Burden of Tick-borne Infections on American Companion Animals

Zenda L. Berrada, PhD and Sam R. Telford III, DSc

This review examines the biology of ticks and tick-borne infections in the United States. The most common tick-borne diseases in dogs and cats are discussed. We demonstrate that there is much interest in tick-borne infections at the level of the lay public (pet owners), describe trends in the distribution and prevalence of tick-borne infections in the United States, summarize some issues in understanding the degree of ill health due to tick-borne infections, and suggest some avenues for research that would clarify these issues.
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More pathogens have been associated with ticks than any other bloodsucking arthropod but mosquitoes. Companion animals have always suffered from tick infestations. As veterinary medicine advances, signs and symptoms of disease that may have been missed before are now being detected. In addition, given the current trends of pet ownership and indeed treating companion animals as one of the family, there is more interest in the possible effects of tick infestation. Burden is an epidemiological concept that is based on the combination of prevalence and capacity of an infection to impact the health of a group of individuals. Therefore, we review the potential burden of tick-borne infections on companion animals and, in particular, those that affect dogs in the United States.

Tick Biology

Hard ticks (ixodids) are so named because of the hardened dorsal shield or scutum. In female hard ticks, the scutum is on the anterior third of the body, with the remainder consisting of pleated, leathery cuticle that allows for tremendous expansion during bloodfeeding. In male hard ticks, which may or may not feed at all, the scutum extends the length of the body. In contrast, soft ticks have no scutum; their entire body is leathery. Soft ticks (argasids) are transient feeders and will only rarely be found attached. We focus our discussion on hard ticks because soft ticks rarely achieve great population

densities and do not comprise a burden. (The spinose ear tick, *Otobius megnini*, may occasionally infest individual dogs in numbers that may cause dermatoses, but these ticks are restricted to small foci in the south-central United States and are not broadly encountered.) Hard ticks require several days to complete their bloodmeal; the number of days depends on the species and stage of the tick. Deer ticks (*Ixodes dammini*) will feed 3 days as a larva, 4 days as a nymph, and 7 days as the female. In the last day, usually in the last 3 or 4 hours of the bloodmeal, the tick takes what has been termed "the big sip," removing a large volume of whole blood, then detaching and dropping from the host.

Because they must remain attached for days, hard ticks secrete a complex mixture of anticoagulant, antiinflammatory, and antihemostatic agents that temporarily disable a host's local inflammatory response,[1] which might inhibit its feeding. Hosts that have never been exposed to ticks will not realize that a tick is attached. In contrast, soft ticks are similar to mosquitoes in their feeding, spending tens of minutes to no more than a few hours feeding, usually as their host is sleeping.

Tick life cycles have an extended duration, usually months or years. Deer ticks, for example, take 2 years to go from egg to egg. For this reason, there is generally no risk associated with hard ticks engorging and dropping off of a companion animal within a patient's home. The engorged tick will not feed again and will take weeks to molt or lay eggs, and, in the interim, usually the relative humidity within the house is too low for extended survival of the tick. Many of the pest tick species have very specific microhabitat requirements, including the need for high relative humidity and thus are found mainly in sites with dense grassy or herbaceous vegetation with a leaf litter understory. Brown dog ticks (*Rhipicephalus sanguineus*) are very resistant to heat and moisture deficits,[2] but require warmer temperatures for their complete life cycle. They are the only hard tick in which a complete life cycle may occur indoors, particularly within kennels.

Ticks Commonly Infesting Dogs and Cats in the United States

There are 800 described tick species globally, and 87 of these have been reported from North America (of which nearly half are hard ticks of the genus *Ixodes*). However, relatively few are common pests in the United States. Virtually all ticks found on dogs or cats are brown dog ticks (*Rhipicephalus sanguineus*), American dog ticks (*Dermacentor variabilis*), Rocky Mountain wood ticks (*D. andersoni*), Western dog ticks (*D. occidentalis*), Lone Star ticks (*Amblyomma americanum*), Gulf Coast ticks (*A. maculatum*), deer ticks (*I. dammini*), blacklegged ticks (*I. scapularis*), and woodchuck ticks (*I. cookei*). With the exception of *Dermacentor* spp (in which the subadults infest only rodents), all 3 stages (adult, nymph, larva) of the other common species may infest dogs. Good photographs are available online and may help identify a specimen to species. However, when ticks are partially fed or engorged, many of the easy morphologic features become obscured. The need for identification is not axiomatic: if dogs or cats are frequently infested, the owner would want to act to reduce infestation regardless of species. Although most concern relates to infectious agents, note that the vast majority of host-seeking ticks are not infected. Other than for the agent of Lyme disease in New England deer ticks (in which prevalence of spirochetal infection is commonly 35% to 65% in adult ticks,[3] typical infection rates for the agents of spotted fever, ehrlichiosis, tularemia, or babesiosis in their tick vectors is on the order of 0.1% to 1%. Accordingly, it might be useful to distinguish dog ticks from deer ticks in New England, if only to be alert for signs or symptoms of Lyme disease. Otherwise, tick identity would not affect a decision to try to reduce risk, either at the level of the individual (a topical formulation for pets, personal protection for the owner) or at the level of yards or neighborhoods (habitat management, judicious use of acaricidal spraying). Although focused on deer ticks, a good source for modes of prevention for any tick may be found at http://www.ct.gov/CAES/lib/caes/documents/special_features/TickHandbook.pdf.

Ticks as Vectors

Ticks are notorious vectors for a diverse array of infections. The vectorial capacity of a bloodsucking arthropod depends on focusing bites on relevant hosts, and competence in sustaining the development of a pathogen and the density of the arthropod.[4] Tick vectorial capacity is a function of (1) the extended duration of their feeding and large amount of blood ingested, thereby concentrating minute amounts of pathogen circulating within the vertebrate vasculature, and (2) the great densities of infestations that might result from environmental perturbation. In addition, very host-specific ticks that feed throughout their life cycle on the same individual animal or at most on a single species of animal efficiently maintain pathogen life cycles by not wasting bites on irrelevant species. Ticks that are more indiscriminate in their feeding habits have many opportunities to transfer potential pathogens between species, thereby serving as "bridge vectors." Ticks have long been known as important veterinary pests and sources of infection. Indeed, the seminal report of the life cycle of the agent of Texas cattle fever (*Babesia bigemina*) by Smith and Kilborne in 1893 served to start the field of medical and veterinary entomology.

Significance of Tick Infestation for Companion Animals

Ill health from tick infestation is due to (1) repeated infestation and engorgement of dozens of adult ticks at a time, promoting anemia or immune suppression, (2) tick paralysis induced by a toxin secreted in the saliva of certain ticks, (3) effects of sensitization or secondary bacterial infection of bite sites, causing granulomatous dermal reactions or pyogenic lesions, and (4) disease resulting from infection transmitted by a tick. Although occasional low-level tick infestations of dogs or cats are arguably harmless and should not incite panic, repeated identification of attached ticks should prompt preventive measures to at least reduce the likelihood of direct injury. Anemia or tick granulomas would be more likely with dense tick infestations, something that few companion animal owners should tolerate.

Tick-borne Infections of Companion Animals

Dogs and cats may become ill because of infection by arboviruses (arthropod-borne viruses), bacteria, and protozoa transmitted by ticks. Good reviews of the biology and clinical features of these infections are available,[5,6] and we provide only a brief overview. The most burdensome of the tick-borne infections for dogs are ehrlichiosis and babesiosis, and for cats, cytauxzoonosis (a form of babesiosis). Canine ehrlichiosis due to *Ehrlichia canis* and canine babesiosis due to species complexes of *Babesia gibsoni* and *B. canis* have been known since the early 20th century. Both significantly contribute to the ill health of dogs across the New World and Old World tropics because of infestations of brown dog ticks. Infections may progress to a chronic disease resulting in immunosuppression and pancytopenia (tropical canine pancytopenia due to *E. canis*) or severe hemolysis and shock due to multiorgan ischemia (babesiosis). Fortunately, severe babesiosis is rare in American dogs, even though *B. gibsoni*-like complex parasites are endemic in some states.[7] Most cases are detected in dogs that were adopted from Latin America, or from small outbreaks in kennels that had kept such dogs. Interestingly, dog bites appear to be an important mode of exposure for canine babesiosis in the United States, undoubtedly because of transfer of parasitized red cells.[8]

Less severe forms of ehrlichiosis due to *Ehrlichia canis* are common in the United States. Although the agent is now classified as *Anaplasma phagocytophilum*, and "human granulocytic ehrlichiosis" is erroneously referred to as "human anaplasmosis,"[9] the disease is indistinguishable from that known as canine granulocytic ehrlichiosis due to *E. ew-*

ingii or even canine infection with *E. chaffeensis*. *Anaplasma phagocytophilum* is transmitted by deer ticks, and *E. ewingii* and *E. chaffeensis* by Lone Star ticks. These ehrlichioses have received much attention because they are zoonotic.[10] In addition, infection by *A. platys*, transmitted by brown dog ticks, is usually subclinical but may be discovered by routine complete blood count because it causes thrombocytopenia.[11] The clinical entities are usually characterized by nonspecific signs such as fever, depression, and lethargy, and may spontaneously resolve.[12,13] Evidence of exposure is not evidence of current infection. Indeed, for human granulocytic ehrlichiosis ("human anaplasmosis") diagnostic antibody titers appear only in convalescence. Although sheep can be chronically infected by *A. phagocytophilum* (leading to immunosuppression), and *E. canis* infection may relapse even after appropriate treatment,[14,15] it is more likely that these infections spontaneously resolve. Re-exposure to infected ticks needs to be ruled out before concluding that infection may persist "silently" and unpredictably cause patent disease.

Cats may acquire cytauxzoonosis due to *Cytauxzoon felis*, a hemoparasitic protozoan. Dog ticks are known vectors, and, although classically most cases are reported from the south-central states, even cats residing in the eastern seaboard states appear to be at risk. A recent analysis reports a >90% case fatality rate (including those euthanized as a result of signs and symptoms).[16] Cats present with acute fever, icterus, and pancytopenia, and rapidly deteriorate.

Lyme disease (borreliosis) due to the spirochete *Borrelia burgdorferi* continues to receive intense attention in the companion animal world since canine disease was first reported in the early 1980s.[17] The distribution and density of the main deer tick vector have changed in the last decade, with expansion from the main coastal New England and upper Midwestern foci of intense transmission. As with human Lyme disease, the diagnostic, clinical, and therapeutic features have elicited controversy, and the reader is referred to the American College of Veterinary Internal Medicine consensus statement on Lyme disease for an excellent review of these issues.[18] Given the great prevalence of spirochetal infection in the recognized Lyme endemic areas, and the likelihood of frequent if not daily exposure to deer ticks, dogs or outdoor cats must sustain numerous infectious bites during their lifetimes. Why superinfection does not seem to occur with resulting frank, objectively definable Lyme disease at epidemic rates is a paradox that speaks to the host-pathogen relationship in canine or feline *B. burgdorferi* infection. A dose-response association is typical for most infectious diseases: the greater the inoculum, the greater the probability that infection results in disease.

The epidemiology of Rocky Mountain spotted fever (RMSF) is undergoing a paradigm shift. Although this infection was thought to be transmitted mainly by *Dermacentor* spp ticks, a small outbreak in Arizona[19] was due to transmission by brown dog ticks. In addition, RMSF has long been noted to vary in severity, from mild to fulminating,[20] and this clinical spectrum has been attributed to the existence of strains of *Rickettsia rickettsii* that were less virulent. In fact, related spotted fever group rickettsiae that were long thought to be tick symbionts are now increasingly being identified as pathogens.[21] These symbionts are more commonly detected in ticks than is *R. rickettsii*, and species such as *R. parkeri* and *R. amblyommii* are being incriminated in milder versions of human RMSF, suggesting that dogs may also become infected by these species and exhibit a range of clinical presentations. There are few evidence-based predictors for why an individual patient (human or dog/cat) might develop severe disease or any disease due to infection by any *Rickettsia* spp, and thus it is not clear that a greater level of concern regarding tick infestation and rickettsial disease in companion animals is warranted at this time.

Although DNA of *Bartonella* spp, particularly *B. henselae*, has been detected in deer ticks, and there is an emerging body of literature that considers ticks to serve as vectors for these bacteria, definitive demonstration of tick vectorial capacity has not been established.[22] We do not consider *Bartonella* further in this review, but note that if ticks are vectors, such a fact would add to the already considerable perceived or real burden of ill health associated with these ectoparasites.

Perceived Burden of Tick-borne Infection

The market for antiectoparasite products targeting companion animals is very large, suggesting that the public has a strong perception that their pets are at risk of ill health due to arthropod infestation. The best-selling topical formulation of fipronil for controlling fleas and ticks on dogs has sold over 1 billion units since its commercial introduction in 1996 (http://www.petproductnews.com/headlines/2009/05/07/update-epa-considers-further-restrictions-on-flea-tick-pet-products.aspx). Issues of infection aside, mere infestation of a cat or dog is now commonly regarded as ill health and potentially hazardous to the owner. In fact, low-level infestations of ticks (fewer than 10) are likely not harmful to the individual animal because, at most, approximately 3000 μL of blood would be ingested by a single adult tick. Ticks would feed to repletion if attached to a dog and would not seek another host (the owner), and if the replete tick was subadult, it could conceivably hide and molt to another host-seeking stage. The environment within homes is generally poor for completing development, with the exception of brown dog ticks, which are resistant to humidity and temperature extremes. However, if pets were kept outdoors, a nuisance infestation could develop quickly within the yard. Indeed, before the introduction of the topical antiectoparasite drugs, American dog ticks (*Dermacentor variabilis*) reproduced mainly on domestic dogs. On the other hand, ticks may be transported into homes, particularly by cats, and seek hosts there if for unknown reasons their transport host is not palatable. In addition, ticks are transported large distances by infesting dogs that accompany their owners on vacation and return with a new infestation.

Web Chatter, Support Groups, Anecdotal Reports

The worldwide web has become an invaluable resource for many pet owners to gather information about tick-borne diseases that may affect their pets. Search results as of May 2009 using the popular search engine Google identified 341,000 results for the keywords "tick borne disease AND dogs"; 86,800 results for "ehrlichiosis AND dogs"; 76,700 results for "babesiosis AND dogs"; 56,400 results for "RMSF AND dogs"; and 51,600 search results for "anaplasmosis AND dogs." Lyme disease is of particular interest; there were 533,000 search results for "Lyme disease AND dogs" using the Google search engine. The highest-ranked web sites under all categories that were searched were generated by animal health care providers, animal hospitals, pet interest groups, and educational institutions. Web sites provided basic disease information including disease signs and symptoms, diagnosis, treatment, and vaccination options (if applicable) to pet owners. A review of the top 50 results for canine Lyme disease found that despite the ongoing debate in the veterinary community over diagnosis and treatment, the information was generally consistent between the sites. This may decrease the opportunity for web searchers to be confused about conflicting information. However, there were several examples in which animal health care providers expressed doubts about current Lyme disease diagnostic paradigms. One extreme example from a web site quoting a veterinarian suggests extended antibiotic therapy, which has not been proven to be valuable for human Lyme disease.[23] Other examples provide good references for evidence-based opinions but conclude with statements that are not justified by peer-reviewed reports. There are many comments within the sampled web sites from concerned owners who question treatment or vaccination, often noting a failure of therapy or protection and then offering their anecdotally based advice.

Despite the possibility of obtaining misleading information from comments posted by laypersons on internet web sites, it is reassuring that many of the highest-ranked sites present basic information on tick-borne disease in an accurate and concise manner. The great amount of online chatter demonstrates the level of concern about ticks and tick-borne infection among pet owners and perhaps reflects a deficit in communication, significant confusion, poor comprehension, or insufficient education efforts of many veterinary practices.

Peer-reviewed Evidence of Burden

Although prospective clinical and seroepidemiologic studies that document the asymptomatic to symptomatic ratio precisely measure burden, such studies are expensive and not practical on a regional or national basis. A quantifiable measure of burden that can be extracted from the peer-reviewed literature comprises prevalence of infection. Even without implying severity or extent of disease, such a review makes the important point that risk is not homogenous across the United States or even within well-known endemic states, and

that seroprevalence estimates may be compared with other known or emerging infections of companion animals to place burden into context. For example, more than 50% of 1000 sera from American dogs were seroreactive to antigen of canine respiratory coronavirus,[24] with rates ranging from 31% to 100% for individual states. Accordingly, a seroprevalence of 5% for American dogs (vide infra) for antibody to *Borrelia burgdorferi* suggests that Lyme disease is on the order of a tenth as burdensome nationally as canine respiratory coronavirus, assuming that antibody wanes at a similar rate for the 2 agents, but that in certain states, the burdens are equivalent. Good serological surveys have been published for Lyme borreliosis, ehrlichiosis, and RMSF.

Lyme Borreliosis

Overall, large-scale serosurvey results closely reflect the geographic distribution of reported human Lyme disease cases with hyperendemic foci found in counties in central and northern California and the New England states.[25,26] Analysis of data from a commonly used antibody test demonstrated that 5.1% of 982,336 dogs tested were seroreactive against the C_6 peptide analyte used in the kit, which indicates recent or current infection with *Borrelia burgdorferi*.[25] When the results were analyzed by region of the United States, the greatest prevalence was found in the Northeast and Midwest (11.6% and 4.0%, respectively), whereas the lowest prevalence was in the Southeast and West (1.0% and 1.4%, respectively). Data mapped by zip code (county level) revealed pockets of relatively high seroprevalence, which represent either known areas of hyperendemicity in humans, areas that encompass good habitat for tick vectors (*Ixodes scapularis*, *I. dammini*, *I. pacificus*), or inclusion of dogs that have previously traveled or resided in Lyme disease–endemic areas.[25] These results are consistent with the findings from other serosurveys of dogs: Westchester County, New York, was between 7.1% and 85.2%,[27] dogs from Dukes County and Nantucket County, Massachusetts, were found to be 50% and 69% seropositive, respectively,[28] and 66.5% of dogs sampled from southern Connecticut were seropositive.[29] Similarly, between 0% and 15% of dogs from endemic California counties were seroreactive to *B. burgdorferi*,[30] and between 40% and 53% in portions of Wisconsin.[31,32] Surveys from nonendemic areas have comparatively lower seroprevalence: 0.6% in the Michigan Peninsula,[33] 0.4% to 2.3% in North Carolina,[34,35] and 2.3% in San Diego County, California.[36] It should be noted that differences among serologic assays between these studies might not heavily influence the large-scale seroprevalence estimates. Nonetheless, given the heterogeneity of risk and our relatively poor understanding of the asymptomatic to symptomatic ratio for canine Lyme disease, testing, vaccination, and treatment decisions should be tailored to specific areas. A one-size-fits-all recommendation would clearly be erroneous. A surveillance case definition for canine Lyme disease should be drafted by a national veterinary organization and adopted to better define its burden.

Domestic cats are exposed to *Borrelia burgdorferi*, with reported seroprevalence rates of 47% to 71% in cats from endemic areas of the northeastern United States.[37,38] It is likely that feral cats are greatly exposed, and their role as hosts for ticks or as reservoirs of the deer tick–transmitted agents needs to be formally studied. Development of disease in cats has not been reported; however, it may be suspected in cats exhibiting clinical signs such as those for dogs (lameness, fever, anorexia).[37,38]

Ehrlichiosis and Rickettsiosis

The burden of ehrlichial and *Anaplasma phagocytophilum* exposure in dogs has been estimated through numerous serologic and molecular assays. A recent study analyzed serologic results obtained throughout the United States and found that overall seroprevalence in dogs for *Ehrlichia canis* or *E. chaffeensis* was 0.6% (6295 of 982,336 dogs tested). When data were analyzed by region of the United States, the greatest prevalence of 1.3% was in the Southeast; the Northeast, Midwest, and West had canine seroprevalences of <1% (0.3%, 0.4%, and 0.6%, respectively). Within the Southeast, seroprevalence was greatest in Arkansas (3.9%), Oklahoma (3.8%), Mississippi (3.1%), Tennessee (2.3%), and North Carolina (2.1%); all other states included in this region had seroprevalence data of <2.0%. Within the Midwest, Kansas and Missouri had the greatest seroprevalence for *E. canis* or *E. chaffeensis* (2.2% and 1.9%, respectively), whereas all other states in this category had seroprevalences of <1%.[25] The states with the greatest seroprevalence in dogs for *E. canis* or *E. chaffeensis* overlap the geographic distribution of the principal tick vector, the lone star tick.[39] Polymerase chain reaction (PCR) and DNA sequencing have been used to demonstrate active infection with *E. ewingii*, *E. chaffeensis*, and *E. canis*. *Ehrlichia ewingii* has been found in as many as 23% of dogs suspected of having acute ehrlichiosis from Missouri; infection with *E. canis* was not found in the same cohort.[40] A study incorporating PCR was used to identify *Ehrlichia* spp in 65 dogs harboring ticks in Oklahoma and found dogs infected with *E. ewingii*, *E. canis*, and *E. chaffeensis*.[41] A similar study looking at the proportion of *Ehrlichia* spp infections in 27 sick kennel dogs in North Carolina reported infection of 56% with *E. canis*, 33% with *E. chaffeensis*, 30% with *E. ewingii*, and 41% as having infection with *A. platys* and/or *E. equi*.[42]

The seroprevalence noted for *Anaplasma phagocytophilum* exposure shows similar geographic distribution to that noted for *Borrelia burgdorferi*.[25] The overall seropositivity was 4.8% of the dogs tested nationwide (23,234 of 479,640), with the greatest seroprevalence found in the Northeast and the Midwest of the United States (5.5% and 6.7%, respectively). The seroprevalence was comparable in the West because of relatively high seroprevalence in Oregon and California (7.4% and 4.8%, respectively).[25] *Anaplasma phagocytophilum* DNA has been identified in clinical cases of "canine granulocytic ehrlichosis" (6 of 17 dogs) in Minnesota and Wisconsin,[43] and also in both healthy dogs (7 of 222) and those diagnosed with "anaplasmosis" (19 of 51 dogs tested) in Minnesota[44]; a similar study in Missouri detected *A. phagocytophium* in only 1 of 88 dogs tested.[40] These results are consistent with the prevalence pattern of human granulocytic ehrlichiosis and Lyme disease cases in humans.

Cats are susceptible to *Ehrlichia canis* and *Anaplasma phagocytophilum* infection; however, few studies have been done to assess the burden of these diseases in the feline population. Natural exposure to these pathogens in the United States has been assessed by serologic and molecular assays; 30% to 38% seropositivity to *A. phagocytophilum* was observed from 84 cats from the northeastern United States,[38] and evidence of infection with the agent was reported from several clinically ill cats from Massachusetts and Connecticut.[45] *Ehrlichia canis* has also been detected by PCR from 3 cats in North Carolina.[46]

In areas where RMSF outbreaks have occurred, canine seroprevalence to *Rickettsia rickettsii* can be relatively high; one study in Arizona found RMSF seroprevalence of 70% of dogs from a community that had 15 human cases[19]; another study in Ohio found seropositivity in as many as 75% of dogs in the vicinity of an RMSF case.[47] Serosurveys of dogs from RMSF-endemic areas tend to show relatively high seroprevalence; a study from Oklahoma found a 38% seroprevalence in 259 dogs,[48] and in North Carolina 5% of 600 dogs were seropositive,[49] whereas 22 of 27 sick Walker Hounds were seropositive.[42] Cats are believed to be resistant to *R. rickettsii* infection, although serologic evidence suggests they are exposed.[50]

Prevention

Before the introduction of topical acaricides, prevention comprised dipping dogs or blowing powders into their fur, using chemicals with a small but measurable toxicity to mammals, such as DDT, derris powder (rotenone), or lindane. The current classes of acaricides are orders of magnitude less likely to be toxic for the patient and the environment, comprising either insect growth regulators that interfere with hormones required for successful feeding and development (eg, methoprene, a juvenile hormone analog); synthetic pyrethroids such as permethrin, which inhibit arthropod nerve de-excitation, or fipronil, which acts on insect gamma-aminobutyric acid receptors, also causing nerve hyperexcitation. Topical applications reduce systemic levels of the active ingredients and, indeed, are localized in the very skin that serves as the critical interface for bloodsucking arthropods. Although there is a recent US Environmental Protection Agency advisory regarding topicals (http://www.epa.gov/pesticides/health/flea-tick-control.html), it is not clear whether an increasing database of adverse events reflects newly recognized toxicity or is a function of random illness with the ever-increasing number of doses administered. Several hundred reports of an adverse event may appear to be significant, but against a denominator of 1 billion (number of doses sold for the best-selling topical) this repre-

sents an infinitesimal risk. The costs and benefits of regularly using topicals to reduce tick infestations on companion animals needs to comprise the estimated and potential burden of ill health due to tick-borne infection or owner attitudes toward ectoparasitism as well as the estimated burden due to documented attributable toxic effects of the preventative. Such an analysis should be formally undertaken, but is likely to conclude that the benefits of topicals outweigh their slight risk of toxicity.

Vaccination is currently available only for Lyme disease. Vaccination against Lyme disease is effective because of a unique mode of immune protection[51] and, indeed, one formulation is virtually identical to the human Lymerix vaccine, which was briefly sold and withdrawn from the market because of poor sales. The Lymerix vaccine itself was considered safe and, indeed, in the decade since it was used, adverse event reports have not accumulated in postdeployment monitoring of vacinees. Vaccination should be considered for dogs that are frequently exposed to habitats with known deer tick infestations and where seroprevalence studies have indicated a greater than national risk. However, vaccination should only serve as a complement to topicals and appropriate grooming. Vaccination to reduce Lyme disease risk does not reduce the risk of other tick-transmitted infections.

Prevention is easiest of all for cats. Cats should remain indoors to prevent exposure to ticks, to reduce direct effects of cats on biodiversity either directly via predation of birds, small mammals, and reptiles, or to reduce indirect effects on biodiversity due to contamination of the environment by feline-maintained infections such as toxoplasmosis.[52]

References

1. Ribeiro JMC: Blood feeding arthropods: live syringes or invertebrate pharmacologists? Infect Agents Dis 4:143-152, 1995
2. Yoder JA, Hedges BZ, Tank JL, et al: Dermal gland secretion improves the heat tolerance of the brown dog tick, *Rhipicephalus sanguineus*, allowing for their prolonged exposure to host body temperature. J Therm Biol 34:256-265, 2009
3. Telford SR, Dawson JE, Katavolos P, et al: Perpetuation of the agent of human granulocytic ehrlichiosis in a deer tick-rodent cycle. Proc Natl Acad Sci U S A 93:6209-6214, 1996
4. Spielman A, Rossignol PA: Insect vectors, in Warren KS, Mahmoud AAF (eds): Tropical and Geographical Medicine. New York, McGraw Hill, 1984, pp 167-183
5. Shaw SE, Day MJ, Birtles RJ, et al: Tick-borne infectious diseases of dogs. Trends Parasitol 17:74-80, 2001
6. Otranto D, Dantas-Torres F, Breitschwerdt EB: Managing canine vector-borne diseases of zoonotic concern: part one. Trends Parasitol 25:157-163, 2009
7. Kjemtrup AM, Conrad PA: A review of the small canine piroplasms from California: *Babesia conradae* in the literature. Vet Parasitol 138:112-117, 2006
8. Birkenheuer AJ, Correa MT, Levy MG, et al: Geographic distribution of babesiosis among dogs in the United States and association with dog bites: 150 cases (2000-2003). J Am Vet Med Assoc 227:942-947, 2005
9. Telford SR, Goethert HK: Emerging tickborne infections: rediscovered and better characterized or truly new? Parasitology 129:S301-327, 2004
10. Dumler JS, Madigan JE, Pusterla N, et al: Ehrlichioses in humans: epidemiology, clinical presentation, diagnosis, and treatment. Clin Infect Dis 45:S45-S51, 2007
11. Harvey JW, Simpson CF, Gaskin JM: Cyclic thrombocytopenia induced by a *Rickettsia*-like agent in dogs. J Infect Dis 137:182-188, 1978
12. Ewing SA, Dawson JE, Panciera RJ, et al: Dogs infected with a human granulocytotropic *Ehrlichia* spp. (Rickettsiales: Ehrlichieae). J Med Entomol 34:710-718, 1998
13. Neer TM, Breitschwerdt EB, Greene RT, et al: Consensus statement on ehrlichial disease of small animals from the infectious disease study group of the ACVIM. J Vet Intern Med 16:309-315, 2002
14. Foggie A: Studies on the infectious agent of tickborne fever in sheep. J Pathol Bacteriol 63:1-15, 1951
15. Iqbal Z, Rikihisa Y: Reisolation of *Ehrlichia canis* from blood and tissue of dogs after doxycycline treatment. J Clin Microbiol 32:1644-1649, 1994
16. Birkenheuer AJ, Le JA, Valenzisi AM, et al: *Cytauxzoon felis* infection in cats in the mid-Atlantic states: 34 cases (1998-2004). J Am Vet Med Assoc 228:568-571, 2006
17. Lissman BA, Bosler EM, Camay H, et al: Spirochete-associated arthritis (Lyme disease) in a dog. J Am Vet Med Assoc 185:219-220, 1984
18. Littman MP, Goldstein RE, Labato MA, et al: ACVIM Small Animal Consensus Statement on Lyme Disease in dogs: diagnosis, treatment, and prevention. J Vet Intern Med 20:422-434, 2006
19. Demma LJ, Traeger MS, Nicholson WL, et al: Rocky Mountain Spotted Fever from an unexpected tick vector in Arizona. New Engl J Med 353:587-594, 2005
20. Warner RD, Marsh WW: Rocky Mountain Spotted Fever. J Vet Intern Med 10:1413-1417, 2002
21. Parola P, Paddock CD, Raoult D, et al: Tick-borne rickettsioses around the world: emerging diseases challenging old concepts. Clin Microbiol Rev 18:719-756, 2005
22. Billeter SA, Levy MG, Chronel BB, et al: Vector transmission of *Bartonella* species with emphasis on the potential for tick transmission. Med Vet Entomol 22:1-15, 2008
23. Wormser GP, Dattwyler RJ, Shapiro ED, et al: the clinical assessment, treatment, and prevention of Lyme disease, human granulocytic anaplasmosis, and babesiosis: clinical practice guidelines by the Infectious Diseases Society of America. Clin Infect Dis 43:1089-1134, 2006
24. Priestnall SL, Brownlie J, Dubovi EJ, Erles K: Serological prevalence of canine respiratory coronavirus. Vet Microbiol 115:43-53, 2006
25. Bowman D, Little SE, Lorentzen L, et al: Prevalence and geographic distribution of *Dirofilaria immitis*, *Borrelia burgdorferi*, *Ehrlichia canis*, and *Anaplasma phagocytophilum* in dogs in the United States: results of a national clinic-based serologic survey. Vet Parasitol 160:138-148, 2009
26. Centers for Disease Control and Prevention: Lyme Disease, United States, 2003-2005. MMWR Morb Mortal Wkly Rep 56:573-576, 2007

27. Falco RC, Smith HA, Fish D, et al: The distribution of canine exposure to *Borrelia burgdorferi* in a Lyme-disease endemic area. Am J Public Health 83:1305-1310, 1993

28. Lindenmayer JM, Marsha D, Onderdon AB: Dogs as sentinels for Lyme disease in Massachusetts. Am J Public Health 81: 1448-1455, 1991

29. Magnarelli LA, Anderson JF, Schreier AB, et al: Clinical and serologic studies of canine borreliosis. J Vet Med Assoc 191: 1089-1094, 1987

30. Foley JE, Brown RN, Gabriel MW, et al: Spatial analysis of exposure of dogs in rural north-coastal California to vector-borne pathogens. Vet Rec 161:653-657, 2007

31. Burgess EC: Natural exposure of Wisconsin dogs to the Lyme disease spirochete (*Borrelia burgdorferi*). Lab Anim Sci 36:288-290, 1986

32. Guerra MA, Walker ED, Kitron U: Canine surveillance system for Lyme borreliosis in Wisconsin and Northern Illinois: Geographic distribution and risk factor analysis. Am J Trop Med Hyg 65:546-552, 2001

33. Hamer SA, Tsao JI, Walker ED, et al: Use of tick surveys and serosurveys to evaluate pet dogs as a sentinel species for emerging Lyme disease. Am J Vet Res 70:49-56, 2009

34. Green RT, Levine JF, Breitschwerdt EB, et al: Antibodies to *Borrelia burgdorferi* in dogs in North Carolina. Am J Vet Res 49:473-476, 1988

35. Duncan AW, Correa MT, Levine JF, et al: The dog as a sentinel for human infection: prevalence of *Borrelia burgdorferi* C6 antibodies in dogs from southeastern and Mid-Atlantic states. Vector Borne Zoonotic Dis 5:101-109, 2005

36. Olson PE, Kallen AJ, Bjorneby JM, et al: Canines as sentinels for Lyme disease in San Diego County, California. J Vet Diagn Invest 12:126-129, 2000

37. Levy SA, O'Connor TP, Hanscom JL, et al: Evaluation of a canine C_6 ELISA Lyme disease test for the determination of the infection status of cats naturally exposed to *Borrelia burgdorferi*. Vet Ther 2:172-177, 2003

38. Magnarelli LA, Bushmich SL, Ijdo JW, et al: Seroprevalence of antibodies against *Borrelia burgdorferi* and *Anaplasma phagocytophilum* in cats. Am J Vet Res 66:1895-1899, 2005

39. Centers for Disease Control and Prevention: Diagnosis and management of tickborne rickettsial diseases: Rocky Mountain spotted fever, ehrlichioses, and anaplasmosis–United States: a practical guide for physicians and other health-care and public health professionals. MMWR Morb Mortal Wkly Rep 55(RR04):1-27, 2006

40. Liddell AM, Stockham SL, Scott MA, et al: Predominance of *Ehrlichia ewingii* in Missouri dogs. J Clin Microbiol 41: 4617-4622, 2003

41. Murphy GL, Ewing SA, Whitworth LC, et al: A molecular and serologic survey of *Ehrlichia canis*, *E. chaffeensis*, and *E. ewingii* in dogs and ticks from Oklahoma. Vet Parasitol 79:325-339, 1998

42. Kordick SK, Breitschwerdt EB, Hegarty BC, et al: Coinfection with multiple tick-borne pathogens in a Walker Hound kennel in North Carolina. J Clin Microbiol 37:2631-2638, 1999

43. Greig B, Asanovich KM, Armstrong PJ, et al: Geographic, clinical, serologic, and molecular evidence of granulocytic ehrlichiosis, a likely zoonotic disease, in Minnesota and Wisconsin dogs. J Clin Microbiol 34:44-48, 1996

44. Beall MJ, Chandrashekar R, Eberts MD, et al: Serologic and molecular prevalence of *Borrelia burgdorferi*, *Anaplasma phagocytophilum* and *Ehrlichia* species in dogs from Minnesota. Vector Borne Zoonotic Dis 8:455-464, 2008

45. Lappin MR, Breitschwerdt EB, Jensen WA, et al: Molecular and serologic evidence of *Anaplasma phagocytophilum* infection in cats in North America. J Am Vet Med Assoc 6:893-896, 2004

46. Breitschwerdt EB, Abrams-Ogg A, Lappin MR, et al: Molecular evidence supporting *Ehrlicha canis*-like infection in cats. J Vet Intern Med 16:642-649, 2002

47. Gordon JC, Gordon SW, Peterson E, et al: Epidemiology of Rocky Mountain spotted fever in Ohio, 1981: serologic evaluation of canines and rickettsial isolation from ticks associated with human case exposure sites. Am J Trop Med Hyg 33:1026-1031, 1984

48. Rodgers SJ, Morton RJ, Baldwin CA: A serological survey of *Ehrlichia canis*, *Ehrlichia equi*, *Rickettsia rickettsii*, and *Borrelia burgdorferi* in dogs in Oklahoma. Vet Diagn Invest 1:154-159, 1989

49. Breitschwerdt EB, Moncol DJ, Corbett WT, et al: Antibodies to spotted fever-group rickettsiae in dogs in North Carolina. Am J Vet Res 10:1436-1440, 1987

50. Case JB, Chomel B, Nicholson W, et al: Serological survey of vector-borne zoonotic pathogens in pet cats and cats from animal shelters and feral colonies. J Feline Med Surg 8:111-117, 2006

51. Telford SR, Fikrig E: Progress towards a vaccine for Lyme disease. Clin Immunother 4:49-60, 1995

52. Miller MA, Gardner IA, Kreuder DM, et al: Coastal freshwater runoff is a risk factor for *Toxoplasma gondii* infection of southern sea otters (*Enhydra lutris nereis*). Int J Parasitol 32:997-1006, 2002