CANINE BORRELIOSIS

VECTOR BORNE DISEASE

MSD Animal Health

DR. KATHRYN REIF

Dr. Kathryn Reif is an assistant professor at the Department of Diagnostic Medicine/Pathobiology in the College of Veterinary Medicine at Kansas State University. Her primary research interests center around the control and prevention of ticks and tick-borne diseases important to companion animal, livestock and human health. Current research projects include evaluation of antimicrobial treatment efficacy for anaplasmosis, tick-borne pathogen vaccine development, assessment of tick-borne pathogen genetic diversity, and development of novel techniques to study tick feeding and pathogen transmission. In addition to research pursuits, Dr. Reif enjoys outreach opportunities with the general public and health professionals to discuss the risks of ticks and tick-borne pathogens and tick safety.

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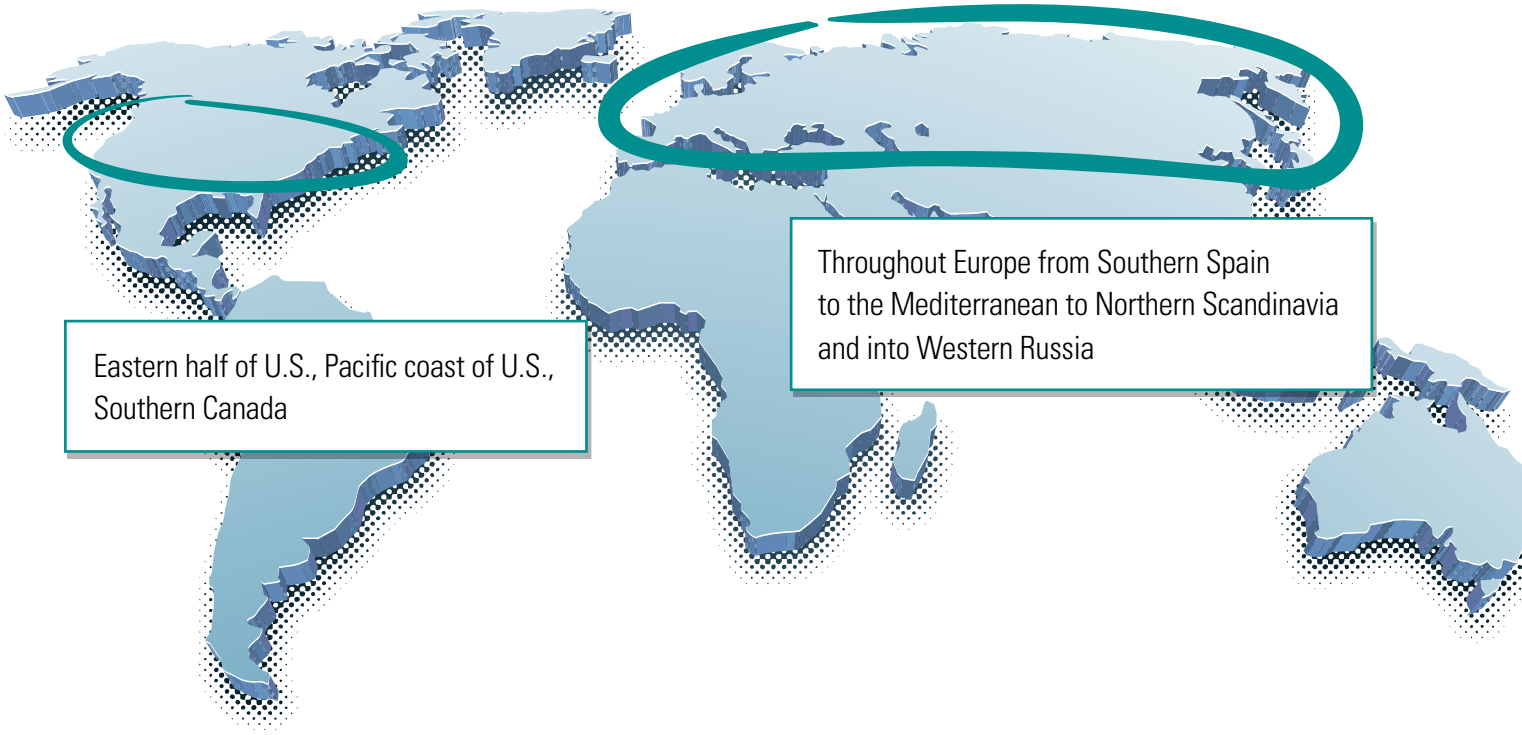
WHERE IS THE DISEASE MOST LIKELY TO BE FOUND?

Canine borreliosis (Lyme disease), caused by *Borrelia burgdorferi* sensu lato species, is the most common tick-borne disease of dogs and humans in the temperate northern hemisphere.

Geography

The primary factor driving the geographic distribution of this disease is distribution of the tick vector species which favor temperate climates. The geographic distributions of tick vectors responsible for transmitting canine borreliosis extend over expansive ranges in **North America** and **Eurasia.**



Within a given geographic area the following factors collectively influence the risk of canine borreliosis:

- Altitude
- Latitude
- Distance from water body
- Temperature
- Humidity (saturation deficit)
- The density and type of host species available to support tick populations
- The density and type of reservoir species available to support *B. burgdorferi* s.l. maintenance.

WHERE IS THE DISEASE MOST LIKELY TO BE FOUND?

Local environment

Within a local environment, tick vector populations have a heterogenous distribution. These tick vector species are most commonly encountered in deciduous or mixed-wood areas that provide favorable habitat for ticks (ambient temperatures and humidity) as well as tick host and *B. burgdorferi* s.l. reservoir species.

Disease risk is highly correlated with tick seasonality and activity.

- Tick encounter risk varies by season, with **adult *Ixodes* species preferring cooler spring and fall months and juvenile stages preferring warmer spring and summer months.**
- The specific months of greatest tick risk vary regionally areas based on local climate differences **(tick activity is common in temperatures over 4°C / 40°F).**

Suitable tick habitat can occur in rural, suburban and urban areas. Dogs and people encounter ticks by brushing against grass or other vegetation where ticks await while questing for a host. Areas with vegetative growth in or near tree canopy overhang and containing vegetative litter overlaying moist soil (e.g. trail edges, landscape edges) are common areas for tick encounters.

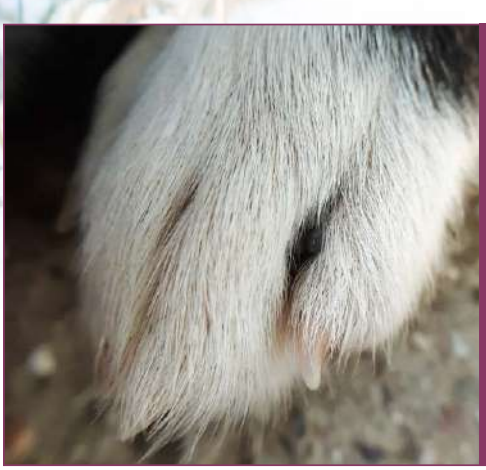
Dogs walking along paths bordering vegetative areas are at risk for tick exposure.

Favorable climate conditions

Canine borreliosis is most commonly reported in temperate global regions with climates suitable for supporting the associated tick vector species.

Humidity and host species availability are factors that greatly influence the population density of the primary tick vector species as these vectors are easily susceptible to desiccation and require hosts to feed upon to progress through their life cycle, respectively.

WHERE IS THE DISEASE MOST LIKELY TO BE FOUND?



Seasonality to the risk of encountering infected ticks

Several environmental variables (e.g. temperature, humidity, host availability, photo period) influence when different tick life stages are actively host-seeking.

The length of time the tick spends questing depends on environmental humidity; ticks can spend more time host-seeking in shaded or protected areas where humidity is greater. Once a tick loses 4-5% of its body moisture, it returns to the ground litter to begin the energy-expensive process of rehydrating before recommencing host-seeking.

Habitats

In general, *Ixodes* species prefer deciduous or mixed-wood forested habitats with dense understory vegetation compared to coniferous habitats. Outside of host-seeking periods, ticks reside in protective microenvironments within understory vegetation in a quiescent state of low metabolic activity termed diapause waiting for environmental conditions to become favorable.

Evidence of infection/disease spread

Increasing and expanding populations of tick vector species are contributing to the increasing spread of canine borreliosis. For example, in North America, geographic distribution of the primary tick vector has more than doubled over the last 20 years. In North America, historic endemic regions included New England and the upper mid-west in the United States; however, the disease is now endemic in most northeastern and mid-Atlantic states and is moving into the Southern Midwest region and westward towards the Great Plains.

Historically endemic areas are experiencing seroprevalence stabilization in dogs or even reduction, however, seroprevalence rates in these areas are still high. Canine borreliosis is now well-established in **Southern Canada** introduced through tick translocation by migratory birds. A warming climate and plentiful host species with ticks enable tick vectors to survive and establish populations in areas north of their previous range limit.

WHERE IS THE DISEASE MOST LIKELY TO BE FOUND?

In Europe, tick vector populations have expanded northward into Scandinavia and into higher altitudes in southern regions, also beyond their historic ranges.

Variables contributing to disease spread include:

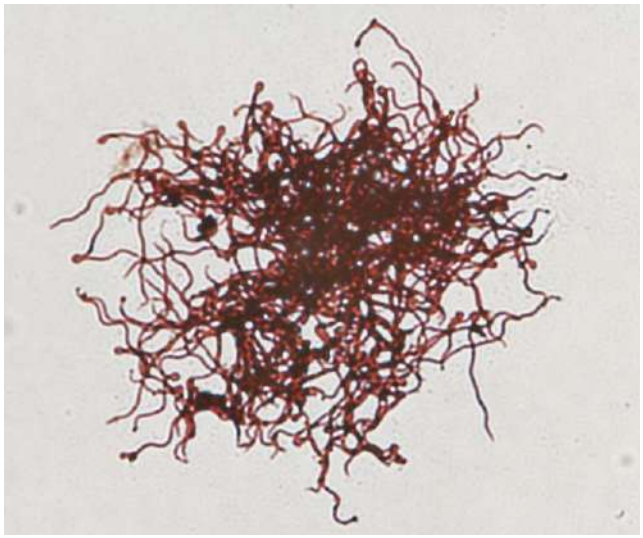
- The increasing distribution of tick vector species
- Host species abundance
- Host species movement (e.g. migratory birds)
- Land use
- Climate change

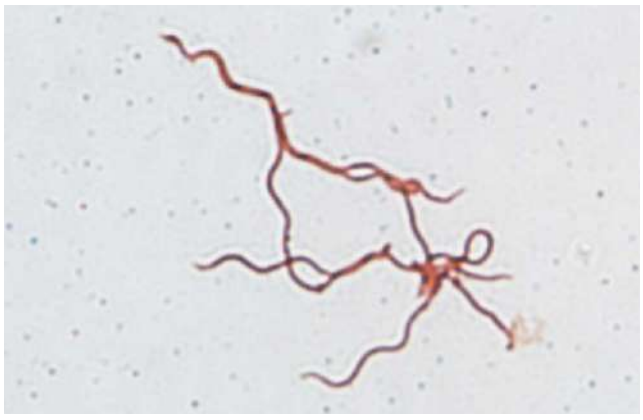
HOW DOES A DOG **BECOME INFECTED?**

An introduction to the causative agent(s)

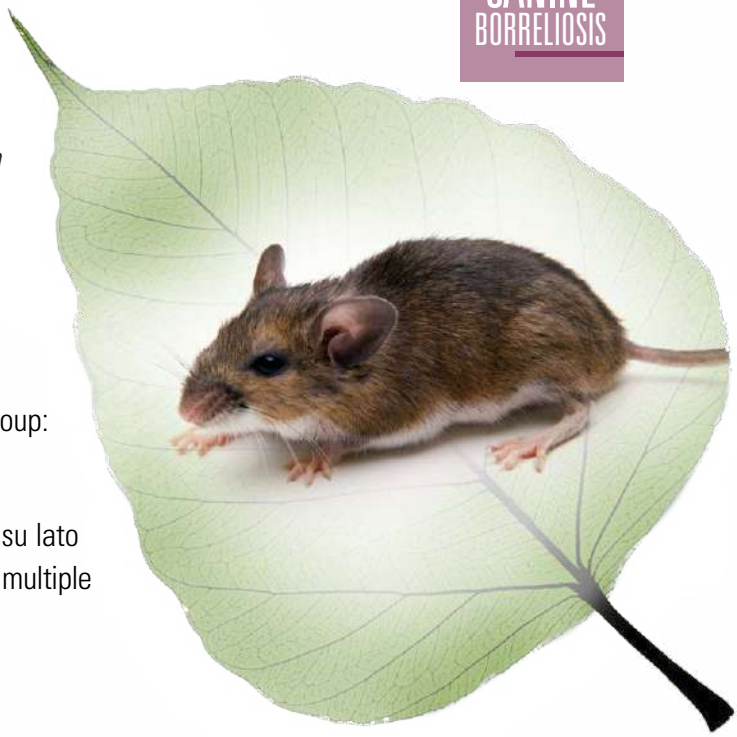
Canine borreliosis (Lyme disease, Lyme borreliosis) is a disease caused by pathogenic tick-borne spirochetal bacteria within the lyme borreliosis group of the genus *Borrelia* in the family Spirochaetaceae.

These bacteria are highly mobile, propelling themselves through the host using periplasmic axial filaments. They are slow-growing, microaerophilic spirochetes with a complex outer membrane composed of lipoproteins and a peptidoglycan layer which classifies them as Gram-negative. Both the ability to move within the host and the ability to vary the composition of their outer surface lipoproteins are important mechanisms these spirochetes use to evade host immune responses.





Borrelia burgdorferi.
Stained, culture propagated *B. burgdorferi* spirochetes (40X).



At least 53 species have been described within the genus *Borrelia* and these can be classified in three groups:

- Agents of lyme borreliosis: approximately 22 species.
- Agents of relapsing fever: approximately 29 species.
- A third genetically distinct and largely uncharacterized group: approximately 2 species, found in reptiles.

Lyme borreliosis bacteria belong to the *Borrelia burgdorferi* sensu lato (s.l.) complex which contains approximately 19 genospecies, with multiple strains comprising each genospecies **(Table 1).**

Table 1

***Borrelia burgdorferi* sensu lato genospecies: their predominant geographic locations and predominant reservoirs**		
***Borrelia burgdorferi* sensu lato genospecies**	**Geographic Location**	**Predominant Reservoir Host**
B. afzelii	Europe, Asia	Rodents
B. americana	North America	Birds
B. andersonii	North America	Birds
B. bavariensis	Europe, Asia	Rodents
B. bissettii	North America, Europe	Rodents, Birds
B. burgdorferi	North America, Europe	Rodents, Birds, Reptiles
B. californiensis	North America	Rodents
B. carolinensis	North America	Rodents
B. garinii	Europe, Asia	Birds
B. japonica	Asia	Rodents
B. kurtenbachii	North America	Rodents
B. lusitaniae	Europe	Reptiles
B. mayonii	North America	Rodents
B. sinica	Asia	Rodents
B. spielmanii	Europe	Rodents
B. tanukii	Asia	Rodents
B. turdi	Asia	Birds
B. valaisiana	Europe, Asia	Birds
B. yangtzensis	Asia	Rodents

*Genospecies detected in dogs are shaded in pink.

Vector (lifecycle)

Ticks in the genus *Ixodes* are the most common vectors of *B. burgdorferi* s.l. Over 18 *Ixodes* species contribute to the maintenance of *B. burgdorferi* s.l. species in nature; however, a handful of species serve as primary transmission vectors of these pathogens to dogs and people. Deer are perhaps the most important wildlife host species maintaining tick populations. Rodents are perhaps the most important wildlife species for maintaining *Borrelia* spp.

The predominant vectors of borreliosis are:

In North America

- *Ixodes scapularis* (blacklegged tick or deer tick)
- *Ixodes pacificus* (Western blacklegged tick)

In Europe

- *Ixodes ricinus* (Castor bean tick, sheep tick)
- *Ixodes persulcatus* (taiga tick)

The broad host range and expansive geographic distribution of these major ***Ixodes* species** underpin their success as *B. burgdorferi* s.l. transmission vectors.

In both North American and Europe, other Ixodes species may serve as vectors for *B. burgdorferi* s.l.; however, these ticks are more involved in enzootic maintenance of the pathogen and less important as transmission vectors of the pathogen to dogs or people.

Ixodes species. Attached *Ixodes scapularis* female and male.

Proportion of infected vectors

The proportion of ticks infected with *B. burgdorferi* in a given area is heterogeneous and can vary dramatically from <1% to almost 100%. The number of bloodmeals a tick has taken is **positively correlated** with infection risk.

In a given tick population, about twice as many adult ticks are infected compared to nymphs.

These ticks generally feed once per life stage, therefore a host-seeking nymph has had one opportunity to acquire the pathogen during its larval blood meal while a host-seeking adult has had two prior opportunities to acquire the pathogen during its larval and nymphal blood meals.

U.S. areas with high proportions of *B. burgdorferi*-infected ticks tend to be in the mid-Atlantic, upper Midwest, and New England areas. In Europe, countries with high proportions of *B. burgdorferi* s.l.-infected ticks tend to be in Central and Eastern Europe.

Factors that influence the proportion of infected vectors:

- The community and abundance of vertebrate host reservoirs
- Land use/land cover
- Physical environment (e.g. weather, humidity)

HOW DOES A DOG **BECOME INFECTED?**

Reservoirs

Canine borreliosis agents are maintained in nature in enzootic cycles involving competent tick vectors and wildlife reservoirs **(see table 1).**

Dogs and humans are accidental and most often dead-end hosts and do not contribute to maintaining these agents in nature. Multiple vertebrate species serve as reservoirs for *B. burgdorferi* s.l. including numerous mammals, birds and reptiles.

Infection with *B. burgdorferi* s.l. has been observed in over 300 vertebrate species; however, not all these vertebrates are equally important in maintaining *B. burgdorferi* s.l. in nature. Depending on the *B. burgdorferi* genospecies, some vertebrate hosts are more important in maintenance than others. Some genospecies have developed highly specialized host preferences and can only infect certain vertebrate species, whereas other genotypes are more 'generalists' in their reservoir species use.

Rodent species serve as primary reservoirs for most *B. burgdorferi* s.l. genospecies.

Avian reservoirs are more common for *B. garinii* and some *B. burgdorferi* s.s. strains.

Reptile reservoirs are more common for *B. lusitaniae*.

Probability of transmission and routes of transmission

The longer an infected tick is attached, the greater the probability of *B. burgdorferi* s.l. transmission.

Although transmission time may vary, transmission of *B. burgdorferi* s.l. is significantly greater once the infected tick has been attached for 36-48 hours.

About 10%	About 70%	>90%
48 hours	72 hours	if the tick feeds completely

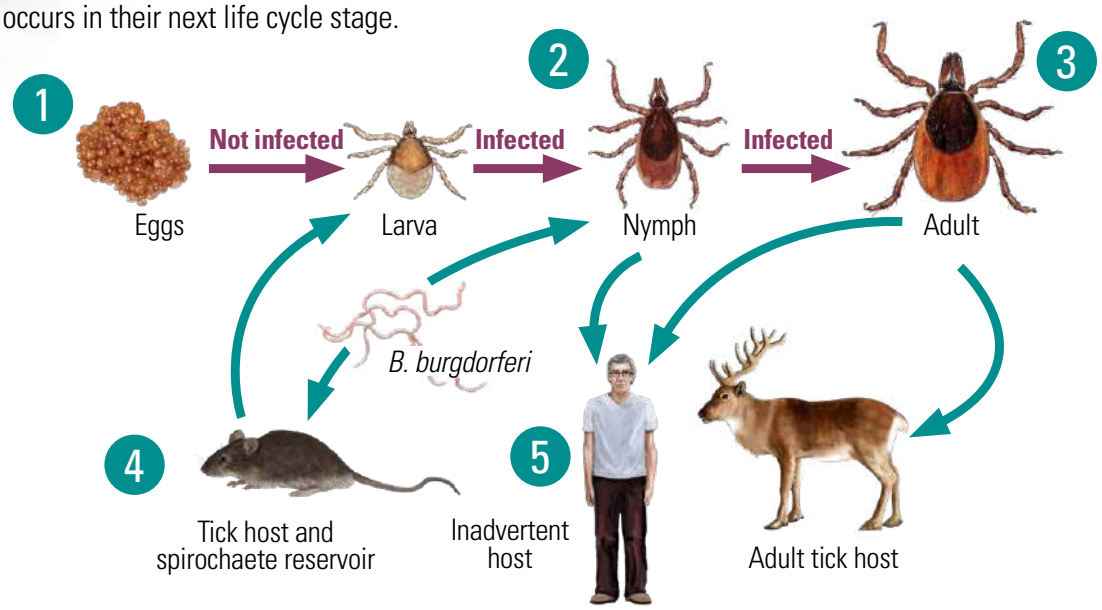
Transmission appears to occur a little more quickly for some European *B. burgdorferi* s.l. genospecies and strains compared to North American strains. Most *B. burgdorferi* s.l. transmission studies used *B. burgdorferi* sensu stricto, and transmission timing information on other genospecies or strains is lacking.

Factors that may influence transmission timing:

- *B. burgdorferi* s.l. genospecies/strain differences
- Interrupted tick blood meal
- Simultaneous feeding of multiple-infected ticks
- Co-infecting microbes in the tick

Transmission mechanisms

Borreliosis agents are typically acquired by ticks during their larval or nymphal blood meals when feeding on an infected wildlife host. Once infected, *Ixodes* ticks can transmit *B. burgdorferi* s.l. during their next blood meal which typically occurs in their next life cycle stage.



1 Transovarial transmission (from a female tick to her progeny) rarely, if ever occurs.

2 When the infected tick identifies and commences attachment and feeding on a new host, quiescent borreliae migrate from the midgut to replicate in the tick salivary glands. In preparation for infection of the new vertebrate host, the borreliae begin rapidly adapting their surface proteins, metabolism, and regulatory pathways prior to inoculation via tick saliva to establish infection in the vertebrate host.

After infecting the tick, *B. burgdorferi* localize and attach to the wall of the midgut, persisting in this tissue for 3-12 months until the tick finds a new host. The *B. burgdorferi* surface lipoprotein outer surface protein A (OspA) is essential for attachment of the borreliae to the midgut epithelium and survival in the tick. OspA is also one primary target for *B. burgdorferi* vaccines.

OspC is one surface protein, and another common target of *B. burgdorferi* vaccines, that is upregulated and expressed during early vertebrate host infection. A combination of tick-derived and *B. burgdorferi*-derived factors are used by the pathogen to escape the initial site of inoculation in the skin and establish infection while counteracting vertebrate host immune responses.

3 Adult *Ixodes* may be more important than nymphs for *B. burgdorferi* s.l. transmission to dogs and experimental studies in dogs usually use adult ticks. Time to clinical disease onset is highly variable in dogs and because there is no pathognomonic clinical sign for canine borreliosis, it is difficult to know which tick life stage most commonly transmits *B. burgdorferi* to dogs.

4 The first opportunity for *Ixodes* ticks to acquire *B. burgdorferi* s.l. is feeding on an infected wildlife reservoir (commonly a rodent or bird) during their larval or nymphal bloodmeals.

These ticks typically feed once per life stage thus their likelihood to transmit the pathogen would occur during their next blood meal in their next life stage. Therefore, in an endemic area, host-seeking adult *Ixodes* ticks are approximately twice as likely to be infected as host-seeking nymphs, while host-seeking larvae are generally not infected.

5 The small size and greater numbers of nymphs means that this life stage of the tick presents the greatest risk to people. Thus the risk to people of Lyme borreliosis is usually determined by assessing nymph population density.

WHAT BEHAVIORS
PUT A DOG AT RISK FOR THE DISEASE?

Activities

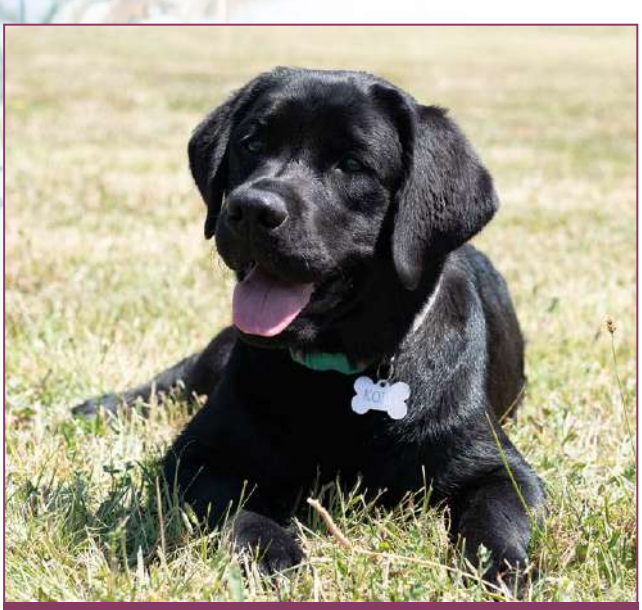
Outdoor activities during seasons when ticks are active in canine borreliosis-endemic areas put dogs at risk for exposure to *B. burgdorferi*-infected ticks potentially leading to the disease.

Activities where dogs travel through **tree canopy, vegetative understory, uncut grass or brushy/shrubby areas,** or areas where tick host species await will increase tick encounter risk and subsequent *B. burgdorferi* s.l. infection risk. Regardless of whether areas are urban, suburban, or rural, if **vegetative habitats with suitable microenvironments and tick host / *B. burgdorferi* s.l. reservoir species** are present, there is a risk of encountering *B. burgdorferi*-infected ticks. Green spaces in urban areas and landscape fragmentation in suburban areas have created plentiful tick habitats. Both dogs and their owners actively using these areas are at risk for tick encounter.

Time of day for increased exposure

Dogs may encounter *B. burgdorferi*-infected *Ixodes* ticks at any time of day. In general, the chance of tick encounter in areas receiving direct sunlight is low during the warmest and driest parts of the day; however, in shaded areas ticks may still actively quest for hosts even during these times. Shaded or protected areas where ticks are most active are also favored by vertebrate hosts. Ticks, especially *Ixodes* populations in warmer regions, will actively quest in the twilight and overnight to maximize their host-seeking duration, taking advantage of times when temperature, humidity, and host activity are more favorable.

WHAT BEHAVIORS PUT A DOG AT RISK FOR THE DISEASE?



Breed-related risks

All dog breeds are susceptible to *B. burgdorferi* s.l. infection; however, greater seroprevalence may occur in Bernese mountain dogs and more severe clinical disease in retriever breeds. These observations require additional study and may be due to over-representation of these breeds in study populations, breed-related genetic predisposition, or a greater likelihood of these breeds being active in tick-infested areas.

Diet

Diet-induced obesity in mice suppresses innate immune responses and correlates with greater borreliosis pathogenicity; however, antimicrobial treatment of obese mice is successful. The influence of diet on canine susceptibility to *B. burgdorferi* s.l. infection or disease severity is unknown. If a *B. burgdorferi*-seropositive dog develops glomerulonephritis with protein-losing nephropathy, then diet modification or other interventions that would normally be used to support renal function (or the function of other affected organs) should be considered.

Contact with other animals

A dog has little risk of directly acquiring or transmitting *B. burgdorferi* s.l. infection directly from or to other animals, because acquired borreliae quickly leave the bloodstream to enter tissues and reside there in low levels. Therefore, dogs diagnosed with *B. burgdorferi*-infection pose minimal risk to their owners and vice versa. Dogs do not acquire borreliosis from eating infected ticks. Dogs are at risk that reside near areas with host species (e.g. deer, mice) that support local tick populations and other species that maintain the pathogen (e.g. chipmunks or squirrels). Dogs (or their owners) may also inadvertently bring ticks home that are crawling on them but are not attached. These ticks may subsequently infest other household pets or people. Ticks are even occasionally recovered from indoor-only cats, presumably after the ticks were unknowingly brought home by other household members.

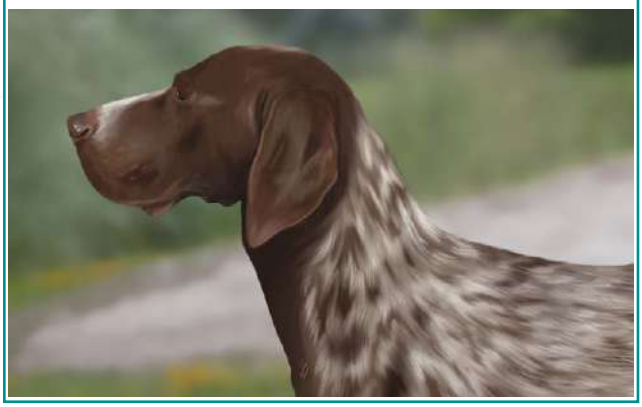
CAN A DOG BE INFECTED AND **NOT SHOW SIGNS?**

Infection *vs* disease

Dogs in endemic areas have a high risk of exposure and infection; however, most dogs (~90%) inoculated with *B. burgdorferi* s.l. by ticks do not develop overt clinical signs of disease. In contrast to dogs, most people infected with *B. burgdorferi* s.l. will develop signs of clinical borreliosis.

Risk to the population from subclinically diseased dogs

There is minimal risk of direct (dog-to-vertebrate host) or indirect (dog-to-tick-to-vertebrate host) *B. burgdorferi* transmission from a subclinically-diseased dog to another host. Subclinical disease is primarily a result of the infected dog's immune response. Dogs are unlikely to be a common reservoir host, although Beagles could serve as transmission reservoirs (successful dog-to-tick transmission) in experiments. We do not know the length of time a dog may serve as a reservoir; the likelihood that dogs contribute to enzootic maintenance; and, whether breeds other than Beagles may serve as reservoirs.



Risk of subclinical disease (frequency in the population)

Subclinical disease occurrence is likely greater than expected. Pathogenesis research studies in experimentally infected dogs (typically using *B. burgdorferi* sensu stricto) commonly report subclinical polyarthritis, periarteritis, and/or perineuritis. Subclinical disease frequency in association with different *B. burgdorferi* s.l. genotypes or strains is not known and likely to be highly variable.

Tests that reveal a subclinically infected dog

Evidence of infection or prior exposure to canine borreliosis agents in an apparent healthy (or subclinically infected) dog is often identified during routine annual serological assessments for exposure to vector-borne pathogens. Dogs seropositive for *B. burgdorferi* s.l. on screening tests should receive additional tests (e.g. CBC, serum chemistry, urinalysis) to monitor for subclinical disease.

WHAT CLINICAL SIGNS
DOES A SICK DOG SHOW AND WHY?

Pathogenesis

B. burgdorferi inoculated via tick saliva into skin disseminate in the blood stream from the tick bite site to distal, typically collagen-rich, tissues. Some *B. burgdorferi* genospecies have a greater predilection for certain host tissues compared to others.

Infection is recognized by the host's immune response and the extent of the response correlates with the amount of pathologic change. **Excessive innate and adaptive immune responses** can occur in the infected tissue (e.g. joint).

> In general, excessive host responses associated with increased tissue damage are more commonly seen in non-reservoir mammalian hosts such as dogs and people.

Excessive innate immune responses can lead to increased disease severity associated with overproduction of proinflammatory cytokines and chemokines upon recognition of bacterial surface proteins by Toll-like receptors. An excessive adaptive immune response also contributes to disease pathogenesis where accumulation of pathogen specific antigen/antibody immune complexes in tissues (e.g. joint, kidney) promote inflammation and immune-mediated disease at these sites.

Early signs

There are no pathognomonic canine borreliosis clinical signs and only about 5 - 10% of infected dogs develop overt clinical signs.

Most common signs:

- Fever
- Lethargy
- Malaise
- Shifting-leg lameness
- Anorexia
- Depression

Unlike the disease in people, dogs generally do not develop clinical signs until several weeks (>4 weeks) to several months postinfection. They are also largely non-specific, making diagnosis difficult based on clinical signs alone. The most common clinical presentation of canine borreliosis is an acute mono- or polyarticular lameness (shifting leg lameness) with joint swelling and fever. Dogs do not develop the characteristic bull's eye rash (*erythema migrans*) reported frequently in people.

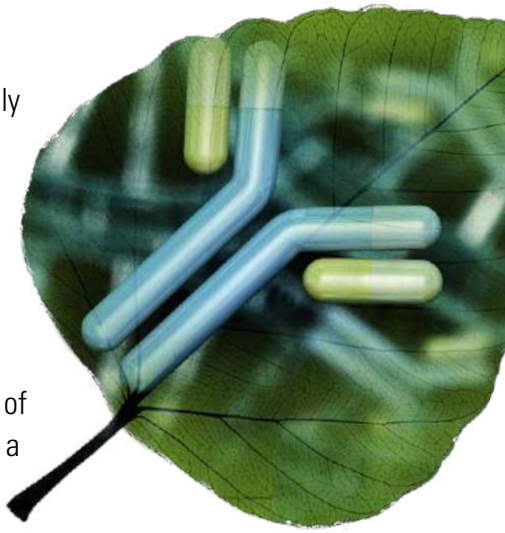
WHAT CLINICAL SIGNS DOES A SICK DOG SHOW AND WHY?

Progression

Most dogs that experience subclinical disease or mild to moderate clinical disease will resolve the infection with or without treatment; however, antimicrobial treatment can greatly facilitate recovery.

Progression to more severe disease occurs in a small percentage (<2%) of infected dogs.

Disease progression is linked to the degree of the individual animal's immune response to infection leading to immune-mediated tissue injury. This is most common in joint tissues (arthritis) and hypothetically in kidneys (nephritis). The specific tissue affected in severe disease is heavily influenced by the infecting *B. burgdorferi* s.l. genospecies. There are experimental studies examining *B. burgdorferi* s.s. disease pathology in dogs, but disease development in dogs caused by other *B. burgdorferi* genospecies is not described.



Prognostic factors

A small percentage of dogs develop clinical signs of disease and seropositive clinically healthy dogs have a good chance of resolving infection with or without treatment.

Seropositive dogs displaying mild to moderate signs of infection (e.g. fever, arthralgia, lameness, anorexia) have a **good recovery prognosis** and tend to rapidly respond to antimicrobial treatment. *B. burgdorferi*-associated lameness should begin resolving within 1-3 days of antimicrobial treatment initiation.

Seropositive dogs with signs of immune-mediated inflammation, possibly a result of *B. burgdorferi* antigen/host antibody complexes in kidney or other tissues, have a poorer prognosis even with antimicrobial treatment.

Recovery indications

Clinical recovery assessment based on observation of reduced pathogen infection level is difficult because clinical signs are more associated with the animal's immune response to the pathogen rather than the pathogen. Quantitative serology assays are available to monitor titers, which should decrease if the animal is not re-exposed or infected during the recovery or treatment period – and re-exposure is likely for dogs living in endemic areas. Seroconversion does not make a dog immune from reinfection or disease, and seropositive dogs remain susceptible to infection with other *B. burgdorferi* s.l. genospecies or heterologous strains of the same genospecies. Dogs experiencing severe immune-mediated disease signs suspected to be caused by *B. burgdorferi*-s.l. infection have a poorer prognosis.

WHAT DIAGNOSTIC TESTS SHOULD BE RUN IN A DOG THAT IS SUSPECTED TO HAVE THE INFECTION/DISEASE?

Rapid, table-side

They are the most common assays used to diagnose canine borreliosis.

These table-side tests are frequently administered during routine annual health assessments to monitor exposure/infection of dogs to *Borrelia* and other vector-borne pathogens. **Multiple commercial table-side assays** are available, with assays differing in the specific pathogen antigens for which they recognize antibody.

> Some assays probe for antibodies against a single antigen target while others test for antibodies against multiple pathogens. These types of assays are qualitative and provide a yes/no answer regarding *B. burgdorferi* s.l. serostatus.

In hospital using microscope or similar equipment

Direct detection of *B. burgdorferi* (e.g. evaluation of thin blood smears, etc.) is not recommended. When spirochetes are observed on a thin blood smear, these are more likely a relapsing fever *Borrelia* species rather than a *B. burgdorferi* s.l. species.

> This approach is difficult and inefficient because the pathogen quickly leaves the bloodstream to sequester in distal, typically collagen-rich tissues.

Detection in histological preps or using molecular assays is also inefficient as the number of organisms in host tissues is low. Growing borreliae from infected host tissue is an option to confirm the infection; however, most hospitals or labs are not set up to conduct these labor and time intensive cultures.

Laboratory testing

There are multiple additional commercial and in-house serologic-based diagnostic assays available from commercial, government, and university diagnostic laboratories.

- These assays may test for antibodies against single antigens or a combination or antigens to evaluate *B. burgdorferi* s.l. exposure/infection.
- Diagnosis by direct observation of the pathogen (biopsy culture) or pathogen DNA (molecular-based tests such as PCR) is difficult, especially at later stages of infection, because the pathogen migrates quickly away from the initial site of inoculation through the bloodstream into favored collagen-rich tissues.

WHAT DIAGNOSTIC TESTS SHOULD BE RUN IN A DOG THAT IS SUSPECTED TO HAVE THE INFECTION/DISEASE?

Test interpretation

Serologic assays, the most common tests used to diagnose canine borreliosis, detect pathogen-specific antibody in the dog, not the pathogen. Seroconversion occurs approximately four weeks after initial infection, therefore recently infected dogs may test seronegative. Dogs rarely display clinical signs of borreliosis before serocoversion.

Based on the serologic assay antigen target, tests may differ in their ability to differentiate:

- **Exposed versus infected dogs.** Tests that detect antibodies to *B. burgdorferi* s.l. proteins not expressed until the spirochete is in the vertebrate host (e.g. VlsE C6 peptide, OspF) can differentiate between vaccinated and naturally-infected dogs.
- **Infected versus vaccinated dogs.** Tests that detect OspA or OspC antibodies are not able to differentiate between vaccinated and naturally-infected dogs because these two proteins are included in most canine borreliosis vaccines.
- Active versus past infection (IgM versus IgG)
- *B. burgdorferi* versus other *Borrelia* species (e.g. relapsing fever *Borrelia* species)

Most serologic-based tests are qualitative and provide a yes/no response; however, laboratory-based quantitative serologic assays are available (can be useful in monitoring antibody titer changes to determine infection progression, treatment response, or reinfection).

For **seropositive dogs,** other laboratory tests (e.g. CBC, serum chemistry, urinalysis to test for proteinuria) are useful to facilitate treatment decisions.

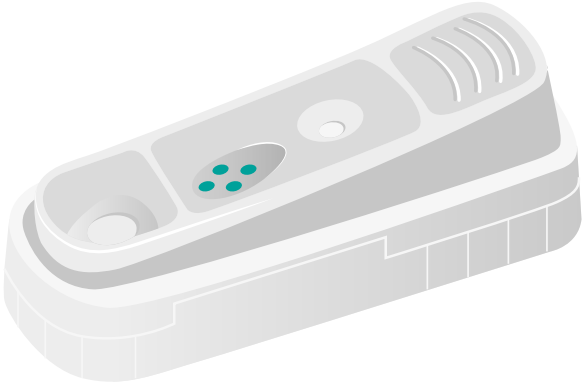
B. burgdorferi-specific antigen/antibodies complexes may be the cause of protein-limiting nephropathy in seropositive dogs; however, no staining techniques are validated for identification of these immune complexes and confirmation of *B. burgdorferi* s.l. instigated nephritis is difficult.

B. burgdorferi seropositive dogs with protein-limiting nephropathy (PLN) were compared to seronegative dogs with PLN and this showed that *B. burgdorferi*-seropositive dogs with PLN were more likely to:

- Be a retriever or retriever-mix
- Have thromobocytopenia, anemia or neutrophila
- Have biochemical evidence of azotemia, hyperkalemia and hyperphosphortemia
- Have hematuria, glucosuria and urine culture-negative pyuria
- Have immune complex glomerulonephritis in renal samples

Acute *vs* convalescent

Titer changes can be used to help discern whether a dog is actively infected or recovering from a previous infection. Monitoring antibody titers can be used to assess treatment response, infection relapse, or re-exposure – which is common for dogs in endemic areas. The best antibodies used for assessing convalescence are against antigens expressed after the borreliae infects the vertebrate host, such as the VlsE C6 antigen or OspF, both of which wane upon successful treatment or natural resolution of infection.



WHAT GENERAL TREATMENT STRATEGY IS RECOMMENDED FOR SICK DOGS?

Types of drugs to use

Tetracycline and beta-lactam antimicrobials are the primary drug classes used to treat canine borreliosis.

Monotherapy or combination therapy

Monotherapy with a tetracycline or beta-lactam antibiotic is usually successful for treating canine borreliosis. Doxycycline and minocycline, at 10 mg/kg for 30 days, are the most frequently used antimicrobial regimens. Several other antimicrobial treatment options including beta-lactams have also been successful. A list of antimicrobial treatment options provided in the ACVIM Consensus is included (Table 2). *B. burgdorferi* s.l. replicate slowly and owner compliance with administering the full antimicrobial regimen is important for successful infection control. Combination therapies may be indicated when a dog is co-infected with other pathogens or supportive care may be needed to manage associated chronic disease symptoms (e.g arthritis or glomerulonephritis) **(Table 2)**. **Treatment** is generally recommended for seropositive dogs displaying canine borreliosis clinical signs or asymptomatic dogs with evidence of protein-limiting nephropathy. However, treatment of seropositive, non-clinical, non-proteinuric dogs is more controversial.

This decision ultimately lies with the owner and veterinarian and should incorporate information based on:

- Patient history (e.g. first time seropositive versus history of being seropositive)
- Transmission risk in the geographic location
- Chronic disease risk (e.g. breed considerations)
- Potential for a drug-associated adverse event
- Concerns over judicious use of antibiotics with regards to curbing antibiotic resistance

Table 2

ACVIM Consensus list of antibacterials used to treat canine borreliosis				
Antibacterial	**Duration of Use**	**Frequency**	**Route**	**Dosage**
Doxycycline or Minocycline	30 days	1-2 times daily	PO or IV	10 mg/kg
Amoxicillin	30 days	3 times daily	PO	20 mg/kg
Azithromycin	10-20 days	Once daily	PO	25 mg/kg
Clarithromycin	30 days	2 times daily	PO	7.5-12.5 mg/kg
Erythromycin	30 days	2-3 times daily	PO	25 mg/kg
Cefotaxime	14-30 days	3 times daily	IV	20 mg/kg
Ceftriaxone	14-30 days	Once daily	IV or SC	25 mg/kg
Cefovecin	28 days	2 times, 14 days apart	SC	8 mg/kg

WHAT GENERAL TREATMENT STRATEGY
IS RECOMMENDED FOR SICK DOGS?

Supportive treatment strategies

Dogs with suspected *B. burgdorferi* s.l.-related arthritis may benefit from:

- Analgesics (preferred)
- Non-steroidal anti-inflammatory drugs
- Glucocorticosteroids (if immune-mediated arthritis is suspected).

In addition to antimicrobial treatment, **supportive treatment** of seropositive dogs with protein-limiting nephropathy or glomerulonephritis should follow recommendations for immune-complex glomerulonephritis standard of care guidelines.

> The International Renal Interest Society Canine Glomerulonephritis Study Group recommends mycophenolate at a dosage of 5-10 mg/kg q12h PO with or without corticosteroids as the first immunosuppressive method to try.

Monitoring for response to treatment

In general, dogs that experience mild to moderate borreliosis clinical signs and receive treatment have a good recovery prognosis and signs generally resolve within the first few days after treatment initiation.

- Treatment response in symptomatic dogs, including dogs with lameness, is often observed within the first few (1-3) days of treatment.
- Dogs that naturally self-resolve infection or are successfully treated can maintain **serum antibody levels** for several months to several years depending on the specific antibody test.

> Assessment of treatment response by evaluating antibody titers can be challenging, especially for dogs living in endemic areas that are at high risk for reexposure infection which would boost antibody titers.

- Dogs who do not recover with treatment many need additional tests to evaluate co-infection with other pathogens or presence of other underlying diseases.

WHAT GENERAL TREATMENT STRATEGY IS RECOMMENDED FOR SICK DOGS?

Management of co-infections

Multiple other **bacterial**, **viral**, and **protozoal** pathogens are carried in the same *Ixodes* species vectors.

Therefore, dogs bitten by these ticks can be co-infected with multiple pathogens. Co-infection or successive *B. burgdorferi* s.l. infection(s) can complicate diagnosis and assessment of treatment response.

- Doxycycline and similar **tetracycline antimicrobials** are commonly used for the treatment of most tick-borne bacterial diseases, and dogs experiencing **co-infection with multiple tick-borne bacterial pathogens** should respond to this treatment as well.
- **Co-infection of other pathogens such as *Babesia* species protozoa**, also transmitted by *Ixodes* species, may complicate the clinical picture and dogs may require additional diagnostic tests to confirm co-infection and may require additional therapeutics for disease management.

Bacterial

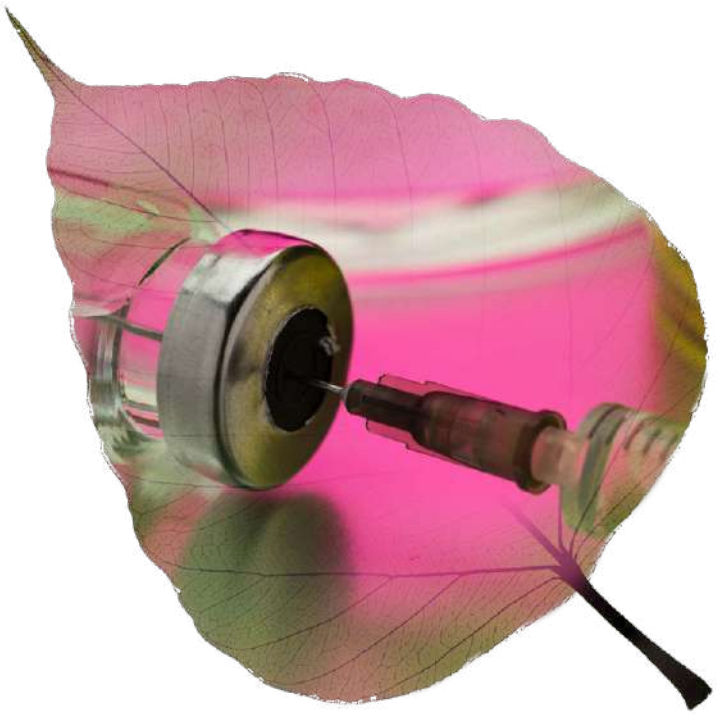
Anaplasma phagocytophilum, Ehrlichia muris, E. canis, Francisella tularensis, Rickettsia spp., *Bartonella* spp.

Viral

Powassan virus, Tick-borne Encephalitis virus

Protozoal

Babesia spp.



ARE OTHER PETS OR PEOPLE IN THE HOUSE AT RISK?

The risks to people from an infected/sick dog

B. burgdorferi infected dogs do not pose a direct risk to other people or pets within the household. This pathogen quickly leaves the bloodstream, and blood-to-blood contact between an infected dog and other household members poses virtually no transmission risk.

Other public health considerations

Owners and dogs share many of the same risk factors for encountering *B. burgedorferi* s.l.-infected ticks, and dogs can serve as sentinels for borreliosis risk in humans. A dog that is seropositive for *B. burgdorferi* s.l. has been in an area with infected ticks. Dogs typically travel with their owners, and it is likely that the owner was in the same area with infected ticks. *B. burgdorferi*-infected ticks can be found in urban, suburban, and rural areas as long as suitable environmental microhabitats, reservoir hosts, and tick vector species are present. Owners living in areas of new tick introduction may be less familiar with the hazard that these parasites represent.

Can cats get this infection/disease?

Cats experimentally-infected with *B. burgdorferi* did not develop clinical signs, however, they seroconverted, and pathogen DNA was recovered from tick inoculation site biopsies.

Cats living in **endemic areas** are susceptible to being bitten by *B. burgdorferi* s.l.-infected ticks.

> Approximately 25% of cats in some areas may be seropositive for *B. burgdorferi*.

Feline borreliosis is controversial and some veterinarians in endemic regions report cases of cats with **clinical signs.** Certain *Borrelia* genotypes or strains may be more likely to cause clinical signs in cats; however, additional research is needed.

> *Ixodes* spp. ticks may transmit other pathogens, including *Anaplasma phagocytophilium*, to susceptible cats and these can cause clinical signs similar to borreliosis, therefore this should be considered in the differential diagnosis.

WHAT ARE SOME RECOMMENDATIONS AROUND PREVENTION STRATEGIES?

How to avoid the vector

Complete avoidance of vector ticks eliminates any canine borreliosis risk; however, this is difficult as vector tick populations are increasing in density and distribution in rural, suburban, and urban areas. To reduce exposure to tick vector species, dogs should avoid or limit the amount of time walking in areas with vegetative ground litter under tree canopies or along areas adjacent to unmaintained vegetative areas and avoid resting in tree- or shrub-shaded areas where other tick hosts may also rest. Check dogs moving through potential infested areas for ticks, focusing especially around the ears, eyes, collar, paws and groin area. Regular 'tick checks' also help prevent inadvertent transfer of ticks at home where other pets or people may get bitten.

Complete avoidance of *B. burgdorferi* s.l.-infected ticks is difficult and may reduce quality of life, therefore dogs should receive tick-preventive products throughout the year. Safe and effective commercial **acaricidal and repellent products** are available for tick control on dogs and cats.

- Products that prevent or rapidly kill attached ticks are preferred to protect dogs from tick-borne pathogens such as *B. burgdorferi* s.l.
- Repellent products that reduce/prevent attachment are primarily synthetic pyrethroid compounds such as permethrin, deltamethrin and flumethrin. These repellent compounds are commonly topically applied and have acaricidal effects that kill ticks upon prolonged contact.

Owner compliance is vital for success and the product that is not administered will not work, regardless of product choice. The "best" tick preventive product is the one an owner will compliantly administer. Longer acting products can help to improve owner compliance with recommended treatment schedules.

Acaricidal and repellent products:

- The systemically acting isoxazolines are highly effective acaricides that may be administered orally or topically (depending on the product) and rapidly kill ticks as they attach to the host.
- Topical ectoparasiticides may be administered directly on the skin (normally between the shoulder blades) or through a slow-release impregnated collar.
- Topical acaricides include amitraz (not used in many areas and a greater adverse reaction potential – use not advisable and only with caution) and fipronil which may be combined with repellent compounds.

WHAT ARE SOME RECOMMENDATIONS AROUND PREVENTION STRATEGIES?

Is routine testing recommended?

Routine annual testing of dogs living in endemic areas is recommended and is often integrated into annual checkups. Annual evaluation of these tests helps to monitor dog exposure, parasiticide products efficacy, vaccine efficacy, and general disease risk for other household members (e.g. other pets or owners) from vector exposure.

General thoughts on preventive treatments

Tick avoidance can be difficult and impractical as a sole prevention method and use of tick preventive products is the best strategy to reduce the likelihood of dogs being bitten by *B. burgdorferi* s.l.-infected ticks potentially leading to canine borreliosis (or infection with other tick-transmitted pathogens).

A changing climate and increasing tick populations are increasing the risks for dogs. In areas where monthly temperature highs exceed 4°C (40°F), dogs will benefit from year-round tick control because ticks are commonly active above this temperature. Risk-based decisions based on location, dog breed, travel, vaccine availability and veterinary consultation will help determine whether a dog would additionally benefit from vaccination.

Strategies to encourage owner compliance with tick preventive products:

- Identifying a product that the client will most compliantly administer.
- Education regarding tick activity.
- Increasing awareness about risk of tick-borne pathogens.
- Client education on the risks of ticks and tick-borne pathogens in their local area can be very effective to keep clients engaged in practicing active tick prevention strategies (e.g. compliantly using tick preventive **products** or vaccination). Owner compliance with treatment administration may improve when the treatment has a longer duration of effect.
- Timely and regionally pertinent information, or links to such information, about ticks and tick-borne diseases in a client's local area are most useful.

WHAT ARE SOME RECOMMENDATIONS
AROUND PREVENTION STRATEGIES?

Is there a vaccine?

For dogs living or visiting canine borreliosis endemic areas, vaccination in combination with use of tick preventive products is an effective strategy for further protection against canine borreliosis. These vaccines are available in many areas and consist of either bacterins (whole killed borreliae) or specific recombinant or chimeric outer surface proteins (e.g. OspA, OspC) and may be adjuvanted or non-adjuvanted. Vaccination-induced antibodies against OspA are thought to work by entering the tick during early stages of feeding and killing the borreliae inside the tick before they are transmitted to the dog. Vaccine-induced antibodies against OspC are thought to help kill or control borreliae during early infection in the dog around the tick bite site. However, because *Ixodes* ticks can carry other pathogens, for which vaccines are not available, it is not recommended to use vaccine in lieu of tick-preventives as the tick species that transmit *B. burgdorferi* s.l. also serve as vectors for other pathogens (e.g. *A. phagocytophilum, Babesia* spp.) that can also infect and cause disease in dogs.

WHAT DOES THE FUTURE LOOK LIKE?

What are the changes being seen with the disease?

Canine borreliosis is an **expanding threat to dogs** and Lyme borreliosis is an **expanding threat to people** as tick vector populations intensify and expand.

Information regarding the prevalence, likelihood of infection, likelihood of disease development, and clinical signs of disease associated with different *B. burgdorferi* genospecies and strains is increasing.

Studies are needed on how disease manifestations differ in dogs infected with different *B. burgdorferi* s.l. genospecies or strains, and such information would be valuable in further developing strategies for disease intervention and therapy.

Most information is derived from investigation of Lyme disease and risks in people; however, this research also helps to understand the risks for dogs.

Is the risk of disease increasing?

Borreliosis is a significant and expanding disease of veterinary and public health concern.

Expanding geographic distributions and densities of tick vectors and *B. burgdorferi* s.l. reservoir hosts (and the multitude of factors that support these) in areas frequented by dogs and owners increase the risk that dogs and humans will encounter *B. burgdorferi* s.l.-infected ticks.

Factors facilitating increased risk of tick exposure and disease risk:

Climate changes

Movement of infected ticks by reservoir hosts

Changes in host and reservoir species composition, richness and abundance

Development of green spaces in urban areas that serve as habitats for tick vectors and transmission and reservoir host species

Suburban sprawl of humans and their companion animals into naturally endemic areas

Increased outdoor activity or recreation in green spaces

Increased movement or travel of dogs into endemic areas

Management of disease risks is complex and requires an integrated approach. Despite the increasing and seemingly omnipresent risk in endemic areas, proper tick control product use and vaccination can effectively mitigate the risk of canine borreliosis. As dogs share many of the same risk factors with their owners, dogs can serve as excellent sentinels of risk, and routine assessment of dog exposure benefits both pets and their owners.

Has resistance to prevention or reduced treatment effect been seen?

Tick populations and borreliosis risk are influenced by a multitude of complex and interwoven variables, and an integrated management plan that considers multiple variables (which may be unique to a given area) is necessary to reduce vector tick populations and mitigate disease risk.

Disease control

Most dogs infected with *B. burgdorferi* s.l. self-resolve infection and have no overt signs of clinical disease. In cases of mild to moderate disease, dogs are most often successfully treated with antimicrobials, although some dogs may require a second round of treatment. *B. burgdorferi* resistance to common antimicrobial treatments used against *B. burgdorferi* s.l. infection has not been definitively demonstrated. As seen in people, individual dog immune responses to infection may trigger immune-mediated damage. In these cases, successful resolution of immune-mediated damage is difficult to achieve and may not be possible when there is extensive damage (e.g. with nephritis).

Tick control

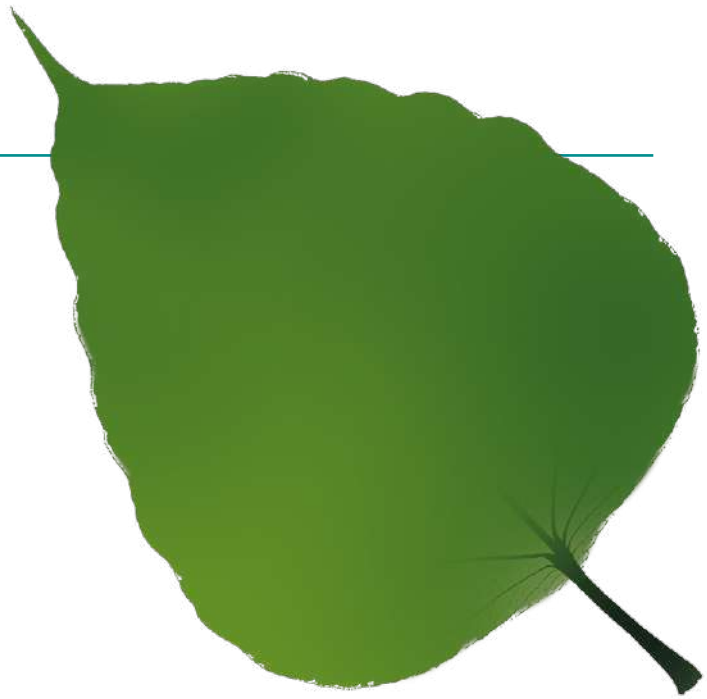
Among *Ixodes* species, development of resistance to tick control chemicals is minimal, due to both the longevity and 3-host life cycle involving multiple individual (mostly wildlife) hosts of these ticks. These factors make mass outdoor chemical treatment efforts impractical and reduce or slow the timeline for resistance development.

Perceived reduced treatment efficacy is most commonly related to compliance issues or occurrence of behavior/activities (timing of administration, method of administration, lack of achieving full body coverage) that may reduce product longevity rather than reduced efficacy or resistance to the specific product. No product is 100% effective; and, an occasional tick may be observed on a dog treated with a parasiticide product.

Environmental control strategies:

- Manipulation of wildlife species (e.g. changes in composition, richness, or density).
- Manipulation of local environments (e.g. chemical application to vegetation or barrier spraying; biological control using parasitoid wasp or entomopathogenic fungus) have had limited broad impacts in reducing tick populations or persistence, or *B. burgdorferi* s.l. prevalence in local vertebrate reservoir populations.

FURTHER READING



Websites

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Companion Animal Parasite Council. https://capcvet.org/

Companion Vector-Borne Diseases: Lyme borreliosis. http://www.cvbd.org/en/tick-borne-diseases/lyme-borreliosis/

European Centre for Disease Prevention and Control: Borreliosis. https://www.ecdc.europa.eu/en/borreliosis

European Scientific Counsel Companion Animal Parasites: Control of Vector-borne diseases in dogs and cats. https://www.esccap.org/uploads/docs/znkh6j1d_0775_ESCCAP_Guideline_GL5_v8_1p.pdf

International Renal Interest Society. http://www.iris-kidney.com/

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