ZOONOTIC DISEASES IN SOCIETY TODAY: LYME DISEASE

An Interactive Qualifying Project submitted to the Cummings School of Veterinary Medicine at Tufts University and the faculty at Worcester Polytechnic Institute in partial fulfillment of the requirements of the degree of Bachelor of Science by

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Abstract

Zoonotic diseases are diseases caused by microorganisms which spread naturally from animals to humans. Humans have been plagued by these types of diseases since the dawn of humankind. Zoonotic diseases account for approximately 61% of all human diseases and it has been found that about 75% of emerging diseases are zoonotic-derived. With the current rise in the global human population, zoonotic diseases are becoming increasingly prevalent. Many factors contribute to the prevalence of zoonotic diseases, including the encroachment by humans into animal habitat, increased livestock production, and increased mixing of different animal species. In addition, with the improvements in global travel, an isolated zoonotic event has the potential to become a global pandemic within a relatively short period of time. In order to get a good understanding of how a zoonotic event occurs, it is important to understand both the animal and human aspect of the particular disease. A better understanding and overlap between human and animal medicine is key in reducing the prevalence of zoonotic diseases. This paper will specifically study Lyme disease, a vector-borne disease prevalent in New England, as an example to explain how human and animal health play a role in the spread of a zoonotic disease.

Acknowledgments

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Last but most certainly not least, we would like to extend our gratitude to Dr. Eric Overstrom, Head of the Biology& Biotechnology Department at WPI, for being our advisor for this project and taking us under his wing. He guided us through the process and steered us in the right directions when we needed it. He also was able to make many connections for us with the faculty at the Cummings School of

Veterinary Medicine, who were able to enrich our experience during this project and give us just a small taste of the broad spectrum of topics that relate to zoonotic disease.

Authorship Page

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-History of Zoonoses

-Surface Protein on Borrelia burgdorferi

-Human Clinical signs/symptoms of Lyme disease

-Diagnostic Testing of Lyme disease in Humans

-Treatment of Lyme disease in Humans

-Prevention of Lyme disease in humans

-Public Health

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-Background on Zoonoses in general

-Background on Lyme disease

-Transmission of Lyme disease

-Antibodies

-Dog Clinical signs/symptoms of Lyme disease

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Introduction

While most people are fully aware of the benefits of having a household pet, few people are aware of the diseases they can contract from their companion animals or that their pets can become infected with some of the same diseases humans do. These diseases are known as Zoonotic diseases, also called zoonoses, and they are caused by microorganisms that can infect both animals and humans (Torrey, 2005). Zoonoses account for approximately 61% of all human diseases and it has been found that about 75% of emerging diseases are zoonotic (Torrey, 2005). Emerging diseases are defined as "diseases that have appeared for the first time, or are increasing in incidence, or have been reported in new areas," (Cleaveland, 2001).

Throughout time, Zoonotic diseases have had a profound impact on human history. From the moment that we evolved into modern man, we carried with us infections agents that came from our animal counterparts. As we evolved, disease causing microorganisms, known as pathogens, also evolved within animal reservoirs; some of these pathogens were able to make the jump from animal to human hosts. Some of the most historical and devastating pandemics can be attributed these types of animal derived pathogens, most notably bacterial and viral pathogens due to their rapid reproductive cycles (Torrey, 2005). Zoonoses have been a problem for as long as we have coexisted with animals (after all we are animals ourselves). Initially, we acquired infections from wild animals that we came in contact with. The earliest mode of transmission were heirloom infections, in which microorganisms were passed from prehistoric animals, to early primates, then on to early hominoids, and finally to humans. The origins of diseases such as malaria and hepatitis A and B date back to prehistoric times and are examples of heirloom infections (Torrey, 2005).

Early humans lived in small nomadic hunter-gatherer societies who followed herds of animals. Their diet consisted mostly of available plants and some animal meat. Their nomadic lifestyle did not allow them to accumulate waste products that would harbor problematic species, like rats. By observing

modern day hunter-gatherers, we know that they lived generally healthy lifestyles without major life threatening infections. As humans shifted towards agricultural communities, diseases became more abundant. We bred animals for livestock and our abundance of crops and organic waste attracted wild animals to move closer to our civilizations. These factors lead to an increase in the prevalence of Zoonotic diseases within the human population (*"The Natural History of Disease"*).

Throughout history, animals and humans have shared a close relationship with each other. Certain animals, both domestic and wild, transmit diseases to us more readily than others. Our pets and livestock like dogs, cats, rabbits, cows, pigs, and birds are prime transmitters of zoonotic infections. In fact, 43% of zoonoses we are battling today are acquired from domesticated household pets like cats and dogs, and 39% account for zoonotic diseases transmitted by livestock such as horses, cattle, sheep, goats and pigs (Torrey, 2005).

Wild animals that are considered pests, like rodents, have fed off of our waste and brought us disease for millennia. Rodents have been a reservoir for ancient zoonotic diseases like rabies (*Rhabdoviridae*), Hemorrhagic fevers (*Bunyaviridae Hantavirus*), and plague (*Yesinia pestis*) (*"The Natural History of Disease"*). By far the most infamous case of plague, and the most destructive pandemic in human history, was the "Black Death" of the 14th century. Strains of *Yesinia pestis* bacteria that caused both bubonic and pneumonic plague spread throughout Europe and Asia during the middle ages. The bacteria were responsible for the death of one third of the entire human population at that time (Chamberlain, 2010). *Y. pestis* was able to proliferate within rodents, but the pathogen's main source of transmission to humans was through a vector organism, the flea (*"Plague", CDC*). Fleas acted as vectors that acquired the plague causing bacteria from rodents and would then transmit the bacteria to humans. At that point in human history we understood little about how microbial infections spread and we lacked basic hygienic practices. However as technologies improved, zoonotic pathogens improved and evolved too.

Primates are our closest relatives and have a great affinity to produce zoonotics. Higher-primates, or simians, are related closely to us evolutionarily and have many of the same anatomical and biochemical features as we do. Therefore, the gap for a simian pathogen to jump to a human host is smaller compared to other animals. The most profound case of a simian derived zoonotic disease that became a global pandemic is the Human Immunodeficiency Virus (HIV) outbreak. HIV was thought to have evolved from a similar virus that infected primates known as Simian Immunodeficiency Virus (SIV) (Wolfe, 1998). This African variant of HIV in primates was able to cross species from primates to humans, and now the virus can be transmitted from person to person which has lead to the globalization of AIDS, the syndrome caused by an HIV infection.

Even with our advancements in the understanding and treatment of infectious diseases, it seems that zoonotic pathogens continue to evolve around our understanding of them. So the question still remains, how can we control the spread of zoonotic diseases? One obstacle that we must overcome is understanding exactly how and why a pathogen makes the jump from an animal to a human host. Most people are aware that zoonoses can spread through direct transmission through an animal bite, scratch, or by inhaling the infectious microorganism. This is perhaps the most preventable form of transmission and examples include rabies, cat-scratch disease, and anthrax (Torrey, 2005). Indirect transmission of zoonoses, spread of microorganisms through food or water contamination, is much more difficult to control due to the expansive transportation, distribution of food products, and the lack of clean water and sanitary food in many countries throughout the world. Contamination of meat products and vegetables has lead to many outbreaks of *E. coli*, salmonella, and mad cow disease (Torrey, 2005). An even more difficult and threatening mode of zoonotic transmission, and one that is making headlines everywhere, is the "animal to human to human" transmission. These infections jump from animals to humans and can then be spread from person to person. H1N1, commonly known as "swine flu", is a reemerging strain of influenza which originated in pigs and then made the jump to humans. However now it has the ability to

spread amongst the human population (CDC, 2009). Other examples of this type of transmission include SARS and other strains of influenza, like H5N1 the "bird flu" virus (Torrey, 2005).

One of the most difficult modes of zoonotic transmission to control is the realm of vector-borne diseases. The diseases involve a secondary organism, typically an insect or parasite like fleas, flies, ticks, and mosquitoes, which become infected with a pathogen from an animal and then passes on that pathogen to a human host (Torrey, 2005). In New England, one of the most rapidly expanding vector borne diseases is Lyme disease. Since the realm of zoonotic diseases can cover an extremely broad range of topics, we have chosen to look specifically at Lyme disease as a specific case study; not only due to its relevance in New England, but also because it is a relatively new emerging zoonotic disease that is on the rise in both humans and animals alike.

History of Lyme

The tick-borne illness we now refer to as Lyme disease was first identified in 1975 by Allen Steere from Yale University after an outbreak of juvenile rheumatoid arthritis in Lyme, Connecticut (Appel, 2002). A few years later in 1982 the pathogen that causes Lyme disease, *Borrelia burgdorferi*, was discovered by Dr. Willy Burgdorfer. The disease has been in existence since the 1880's in Europe but was not fully understood and characterized until the 1970's. By 1983, physicians had begun treated patients who tested positive for Lyme disease with oral and intravenous antibiotic therapy. The vaccine for Lyme disease called LYMErix was approved by the FDA in 1998 but taken off the market just three years later (Nigrovic and Thompson, 2007).

Since the disease was fully characterized in 1982, over 150,000 cases of Lyme disease have been reported to the Center for Disease Control and Prevention. The upper East coast, upper Midwest near the Great Lakes, the Oregon coast, and Northern California are areas of the United States that have experienced concentrated occurrences of Lyme disease, however in total 46 of all 50 states have had reported cases of the disease (Acha, 2001). The United States is the largest endemic area of Lyme disease

infections and 90% of all reported cases of Lyme disease occur in the 10 states that constitute the Northeast region of the U.S. (Appel, 2002). Lyme disease has also been identified in 68 countries worldwide, some of the more prominent regions being many countries in Europe, Australia, China, Japan, and parts of Russia. The disease has highest incidence during the summer months of June and July in the Northern Hemisphere (Acha, 2001).

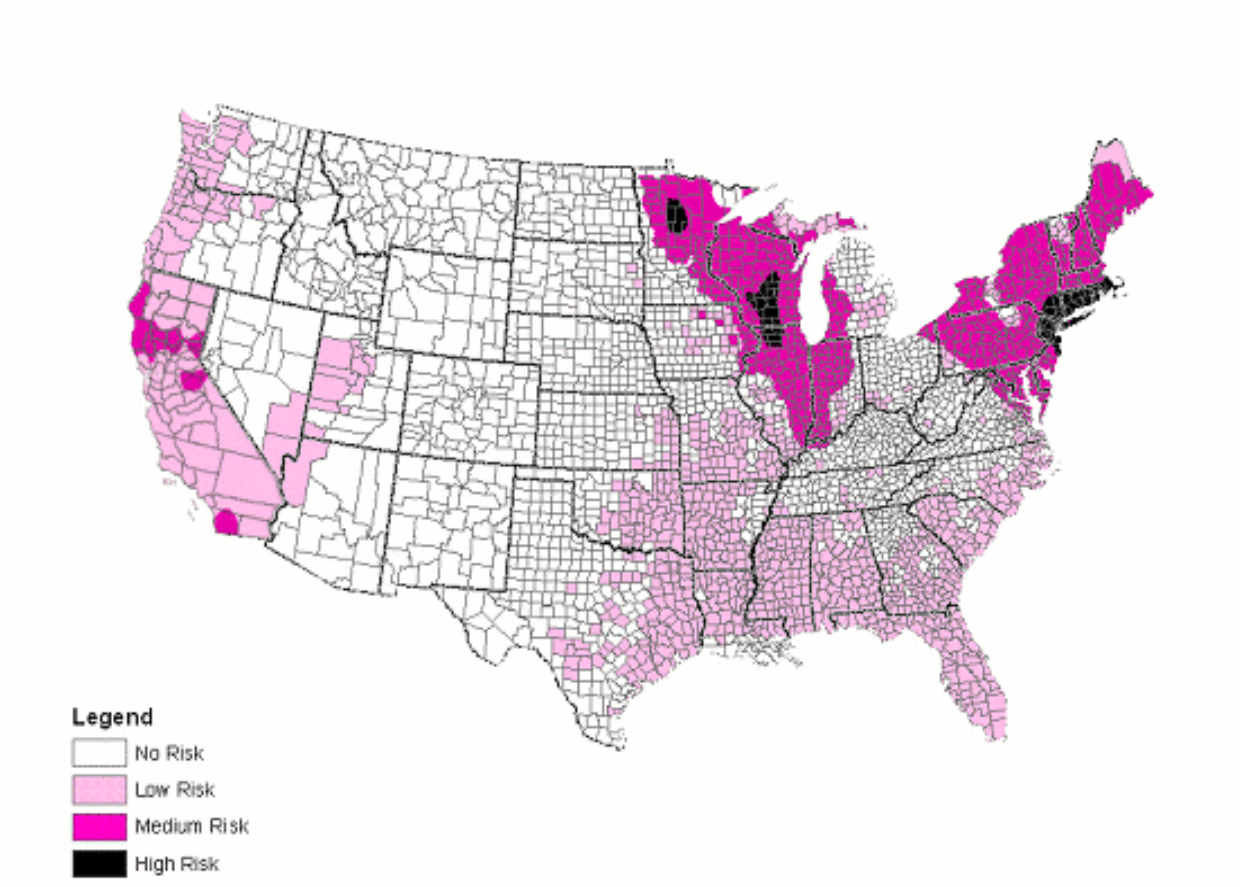


Figure 1. Map of United States Showing Prevalence of Lyme Disease in Humans.

http://www.aldf.com/usmap.shtml.

Lyme disease Transmission

Lyme disease is the most common tick-borne disease in the United States. The disease is a multisystem inflammatory disease which has the ability to spread from the skin to joints and nervous system and even potentially affect other vital organ systems. Humans, horses, and dogs are able to contract the vector-borne disease which is transmitted by deer ticks (*Ixodes scapularis*). Deer ticks have a two year life cycle and just one female tick is capable of producing approximately 2000 eggs each spring (Appel, 2002).

Figure 2. Female Tick with her Eggs.

http://www.bada-uk.org/images/tick%20eggs.jpg.

These eggs grow into larvae which afterwards develop into nymphs. The nymphs lie dormant until late fall when they mature into adults, however even nymphs are able to transmit *Borrelia burgdorferi* but only at an infection rate of about 10-25% whereas the adult tick infection rate is 60% (Appel, 2002).

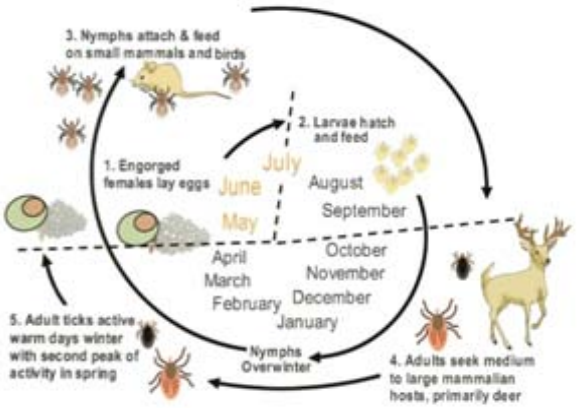


Figure 3. Life Cycle of the Deer Tick

http://www.eradicatelymedisease.org/lyme.html.

White-footed mice and deer act as the reservoir animals for the disease, and once a tick has bitten either of these animals they have then acquired the *B. burgdorferi* bacteria and are then capable of passing it on to other species or animals (Figure 4). The bacteria must move from the ticks mid gut to their salivary glands in order to infect an animal and this process normally takes about 24 to 48 hours (Appel, 2002). *Borrelia burgdorferi* is a spirochete gram negative bacterium which is closely related to the bacteria which also cause leptospirosis and syphilis (Appel, 2002).

Figure 4. Reservoir Animals of Lyme Disease; the White-Footed Mouse and White-Tailed Deer.

http://www.texasbeyondhistory.net/st-plains/nature/images/deer.html.
http://www.nature.com/nature/journal/v423/n6938/fig_tab/423397a_F2.html.

Immunology & Modes of infection

Borrelia burgdorferi, the spirochete that causes Lyme disease, has the ability to trigger multiple clinical symptoms throughout all of the stages of the disease. During the early localization phase of infection the bacteria tend to stay close to the point of entry, the tick-bite, and infect the surround skin tissue causing rashes and inflammation. Once the bacteria migrate to the blood stream in the early dissemination phase, they travel throughout the body and begin to infect multiple tissues groups. The early systemic infection typically affects the tissues of the heart, joints, eyes, peripheral nerves, and cerebrospinal fluid (Sigal, 2007). If the infection persists into the late phase of the disease the bacteria will continue to damage the skin tissue, synovial fluid, and nerve tissue.

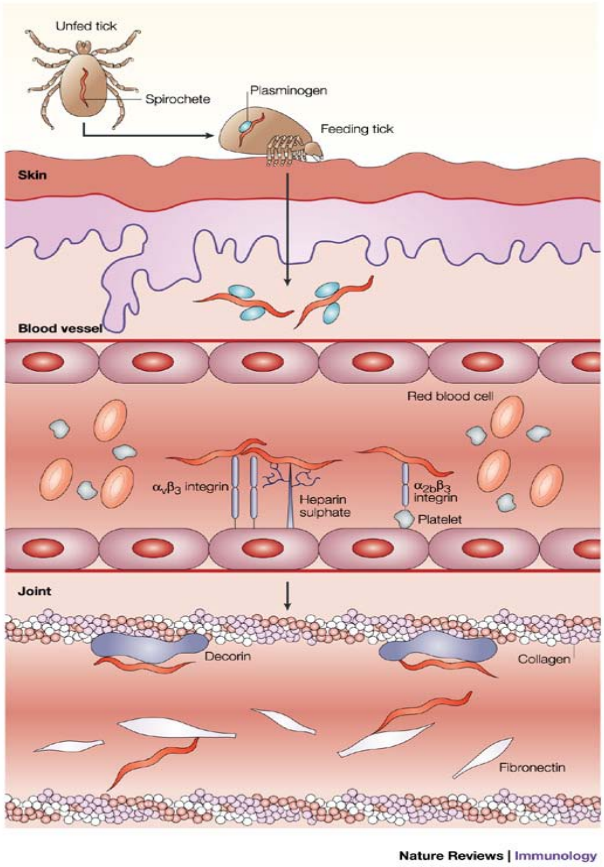


Figure 5. "The Transmission of *Borrelia burgdorferi* to the Mammalian Host and the Dissemination of the Spirochete to the Joint.." Nature Reviews, Immunology.

http://www.nature.com/nri/journal/v4/n2/fig_tab/nri1267_F1.html.

B. burgdorferi, like most other infectious bacteria, has an arsenal of cell surface molecules that they use to successfully infiltrate the host organism. The bacteria's entry into the host begins with the attachment of the vector, in this case and infectious tick. The tick itself can increase the virulence of *B. burgdorferi* by secreting saliva rich in anticoagulants and anti-inflammatory molecules into the bite-site (Sigal, 2007). This allows the tick to receive a continual flow of blood, but it also provides a "smoke-screen" for the bacteria to enter the body undetected. Once the bacteria enter the dermal layer they begin to radiate outwards within the dermis. This radiation of the bacteria within the dermal layer is what causes the indicative erythema migrans rash (Sigal, 2007). The spirochete bacteria migrate through the skin by associating with host plasminogen. Plasminogen is the precursor to plasmin, a protolitic enzyme that degrades fibrin in the blood (Hu, 1995). The plasminogen associated with the bacteria gets activated into plasmin by urokinase-type plasminogen activator. The active plasmin allows the bacteria to penetrate through the endothelial cells and move into the bloodstream. The presence of *B. burgdorferi* in the blood is known as spirochetemia (Sigal, 2007).

Once the bacteria become systemic they can penetrate further into their target tissues by associating with extracellular matrix (ECM) complexes located on platelets and endothelial cells that line the blood vessels. The bacteria penetrate the endothelial layer into their target tissue by binding to cell surface proteoglycans, like heparin, via a glycosaminoglycan receptor (Sigal, 2007). The bacteria also bind to $\alpha_{2b}\beta_3$ intergin on the surface of both the platelets and endothelial cells, and this may play a role in increasing spirochetemia (Sigal, 2007).

Once the bacteria have successfully made it to their target tissues, typically joint fluid and connective tissue, they cause further pathogenesis by anchoring to fibrous proteins associated with the ECM of these tissues. The spirochetes are able to associate indirectly with collagen fibers by binding to decorin, a glycosaminoglycan molecule that binds directly to collagen, through a bacterial receptor known simply as the decorin binding protein ("Pathogenesis", Brown University). The bacteria can also bind

indirectly to other ECM components by anchoring to fibronectin. The full pathogenesis of *B. burgdorferi* is outlined in (Figure 6).

The surface proteins of *B. burgdorferi* play an important role in helping the bacteria proliferate within the host organism; however, they can also act as antigens that elicit an immune response. The most notable antigens are the class of bacterial outer surface proteins (Osp). There are 7 known Osp molecules, A-G, and they carry out various functions. For example, association between plasminogen and *B. burgdorferi* is mediated OspA (Sigal, 2007). The expression of these Osp proteins can vary depending on environmental and pathogenic conditions (Figure 7).

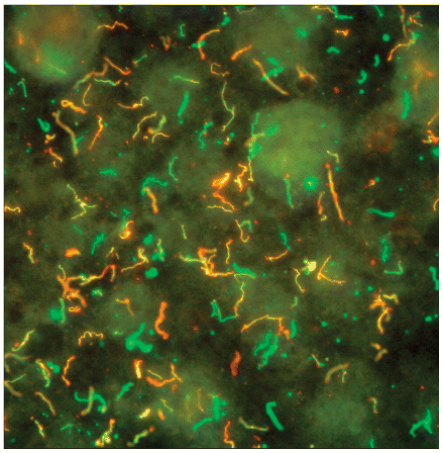


Figure 6. "Expression of *B. burgdorferi* Outer Surface Proteins." ***Rocky Mountain Laboratories*.**

http://iai.asm.org/content/vol76/issue5/cover.dtl.

OspA and OspB are both expressed in spirochetes located in the mid-gut of unfed *Ixodes scapularis* nymphs, whereas OspC and OspD are almost exclusively expressed in spirochetes within the host organism.

The expressions of surface proteins on the cell surface of the bacteria vary between tick and mammalian hosts (Figure 8A). OspA proteins are heavily expressed in spirochetes that reside on unfed

ticks. However once the tick makes contact with the host blood, Osp A is down regulated and OspC becomes heavily expressed (Bunikis, 2003).

In addition to the outer surface proteins, *B. burgdorferi* also expresses p66 and p13, short transmembrane proteins that are displayed in the surface of the bacteria. Both p66 and p13 can act as immune system antigens, however they are often shielded from antibody attachment by the larger outer surface proteins (Figure 8B) (Bunikis, 2003).

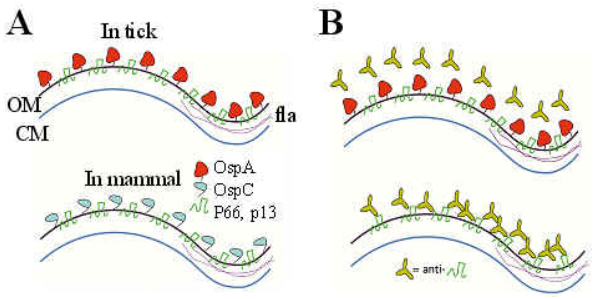


Figure 7. "A Model of the Outer Membrane of *B. burgdorferi*." *Structure and Function of the Surface Proteins of Borrelia Spirochetes* .

http://www.zooeco.org/zooeco/soczee/meetings/CRTBI/abstract/bunikis.asp.

Lyme Disease in Humans

Clinical Signs & Symptoms of Lyme Disease in Humans

The symptoms in Lyme disease patients share many similarities to those of arthritis patients. In fact, the discovery of the disease was initially reported as multiple cases of 'juvenile rheumatoid arthritis in Lyme, Connecticut (Nigrovic, 2007). These cases later turned out to be caused not by an autoimmune condition, but by a bacterial infection. The development of Lyme disease can be broken up into three phases ("Lyme Disease – Symptoms", Arthritis Health Center). Phase one is the early localization of the infection. This initially takes place at the site of the tick bite where the *Borrelia* bacteria have entered the body. A very common symptom in the early onset of the disease is the formation of a circular "bull's-eye" shaped rash, known as an erythema migrans, around the tick-bite (Figure 10). The rash typically appears 3-30 days prior to exposure and occurs in approximately 70-80% of Lyme disease cases ("Lyme Disease Symptoms", CDC). Even though the erythema migrans rash is considered a tell-tale sign of Lyme disease, not all infected persons develop it.

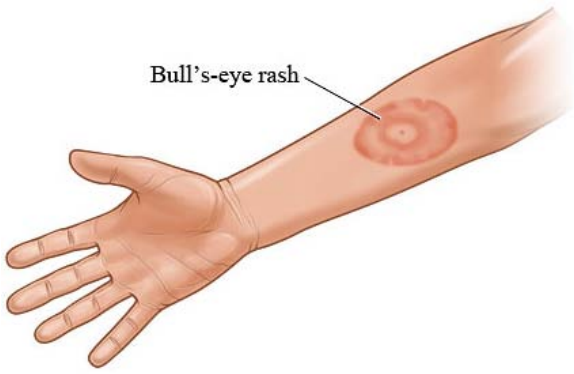


Figure 8. "Erythema Migrans." Lyme Disease rash.

https://hvelink.saintlukeshealthsystem.org/library/healthguide/en-us/support/topic.asp?hwid=zm6245.

Other common non-specific symptoms in the early localization of the infection include chronic fatigue, fever, chills, swollen lymph nodes, joint pain, and stiffness of the neck ("Lyme Disease – Symptoms", Arthritis Health Center).

The second phase in the progression of the disease is early dissemination of the infection. In this phase the *Borrelia* bacteria begin to infect other tissue groups and spread throughout the body. This later onset of the disease is often allowed to occur when patients do not exhibit any of the early localized symptoms, like erythema migrans, or do not have severe enough symptoms to seek treatment initially. Symptoms of early dissemination of the infection include an exacerbation of the early localized symptoms and the onset of additional neurological and muscular symptoms, most notably numbness of the extremities and paralysis of the facial nerves, known as facial palsy (Figure 11). Patients in the early dissemination phase of the disease may also develop conjunctivitis ("Lyme Disease – Symptoms", Arthritis Health Center).

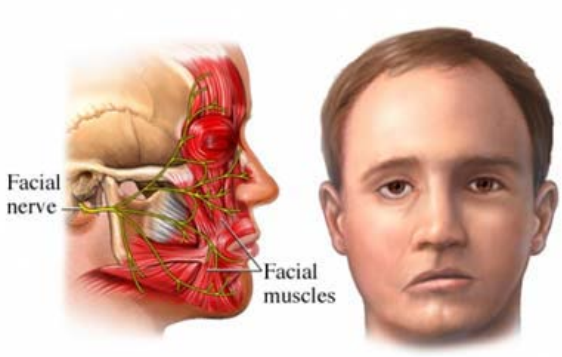


Figure 9. "Bell's (facial) Palsy."

http://www.beliefnet.com/healthandhealing/getcontent.aspx?cid=12019.

The third phase in the development of the disease is the late dissemination phase. Here the bacteria cause further joint and nerve damage. Approximately 60% of the patients who enter the chronic phase have severe arthritis and inflammation of the joints, especially in the large joints like the knee

("Lyme Disease Symptoms", CDC). Patients also experience sharp pains, increased numbness of the extremities, and short term memory loss.

Diagnostic Testing for Lyme disease in Humans

Testing for Lyme disease has raised many questions as to the sensitivity and specificity of the diagnostics currently in use. When a person presents with symptoms typical of Lyme disease, the physician attending them would run either an Indirect Fluorescent Antibody (IFA) test, or more commonly, an Enzyme-linked Immunosorbent Assay (ELISA). Both of these tests detect antibodies for *Borrelia burgdorferi* ("Lyme Disease Diagnostics" CDC, 2009). These two serological tests are meant to be very sensitive. Once a positive result is acquired from either of these two tests, a Western Blot is performed for better specificity in terms of the stage of the disease. The Western Blot tests for the levels of IgM and IgG antibodies in the blood. The IgM antibody is the first line of defense but will not peak until three to six weeks after the patient has been infected, and peak IgG levels are reached later, months to years after the onset of the disease ("Lyme Disease Diagnostics" CDC, 2009). . Due to the length of time required to see an immune response, many patients who have been infected will go weeks without being treated. This lapse in detecting the IgG and IgM antibodies contributes to the issue of early detection of Lyme disease. If a negative Western Blot result is received, then the initial positive result was a false positive.

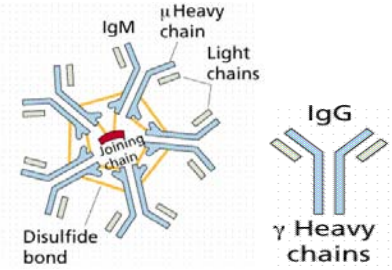


Figure 10. IgM and IgG Antibodies which are recruited during an Immune response to a *B. burgdorferi* infection.

http://www.cartage.org.lb/en/themes/sciences/lifescience/GeneralBiology/Physiology/LymphaticSystem/Antibodymediated/Antibodymediated.htm.

Many false positives are experienced using the antibody testing method however because it is such a sensitive test, so other methods have been explored. Antigen testing experiments have been completed to test whether or not this form of diagnostic testing would be a more specific and more sensitive method than antibody testing. Antigen tests are considered a more direct method of diagnosis than antibody testing. This method proved to be more sensitive than antibody testing but less specific. The method is superior to an ELISA test however for diagnosing early stage Lyme disease. It is also useful in recognizing false-positive ELISA tests. The drawback that will prevent this method from becoming more widely used is the more in depth protocol required for antigen testing (Magnarelli, 1987).

Treatment of Lyme Disease in Humans

Since Lyme disease is caused by bacteria, antibiotics are used to eradicate the spirochete bacteria from the body. Lyme disease is treatable in most stages of the disease with the proper dosage of antibiotics administered orally or intravenously. Exactly which antibiotic is used differs for adults and children and also depends how far the disease has progressed in the individual. Specific antibiotics used for different stages of the disease are outlined in *Table 1*. If the disease is caught early, the most likely course of treatment in adults is an oral regiment of doxycycline. For children younger than nine years old and women who are pregnant, penicillin, amoxicillin, and erythromycin are all effective alternatives to the oral doxycycline treatment. In many cases an early course of antibiotics within 72 hours post-infection can completely eliminate the development of the disease (Nigrovic, 2007). An intravenous regiment of antibiotics may be administered to patients who do not respond to the initial oral antibiotic regiment or in patients who present with chronic symptoms of Lyme disease.

Table 1. Treatment Regimens for Lyme disease in Humans

Early Infection - (Local or Disseminated)	
Adults	Doxycycline, 100 mg orally 2 times/days(d) for 20 to 20d Amoxicillin, 500 mg orally 3 times/d for 20 to 30d *Alternatives in case of doxycycline or amoxicillin allergy*: Cefuroxime axetil, 500 mg orally twice daily for 20 to 30d Erythromycin, 150 mg orally 4 times a day or 20 mg/kg/d in divided doses for 20 to 20d
Children (Age 8 or less)	Amoxicillin, 250 mg orally 3 times a day or 20 mg/kg/d in divided doses for 20 to 30d *Alternatives in case of penicillin allergy:* Cefuroxime axetil, 125 mg orally twice daily for 20 to 30 d Erythromycin, 250 mg orally 3 times a day or 30 mg/kg/d in divided doses for 20 to 20 d
Arthritis	
(Intermittent or Chronic)	Doxycycline 100 mg orally 2 times/d for 30 to 60d Amoxicilln 500 mg orally 4 times/d for 30 to 60d **or** Ceftriaxone 2g IV once a day for 14 to 39d Penicillin G, 20 million U IV in 4 divided doses daily for 30d
Neurologic Abnormalities	
(Early or Late)	Ceftriaxone, 2g IV once a day for 14 to 30d Penicillin G, 20 million U IV in 4 divided doses for 30 d *Alternative in case of ceftriaxone or penicillin allergy:* Doxycycline, 100 mg orally 3 times a day for 30d
Facial palsy alone	Oral regimens may be adequate
Cardiac Abnormalities	
First-degree AV block (P-R interval >0.3 sec)	Oral regimens, as for early infection
High-degree AV block	Ceftriaxone, 2 gm IV once a day for 30d** Penicillin G, 20 million U IV in 4 divided doses daily for 30d**

Lyme Vaccination for Humans

Once Lyme disease was recognized as a bacterial infection in 1977 a demand for a vaccine against the bacteria arose. Pharmaceutical companies began to develop vaccines that would expose the body's immune system to some of the bacterial surface proteins. The obvious target for a vaccine would

be the characteristic *B. burgdorferi* outer surface proteins. In the early 90's two major vaccines were developed, LYMErix™ and ImuLyme™, that both used an OspA recombinants as the immugen (Nigrovic, 2007). Both immunizations went into clinical trial and showed success in both animal and human test subjects. In 1998 LYMErix™ gained FDA approval and went into clinical practice. ImuLyme™ never sought FDA approval, even after success in clinical trials (Nigrovic, 2007).

Although this seemed like a great victory against limiting the spread of Lyme disease, the LYMErix™ vaccine ended up being a catastrophic failure and it was pulled from the market in 2002 (Nigrovic, 2007). There were many factors that limited the success of the Lyme disease vaccine. One of the key limitations in the vaccine was that it required multiple inoculations in order to be effective. The vaccine would be administered a total of three times (initial inoculation [i], [i]+1 month, and [i]+ 12 months) in order for patients to receive full immunity (Nigrovic, 2007). Most patients looking to be vaccinated, want a "quick-fix", and do not want the hassle of having to return to the doctor's office for multiple vaccinations. Patients having to receive multiple inoculations also meant that there was a latent period where the patients were "partially immune" and still susceptible to infection. Another limitation in the success of the vaccine was that it was only 80% effective, which meant that 20% of the people who received the full immunization treatment were still at risk (Nigrovic, 2007). Because the vaccination lacked strong effectiveness, it actually contributed to the increased prevalence on the disease. Unsuccessfully immunized patients gained a false sense of security and ignored simple preventive measured when they went into tick infested areas. Other downfalls in the success of the vaccine were that its effectiveness in young children, a high risk demographic for contracting Lyme disease, was unknown, and the vaccine was only effective against the North American strain of *B. burgdorferi* not similar European spirochetes (Nigrovic, 2007).

The vaccine's poor success was due to both scientific barriers and human behavioral problems. From a behavioral perspective, people simply aren't highly concerned about Lyme disease. Although the disease causes devastating symptoms, it is seldom fatal and typically responds well to antibiotic treatment

if it is caught early. Also, shortly after the vaccine was licensed by the FDA, there were multiple reported cases of autoimmune side-effects like arthritis, after patients had received the vaccine. The FDA investigated these allegations and found no substantial evidence to revoke the vaccine's license (Nigrovic, 2007). In 1999, a Philadelphia law-firm went on to file a class-action lawsuit against SmithKlineBeecham, the company that manufactured LYMErix™, claiming that 121 people who received the vaccine suffered multiple adverse side effects (Nigrovic, 2007). This had huge effects on the credibility and public opinion of the vaccine. To make matters worse, LYMErix™ was released in the middle of an anti-vaccination movement in the US, which caused the media to negatively portray the fledgling vaccine (Nigrovic, 2007). In lieu of the pending lawsuit, unpopularity, and low profit margins associated with the vaccine SmithKlineBeecham ceased production of the LIMErix™ vaccine in 2002.

A current vaccine is being developed against *B. burgdorferi* OspC (Earnhart, 2007). The original vaccines against OspA were designed to attach the spirochetes that expressed OspA in the tick's midgut. Since OspC is expressed more than OspA in spirochetes located in the host's plasma, the OspC vaccine should be more effective than the OspA vaccine. However after the catastrophic failure of the first Lyme disease vaccine, most pharmaceutical companies are steering clear from Lyme disease specific treatments, for fear of releasing the next LYMErix™.

Canine Lyme Disease

Clinical Signs Symptoms of Lyme Disease in Dogs

The first suggestion that dogs could also contract Lyme disease through tick exposure occurred in 1984 and 1985 (Littman, 2006). In contrast to human response to *Borrelia burgdorferi*, dogs' immune systems take much longer to respond to spirochete infection. Due to this latent exposure period, dogs will not develop symptoms to the bacteria for weeks to months after the initial exposure. Most cases of canine Lyme disease are reported during the summer or early fall because the dogs have been exposed during the spring or summer at some point. Only 10% of humans infected with *B. burgdorferi* are asymptomatic as opposed to 95% of infected dogs who are asymptomatic (Veterinary Partner, 2010). Another difference between Lyme disease in humans and dogs is the prevalence in the U.S. As you can see from the map below (Figure 11) which compares human and dog Borrelia burgdorferi infection, Lyme infection in dogs is much more widespread than it is in humans. Although it is most prevalent in the Northeast region, Lyme disease does occur elsewhere in the country. The main symptoms associated with Lyme disease in dogs are lameness or arthritis, anorexia, and fever. However these symptoms are also common clinical signs for other tick-borne diseases such as Rocky Mountain spotted fever, Anaplasmosis, and Ehrlichiosis (Littman, 2006). In order to differentiate between Lyme disease and other tick-borne illnesses, diagnostic testing is required.

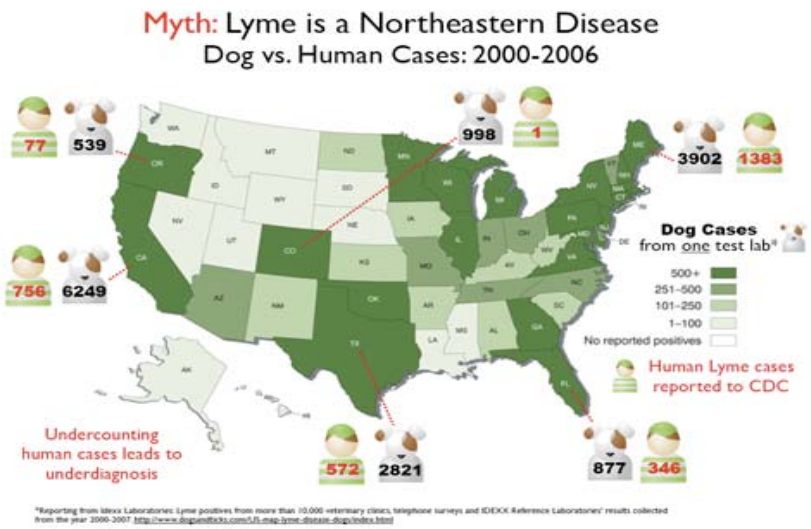


Figure 11. Map of the United States Comparing Prevalence of Lyme disease in Humans and Dogs by Region.

http://underourskin.com/blog/?p=337.

Untreated Lyme disease in dogs can lead to a condition known as Glomerular disease in which excessive amounts of protein are being excreted in the urine. The immune system is trying to fight off the *B. burgdorferi* infection and remove the bacteria from the body. In the process, antibodies end up accumulating in the kidneys and can cause damage. To test a Lyme positive dog to see if they are losing extra protein in their urine a urinalysis is done. A urine sample is gathered from the dog and a urine protein to creatinine ratio test is performed. This test compares the amount of protein and creatinine being excreted in the urine in the form of a ratio and indicates whether or not too much protein is being lost in the urine. If a dog is losing excess protein in their urine this could lead to kidney disease and in time develop into renal failure (Veterinary Partner, 2010). This is the major, long term health concern with dogs that test positive for Lyme disease.

The steps that should be followed when diagnosing a dog that may have Lyme disease are:

I. Evidence of Exposure to *Borrelia burgdorferi*
   A. Positive 4DX or 3DX test
   B. C6 qualitative test to show level of infection

II. Clinical signs typical of Lyme disease
   A. Lameness
   B. Arthritis
   C. Anorexia
   D. Fever

III. Consideration of other possible causes of symptoms
   A. Anaplasmosis
   B. Erhlichiosis
   C. Rocky Mountain Spotted Fever

IV. Response to treatment
   A. Most Lyme positive dogs will respond to treatment with Doxycycline within two days of starting the medication (Littman, 2006).

In addition to these steps diagnostic testing should also be done to verify that it is in fact Lyme disease and rule out other possible diseases with similar symptoms.

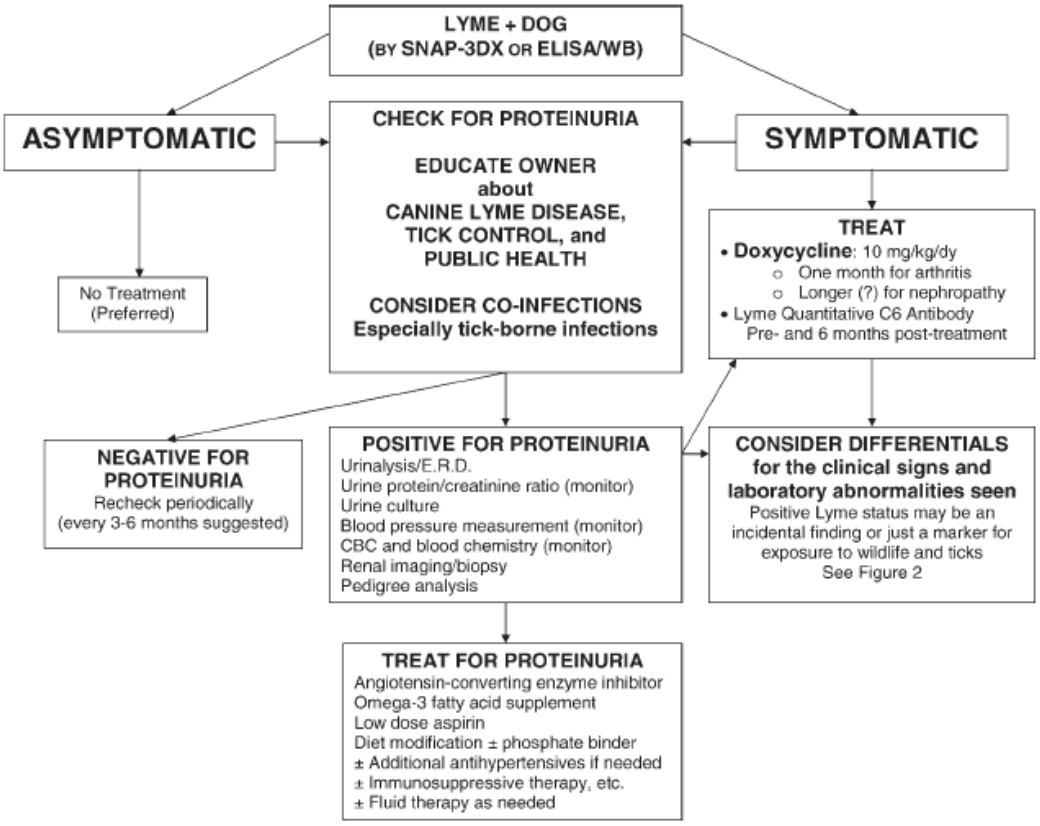


Fig 3. Flowchart for the Lyme-positive dog.

Figure 12. Flowchart of How to Treat and Test a Lyme Positive Dog.

http://www3.interscience.wiley.com/cgi-bin/fulltext/120715308/PDFSTART.

Diagnostic Testing for Lyme disease in Dogs

The greatest challenge that small animal veterinarians are met with when treating dogs in areas endemic for Lyme disease, is that about 90% of dogs in that area will have developed antibodies against the Lyme spirochete ("Lyme Disease," Veterinary Partner). This is due to the fact that many dogs may have been bitten by a deer tick and be exposed to the spirochete, but do not have a full blown immune response to the infection. These dogs have essentially, immunized themselves to the disease by being bitten by the tick and not having the tick intact for a long enough period of time that the spirochete was able to completely transfer to its new host. These antibodies the dogs have developed due to that small amount of exposure will last for years afterwards ("Lyme Disease," Veterinary Partner).

There are a few ways of testing for Lyme disease. However many of these methods are difficult, time-consuming and expensive so normally faster and easier methods are utilized in a clinical setting. Enzyme-linked immunosorbent assays (ELISAs) and Indirect Fluorescent Antibody Assays are two types of antibody tests that detect *B. burgdorferi* in the blood serum. However, these antibody tests are not typically utilized in clinics because most dogs will not exhibit clinical signs of infection for a few months after infection, and therefore the IgM and IgG antibodies on is full blown (Grodzicki, 1988). Whereas ELISA tests give a qualitative result, positive or negative, Western blots allow medical professionals is more specific and quantitative, allowing one to see how many antibodies are directed against each pathogen. Western Blots with a variety of antigens are useful for differentiating the source of the antibody response. Bands in the p58, p37, p35, and p30 areas have been shown to indicate a dog that was infected through exposure to a tick and who had never received a Lyme vaccine. When the p93, p34, p31, and p28 bands appears on a Western Blot, it is an indication of a dog that has been vaccinated, not infected through a tick bite (Guerra, 2000).

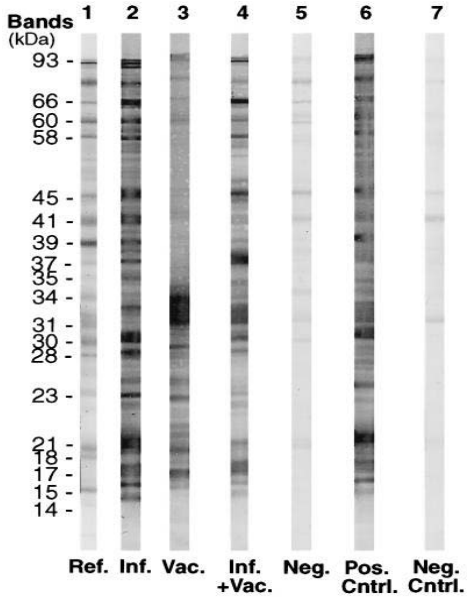


Figure 13. The Inf. Lane on the left hand side of the Westernblot indicates that the result for a dog who had naturally been infected in an endemic area. The Vac. Lane indicates the result for a dog who had received the Lyme vaccine and lived in an endemic area. The Inf. + Vac. Lane indicates a dog that had been vaccinated but did not live in an endemic area.

http://www.ncbi.nlm.nih.gov/pmc/articles/PMC86982/.

When a dog presents to a small animal veterinarian with the classic Lyme symptoms, the next step the veterinarian would normally take is performing a blood test. In most clinics 3DX or 4DX is used to test for Lyme disease, along with two other common tick-borne diseases and possibly even heartworm. Whole blood is used for the test and the blood is mixed with a conjugate and then transferred into a "Snap test." This is an in-house test which takes a total of approximately 10 minutes for results ("Snap 4DX Test," IDEXX). The result of this test simply indicates whether or not the C6 peptides that indicate a natural Lyme infection are present. However this only results in a ***qualitative*** test result, whether or not C6 peptide is in the blood, and does not specify the level of infection. Antibodies against the C6 peptide can be detected within three to five weeks of infection and a positive result will normally occur if the dog is retested afterwards for up to 69 weeks (Magnarelli, 1987).

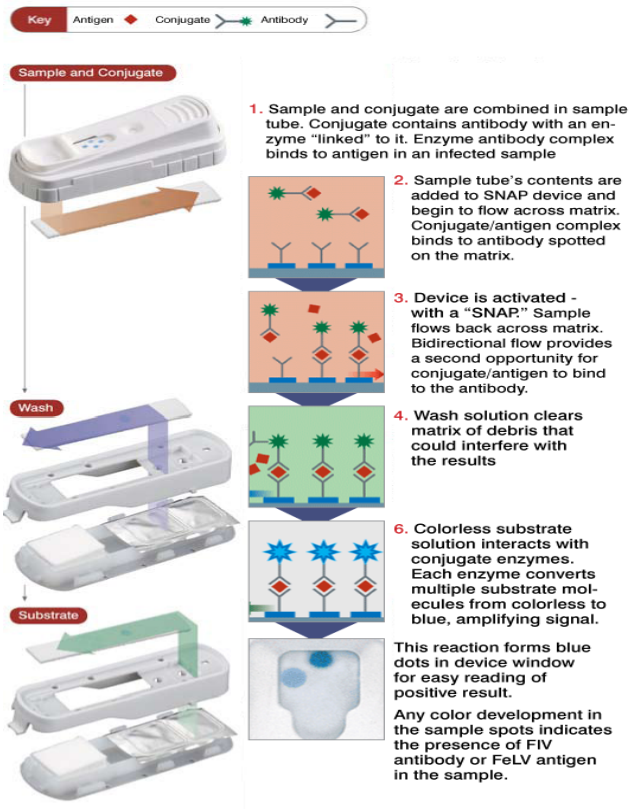


Figure 14. Snap 3DX/ 4DX Test used to Test Dogs for Lyme Disease.

http://www.idexx.com/view/xhtml/en_us/smallanimal/inhouse/snap/common/technology.jsf.

Once a positive result for Lyme disease is procured, a follow up test is performed which is called a C6 ***quantitative*** test to test the level of antibodies in the blood. Quantifying the level of antibodies developed against the spirochete gives the practitioner a better idea of the specificity and severity of the infection. The test analyzes the antibodies produced against the C6 peptide, which is a part of a surface antigen of *Borrelia burgdorferi* ("Lyme Disease," Veterinary Partner). A significant C6 result is a quantity greater than 30U/ml antibody level ("Snap 4DX Test," IDEXX). This method of Lyme disease detection is useful because the C6 peptide is not found in the Lyme vaccine administered to dogs ("Lyme Disease," Veterinary Partner). This means that a true *Borrelia burgdorferi* infection and an immunization response will not be confused because a vaccinated dog will not test positive. This also eliminates the possibility of a dog testing positive because of other underlying health issues. This test is specific to Lyme disease only ("Lyme Disease," Veterinary Partner). The C6 quantitative test does need to be sent out to a diagnostic lab and results are typically acquired within 48 hours.

In addition to getting a quantitative idea of the level of infection, most veterinarians will also recommend running some blood work to make sure that the immune system is operating properly to fight off the *Borrelia burgdorferi* infection. These blood tests with also indicate whether or not there are other underlying health concerns related to the Lyme disease (Dr. Battiston, 2010).

Treatment of Canine Lyme Disease

Once Lyme disease has been detected in a dog who has presented with the typical clinical symptoms of Lyme, an antibiotic regimen is prescribed. The most commonly used antibiotic is Doxycycline, 10 mg/kg by mouth once daily for approximately 30 days. Doxycycline is from the family of tetracycline antibiotics which inhibit protein synthesis of bacteria. These types of antibiotics also are effective against a great variety of gram-negative and gram-positive bacteria (Chopra, 2001). This antibiotic is also chosen frequently because it can take care of other tick-borne infections as well. Doxycycline is inexpensive and has anti-inflammatory properties to help with any joint swelling as result

of infection (Littman, 2006). After a day or two of being on Doxycycline, most dogs show much improvement. If the dog has a bad reaction to the Doxycycline, amoxicillin can be substituted as antibiotic therapy. However, because the *Borrelia burgodorferi* bacterium is so good at hiding within the cells, even after an antibiotic regimen, most dogs will test positive for the infection. Once a dog tests positive for Lyme, the owner is recommended to bring their dog in every 6 months (for the rest of the dog's life) for a recheck of the C6 quantitative test and a urinalysis (Littman, 2006).

Prevention of Lyme disease in Dogs

Tick control in endemic areas is not only important for the prevention of Lyme but is also essential to prevent infection with other tick-borne diseases. Although these prevention methods may be costly, it has been shown that using multiple methods or products together works best for Lyme disease prevention. The easiest form of tick control is a tick collar such as a Preventic™ collar. These collars are made with a chemical called amitraz which is a topical anti-parasitic. These collars prevent tick attachment and if a tick does happen to attach itself to the dog, it kills the tick in less than 24 hours to prevent transmission of the *B. burgdorferi* bacteria. Preventic™ Collars are 97% effective against ticks for up to 3 months of use (Littman, 2006). However, just as with all other topical products, because amitraz is a harsh chemical there is a chance that it can cause some skin irritation such as a rash or even hair loss. Another important warning when using this product is that amitraz is a monoamine oxidase inhibitor, a powerful antidepressant drug. Humans who are on MAOI's that are applying this product to their dog need to take extra precaution (Drugs.com Veterinary Edition, 2010).

Figure 15. Preventic™ Tick Collar made by Virbac.

http://www.drsfostersmith.com/product/prod_display.cfm?pcatid=1254.

Topical monthly tick control medications include Frontline™ and Advantix™. Frontline™ contains a chemical called Fipronil that is absorbed into the skin but does not enter the bloodstream. Fipronil blocks the passage of chlorine through the cell membranes of the insect causing the tick to become paralyzed (Nash, 2010). It is also an antiparasitic which kills ticks after their second day of attachment. The effects of Frontline™ only last approximately a month however and it's recommended that reapplication takes place every 30 days. Advantix™ is also a topical solution which contains the chemicals imidicloprid and permethrin. It works in a similar way to Frontline™ in that it kills ticks, however unlike Frontline™, it is also able to repel ticks from attaching in the first place. Advantix™'s two active ingredients use similar modes of action to kill ticks. Both chemicals interfere with the nervous system of an attached insect; however imidicloprid blocks nerve receptors while permethrin causes repetitive nerve impulse firings (Nash, 2010).

Figure 16. Frontline™ and K9 Advantix™, used as Tick Preventatives in Dogs.

http://www.petcarerx.com/pcrx/ProductPages/Product.aspx?pid=13040&k=Frontline%20Plus%20One%20Year%20Supply%20Special.
http://cheap4you.wordpress.com/.

If a dog should by chance ingest some of these chemicals the owner should call poison control. Just as with Preventic™ collars, these are strong chemicals and can cause damage if not used properly. Also, there is also a chance that both of these tick preventatives could cause skin irritation such as a rash or skin loss (Drugs.com Veterinary Edition, 2010).

Figure 17. Rash that Developed on a Canine's Skin due to an Allergic Reaction to Advantix™.

http://www.elversonpuzzle.com/advantix.jpg.

Due to the fact that cats tend to clean themselves more than dogs do, they are at a greater risk of ingesting these topical insecticides which are poisonous if ingested. For this reason, only certain tick preventatives can be used safely on cats. Also many products are made to work specifically with the

canine physiology and many of these chemicals are easily digested by dogs while cats are unable to metabolize them (National Pesticide Information Center, 2010).

Much controversy has been raised over whether or not people should have their dogs vaccinated for Lyme disease. Although there is the possibility of adverse reactions to the vaccination, the benefits of vaccination have been shown to outweigh the cons. The first factor that should come into consideration is whether or not the dog resides in an endemic area. Most dogs that do not live in areas where the Lyme prevalence is high will not need the Lyme disease vaccination. Also many small dogs that do not go outside often and are at a lower chance of getting infected may not need to receive the vaccine either. Many owners are worried about adverse reactions their pet may have to the vaccine but studies have shown that less than 2% of dogs who have received the vaccine had adverse reactions (Littman, 2006). Dogs can be lethargic the day or two after vaccination, but this is a typical side effect of most vaccinations. This is similar to how humans are sore the day or two after they receive an immunization. Once a dog is started with the Lyme vaccine it should receive an annual booster for the rest of their life, unless they become infected.

There are currently three Lyme vaccinations available for use in dogs. LymeVax™ is made by Fort Dodge Animal Health, RECOMBITEK™ Lyme, made by Merial, and Galaxy Lyme™ which is made by Schering-Plough Animal Health. The RECOMBITEK™ Lyme vaccine, made by Merial, works by generating anti-OspA antibodies which kill the *B. burgdorferi* within the tick. A study was done to test the efficacy of the Osp-A vaccine. Three months after the study had begun, 9 of the 11 (82%) control canines were Lyme positive, whereas none of the vaccinated dogs tested positive during that time span and continued to be Lyme negative a year after the study began (Wikle, 2006). LymeVax™ made by Fort Dodge and Galaxy Lyme™ made by Schering-Plough Animal Health are bacterin vaccines, meaning that that actually have a small amount of weakened *B. burgdorferi* bacteria in them. The vaccine introduces the immune system to the bacteria at a low level to mount a primary immune response. Should the dog get naturally infected later in life the secondary response to the bacteria will be much faster and efficient.

A study similar to the one performed using the RECOMBITEK™ Lyme vaccine was done to test the efficacy of the bacterin vaccine. This study has a larger test group and all dogs in the study lived in the Connecticut River Valley area, a highly endemic location for Lyme disease. The results showed that 64% of non-vaccinated dogs had been infected and only 5% of the dogs who had been vaccinated annually with the bacterin vaccine tested Lyme positive (Levy, 2002).

If a dog is a good candidate for receiving the Lyme vaccine, they would typically be started with their first booster at 9 or 12 weeks of ago. They would then receive a second booster 2 to 4 weeks after the initial vaccine. From then on, the dog would receive the Lyme vaccine on an annual basis. However, a dog should be tested for Lyme before the vaccine is administered (Battiston, 2010). As Dr. Tanya Battiston DVM explains, "An infected dog, in theory, could be at higher risk for complications if they were given a vaccine when their immune system is already exposed, and fighting the infection. We are concerned about auto-immune consequences." The most important consideration to take into account when deciding whether or not to vaccinate your dog if you live in an endemic area, is that if you do not vaccinate them and they become infected, even after treatment your household pet has become a reservoir animal for *Borrelia burgdorferi* (Littman, 2006). Once your dog has become a reservoir animal for Lyme disease, they could then potentially pass the disease onto you.

Table 2. Pros and Cons of Canine Lyme Vaccination

Proponents Say …	Naysayers Say…
Private practitioners have given many doses of *Bb* vaccines since 1990 without side effects.	39 diplomates do not recommend vaccine, only 2 recommend vaccine, and 4 use it rarely.
Because you might not always clear the infection and some dogs get serious illness from *Bb*, it is best to attempt to prevent infection with vaccination.	Most *Bb* infections are subclinical or respond rapidly to cheap/safe/oral antibiotics. The dogs that develop serious illness from *Bb* are probably genetically predisposed to having immune-mediated disease triggered by Lyme antigens and vaccine might not be best for them.
Owners might not want to use tick control products and prefer a vaccine. Owners are worried about Lyme disease in their area.	We need to use good tick control in Lyme endemic areas anyway because of *Anaplasma*, RMSF, *Ehrlichia*, *Babesia*, *Bartonella* spp., etc.
Private practitioners using vaccine say they are seeing fewer Lyme disease cases now.	Practitioners not using vaccine are also seeing fewer Lyme disease cases.
Efficacy	Efficacy
• Bacterin preventive fraction for illness = 78%[84] • Bacterin preventive fraction for seroconversion = 90%[85] or 92%[61] • rOspA 100% efficacious[86] • Need annual boosters (economic incentive)	• Variable, 50–100% • Not that good for preventing signs • Preventive fraction for illness is more important than preventing seroconversion • rOspA only 50% efficacious[27] • rOspA only 60% efficacious[85] • Need annual boosters
Safety	Safety (see text for more references)

• <2% adverse effects[84]
• "Post-vaccinal Lyme-like syndrome" might be a result of misinterpretation of Western blots (carrier dogs' patterns can appear as those vaccinated with bacterin), *Anaplasma* infection, or other causes.
	• Possible anaphylaxis; adverse effects are "moderate"[87]
	• "Post-vaccinal Lyme-like syndrome"[88] needs more study
	• Many respondents associated adverse effects (PLN, IMPA) with Lyme vaccines
	• Molecular mimicry
	  ○ OspA/LFA-1 (HLA-DR4 predisposed)
	  ○ Myelin, myosin, cardiolipin, thyroid
	• OspA is in all vaccine types
	  ○ OspA is proinflammatory
	  ○ OspA sensitizes
	  ○ OspA in human chronic Lyme arthritis
	  ○ OspA in Lyme nephropathy
	  ○ Canine Lyme nephropathy is an immune complex disease
	  ○ 30% of Lyme PLN dogs were vaccinated
	  ○ Postvaccinal Lyme nephropathy (Fincham, personal communication)

Treat all positive dogs with doxycycline for 1 month and vaccinate with bacterin at 0, 14 days.[34]	No evidence that vaccinating seropositive dogs is a good idea; it could even be harmful to some.

http://www3.interscience.wiley.com/cgi-bin/fulltext/120715308/PDFSTART?CRETRY=1&SRETRY=0.

Methods for Reducing Tick Population

The infectivity of deer ticks is completely dependent on their reservoir mammal hosts. Many proactive methods of reducing the tick population in endemic areas of the country have been postulated, however most ideas are too expensive or inhumane to be used widespread. Controlling the population of

the white-tailed deer would be easiest due to their size and the fact that they are already hunted for sport. The white-footed mouse is more difficult to control because of its smaller size and its ability to reproduce quickly (CCELD, 2010).

The normal deer population for Connecticut was calculated to be 10 deer per square mile of land. According to the Connecticut Coalition to Eradicate Lyme Disease (CCELD) by simply reducing the deer population to normal levels will help eradicate Lyme disease.

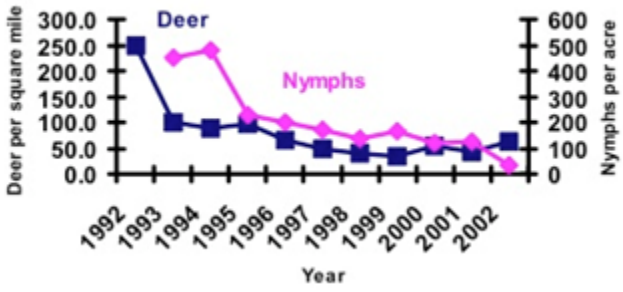


Figure 18. Graph Showing the Decline in the Number of Deer Tick Nymphs due to Reduction of the Deer Population to Natural Levels.

http://www.eradicatelymedisease.org/lyme.html.

Another preventative method that has been in use in some areas are the '4 Poster' Deer Treatment Bait Stations. The device was invented by the Argiculture Research Service branch of the USDA and was patented in 1994. These stations attract deer with whoel kernel corn and when the deer eats the bait, rollers apply 10% permethrin tickicide to the deers ears. Research has found that 90% of adult feeding ticks attach to a deers ears or the deers head area. When the deer groom themselves they can also spread the tickicide to other areas of their bodies. Studies have shown that using this device can decrease the free-living tick population by 92-98% over a time span of three years. This Lyme disease control method is being used in the Northeast region of the U.S. as well as in Maryland and Texas (ALDF, 2010). It serves as a promising method for controlling tick populations due to its humane mechanism of action and its lack of disturbance to the ecosystem.

Figure 19. 4 Poster Deer Treatment Bait Station

http://www.aldf.com/fourPoster2.shtml.

Figure 20. The figure on the right shows the number of attached ticks on a deer's ears before treatment and the figure on the left shows the absence of ticks after treatment.

http://www.aldf.com/fourPoster2.shtml.

Public Health / Prevention

We certainly will not be able to accurately predict exactly when or where the next major zoonotic disease will spring-up, or even what type of infection for that matter. We can hypothesize where the next major outbreak *might* occur based on factors like regional population densities, economics, and proximity to animals. However, these factors are not always absolute indicators of a zoonotic outbreak, as was the case with Lyme disease developing in a rural economically prosperous area. The emergence of a new zoonotic can be viewed as a phenomenon, a “perfect storm”, where all of the conditions required for

disease propagation are present. This is why public health organizations are placing more efforts into preventing and controlling the spread of infectious diseases as opposed to predicting where and when they will emerge. Fighting the spread of zoonotic diseases, whether new or reemerging, is an uphill battle that begins first with a positive identification of a disease outbreak. Prompt recognition and response to a zoonotic threat can make the difference between a few localized cases to a global pandemic. Minimizing the amount of time it takes to identify and respond to an outbreak can be accomplished through effective communication between different public health organizations.

In order to understand how information related to zoonotic diseases (or simply infectious diseases in general) gets passed on, we must first understand the structure of the public health system. At its most basic level, the public health system begins in a doctor's office or veterinary clinic, where the practitioner positively diagnoses a person or animal with a "reportable disease". The practitioners then report the incident to local town public health boards, who then report the incident to the state department of public health (DPH). The state DPH will then monitor the number of cases reported throughout the state, while providing support to the local public health boards in dealing with the potential outbreak. If the disease begins affect a large population within the state, the state DPH will then repost the cases to the Centers for Disease Control and Prevention (CDC). The CDC is a federally funded organization that has national jurisdiction when it comes to matters of public health (especially emerging infectious diseases). If the disease begins to spread throughout a larger region of the United States, the CDC may notify the World Health Organization (WHO) about the epidemic. The WHO a UN sponsored organization that monitors public health and disease prevention on a global scale, and it is at the top of the public health's chain of command.

This is ideally how disease information is passed on in the public health system. However, in reality communication and information sharing between public health organizations can be an obstacle. In the United States the infrastructure of public health can be described as a convoluted web of jurisdictions and policies. The public health system in this country has evolved over the centuries, and it was not

always governed at the federal and state levels. In fact informal local public health boards existed long before any official public health departments were established. Because of this, each local and even state department of public health has its own way of doing things. "As a whole, we (public health organizations) do a pretty good job of passing on information about the prevalence of certain diseases within our jurisdiction", says Dr. Catherine Brown who is Massachusetts's state public health veterinarian. She went on to say that information sharing between state public health departments is often informal and done over the phone. However there is no standard database that all of the states or local health departments input data into

Varying policies between public health organizations is just one of the factors that inhibit the flow of disease related information. Another example is the concept of which diseases are reportable and which ones are not. Exactly which diseases are reportable vary between regions and states, and also between humans and animals. For example, positive identification of Lyme disease in humans is reportable but it is unrepeatable in animals. This variation in the reportability of a disease can cause a misrepresentation the prevalence of a disease within both human and animal populations. Social and economic barriers also inhibit the flow of zoonotic information sharing in the public health system. This is especially true with animal healthcare. Dr. George Saperstein, a large animal veterinarian at Tufts University's School of Veterinary Medicine, described this concept well by providing an anecdote,

> "As a large animal veterinarian who has discovered a salmonella infection in a single cow, I would be pressed with an ethical dilemma. On one hand the farmer is my client and my source of income; should I report him and potentially get his farm shut down by department of agriculture? On the other hand I would not want the salmonella infection to spread further into the animal or human population. As veterinarians we take an oath to protect both animal and human health, and these are the types of dilemmas we face on a regular basis."

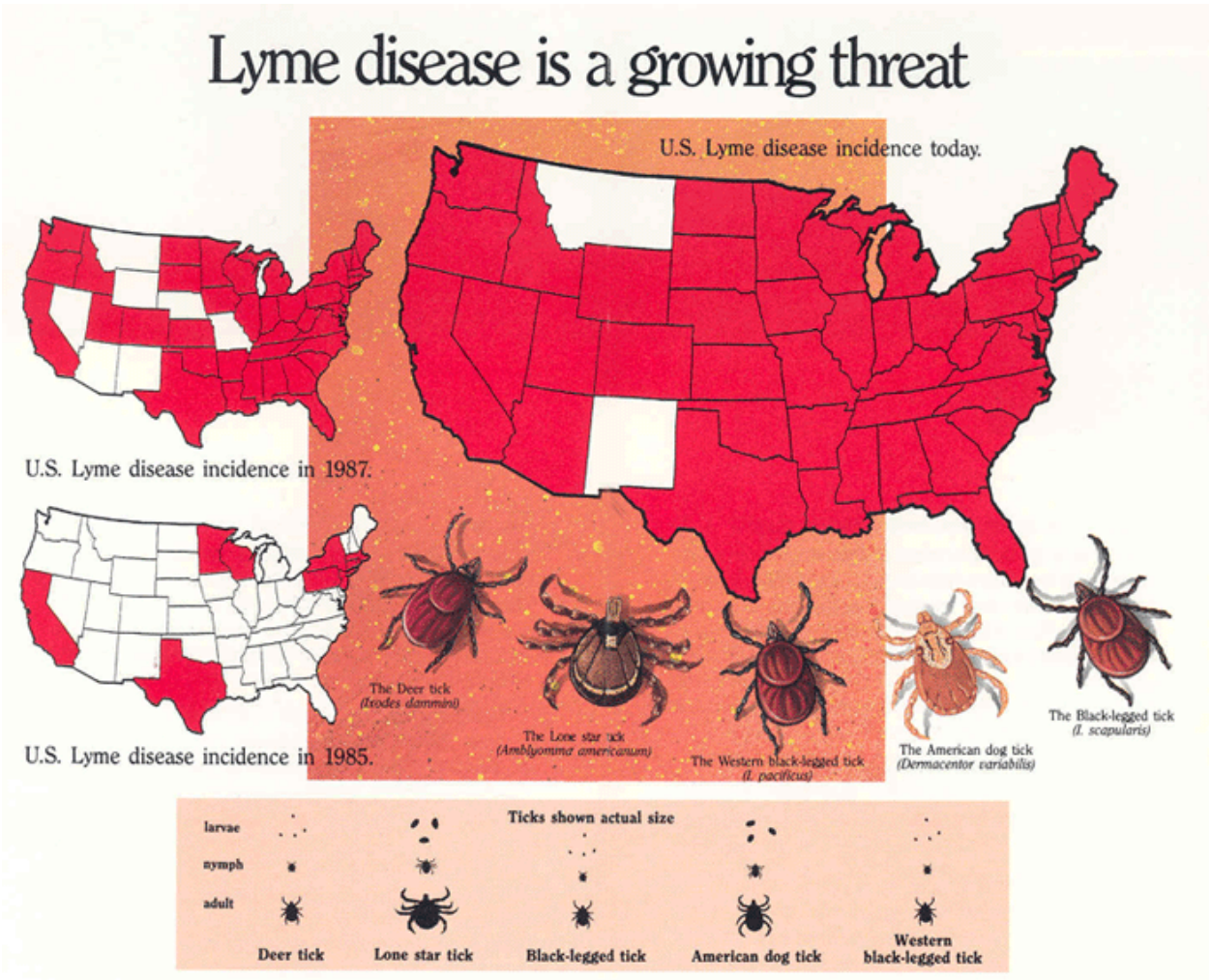


Figure 21. Maps Showing the Increasing Prevalence of Lyme Disease in the United States Over the Past Two Decades.

http://www.avhnj.com/nss-folder/pictures/lymemap.gif.

Education

One of the main roles a health care professional must fill is the role of educator. If a physician or veterinarian simply treats a patient for an ailment and never takes the time to educate that patient or patient's owner, they have not fully done their job. It is essential to make people aware of the health risks they face in order to help them create a disease-free life style for

themselves. Treatment alone may work over the short term, but education is needed in order to ensure a reoccurrence of disease or re-infection in the future. Many times this education entails recommendations for behavior modification. While interviewing faculty members from Cummings School of Veterinary Medicine, in addition to a small animal veterinarian and the State Public Health Veterinarian of Massachusetts, the reoccurring theme of our discussions was education as a means of disease prevention and control. Dr. Catherine Brown of the Massachusetts DPH described how the Principle of KBA (Knowledge, Behavior, and Attitudes) affects prevention of disease. She explained that Lyme disease is still on the rise in humans, even though it is a widely known and well studied disease. The main factor that contributes to its continued state as an uncontrolled infectious disease is that it is not a fatal disease in most cases and therefore has been given lower priority in comparison to health risks such as cancer.

In order to spread education and awareness of Lyme disease to our college campus, the IQP team put together an educational flyer. This flyer contained the basic facts about Lyme disease in humans and dogs and important information on prevention. The flyer was distributed at the Pre-Health Formal dinner to Pre-Health students and Biology department faculty members and distributed at the WPI Health Services office. A representative from the Health services office welcomed the educational flyers and said, “Education- that’s what we’re all about!”

Lyme Disease

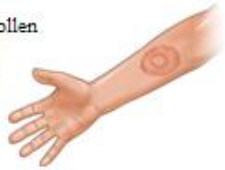
Deer Tick (Nymph & Adult)—Common carriers of *Borrelia burgdorferi*, the bacteria that cause Lyme disease.

Prevention for you and your dog

Lyme in Humans

Signs & Symptoms

Common Early Symptoms
- Fatigue, Chills, Fever, Joint Pain, Swollen Lymph Nodes
- *Erythema migrans* -"Bull's eye" rash around bite site →



Late Disease Symptoms
- Facial Palsy - drooping of one side of the face
- Arthritis and inflammation of large joints (especially the knees)

Treatment

- If diagnosed early, the most common course of action is a 2-4 week oral antibiotic treatment.
- If symptoms persist, an aggressive intravenous regiment of antibiotics may be recommended by your physician.

How to Protect Yourself

- Avoid tick infested areas
  - Ticks prefer densely wooded areas with tall grass and heavy ground leaf coverage
- Wear lightly colored clothing to make tick identification easier
- Wear a hat, long-sleeved shirt, and tuck your pants into your socks
- Use Insect repellent containing DEET on clothing and exposed areas on your body
- Do a thorough body check for ticks everyday, and remove ticks immediately

- Tick populations are most active during the months of **May, June, and July**

Lyme in Dogs

Signs & Symptoms

- Lameness
- Arthritis
- Anorexia
- Fever

*Symptoms take weeks to months to set in

*Many of these symptoms are also common to other tick-borne diseases

Treatment

- Doxycycline, 10 mg/kg by mouth, once daily for approximately 30 days
- Inexpensive
- Anti-inflammatory properties
- Dogs respond quickly to this treatment

How to Protect Your Dog

- Preventic™ Collars
- Frontline™
- Advantix™
- Check your dog daily for ticks and remove them immediately if found
- Talk to your Veterinarian about whether or not your dog is a good candidate for the canine Lyme vaccine
- Best method of protection is using multiple preventative products together

---

Tick Removal

- Using a fine set of forceps or tweezers, clasp the tick at the base of the skin →
- Pull up slowly until the whole tick is removed. Do not twist.
- Place the tick in a sealed container for future testing.
- Clean the bite site with an antiseptic (70% Alcohol).
- Continually clean and monitor the bite site

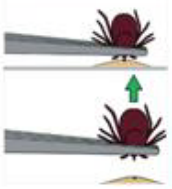


Figure 22. Handout that was Generated to Educate the Public on Human and Canine Lyme Disease and its Prevention.

Human and Canine Overlap

As with many other zoonotic and vector-borne diseases, there is more than just one side to this disease. Treating a person or dog that presents with Lyme disease only solves half of the problem at hand. Unless prevention and control methods are put in place and applied, the disease will continue to spread. Where the disease originates from and how it is transmitted needs to be taken into consideration in order to proactively prevent the disease. Establishing a method for controlling the movement of Lyme disease from its reservoir hosts, to a human or dog is required in addition to treatment of the disease itself. However, while attempting to accomplish this, the impact any of these control methods might have on the environment must be taken into consideration as well.

When the IQP team met with Dr. George Saperstein from the Cummings School of Veterinary Medicine, Dr. Saperstein stressed the importance of a "One Health" approach to medicine that is essential for the control of all zoonotic diseases. He explained that this approach strives to maintain the health of humans, animals, and ecosystems all together. Since humans, animals and the environment all impact each other, working towards optimal health for all three will create a healthier world for everyone.

While Ben researched all aspects of Lyme disease in humans, and Carrie researched all aspects of Lyme disease, many overlaps were found. Some of the symptoms experienced by humans were similar to the clinical symptoms that dogs exhibit as well. Diagnostic methods and testing were also similar with the use of ELISA blood tests, and treatment using antibiotic regimens is almost identical in both species. While discussing these similarities and differences, the IQP team decided to create a Venn diagram of the human and canine overlap in Lyme

disease. This is just further illustration of how vital it is to understand some aspects of veterinary medicine as a human physician, and vice versa.

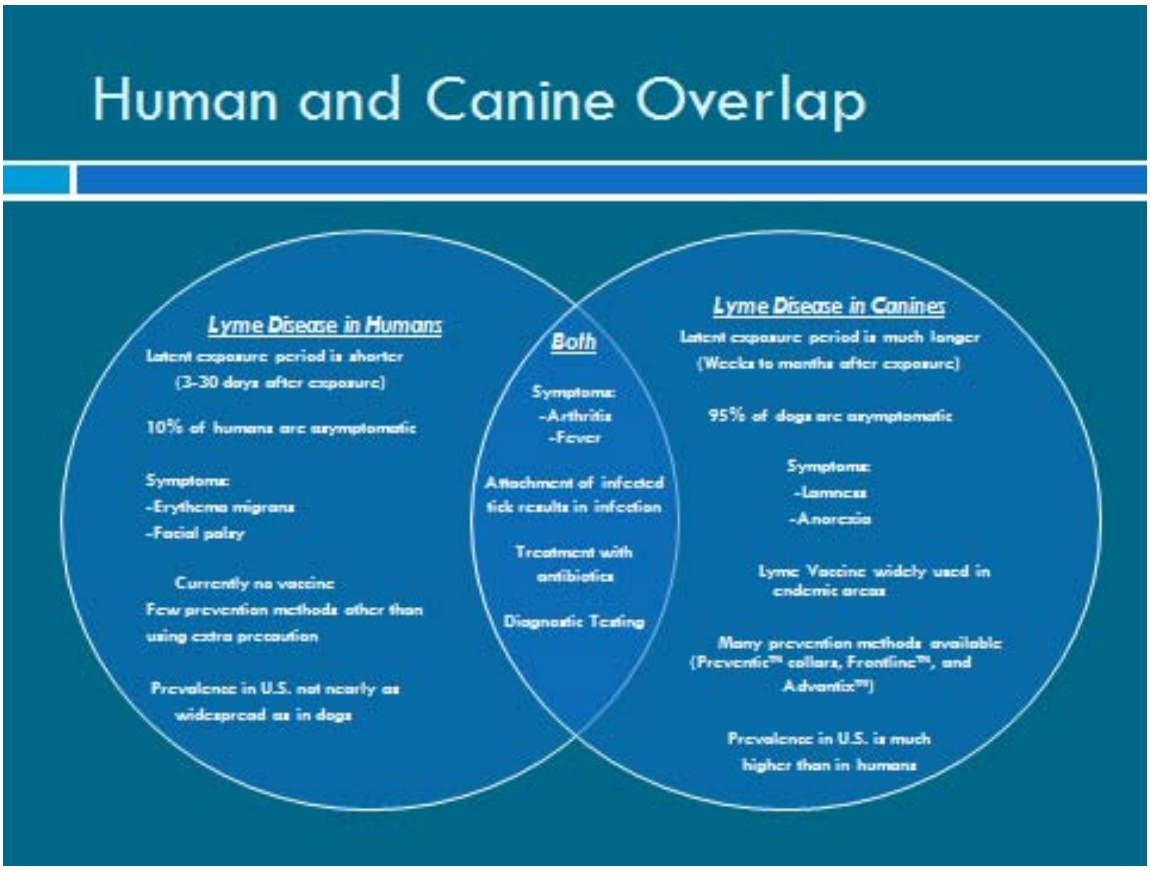


Figure 23. Venn Diagram of Human and Canine Lyme Disease Comparison.

Interactive Project Element

At a dinner held by the Mu Sigma Delta Pre-Health Society at WPI, on April 20th, 2010, the IQP team gave a lecture on Lyme disease. In attendance were Pre-Health students, mainly Pre-Medical and Pre-Veterinary students, as well as WPI Biology and Biotechnology Department faculty, and some Health care professionals from the community. The Health care professionals were a mix of human medicine and veterinary medicine professionals. The IQP

team decided this would be an excellent forum for discussing a disease that is so widely acknowledged yet continues to be on the rise.

Figure 24. IQP Team giving a talk on Lyme Disease at the Pre-Health Formal Dinner at WPI.

Not only were all facets of Lyme disease in both humans and dogs discussed, but the IQP team also stressed the importance of education as a prevention method of disease and the importance of an overlap in human and animal medicine. A PowerPoint presentation was made from all of the compiled research. While the IQP team had the attention of local doctors and veterinarians as well as future doctors and veterinarians, the ideal opportunity was discovered to share the relevant information found while researching zoonotics and Lyme disease. After giving some background on zoonotics, history of Lyme disease, and explaining how it is transmitted, Ben discussed how a *Borrelia burgdorferi* infection affects humans. Carrie then took over and

explained how a Lyme infection is dealt with when a dog presents to a veterinarian with the common clinical symptoms of Lyme disease. The IQP team wrapped up the lecture by speaking about the importance of education when controlling disease and preventing infection or even re-infection. Also discussed was the need for a greater synergy between human and animal health care in order to combat zoonotic diseases, which are currently on the rise.

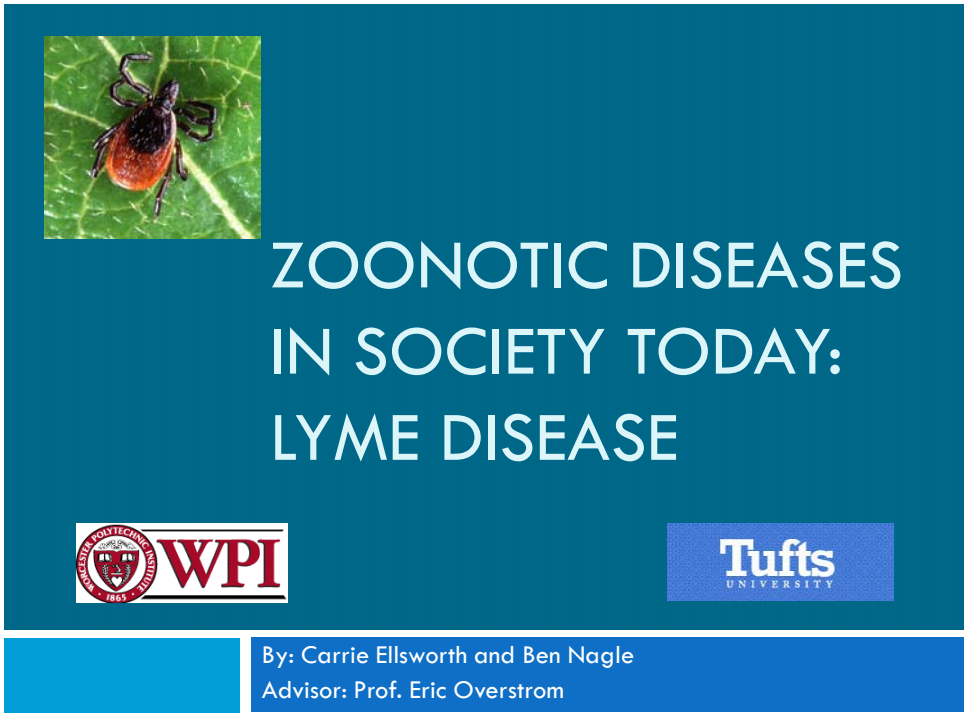


Figure 25. Title slide of PowerPoint presentation on Lyme Disease.

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Appendix

1.) Interview with Dr. Giovanni Widmer from Cummings School of Veterinary Medicine at Tufts University

Questions for Dr. Widmer:

CARRIE

-What specifically interests you about zoonotic diseases?

-Do you believe that the importance of educating people about zoonotic diseases has been understated in current society especially due to its prevalence right now?

-What do you believe is the greatest contribution to the spread of zoonoses?

-What do you consider to be the greatest zoonotic threat facing the world today?

-Do you believe that more emphasis should be put into studying emerging animal diseases and pathogens to prevent their possible spread to humans in the future?

-(If yes) What specific area of zoonoses should be more extensively studied?

-Can you tell us about the research you are currently working on with Cryptosporidium and Giardia and what you are hoping to achieve?

-How effective do you believe the giardia vaccine is in terms of reducing the spread and re-infection of giardia?

BEN

-What other medical methods, besides vaccination, have proven to be affective against the spread of zoonotic derived diseases?

-Who controls the distribution and production of vaccines? Is it strictly the federal government, or are there private companies authorized to produce vaccine?

-What are the regulations for the importation of live/butchered animals into the US? What are the policies in other countries?

-What are the socioeconomic effects of a global zoonotic disease pandemic?

-How do different countries deal with epidemics and are those methods successful?

-When studying virulent Zoonotic pathogens in the lab, what security measures must be taken?

-What do you believe is the most effective method for controlling the spread of zoonotic derived diseases?

Notes from Meeting with Dr. Widmer: 12/11/09

-Level 2 Lab on campus not yet up and running so people are allowed to walk through

Current Research:

-Cryptosporidia

- What genes determine certain properties/ which genes confer certain traits
- Investigating treatments options
  - Cell line which works as indicator
  - Fluorescence stain
  - Episome (plasmid) transfected
  - Promoter responds to presence of protozoa

-Giardia

- High throughput system
- Molecular markers test cysts
- Micro-ray analysis
- Vaccine most likely passive and introduces fixed tropozoites to body

Focus of paper:

- -Specific area of the world
- -Form of transmission
- -Emergent diseases (ex. Ebola)
- Host range (predicting path /mutations)

Major Contributors to spread of zoonoses:

- Movement/ importing of animals
- New types due to immune-compromised patients
- Environmental degradation
- Deforestation
- Antibiotic resistance of livestock due to over use
- Difficult to control

*Preventative measures important in aiding in reduction of zoonoses

-Influenza strains are the greatest zoonotic threats today because they easily and quickly mutate and because of antibiotic resistant bacteria

-Education helped reduce the spread of HIV

-Current technology is not keeping us from discovering new emerging pathogens

Examples of interesting areas in zoonotic disease:

- Rift Valley Fever (Africa)
- Sleeping Sickness (Africa)
    - Sterile male Tse Tse flies used to compete with fertile males and decrease tse tse fly population
- Origin of Malaria (Evolutionarily)

2.) Interview with Dr. George Saperstein from Cummings School of Veterinary Medicine at Tufts University

Questions for Dr. George Saperstein:

-Tell us about your research that you did in Asia with the avian flu.

-I read that you have also done some work in the Middle East to control the spread of disease in livestock. Could you tell us what specifically you were working with there?

-I saw that listed under your general research areas was xenotransplantation. This is a term that came up a couple times during my research and I was very interested in exploring. Can you tell us a little bit about that?

-Do you believe that the importance of educating people about zoonotic diseases has been understated in current society especially due to its prevalence right now?

-What do you believe is the greatest contribution to the spread of zoonoses?

-What do you consider to be the greatest emerging disease facing the world today?

-Do you believe that more emphasis should be put into studying emerging animal diseases and pathogens to prevent their possible spread to humans in the future?

-(If yes) What specific area of zoonoses should be more extensively studied?

- It seems like emerging infectious disease scares disappear from public concern over time (ex Bird flu, SARS, and more recently H1N1). Is this due to the success of Public Health Organizations, or just the natural decline in the prevalence of the pathogen? Dose the media play a role?

- It seems like we were successful at controlling the recent H1N1 outbreak. In your opinion why were we successful and what could we have done better?

- As a veterinarian, how would you go about reporting an incident of a potential threat to public health? Who are the governing bodies in Public Health at the local, state, federal, and global levels?

-What other medical methods, besides vaccination, have proven to be affective against the spread of zoonotic derived diseases?

-What are the regulations for the importation of live/butchered animals into the US? What are the policies in other countries?

-How do different countries deal with epidemics and are those methods successful?

-What do you believe is the most effective method for controlling the spread of zoonotic derived diseases?

Meeting with Dr. Saperstein: 1/25/10

-Animals-> Humans-> Animals transmission possible

Ex. MERSA

-USDA in charge of keeping animals (especially livestock) healthy

Developments that contributed to decrease in spread of zoonoses/ would help:

-sewer systems

-chlorination of water

*Emphasis switched from infectious disease to non-infectious diseases/ health concerns

(ex. cancer and smoking)

Funding is provided to fix problems not prevent them

*Infectious disease control in animals (livestock) means greater profit for agriculture workers

In veterinary medicine the current trend is prevention of disease instead of treatment

(Breeding is being done to prevent disease)

*In 1900's USDA attempted to eradicate brucellosis and tuberculosis (both transmitted around or through milk)- programs that were established to do this are still in existence even though both have been almost completely eradicated

*Animal exports are huge in US so public funds are allocated to animal health- this money goes to efforts to keep out diseases we don't have (ex. Foot and Mouth Disease)

*17% of US population has jobs that depend on agriculture

*Economics play a big role in disease control because of the impact a disease outbreak could have on importation/exportation business

2 Mammalian Sources of zoonotic diseases:

-domestic animals

-wildlife (most most from these)

Agroterrorism= sabotage of livestock health (bringing in Foot and Mouth disease)

Dr, Saperstein's work with H5N1 (Avian Flu) in Indonesia:

-still a threat

-media is simply tired of covering it and human mortality rates have dropped

-still prevalent in Indonesia and Egypt (Dr. Saperstein worked on program in Indonesia)

-Vietnam and Thailand were able to control H5N1 quickly

-Dr. Saperstein's job was to train animal workers and veterinarians how to respond to the disease and how to control the spread of it

*He had to work with the native peoples' superstitions and respect their culture while introducing the science concepts behind the spread of zoonoses and educating the people

*70% of Indonesian people keep birds in their domestic setting

What made H5N1 such a problem in Asia?

-The disease was spreading from commercial to domestic animals

-Many humans were in very close contact with the diseased birds

-The H5N1 reservoir was in animals but people were more concerned with treating humans even though it is cheaper and more effective to treat the birds that were spreading the disease before it jumps to humans

*In the 1980's the USDA killed a flock of birds found in Pennsylvania that were infected with H5N1- utilizing the "Stamping Out" method of dealing with an outbreak

*Areas where zoonoses are most likely to spring up are areas that have a large wildlife population and the humans are encroaching on the wildlife habitats- these areas also have little infrastructure for dealing with disease outbreaks

*Veterinarians in these "hotspot" areas need to be educated

****"One Health Approach"** = maintaining the health of Humans, Animals, and Ecosystems all together

Dr. Saperstein's work in the Middle East:

- Part of the Camp David Accord with Egypt and Israel was that the US was to provide resources to improve livestock health and productivity (Palestine and Jordan were also added to this agreement because they were not as sophisticated as Egypt and Israel)

-spread of diseases in Middle East is so prevalent because of the clustered boarding countries, the nomadic culture of the people with their ruminant livestock

-Research and work was mainly directed at Foot and Mouth disease, Brucellosis, and small ruminant health issues (neonatal diseases)

Xenotransplantation:

-In the 1970's experiments began with transplanting primate organs in humans

-ethics was a concern because primates were being killed for their organs

-the primate organs did not work well and were rejected

-experiments began with swine organs because they are the next most anatomically similar non primate animal (less concern with ethics is the pig would have been sent to slaughter anyways)

-The sugar α-gal is present on the surface of all swine cells however and human's cells do not recognize these so organs were rejected

-breeding of pigs without α-gal on their cell surface began (some was even being done at Tufts)

-neurons were also being harvested from fetal pigs to be injected into the brain of late stage Parkinson's disease patients to bridge gaps in neuronal impulse propagation

-then islet cells from fetal pigs were being harvested to transplant into diabetic patients pancreas'

-swine livers were being used to cleanse human blood in patient with liver failure

*Many of these experiments did not get past FDA approval phase trials because there was not enough conclusive evidence

<u>Endogenous retroviruses**</u>= pieces of old viruses that are part of our genomes

<u>Reporting Zoonotic Diseases in Animals:</u>

-If a veterinarian treats with antibiotics they could create animals who are carriers for the disease

-Are the animals economically or medically worth treating?

-Diagnostic labs should compile data and report cases

-USDA inspects slaughterhouses at critical control points (Hazard Analysis)

-Real time PCRs performed in plants to test food products

Ways to prevent the spread of disease:

-Vaccination

*Ring vaccination (vaccinate hotspot areas only instead of widespread vaccination)

*Plum Island, NY maintains banks of vaccine concentrate TOP SECRET

-"Stamping Out" method

*Mass Emergency Management Agency

*1929 was the last outbreak of Foot and Mouth in the US and it occurred in Mass.

<u>Risk Communication:</u>

-not presenting the facts or accurate risks

-attempting the squelch panic

-media will twist medical professional's words and misconstrue the facts

*Import/export of animals covered by USDA-APHIS

*World Trade Organization deals with animal products (tariffs)

*World Animal Health Organization (OIE) sets standards for animal disease control

1918 Spanish Flu Pandemic had possible origins in animals and was spread during WWI due to the transportation of soldiers between continents

**Educating public about zoonoses is vital but physicians need to be better educated as well

**Need a better mix of Human and Animal Health

3.) Interview with Dr. Jean Mukherjee from Cummings School of Veterinary Medicine at Tufts University

Meeting with Dr. Mukherjee: 1/27/10

Her background:

-educated in microbiology and immunology

-regulatory and selective agent work

-monoclonal antibodies and small molecule therapeutics

Other Zoonoses that a prevalent in New England area:

-Leptosporosis

-E. coli

-Salmonella

-Staph

What to cover in our project:

-Biology of Organism

-Where it is in population

-How it is transmitted

-Tests for pathogen

*What are they testing? (Antibodies or antigens)

-Differences between human and animal infection

-How the organism and its host interact

Preventative measures and Treatment options:

-Tick prevention

*Frontline

*Advantage (imidacloprid)

*Revolution (selamectin)

*Program and Sentinel tablets (lufenuron)

-eradicate white-footed mice and deer

-get rid of ticks

-antibiotics (Doxycycline)

-Lyme vaccine

*Lyme vaccine currently in use for animals was once used for humans but was taken off the market for humans

4.) Conference Call with Dr. Catherine Brown, State Veterinarian for The Massachusetts Department of Public Health

Questions for Dr. Catherine Brown

What is your role in the Mass DPH?

How closely do you work with other state health officials in the region to combat regional threats to public health?

Who falls under your jurisdiction, and who would you report up to about matters pertaining to emerging infectious diseases?

Do you see any flaws in the public health system, and if so how can they be addressed?

Have zoonotic diseases presented a major problem for the state, over the past few years?

Where does Lyme disease rank on your priority list as an emerging infectious disease?

What measures has the state taken to try and limit the spread of Lyme disease? How effective have these methods been?

Are you familiar with the LIMErix vaccine for *Borrelia* bacteria, and if so why was it taken off of the market? Is there another vaccination in progress?

What are some of the most pressing issues you are faced with in your job?

What are some of the most prevalent zoonotic diseases in Massachusetts and are they different from neighboring states?

Which zoonotic diseases do you continue to see and increase in and are still in the process of being controlled?

Are there any zoonotic diseases that you predict we will see an outbreak in in the near future?

Which wild animals present the biggest risk in terms of spreading diseases in Massachusetts?

What types of restrictions and regulations does the state put on petting zoos and other areas where exotic animals are housed to prevent the spread of diseases or introduction of new diseases to the area?

Can you tell us about the work you are doing with rabid coyotes and what advancements you are hoping to make or have made?

What is the protocol for dealing with an animal that is suspected to be rabid?

Once an animal tests positive for rabies what measures are taken next?

What has been done in Rabies-free areas of the world to keep out or eradicate the disease?

What can you tell us about the prevalence of Lyme disease in Massachusetts?

Conference Call with Dr. Catherine Brown: 2/10/10

State Public Health Veterinarian:

-responsible for overseeing surveillance and education of public

-collects data, analyzes, figures out what risks are posed to humans, and educates people

*Lyme disease tends to be separated out from zoonotic diseases with other vector-borne diseases

Main Zoonoses and Vector-Borne Diseases in Mass.:

1. Rabies

-2-3 human deaths per year due to rabies

-1985 was last case of Rabies in Mass. And individual was infected outside of the state

2. Lyme

-affects more individuals than Hepatitis A and B combined

3. Tularemia

-Prevalent in Martha's Vineyard

4. Eastern Equine Encephalitis (EEE)

*120 infectious diseases in Mass. , 42 of which are zoonotic

Home Rule (Local jurisdiction)

-351 towns and each have their own local health dept

-each town has different protocols, opinions, and priorities

Mass. Department of Public Health (State jurisdiction)

CDC (Federal jurisdiction)

No database to record diseases- human patient confidentiality prevents reporting most human diseases

Reportable human diseases are reported to the DPH

Reportable Animal diseases are reported to the Agriculture Dept

*4 Reportable animal diseases- West Nile Virus, EEE, plague, and anthrax

Lyme Disease:

-Ecological factors

*deer and mice populations

*human habitats

-humans indirectly responsible for spread

-people must take personal actions

*wearing long sleeves and pants

*using tick repellants

*checking for ticks

*Ecological modifications often lead to negative consequences

KBA (Knowledge Behavior and Attitudes)

-pesticides (expensive)

-not fatal disease

-more concerned about other diseases or health threats

*Climate change and distribution of different vectors

Enteric Zoonoses most common- salmonella and E. coli

Rabies:

*Bats pose biggest risk

*Can only test for Rabies post-mortem

*Many island countries have never been exposed to Rabies and have managed to keep it out

Behavioral signs of Rabies:

-Furious Rabies (Aggressive)

-Dumb Rabies (Sleepy)

* Oral vaccine used for raccoons in Cape Cod

*From the 1950's to now huge improvements and advancements have been made with Rabies Human Vaccine:

-3 series

-Unpopular

-came out during anti-vaccine movement

-adverse reactions

-reluctance to undertake project again due to failure

-made no money

-no vaccine is currently close to clinical trial stage yet

Imported Animals:

-strict regulations on testing

-quarantine period before being put in with other animals

-lots of hoops to jump through to import animals

-illegally imported animals are a larger and growing problem

*Dept. of Agriculture

*USDA

*Dept. of Fish and Game

Mass DPH offers recommendations to petting zoos in order to prevent spread of disease

*Salmonella outbreak in Mass. School due to owl pellet dissection

5.) Electronic interview with Dr. Tanya Battiston DVM who is co-owner and practitioner at a small animal practice in Farmington, CT

Questions for Dr. Battiston: 3/17/10

-How do you educate your clients about Lyme disease?

We spend a lot of time educating clients on prevention, control, etiology, signs, testing and treatment of Lyme disease. Our clinic has composed a protocol based off of the 2006 ACVIM consensus on Lyme disease. We give clients this handout and follow the protocol (see attached). We also discuss potential complications from the disease as well as availability of vaccinations to prevent disease. We stress tick control as the hallmark of prevention for Lyme disease. We also explain that we need to test for Lyme disease, via 4DX, each year before vaccinating.

-What suggestions do you make to your clients for how they can attempt to prevent their dog from contracting Lyme disease?

We explain that there is no method that is 100% at preventing Lyme disease in our Lyme endemic area. Tick control, avoidance of tick habitats, careful landscaping, and daily checking for ticks is paramount in prevention. Vaccination should be considered in high risk animals. As deer ticks can be active year-round in our state, topical product to kill/repel ticks,

such as Preventic (amitraz) collars +/- Frontline (fipronil), Revolution(selamectin), Advantix (imidicloprid/) are recommended year-round.

-What procedure do you normally follow when you have a dog present with the signs and symptoms that a veterinarian would associate with Lyme disease?

If history and physical examination findings are consistent with Lyme disease, we run a fast and easy, in-house blood test to confirm exposure (IDEXX 4DX snap test). This tests for presence of a C 6 peptide that is present only in natural exposure or infection. If this test is positive, we will run a Complete blood count, Serum Chemistry, urinalysis, and a Lyme Quantitative C6 peptide. If positive for Lyme and symptomatic, we usually prescribe a 30 day course of Doxycycline +/- pain medication for comfort. We would then screen this dog **every 6 months,** for life, with a urinalysis and C 6 Quantitative analysis. Our hope is that we will be able to identify, treat, and control dogs with active chronic Lyme, recrudescence of Lyme, or re-infected dogs.

What types of tests would you run?

See above

-If a dog tests positive for Lyme disease how do you go about treating them and what recommendations would you make to their owner?

(See above) We treat the dog with a 30 day course of doxycycline, and then recheck the Lyme quantitative C6 +/-, a CBC, and urinalysis every 6 months to monitor, and retreat as symptoms recur.

-Can you describe the Lyme vaccination protocol you follow for dogs at your clinic? Why do you cease administering the Lyme vaccination to a dog that has tested positive for Lyme?

*Lyme vaccine protocol would be started at 9 weeks of age or older with a series, starting with an initial vaccination followed by a booster 3 to 4 weeks later. If we start the vaccine at 6 months or younger, we do not need to Lyme test prior to vaccinating. We then recommend retesting via 4DX every year prior to giving a booster. Lyme is not a core vaccine as determined by the AHAA vaccine guidelines for veterinarians. As with any non-core immunization we have discussions of risk verses benefit with the owner. We do not usually start adult dogs with Lyme vaccination as 70-90% of dogs in Connecticut have already been exposed.

We **do not** vaccinate dogs who have tested positive for the Lyme. An infected dog, in theory, could be at higher risk for complications if they were given a vaccine when their immune system is already exposed, and fighting the infection. We are concerned about auto-immune consequences. This is exactly why we screen dogs for Lyme on the dog of their vaccination.

-Do you keep track of how many dogs that are patients at your clinic contract Lyme disease on a yearly basis? Have you noticed an increase in the number of Lyme positive dogs?

*No, we do not specifically track the dogs that contract Lyme disease on a yearly basis. However, we issue computer-generated reminders to clients who have patients with Lyme disease. The reminded is every six months to have their animal's Lyme C6 levels and urinalysis evaluated.

*Subjectively, we have noticed an increase in the number of asymptomatic dogs that test positive when we routinely test for Lyme disease via 4DX before re-vaccinating. Most dogs in Connecticut will be exposed at sometime in their life

-Why is it that you don't hear much about cats getting Lyme disease? Are they able to contract the disease and just don't exhibit the symptoms that dogs do?

*Cats can get Lyme disease, although it is extremely rare. Cats can seroconvert, but usually do not develop symptoms.

-Do you believe that increased public education on Lyme disease would help decrease the prevalence of the disease (both in humans and animals) in the United States?

Educating people on tick control, avoidance of tick habits, regular tick checks and removal, as well as Lyme disease are important steps. As a veterinarian, I believe that our hospital educates the public as well as possible relating to Lyme disease in dogs. I would like to see more human-related Lyme awareness from the human medical sector.