dirofilaria*

immitis and mosquitoes transmit the disease between dogs. Today in the US, dogs in all 50 states are at risk. Heartworm disease has also spread into Canada, although infection rates there are lower than in much of the US [8]. Rates of infection in any area are influenced by the number of infected dogs in the neighborhood, the mosquito numbers in a specific area, and the use of heartworm preventatives. Now, however, some *D. immitis* are resistant to heartworm preventatives. While still rare, the frequency of resistance is increasing and creates a situation where heartworm can spread to dogs receiving heartworm prevention. Resistance to the agents commonly used in monthly preventatives, moxidectin and ivermectin, is most frequent in the Mississippi Delta region of the United States [9]. The resistance is believed to be due to genetic changes in the parasite similar to changes causing resistance to this class of drugs in other parasites [10]. The good news is that these drugs still prevent most heartworm infections. In addition, infections with the resistant parasites generally should have low numbers of adults because the preventatives will kill most young heartworms, leaving the small number that are resistant. The resulting adults can still be killed since the drugs used to treat affected dogs are in a different class of drugs than the preventatives [9]. Owners may want to discuss resistance to preventatives with their veterinarian, particularly if they live in, or will be traveling to, a high risk region of the country.

Fleas as vectors of canine disease

The "cat flea," *Ctenocephalides felis*, is actually the common flea of the dog. It is well known for its role in tapeworm transmission in dogs [11]. This flea is also increasingly implicated in transmitting infections due to a number of pathogenic bacteria, most notably *Bartonella*, small intracellular bacteria that infect blood cells of many different species [11-13]. *Bartonella* infections can also be transmitted by sand flies and

ticks. *Bartonella* infections of cats are common in cats living in houses with flea problems and fleas appear to spread the organism between cats. The common *Bartonella* of cats, *Bartonella henselae*, may actually be transmitted through bites and scratches from the cat that are contaminated with the feces of the flea (flea dirt). A small study of veterinary personnel (veterinarians and veterinary technicians) indicates that they may be commonly infected with *Bartonella*, with 28% of veterinary personnel having evidence of infections (DNA by PCR) as opposed to none of those with other occupations [14]. The risks associated with the infections in veterinarians and veterinary technicians have not been identified.

Dogs can also get *B. henselae* infections but I know of no reports of dogs transmitting *B. henselae* infections to humans. The Vector Disease Diagnostic Laboratory at the North Carolina State University College of Veterinary Medicine receives diagnostic samples from dogs throughout the United States. Data from that lab suggest infections in dogs are less frequent than in cats and veterinarians - among 14,496 serum samples, 3.8% showed evidence of exposure to *B. henselae* and 1.5% showed evidence of exposure to *Bartonella vinsonii subsp. berkoferii* [15].

Once *Bartonella* infections are established, they tend to persist, particularly within red blood cells and the endothelial cells which line blood vessels [16]. However, the levels of circulating *Bartonella* vary greatly with time, and intermittent circulation in the blood is characteristic [16]. Because *Bartonella* hide within cells, they can often evade the immune response of individuals they infect. The combination of a poorly responsive immune system and intermittent circulation makes diagnosis difficult. That is because diagnostic tests often rely upon finding the organism's DNA in circulating blood or the antibodies the dog produces when its immune system recognizes the organism. The tests cannot identify an organism if the blood is drawn when it is hidden and if the immune system has

AKC Canine Health Foundation

Tick-Borne Disease Research Initiative

The AKC Canine Health Foundation (CHF) recently announced that it has met the Year I fundraising goal of \$250,000 for its Tick-Borne Disease Initiative, launched in February 2016. Funds raised were matched dollar-for-dollar by the American Kennel Club (AKC).

Building on this progress, CHF will carry this important Initiative into Year II, and once again, all donations to the CHF Tick-Borne Disease Initiative during 2017 will be generously matched dollar-for-dollar by the AKC, up to \$250,000.

"The AKC is proud of the progress made through CHF's Tick-Borne Disease Initiative, and we are pleased to once again provide these matching funds to the Initiative in 2017," said Harvey Wooding, AKC Board of Directors. "Tick-borne disease has far-reaching impacts on both dogs and humans, and the AKC supports this work for the health of dogs."

"We are grateful to the AKC for continuing their generous match of funds raised through the Tick-Borne Disease Initiative, and we also thank the many individuals, dog clubs and foundations who have supported this important Initiative to help us reach our Year I goal," said Dr. Diane Brown, CHF CEO. "We believe, through this dedicated research effort, we can make a long-lasting impact on these diseases in dogs and their human companions."

The AKC Canine Health Foundation also thanked the Golden Retriever Foundation for kicking off its 2017 Tick-borne Disease Initiative with their generous, \$15,000 match-eligible Charter Sponsorship. To learn more about the current research being funded, to access educational materials and read about the current request for new research proposals, see www.akcCHF.org/ticks.

not responded. Recent advances in diagnostic procedures have improved this situation and are helping establish a role for *Bartonella* in some clinical diseases [17].

In people, one disease known to be caused by *B. henselae* is "cat scratch disease [13]." Infections of the lining of the heart (endocarditis) and liver disease have also been attributed to *Bartonella* [16, 17]. *Bartonella* have also been isolated from people with neurologic disorders and arthritis, although it is not yet clear if these were caused by *Bartonella* [18, 19]. In contrast, diseases characterized by proliferation of blood vessels, the vasoproliferative diseases, are strongly associated with *Bartonella* infections in people, particularly in the immunosuppressed [16]. Similarly, there is a case report of a dog treated with immunosuppressive drugs that developed skin nodules comprised of blood vessels lined by enlarged endothelial cells containing *Bartonella*. The nodules resolved with antibiotic treatment [20]. The tendency for *Bartonella* to cause proliferation of blood vessels has been attributed to their ability to stimulate cells to produce the growth factor, VEGF, which causes proliferation of the cells lining blood vessels, the endothelial cells [16, 21-23]. *Bartonella* have also been identified in tumors of humans and dog that are characterized by vascular proliferation, including some hemangiopericytomas and hemangiosarcomas of dogs [16, 24]. The combined identification of *Bartonella* in some hemangiosarcomas and the ability of *Bartonella* to cause the release of growth factors stimulating vascular proliferation has caused at least one research group to hypothesize that *Bartonella* may contribute to the development of hemangiosarcoma in dogs [16]. While that hypothesis remains to be fully investigated, owners may want to talk with their veterinarians about flea control while those studies continue.

Ticks as vectors of canine disease

Eight tick-transmitted organisms are especially important in the United States: *Rickettsia rickettsii* (the cause of Rocky Mountain Spotted Fever), *Ehrlichia canis*, *Ehrlichia ewingii*, *Ehrlichia chaffeensis*, *Babesia canis*, *Anaplasma platys*, *Anaplasma phagocytophilum*, and *Borrelia burgdorferi* [25]. The most frequent infection in dogs is with *Borrelia burgdorferi* (the cause of Lyme disease). From 2008-2010, 8.3% of samples sent to the Vector Disease Diagnostic Laboratory indicated exposure to this pathogen [26]. The Companion Animal Parasite Council (CAPC) maps of parasite prevalence for 2016 indicate a similar frequency, with ~1 in 16 (6.25%) positive for *B. burgdorferi*. *B. burgdorferi* is also spreading from its traditional location in the northeast US to other regions, notably portions of Canada and the southern US [26-28]. *B. burgdorferi* can cause clinical disease in dogs, most notably kidney disease and joint pain (polyarthritis) [29]. Avoiding *B. burgdorferi* infection is particularly important for Golden Retrievers because Golden Retrievers and Labrador Retrievers are reportedly at increased risk for developing fatal kidney disease (Lyme nephritis) after *B. burgdorferi* infection [30].

As noted above, a number of other organisms can be transmitted by ticks. The 2016 CAPC map indicated that 1 in 35 samples were positive for exposure to the genus *Ehrlichia*, and 1 in 30 were positive for exposure to the genus *Anaplasma* [31]. Like *Bartonella*, species of *Ehrlichia* and *Anaplasma* that infect dogs manage to avoid the normal immune response of dogs, in part by hiding within blood and or endothelial cells so that persistent infections are possible [32, 33]. *Anaplasma*

phagocytophilum can infect people as well as dogs, and cases are increasing in the United States [26]. This organism can cause a variety of clinical signs including fever, appetite loss, lameness, nose bleeds, immune-mediated hemolytic anemia and low platelet counts in dogs [34]. Dogs with *Ehrlichia* infections may be depressed, lose weight and sometimes have a tendency to bleed, which can cause little red spots in the gums or nose bleeds. Less frequently, *Ehrlichia* infections can cause muscle and joint pain or neurologic disease [35]. Several different species of *Ehrlichia* can cause disease in dogs and they are all transmitted by ticks. A recent case report suggests that some ticks may also be able to transmit *Bartonella* infections [19]. Responding to this, the AKC Canine Health Foundation has begun a tick-borne disease research initiative and some very nice online articles are now available on canine tick-borne disease and their prevention [36-38].

Ticks are highly effective in transmitting the organisms that cause a number of important canine diseases. Fortunately, for most but probably not all vector-borne infections, ticks need to be attached for a period of time, called the attachment time, before the vector-borne infection is transmitted. For *B. burgdorferi* (the cause of Lyme disease), the risk of transmission to people and mice increases greatly after 36-48 hours of attachment, although successful transmission has been reported when infected ticks were attached for shorter time periods [39-41]. This is not as well studied in dogs. What is abundantly clear is that for most vector-borne diseases, the risk of transmission increases the longer the tick stays on the dog [25]. Therefore, some vector-borne infections of dogs may be prevented by inspecting a dog for ticks and carefully removing them shortly after they are acquired. Instructions for tick removal are available from the Centers for Disease Control and Prevention [42]. Chemicals which kill ticks (acaricides) and/or repel them have been documented to be highly effective in reducing the risk for many vector-borne infections of dogs in several studies [25, 43-46].

Preventing the fleas and ticks

Fortunately, vector-borne diseases can often be prevented by controlling fleas and ticks. The Companion Animal Parasite Council currently recommends that all dogs and cats stay on treatment throughout the year to prevent flea and tick problems [11, 39]. In regard to flea control, the most important things to remember are that a female flea begins to produce eggs within a day of her first blood meal, produces roughly 40-50 eggs per day and will live up to 2-3 months on an untreated dog. The eggs fall off and land in the environment. The emergence of adults can be delayed up to 30 weeks under some environmental conditions [11]. In short, the key to flea control is preventing the establishment of a population.

Similarly, tick prevention is key to preventing vector-borne diseases in dogs [25]. The effectiveness and safety of flea and tick products sometimes vary depending upon the geographic area and what the dog does. For example, some products do not work well when dogs swim frequently and many products have not been evaluated for safety in breeding dogs. For products that have been evaluated in breeding dogs, some appear safe while findings in others may be concerning. The product labels often contain critical information regarding whether or not the product is safe for breeding dogs. Pesticide resistance can also vary in different areas. Some products are better for fleas and some for ticks. Importantly, in a 2008 study, monthly

acaricide treatment was more common in healthy Golden Retrievers than in Golden Retrievers with lymphoma (cancer of the lymph nodes) [47].

The take home message is that owners should talk frequently with their veterinarians about how to prevent fleas and ticks and vector-borne diseases in their Golden Retrievers. When owners make plans to travel with their Golden Retrievers, an updated discussion may help guide precautions for safer travels.

Additional important considerations

Because so many different organisms can be transmitted by fleas, ticks and mosquitoes, dogs can be infected with more than one vector-borne agent. Individual differences between dogs and the presence of more than one infectious agent can influence the signs shown by an individual dog [34, 48]. That is part of the challenge in diagnosing and treating these agents. In addition, the agents causing vector-borne disease and the vectors transmitting them are more frequent in some geographic regions than in others. This means that discussions with the attending veterinarian can be a particularly important when preparing to travel with your dog(s). Maps showing the geographic distributions of cases of heartworm disease, Lyme disease, *Ehrlichia* and *Anaplasma* in the U.S. are available online at <https://www.cpcvet.org/parasite-prevalence-maps/>. These are wonderful resources when traveling to an unfamiliar area in the U.S. For example, a quick look at **the 2016 map reveals a high frequency of Lyme Disease and Ehrlichiosis in Maryland where the 2017 GRCA National Specialty will be held.**

Useful Links

Companion Animal Parasite Council

Parasite Prevalence Maps

<https://www.cpcvet.org/parasite-prevalence-maps/>

Current Advice on Parasite Control: Ectoparasites - Fleas

<https://www.cpcvet.org/capc-recommendations/fleas/>

Current Advice on Parasite Control: Ectoparasites - Ticks

<https://www.cpcvet.org/capc-recommendations/ticks/>

AKC Canine Health Foundation

Tick-borne Disease: Prevalence, Prevention, and Treatment

<http://www.akcchf.org/canine-health/sporting-field-dogs/tick-borne-disease.html>

Tick Borne-Disease Initiative

<http://www.akcchf.org/canine-health/your-dogs-health/caring-for-your-dog/ticks.html>

Canine Tick-Borne Disease

<http://www.akcchf.org/canine-health/your-dogs-health/caring-for-your-dog/canine-tick-borne-disease.html>

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From the Health and Genetics Committee, *continued*

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