Most common vector-borne diseases in dogs in Europe: a review

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The wide variety of infectious and parasitic disorders known as vector-borne diseases are spread by blood-feeding parasites such as ticks, fleas, lice, and mosquitoes. Anaplasmosis, ehrlichiosis, babesiosis, and borreliosis are important for both animal welfare and their potential to spread to humans. In addition, several social and environmental factors, such as shifts in the planet temperature and ecosystems, an increase in animal and human mobility, and chemoresistance to insecticides and acaricides are constantly changing the epidemiological scenario of vector-borne diseases. When these arthropods feed on an infected animal, they pick up the disease-causing pathogens. When, subsequently, they feed on a healthy animal, they can transmit the pathogen to that animal through their saliva. Early detection and treatment of these diseases is critical to ensure the best possible outcomes for affected dogs. The aim of the article was to discuss the most common vector-borne diseases in dogs in Europe, looking at the prevalence of the diseases and the health risks for dogs. We attempted to summarise the latest literature on various aspects of the disease pathophysiology, epidemiology, advantages and disadvantages of diagnostic techniques, available treatments, and methods for prevention in dogs.

Keywords: canine vector-borne diseases, canine anaplasmosis, canine ehrlichiosis, canine babesiosis, canine borreliosis

INTRODUCTION

Infectious diseases spread by ticks due to climate change are an increasing problem in Europe. The prevalence of vector-borne diseases in the dog population varies from year to year in different European countries. The literature discusses the epidemiological situation in different countries regarding Anaplasmosis spp., Borrelia spp., Babesia spp. and Ehrlichia spp., but there is no generalised discussion of the epidemiological situation of these diseases. In this paper, we will review the literature and assess the epidemiological situation in different regions of Europe, the main clinical pathologies caused by these diseases, the most effective methods for detection, and possible disease treatments by veterinarians.

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METHOD

For this literature review on the epidemiological situation of vector-borne diseases in Europe and the latest detection methods and treatment options, 47 articles, published between 2015 and 2023, were selected. Other articles in the literature were used to describe vector-borne pathogens or late history when pathogens were discovered. The selection of the articles was based on the materials and methods, the epidemiological situation in a European region where the vector-borne disease was studied, and the novelty of the article. The latest article discussing the vector-borne pathogen *Borrelia* spp. is from 2015 (Bouchard et al., 2015), and the earliest discussing the *Ehrlichia* spp. is from 2023 articles (Poolsawat et al., 2023). Clinical case reports were not included in the selection of the articles.

ANAPLASMOSIS

*Anaplasma* is an obligate intracellular, Gram-negative alpha-proteobacterium of the family *Anaplasmataceae*, which is the cause of canine anaplasmosis, a vector-borne infectious disease that affects dogs. The first dog cases were documented in 1982 in the United States and in 1988 in Europe (Madewell, Gribble, 1982). The classifications of the species in the genus *Anaplasma* include *A. marginale*, *A. centrale*, *A. bovis*, *A. ovis*, *A. caudatum*, and *A. phagocytophilum*. Granulocytic anaplasmosis and infectious canine cyclic thrombocytopenia are two zoonotic diseases mostly affecting dogs and wild canids that are brought on by *A. platys* and *A. phagocytophilum*, respectively (Atif et al., 2021). The entire genome of *A. phagocytophilum* was sequenced, and it was determined that it included a circular chromosome of a size of 1.2–1.5 × 10^6 bp. The genomic size of *A. platys* is 1.196 × 10^6 bp. Although it is dogs that are usually infected with *A. platys*, it has also been detected in cats, camels, and people (Llanes, Rajeev, 2020). In Europe, ixodid ticks of the genera Ixodes, Dermacentor, Haemaphysalis, and Amblyomma are the major carriers of *A. phagocytophilum* (Atif et al., 2021).

Canine granulocytic anaplasmosis is the term used to describe an infection with *A. phagocytophilum* in dogs. Granulocytes are frequently infected by *A. phagocytophilum*, which results in leukopenia and thrombocytopenia. This modifies the host's immune system, controls several tick genes, and positively regulates cellular cholesterol (Atif et al., 2021). The pathogen attaches to the ligands on the cell surface, enters the cell by receptor-mediated endocytosis, and reproduces in membrane-bound vesicles to create the so-called morulae. Cytolysis releases it, and it then infects further cells (Chirek et al., 2018). Later these pathogens parasitise platelets, monocytes, and erythrocytes, which circulate blood cells. Lethargy, petechiae, pale mucous membranes, nasal discharge, bilateral uveitis, epistaxis, fever, anorexia, weight loss, lymphadenomegaly, and uveitis are all symptoms of the disease (Atif et al., 2021). The pathogenic bacterial strain, the host's sensitivity, and the stage of bacterial growth all affect the seriousness of the infection. Neutrophils and leukocytes are less abundant in the blood of the affected host, which results in immunosuppression and a propensity for opportunistic infection (Woldehiwet, 2010). The unspecified haematological and biochemical profile changes linked to this illness include thrombocytopenia, anaemia, morulae in neutrophils, and elevated liver enzyme activity. Although this information concerns dogs, it is not yet known whether certain clinical symptoms and clinicopathological abnormalities are associated with this disease. (El Hamiani Khatat et al., 2021). Lethargy and decreased activity (83%), fever (67%), and inappetence (63% of the *A. phagocytophilum*-positive dogs included in the study) were the most prevalent clinical symptoms. The most frequent laboratory abnormality was thrombocytopenia (86%), which was followed by hyperbilirubinemia (77%), anaemia (70%), hypoalbuminemia (62%), and leucocytosis (27%) (Chirek et al., 2018).

In dogs with severe thrombocytopenia, reinfection with *A. platys* may occur after two weeks of incomplete recovery. It may be a result
of immunologically-mediated processes that directly harm platelets and immune cells. Megakaryocytes and promegakaryocytes can also become infected with *A. platys*, which mostly affects platelets and causes thrombocytopenia (Atif et al., 2021). *A. platys* infection may also include different symptoms such as muzzle hyperkeratosis, eye discharge, spot bleeding on the eye, oral mucosa, or skin (Bouzouraa et al., 2016). Canine granulocytic anaplasmosis caused by *A. platys* could also manifest in intense vomiting, diarrhoea, polyuria, jaundice, epistaxis, lymphatic adenomegaly, and splenomegaly (Nair et al., 2016).

Many investigations have shown that there is a wide range of genetic variability, as well as host tropisms and pathogenicity. Yet, the relation between genetic diversity and altered pathogenicity it is still unclear. For the identification of the aetiological agent and disease diagnosis, numerous conventional, serological, and molecular techniques have been validated. In the acute stage of the disease, newly produced stained blood smears (Giemsa, Diff-Quik) collected from a vein are utilised for conventional light microscopy. *A. phagocytophilum* infection leads to the formation of 'morulae', a combination of mulberry-type colonies developed in the neutrophils and eosinophils of infected organisms (Woldehiwet, 2010). Parasites can be found in a blood smear only in the early stages (4–14 days after infection), after which not all samples will contain morulae. Anaplasma morulae typically resemble inclusion bodies that are dark blue to purple. On the other hand, anticoagulant-mixed chilled samples can be processed in 24–48 hours. This is the quickest, least expensive, and most effective technique to see germs up close before beginning antibacterial therapy. However, in the cases of prolonged infection accompanied by monocytopenia, neutropenia, thrombocytopenia, and anaemia, this technique is less responsive to reducing bacteraemia. For *A. platys* and *A. phagocytophilum* morulae, it is preferable to use a leukocyte smear rather than whole blood. This enhanced fraction is very helpful for identifying cases of leucopenia and thrombocytopenia manifesting as clinical sequelae since these organisms are restricted to platelets and leukocytes (Eddestone et al., 2007). For diagnosis, nucleic acid detection techniques such as conventional, nested and semi-nested PCR, real-time PCR, and LAMP (loop-mediated isothermal amplification) have been used. The typically targeted genes for the molecular diagnosis of anaplasmosis are the 16S rRNA, citrate synthase, heat shock, and major surface proteins (Msp1, Msp2, Msp4, and Msp5) (Silaghi et al., 2017). Real-time molecular diagnostic techniques that target numerous genes have been developed for direct detection of *A. phagocytophilum* genes in blood, tissue, ticks, and vectors. These techniques can then be applied to taxonomic and phylogenetic research. *A. phagocytophilum* and *A. platys* have both had their whole genomes sequenced. This will support the development of vaccines as well as diagnostic and management strategies for these significant microorganisms (Diaz-Sanchez et al., 2018).

Tetracycline is the recommended medication for treatment of anaplasmosis infections. Doxycycline successfully treated infections in Doxycycline successfully treated the infection in dogs after 7–10 days of treatment, and no relapses have ever been noted. Rifampin therapy should be taken into consideration for patients who are at risk for negative medication reactions. *A. phagocytophilum* vaccines are not yet accessible, although numerous vaccine candidates have been proposed. However, developing an effective vaccine has proved to be a challenge so far (Stuen et al., 2013). Studies show that the treatment with doxycycline resulted in resolution of all clinical abnormalities in about 30 to 60 days following the start of treatment; the blood of the affected canines tested PCR-negative. Additionally, all post-treatment PCR results from lymph node biopsies were negative (Yancey et al., 2017). Nevertheless, a small number of authors saw clinical relapse following doxycycline therapy or an insufficient response to treatment, including three of 12 dogs from the north-central part of the United States, who were identified as having *A. phagocytophilum* serology-based disease
The best and least expensive defence against anaplasmosis is vaccination. It should be noted that whole genomes of both *A. phagocytophilum* and *A. latys* have been sequenced. This can aid in the exploration of numerous novel genes that might make good vaccine candidates. Nine anaplasma proteins, namely, the Asp14, Asp55, Msp5, Msp2, AipA, OmpA, APH 0032, and APH 1384 antigens of the type IV secretion system of *A. phagocytophilum*, have the ability to elicit an immune response (Chirek et al., 2018).

Due to worldwide distribution and possible endemicity, anaplasmosis can be found in 43 different countries. Due to the high variability in the quantities of ticks in different areas and in the frequency of diagnostic tests used, the epidemiological situation of anaplasmosis varies from one region to another and from one animal species and breed to another. *Anaplasma phagocytophilum* and *A. platys* are found on each continent. *A. phagocytophilum* has the ability to infect a variety of domestic and wild animals as well as people; in contrast, *A. platys* typically affects dogs and infrequently cats (Stuen et al., 2013). According to the studies, the highest numbers of *A. phagocytophilum* are observed in Europe (Karshima et al., 2022). *A. phagocytophilum* infections have mostly been reported in northern and central Europe. *A. phagocytophilum* was found in 3% to 57% of dogs in epidemiological studies conducted in Europe that assessed the seroprevalence (rarely a DNA-based study). Results of real-time PCR analysis for *A. phagocytophilum* in Lithuania demonstrated the presence of *A. phagocytophilum* in 35% of dogs (Radzievskaia et al., 2020). However, various studies looked at various dog populations, including both healthy and ill dogs, and they employed various techniques, the immunofluorescent antibody test (IFAT) and the enzyme-linked immunosorbent assay (ELISA) among them. The true seroprevalence may also be overestimated because of serological cross-reactivity with other *Anaplasma* species, such as *A. platys* (Sainz et al., 2015).

**EHRlichiosis**

*Ehrlichia canis*, a gram-negative, obligate intracellular bacterium, is the cause of canine monocytic ehrlichiosis (CME), a tick-borne disease that affects dogs all over the world and is transmitted by ticks (Pugliese et al., 2022). Donestein made the initial discovery of the *E. canis* pathogen strain in Algeria in 1935. In the 1970s, when military canines were infected in Vietnam, and it developed into a serious illness. Consequently, it was also known as ‘tracker dog disease’ and ‘tropical canine pancytopenia’. The infection was then discovered in other locations around the world, including the United States, countries in South America, Africa, and Asia (Hai, Khuong, 2021). The infection primarily affects the leukocytes (monocytes, macrophages, and neutrophils) of the mammals as well as the salivary gland, the gut, and hemocoel cells of tick. *E. canis*, *E. chaffeensis*, *E. ewingii*, *E. muris eauclarensis*, *E. ruminantium*, and *E. minasensis* are the six species that now make up the genus (Diniz, Moura de Aguiar, 2022). The tick *Rhipicephalus* referred to as the brown dog-tick is the primary and perhaps the only vector for *E. canis* in Europe. Experimental evidence suggests that this tick is a capable vector for *E. canis*. According to a recent study, *E. canis* transmission by *Rhipicephalus sanguineus* ticks begins three hours after the tick attaches to the dog (Fourie et al., 2013). The only Ehrlichia species isolated from dogs in Europe is *E. canis*. Dogs from Europe have not tested negative for other *Ehrlichia* species, including *E. chaffeensis*, *E. ewingii*, *E. muris*, and *E. ruminantium*. *E. canis* has a zoonotic potential as it has been reported as causing infection in humans (Sainz et al., 2015).

*E. canis* infection mostly happens in the summer months when the vector tick is active. The majority of dogs recover from the acute and subclinical periods. All dog breeds can contract *E. canis*, but German shepherds seem to be more vulnerable because this breed exhibits more severe form of the disease and has a greater morbidity and mortality.
rate compared other breeds (Harrus, Waner, 2011). In other studies, it was demonstrated that the risk of *E. canis* infection does not depend on the breed (Hai, Khuong, 2021). Due to the several phases and numerous clinical presentations of the disease, diagnosis can be difficult. The acute phase of ehrlichiosis develops over 1–3 weeks and is characterised by listlessness, swollen lymph nodes, anorexia, fever, and ocular and nasal discharge, among other clinical symptoms. Together with the symptoms of the acute phase, the chronic phase also includes widespread haemorrhage, increased mononuclear cell infiltration of organs, nose-bleeds or other abnormal bleeding, and weight loss. Anaemia, leucocytosis, hyperglobulinemia, hypoalbuminemia, and an increase in blood urea nitrogen and creatinine are also detected in cases of erlichiosis (Pugliese et al., 2022). High fever, depression, lymphadenomegaly, splenomegaly, and epistaxis are some of the clinical symptoms that are present during the acute phases of ehrlichiosis. Ophthalmological abnormalities are common and include bullous retinal detachment, anterior uveitis, chorioretinitis, papilledema, retinal haemorrhage, and the presence of retinal perivascular infiltrates. Blood hyperviscosity can cause sub-retinal haemorrhage and retinal detachment, which can end in blindness (a variety of neurological symptoms might ensue from meningitis and/or meningeal bleeding). The most noticeable haematological change that takes place during the acute period is thrombocytopenia (Harrus, Waner, 2011). Pale mucosa, skin inflammation, eye discharges, clouded eyes, hair loss around the eyes, diarrhoea, belly skin bleeding, constipation, ascites, vomiting, salivation, and metritis are some of the symptoms (Hai, Khuong, 2021). Pancytopenia brought on by the suppression or devastation of bone marrow characterises the chronic phase of the disease. Serum biochemical abnormalities in ehrlichiosis are monoclonal; gammapathies can occasionally happen, and polyclonal hypergammaglobulinemia is most frequently detected by serum protein electrophoresis. During the acute phase, dogs frequently have slight elevations in their alanine aminotransferase (ALT) and alkaline phosphatase (ALP) levels. Clinical ehrlichiosis may result in an increase in acute phase protein concentrations. *E. canis* vaccination in five dogs demonstrated that plasma C-reactive protein (CRP) values rose between 4 and 16 days and peaked between 15 and 42 days later (Poolsawat et al., 2023). Canine ehrlichiosis can manifest at any age. The predisposition to the disease is not linked to the sex of the animal. Older dogs had greater seropositivity rates in epidemiological investigations (Sainz et al., 2015).

Haematology, cytology, serology, and isolation are useful diagnostic methods for *E. canis*, but molecular approaches are necessary for a conclusive diagnosis of infection. The veterinary field uses serology-based indirect immunofluorescence antibody (IFA) tests and commercially available point-of-care (POC) immunochromatography tests for *E. canis* as part of a routine annual vector-borne disease screening programme and as a diagnostic tool when dogs exhibit clinical signs (Lara et al., 2020). Additionally, during the first two weeks of infection, antibodies against *E. canis* are typically lacking and can cross-react with several other ehrlichial species. However, sensitive techniques for identifying and characterising *E. canis* DNA include PCR and sequencing. There are several tests based on various target genes (such as 16S rRNA, p28, p30, dsb, and VirB9), but the 16S rRNA and p30-based PCR assays are the most widely used. These methods might be helpful for distinguishing between various ehrlichial species and strains. PCR (conventional or real-time) has various benefits over serology, including early identification of DNA before seroconversion, better sensitivity, the absence of anti- *E. canis* antibodies, and the presence of ehrlichial DNA, which suggests an ongoing infection rather than exposure (Abdel fattah et al., 2019). The primary immunoreactive protein TRP36, which is encoded by the *trp36* gene in *E. canis*, has been utilised to successfully define the genetic diversity of this pathogen worldwide (Pugliese et al., 2022). PCR and sequencing are sensitive techniques for
detecting and identifying *E. canis* DNA. With relatively low annealing temperatures, when pollutants are present or when non-specific amplification takes place, false positive results can be produced. While a negative PCR result indicates that no target DNA was found, it does not imply that there was no DNA in the sample. Concentrations have been reported to grow between 4 and 16 days and peak between 15 and 42 days following inoculation with *E. canis* in five dogs, with detection of DNA possible as early as 4–10 days post-inoculation (Stich et al., 2002). A rapid, sensitive, specific, and accurate diagnosis of ehrlichiosis is essential for both treating the condition and halting its spread. Due to its excellent performance in terms of specificity and sensitivity, nucleic acid detection is one of the most trustworthy assays that is being employed more frequently for the identification of infections. Conventional PCR methods have been widely utilised to diagnose *E. canis* by focusing on some DNA regions, such as the 16S rRNA, trp36, and p30 (Yukhet et al., 2021).

Antimicrobial therapy should be given to dogs who have consistent clinical and clinicopathologic abnormalities, also seroreactivity to *E. canis*, and/or molecular or cytological evidence of *E. canis* infection (Mylonakis et al., 2019). Tetracycline-family medicines are typically effective in treating ehrlichiosis. Doxycycline at 5 mg/kg twice day or 10 mg/kg once daily for four weeks is the preferred treatment. In most instances, this regime ensures a thorough response. In some studies, experimentally infected dogs continued to be infected and developed into subclinical carriers even when given the required doses of doxycycline. As a result, a four-week therapy course is advised (Sainz et al., 2015). Ehrlichiosis has traditionally been treated with other medications. Although chloramphenicol was used in puppies, it is not advisable to do so when doxycycline is readily available. Additionally, imidocarb dipropionate has been mentioned as a potential treatment for canine ehrlichiosis. Recent research found that imidocarb dipropionate was ineffective against *E. canis*, both in vitro and in experimentally infected dogs (Eddlestone et al., 2006).

*E. canis* is primarily found in tropical and subtropical regions, particularly in countries with higher temperatures and higher numbers of tick vectors. It is most reported in areas such as southern Europe, including Spain, Portugal, Italy, and Greece. However, the epidemiological situation of *E. canis* in Europe may have evolved (Weber, 2022). Birds are frequently mentioned as hosts of ticks and other blood-sucking arthropods that can spread vector-borne infection. In Europe, the prevalence of *E. canis* infection varies among countries and regions. Some studies report relatively high prevalence rates in certain areas, especially in countries with a Mediterranean climate. However, it is important to note that *E. canis* is not uniformly distributed across Europe, and there may be variations in prevalence and incidence rates within different regions and over time (Stich et al., 2002). Additionally, companion dogs had a higher seropositivity rate for *Ehrlichia* spp. than hunting dogs. The likelihood of *Ehrlichia* spp. seropositivity was higher in animals that had not received antiparasitic treatment, for example, endo- and/or ectoparasiticides active against vectors or vector-borne pathogens, such as milbemycin, fipronil, permethrin for 12 months prior to sampling compared to animals that had not received treatment in the previous 6 to 12 months, three to six months, or less than three months. Regarding climatic conditions, dogs living in areas with an average temperature of 15.9°C were more likely to be seropositive for *Ehrlichia* spp. than dogs living in areas with an average temperature below 15.9°C. Similarly, when compared to the dogs in locations with higher total annual rainfall, dogs living in areas with lower total annual rainfall were more likely to be seropositive to *Ehrlichia* spp. (Angelou et al., 2019). With a tendency of lowering test positivity rates for the ehrlichiosis pathogen, the overall number of results for tick-borne infections in Europe grew each year. Higher *Ehrlichia* spp. antibody test positivity rates (>3%) were observed in Greece, Italy, Lithuania, the Netherlands, Portugal, Romania, Russia, Spain, and Switzerland; positivity rates were lower (<1%) in Denmark,
Estonia, Finland, Hungary, Norway, Slovakia, Slovenia, and Sweden. Greece had the highest percentage of positive outcomes (19.6%), while Denmark, Estonia, Hungary, and Slovenia all had low percentages of positive results (0.5%) (Miró et al., 2022).

**BORRELIOSIS**

The diversity of other pathogens carried by *Ixodes* and other ticks and the numerous *Borrelia* species that occur have become better understood over the past ten years (Adaszek et al., 2022). The discovery that most *Borrelia* seropositive dogs exhibit no clinical signs of the disease, either in the laboratory or in the field, has not altered. The most common tick-borne disease, Lyme borreliosis, is caused by the spirochete bacterium from the *B. burgdorferi* sensu lato (s.l) complex, which is transmitted enzootically between ticks and their hosts. *B. burgdorferi* s.l. controls the expression of specific genes to enable it to survive in ticks and mammals. By doing this, *B. burgdorferi* s.l. can adjust to the dietary and environmental alterations that result from its transmission between the two hosts. Every stage of the enzootic cycle involves specific interactions between the spirochete and its host, and these interactions determine whether the spirochete will live to the next stage (Helble et al., 2021). *B. burgdorferi* s.l. was separated into numerous species based on numerous independent genomic investigations. In North America, *B. burgdorferi* sensu stricto (s.s.) is the main cause of Lyme disease. In Europe and Asia, the causing agents are *B. burgdorferi* s.s., *B. afzelii*, *B. garinii*, and *B. bavariensis*. Other species have been found, but they have not been definitively linked to overt clinical disease (Marconi et al., 2020).

The *Borrelia* spp. in the tick do not instantly spread to the vertebrate host after a tick bite. Instead, during the first 12 to 24 hours after biting the host, the organisms go through a change in their outer surface to increase their chances of survival in the host (Parry, 2016). Both dogs and humans can experience clinical effects from infection, despite neither species being important in the maintenance of the disease or its subsequent transmission to other ticks. Erythema migrans (red rash) and flu-like symptoms are frequent early signs of infection in humans. Clinical indications related to the neurological system, heart, and joints may appear as the infection spreads throughout the body. Except for erythema migrans, the clinical presentation in dogs is similar and includes fever, lethargy, arthritis, joint swelling, and lymphadenopathy (Liu et al., 2019). It is uncommon and poorly understood in canines to observe dermatologic, neurological, or cardiac manifestations as they manifest in human patients. Lyme nephritis, the most severe (potentially associated) type of Lyme borreliosis in dogs, is less frequent than Lyme arthritis (Littman et al., 2018). Clinical symptoms of canine borreliosis often start out nondescript and progress slowly. Another common acute presentation of Lyme disease in dogs is lameness caused by joint swelling, reported in 9–28% of dogs. In seropositive dogs, polyarthritis often occurs after exacerbation of Lyme disease. An acute chronic infection can lead to progressive renal failure and causes protein-losing glomerulopathy, cardiovascular blockage, and neurological issues. Tissues, synovial membranes, joint capsules, and related tendon sheaths frequently have microlesions and are inflamed. Additional possible complications include glomerulitis, hyperkeratosis, lymphoplasmacytic vasculitis, arteritis, perineuritis, meningitis, joint pannus, and chronic supplicative arthritis. Although infected dogs exhibit a strong Ab response to *B. burgdorferi*, the humoral immune response is typically insufficient to eradicate the infection that has already developed. Protection from natural infection that may arise is often strain-specific and short-lived (Parry, 2016).

Aside from azotaemia, other non-specific disorders in these dogs include thrombocytopenia, hypoalbuminemia, and non-regenerative anaemia. In the few cases of Lyme nephritis that have been reported, progressive renal failure was linked to Lyme borreliosis serology; symptoms in affected dogs may include non-regenerative anaemia, stress leucogram, thrombocytopenia, hypoalbuminaemia, azotaemia,
hypercholesterolaemia, hyperphosphataemia, and occasionally hyperkalaemia and hyperbilirubinaemia. Oliguria, reduced concentration (urine specific gravity frequently below 1.022), haemoglobinuria, haematuria, glucosuria, and bilirubinuria are other possible findings in dogs with Lyme nephritis. In dogs with Lyme nephropathy, glomerulonephritis with diffuse tubular necrosis and regeneration, as well as lymphoplasmacytic interstitial nephritis have been characterised as a distinct histological lesion in the kidneys. The cause of this lesion, which is thought to be immune-mediated rather than the result of spirochaetes invading the kidneys, has not yet been established (Parry, 2016). Some ticks have the ability to emit poisons which can cause tick paralysis. The ticks feed ferociously after becoming attached to a host. A tick communicates with its vertebrate host while it feeds over protracted periods of time. By suppressing the immunological response and tying up any antibodies the host may have produced in an effort to get rid of the blood-sucking parasite, it can weaken the immune system of the host (Hai, Khuong, 2021).

Though *B. burgdorferi* s.l. culture from tissue or blood is the gold standard in laboratory diagnosis of Lyme disease, this test has limited sensitivity, necessitates incubation times of up to 6–8 weeks, and is normally employed exclusively in research settings (Bouchard et al., 2015). The primary method of diagnosis is serology, and it is based on an immune enzymatic test and a Western blot confirmation test. The PCR approach, which amplifies borrelial DNA and may produce results quickly (within a few hours) is widely practised despite being expensive. However, this method should not be used as the sole diagnostic tool when clinical Lyme disease is suspected, because it cannot distinguish between living and dead spirochaetes, and false-negative results are frequently obtained as *Borrelia* organisms are hard to detect in naturally infected dogs due to low spirochaetal burdens. Spirochaetes are rarely found in bodily fluids like blood, urine, synovial fluid, or cerebrospinal fluid; instead, they are more frequently found in the tissues of animals with persistent infections, such as the skin, connective tissue, and joint capsule. Tissue samples are therefore advised for PCR testing (Parry, 2016). The most widely used test for *B. burgdorferi* s.l. infection uses extremely sensitive and specific serological assays for the detection of specific antibodies to *B. burgdorferi* s.l. in serum (Bouchard et al., 2015).

Chronic disease is typically prevented by early therapy with antibiotics like doxycycline or amoxicillin for four weeks. Tick prevention measures, such as tick repellents, are very effective at halting the spread of the disease. The symptoms of Lyme arthritis, which are present in a small percentage of infected dogs, are transient or rapidly improved by oral antibiotics (Littman et al., 2018). Tetracyclines, penicillins, macrolides, and cephalosporins can all cause side effects for the animal in the treatment of *Borrelia* spp. They can be administered intravenously or orally and are used in the early and late stages of the disease. In both human and veterinary medicine, beta-lactams and tetracyclines are frequently used to treat individuals with Lyme disease since they have also been found to be effective. Doxycycline is advised as the primary choice for the majority of sick dogs with suspected borreliosis due to its simplicity of administration and effectiveness against coinfections. In some countries, doxycycline is recommended for puppies and kittens as young as four weeks old. In the cases of tetracycline sensitivity, other groups of antischrochetal medicines are used (Littman et al., 2018). Despite most early-cured Lyme disease cases receiving good therapy, recurrence may happen when antibiotic delivery is stopped. *B. burgdorferi* s.l. can cause the host to remain infected for an extended period. According to some research, dogs treated with antibiotics may also experience PCR positivity in the absence of culture positivity (Milkovičová et al., 2023). There are vaccines available to lessen infection transmission and clinical symptoms in canines. Several different types of *B. burgdorferi* s.s. vaccines are currently commercially available in the USA, including several bacterins (e.g., LymeVax®, Zoetis; Nobivac®Lyme, Merck Animal Health),
recombinant OspA subunit vaccines (e.g., RECOMBITEK® Lyme, Boehringer Ingelheim), and a chimeric recombinant OspA and OspC vaccine (VANGUARD® crLyme, Zoetis) (Vogt, Stevens, 2021). There are currently no experimental field trials evaluating the effectiveness of canine B. burgdorferi vaccinations available. Lysate vaccines made with B. burgdorferi s.s., B. garinii, and B. afzelii are available in Europe; however, additional pathogenic species may be present in ticks, and complete cross-reactive immunity from the vaccine-induced antibodies has not been established (Chomel, 2015).

Since the 1970s, there have been changes in the prevalence and distribution of canine vector-borne illnesses, including Lyme disease, across Europe. In addition, importing dogs from endemic regions, traveling with dogs, and tourism all greatly contribute to the spread of canine vector-borne diseases to new places (Milkovičová et al., 2023). In assessing the public health risk of Lyme disease, tracking the prevalence of B. burgdorferi s.l. has been deemed essential. Because its uninfected life stages (larvae, nymphs, and adults) can feed on infected wildlife reservoirs, get infected, and then spread the illness to other mammals while taking their next blood meal, Ixodes spp. is a significant vector of Lyme disease. Due to ticks’ indiscriminate host selection, B. burgdorferi can spread from wild animals to domestic pets and people (Vrhovec et al., 2017). The meta-analysis (Strnad et al., 2017) revealed that the mean prevalence of B. burgdorferi s.l. in ticks across Europe was 12.3%, with the highest incidence occurring in Romania, Serbia, and Bosnia and Herzegovina (18.5%), as well as Central Europe (Austria, the Czech Republic, Germany, Hungary, Poland, Slovakia, and Switzerland), and the Balkan Peninsula (19.3% and 18.5%, respectively). Slovakia has a long history of studying the ecology of ticks and the epidemiology of diseases spread by ticks. Incidence of borrelia in Slovakia’s hunting dogs is among the highest in all of Europe, yet it varies greatly in suburban forests around 4.4% in northern Slovakia (Pangrácová et al., 2016). Seventy-five healthy dogs living in rural countryside in the Netherlands and 448 hunting dogs were tested in recent research for antibodies against B. burgdorferi s.l. using a whole-cell ELISA. The dogs’ ages and breeds varied. In 18% of hunting dogs and 17% of pet dogs, antibodies against B. burgdorferi were found. Individuals in the hunting dog group appeared to have a greater risk of exposure (22%) than younger dogs (9–11%), and the seroprevalence among hunting dogs over 24 months of age remained consistent at roughly 22%. When compared to humans, whose seroprevalence can persist somewhat longer, dogs older than 24 months may show no significant increase in seroprevalence, suggesting that seropositivity following B. burgdorferi infection in dogs is brief, lasting only about a year (Goossens et al., 2001).

BABESIOSIS

Babesia spp. are tick-borne protozoan parasites that infect the erythrocytes of domestic and wild animals as well as humans. They are members of the phylum Apicomplexa, class Piroplasmea, order Piroplasmida, and family Babesiidae. The virulence of the various species and strains involved in the babesia infection and other factors that affect the host’s response to infection, such as age, individual immune status, and the presence of concurrent infections or other diseases, can all affect the clinical manifestations of the disease (Baneth et al., 2018b). Ixodes and Dermacentor ticks are the main vectors for babesiosis in Europe (Köster et al., 2015). In the past, Babesia infection in dogs was largely determined by the parasite’s morphology in erythrocytes; all large forms were called Babesia canis, whereas small forms were called Babesia gibsoni. Based on cytological analysis of stained blood samples, it was once believed that B. canis (large Babesia) and B. gibsoni (small Babesia) were the culprits behind canine babesiosis. Molecular methods have shown that several Babesia species, including B. canis, B. vogeli, and B. rossi (large forms) and B. gibsoni, B. conradae, and B. vulpes (small forms), infect canines (Panti-May et al., 2020).
The various *Babesia* species involved and their unique virulence, as well as factors that affect the host’s response to infection, such as age, individual immune status, and coinfections with other pathogens, affect the clinical manifestations of canine babesiosis. Clinical signs of babesiosis in dogs include temperature and lethargy, and later they may develop develop anemia, liver, pulmonary, renal, or cerebral dysfunction, as well as haemostatic abnormalities (Baneth et al., 2018a). *Babesia* spp. infections can cause a variety of clinical symptoms, from asymptomatic infections to multiorgan failure with a risk of death (Solano-Gallego et al., 2016). Haemostasis and inflammation are closely linked pathophysiologic processes that may have a significant impact on one another. All elements of the haemostatic system, including vascular endothelial cells, platelets, the plasma clotting cascade, the physiological anticoagulant pathways, and fibrinolytic activity, are involved in extensive crosstalk between the immune and haemostatic systems (Kuleš et al., 2017). Fever, splenomegaly, inappetence, weakness, lethargy, generalised lymphadenopathy, anaemia, haemoglobinuria, and collapse linked to intra- and extravascular haemolysis, hypoxic injury, systemic inflammation and pigmenturia are the main symptoms of the disease. At an advanced stage, abnormalities in numerous internal organs, including the lungs, kidneys, pancreas, and heart, have also been reported (Obeta et al., 2020). Jaundice and pigmenturia can all be brought on by *Babesia* species. Although thrombocytopenia is regularly found to varied degrees, petechiae or ecchymosis are less frequently found. When present, thrombocytopenia can range in severity from mild to severe, just like anaemia. In terms of thrombocytopenia, the *B. canis* genotype 18S rRNA-B strains were discovered to be more virulent (Adaszek et al., 2009). In addition, abnormalities such as hypoalbuminemia and hyperbilirubinemia can be found. Anaemia is brought on by a combination of intravascular and extravascular haemolysis brought on by red blood cell damage and rupture brought on by parasites, enhanced osmotic fragility of the cells, and the action of secondary immune-mediated mechanisms in all species (Jacobson 2006). In Europe, 31% of dogs affected by *B. canis*, need to be admitted to the hospital for intensive care. The infection is marked by a multitude of consequences, many of which are deadly (30%), in addition to haemolytic anaemia (intravascular and extravascular), the characteristic presentation of infections with *Babesia* spp. When erythrocytes are destroyed, anaemia can range in intensity from mild haematocrit (Ht, 0.15–0.30 L/L) to severe (Ht <0.15 L/L). The fact that anaemia can be severe even in cases with low parasitaemia suggests that such non-parasite processes as peripheral capillary sludging, erythrophagocytosis by the spleen and liver, and perhaps immunoglobulin and complement-mediated erythrocyte destruction are involved (Köster et al., 2015). Anaemia does not always show up in the clinical indications of canine babesiosis, though. In 62% of sick dogs, anaemia-related laboratory symptoms were discovered. Haematologic analysis findings revealed that in 38% of the sick dogs, no changes in blood morphology were found. Marked thrombocytopenia has been reported in 62% of the *Babesia*-infected dogs, although there has been no discernible decline in the erythrocyte count, haematocrit, or haemoglobin concentration. It was also shown that the haematological abnormalities of sick dogs frequently caused leukopenias (neutropoenia, lymphopenia, and monocytes) (Zamokas et al., 2014).

An effective diagnostic method for canine clinical babesiosis is blood smear analysis. For most veterinarians, a microscopy evaluation remains the simplest and most accessible diagnostic procedure. It can help the veterinarian make a good diagnosis, but it is less sensitive than molecular testing and is more reliant on the *Babesia* species infecting the dog. A blood smear can be used to distinguish between the large and small forms of *Babesia*. The majority of sick dogs that have been infected by the big types of *Babesia* (such as *B. canis*) can be diagnosed using light microscopy. Also, morphological inspection is insufficient for identifying the species of piroplasm,
necessitating the use of molecular methods like PCR and sequencing (Solano-Gallego et al., 2016): (1) PCR detection is more accurate than a straightforward blood smear test, (2) the presence of DNA for a particular pathogen in a clinical environment may indicate an ongoing infection that is still alive, and (3) PCR enables a more accurate identification of the causal species infecting the dogs as opposed to direct detection by optical microscopy or serology (Solano-Gallego et al., 2016). Babesia species can be recognised and distinguished using various molecular methods. These include reverse line blotting, PCR-restriction fragment length polymorphism analysis, and semi-nested PCR. Additionally, several genes are frequently utilised to distinguish between Babesia species. Typically, these include the two internal transcribed spacers (ITS1 and ITS2) and the nuclear ribosomal RNA genes (Yisaschar-Mekuzas et al., 2013). The molecular analysis of 18S rRNA and Bc28.1 genes of B. canis reveals that genetically heterogeneous B. canis strains circulate in Lithuania. Based on two single nucleotide polymorphisms, 18S rRNA gene sequences were divided into three genotypes by molecular analysis (Radzijevskaja et al., 2022).

The side effects of imidocarb dipropionate, an aromatic diamidine, can be explained by several different mechanisms. One theory is that it prevents Babesia spp. infected erythrocytes from absorbing inositol, which leads to their starvation (McHardy et al., 1986). The second theory is that it reacts with Babesia DNA and damages nucleic acids while preventing cell repair and further replication. The liver and kidneys eliminate imidocarb dipropionate. Imidocarb dipropionate is frequently used in Europe to treat parasitosis brought on by B. canis, but it has also been shown to have an impact on smaller Babesia species, such as B. gibsoni. However, imidocarb dipropionate has an inadequate effect when used to treat B. gibsoni, thus its usage is not advised (Solano-Gallego et al., 2016). Other variations of therapy protocols have been applied in the management of the B. gibsoni infection in addition to the previously listed combinations. Clindamycin (30 mg/kg body weight orally every 12 hours), diminazene aceturate (3.5 mg/kg body weight intramuscularly once only at the start of treatment), and imidocarb dipropionate (6 mg/kg body weight subcutaneously once only at the start of treatment, 24 h after diminazene application) are three drugs that have been combined to explore the effects. After the treatment was finished, 11 out of the 13 observed dogs did not achieve a full clinical cure, and relapses occurred soon (Lin, 2012). In a different study (Suzuki et al.), the combination of clindamycin (25 mg/kg of body weight orally every 12 hours), metronidazole (15 mg/kg of body weight orally every 12 hours), and doxycycline (5 mg/kg of body weight orally every 12 hours) was examined. Three of the four dogs examined showed the elimination of parasitemia, while the fourth dog experienced a rapid recurrence of the illness (Suzuki et al., 2007).

The spread of D. reticulatus range is directly related to the rise of canine babesiosis caused by B. canis (Dwużnik-Szarek et al., 2021). Canine babesiosis affects both well-known endemic locations (Central Europe) and newly discovered ones (Northeastern Europe, including the Baltic countries) (Rubel et al., 2016). Dogs in Europe are infected by both the large and small forms of Babesia species, and the geographic distribution, transmission, clinical symptoms, course of therapy, and prognosis are very different for each species (Solano-Gallego et al., 2016). The substantial epidemiological and genetic data gathered indicate the proliferation (and emergence) of novel piroplasm species across central, northern, and north-eastern Europe, despite inconsistencies in the methodologies used in the studies covered by this review, preventing direct comparisons in many cases. For instance, despite the absence of the primary vector in the majority of these nations, occasional cases of canine babesiosis caused by B. gibsoni have been documented in Austria, the Czech Republic, Slovakia, Germany, Hungary, Poland, and Sweden. B. gibsoni infections may have been brought or spread via unorthodox means, such as dogfights, dog bites, or transplacentally (Cannon et al., 2016).
Using molecular detection methods, an epidemiological survey of vector-borne diseases was carried out in six different regions of Lithuania. Based on PCR-RFLP and sequence analysis, the molecular characterisation of 18S rRNR and \( Bc28.1 \) genes of \( B. \) \textit{canis} revealed the existence of genetically heterogeneous \( B. \) \textit{canis} strains in Lithuania. \( B. \) \textit{canis} genotypes with varying rates of prevalence were detected in different regions in Lithuania (Radzijevskaja et al., 2022). Accordingly, regions with a high proportion of infected ticks in eastern Poland, western Ukraine, or southwest Lithuania are known to have the highest frequency of canine babesiosis (5–250 cases/1000 dogs) (Radzijevskaja et al., 2018; Levytska et al., 2021). A recent study showed a significant prevalence of diseases transmitted by ticks and mosquitoes in Lithuanian dogs, and it was discovered that co-infections with anaplasmosis, borreliosis, babesiosis, and dirofilariosis co-occurred: double, triple, or even quadruple coinfections were found (Radzijevskaja et al., 2020).

**CONCLUSIONS**

The most common vector-borne canine diseases in Europe are anaplasmosis, Lyme disease, babesiosis, and ehrlichiosis.

Canine granulocytic anaplasmosis is the term used to describe \( A. \) \textit{phagocytophilum} infection in dogs. Leukopenia and thrombocytopenia are frequently brought on by \( A. \) \textit{phagocytophilum} infections of granulocytes. \textit{Ehrlichia canis} causes canine monocytic ehrlichiosis. The acute phase of infection is characterised by listlessness, swollen lymph nodes, and ocular and nasal discharge; the chronic phase also manifests in widespread haemorrhage, decreased mononuclear cell infiltration of organs, nosebleeds or other abnormal bleeding, and weight loss.

Canine borreliosis caused by the spirochete bacteria from the \textit{Borrelia burgdorferi} s.l. complex. Clinical symptoms often start out nondescript and progress slowly, and Lyme nephritis is the most severe type of Lyme borreliosis in dogs.

Canine babesiosis is caused by various species of the protozoan genus \textit{Babesia}. The vast majority of clinical babesiosis cases in European dogs are caused by \( B. \) \textit{canis}. \textit{Babesia} spp. infections can cause a variety of clinical symptoms, from asymptomatic infections to multi-organ failure with a risk of death. Clinical symptoms of babesiosis in dogs include fever and lethargy, and they may later develop anaemia, liver, pulmonary, renal, or cerebral dysfunction, and haemostatic abnormalities.

Treatment of vector-borne diseases in dogs is usually associated with antibiotic therapy or antidote therapy, which is usually successful if the causative agent has not caused fatal or long-lasting complications.

It is important for dog owners to take preventative measures to protect their pets from these vector-borne diseases by using appropriate tick and flea control products, avoiding areas where these diseases are prevalent and having their dogs screened for diseases regularly.

**References**


44. Panti-May JA, Rodríguez-Vivas RI. Canine babesiosis: A literature review of prevalence, distribution, and diagnosis in Latin America and the Caribbean. Veterinary Parasitology: Regional Studies and Reports. 2020;21:100417.


60. Vrhovec MG, Pantecev N, Failing K, Bauer C, Travers Martin N, Zahner H. Retrospective
analysis of canine vector-borne diseases (CVBD) in Germany with emphasis on the endemicity and risk factors of leishmaniosis. Parasitol Res. 2017;116:131–44.


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DAŽNIAUSIOS EUROPOJE VEKTORIŲ PERNĖŠAMOS ŠUNŲ LIGOS

Santrauka

Įvairias infekcines ir parazitines ligas, vadinamas pernešėjų platinamomis ligomis, skleidžia krauju mintantys nariuotakojai, pavyzdžiui, erkės, blusos, utelės, uodai ir flebotominės smėlio musės. Anaplazmozė, erlichiozė, babeziozė, boreliozė yra pagrindinės pernešėjų platinamos ligos, aktualios tiek dėl gyvūnų gerovės, tiek dėl galimybės užkrėsti žmonių populiaciją. Planetos temperatūros ir ekosistemų pokyčiai, padidėjus gyvūnų ir žmonių mobilumas, cheminis atsparumas insekticidams ir akaricidams nuolat keičia pernešėjų platinamų ligų epidemiologinį scenarijų. Maitindamiesi liga užskrėtusio gyvūno krauju pernešėjai perima ligą sukeliančius patogenus, vėliau migruoja ir maitindamiesi sveiko gyvūno krauju per seiles perduoda ligos sukélėjus. Ankstvais šių ligų nustatymas ir gydymas yra labai svarbus siekiant išvengti ligų komplikacijų ir užtikrinti efektyvų bei greitų sergančių šunų sveikimą. Straipsnio tikslas – aptarti Europoje davęsios pernešėjų platinamos ligas, apžvelgti jų paplitimą ir riziką augintinių sveikatai. Straipsnyje apibendrinami naujai literatūros duomenys apie vektorių pernešamų ligų patogenezę, epidemiologiją, diagnostikos metodų naudą ir riziką, gydymo galimybės ir šunų profilaktiką.

Raktažodžiai: vektorių pernešamos ligos, šunų anaplazmozė, šunų erlichiozė, šunų boreliozė, šunų babeziozė