



Backgrounder

Canine Vector-Borne Diseases (CVBD)

1. Tick-borne infectious diseases of dogs

Tick-transmitted infections are an emerging problem in dogs. In addition to causing serious disease in traditional tropical and semi-tropical regions, they are now increasingly recognized as a cause of disease in dogs in temperate climates and urban environments. Being haematophagous, ticks are well designed to transmit disease agents such as viruses, bacteria and protozoa.

Ticks attach securely to their hosts, facilitating not only effective transmission of infectious agents, but also the spread of both ticks and microorganisms to different geographical habitats via travelling pets. Between 1995 and 1998, 36% of cases of monocytic ehrlichiosis reported in Germany occurred in dogs that had travelled for short periods to the Mediterranean area. In addition, during the same period, both *Ehrlichia canis* infection and infestation with *Rhipicephalus sanguineus*, the ehrlichiosis vector traditionally found in Southern Europe, were found in dogs that had never been outside Germany.

The zoogeographical range is also increasing because tick species are finding niches in different climatic conditions. Since the 1980s, *Ixodes ricinus* has extended its range in Sweden to include more northern and western areas and



Dermacentor variabilis, the major vector of Rocky Mountain Spotted Fever (RMSF), has extended its range to include the North-eastern USA. Furthermore *Dermacentor reticulatus* (ornate cow tick) becomes more important as common vector in Europe and Central Africa because of its spreading occurrence based on tourism activities.

The most important tick-transmitted infectious diseases causing severe clinical illness in dogs are babesiosis, ehrlichiosis and, in the USA, RMSF. Several of the tick-borne infections that affect dogs can cause serious disease in humans, notably borreliosis, ehrlichiosis, RMSF, *R. conorii* infection and tick-borne encephalitis.

Infection with multiple tick-transmitted pathogens, or with multiple genotypes of the same pathogenic species, can occur in an individual animal following heavy exposure to ticks. The same tick species can be a vector for several pathogens and coinfection of individual ticks can occur. Infection with tick-borne pathogens can also be complicated by other arthropod-borne diseases that share the tick biohabitat, such as leishmaniosis. In dogs, coinfection with combinations of *Ehrlichia*, *Bartonella*, *Babesia*, *Hepatozoon*, *Leishmania* and *Rickettsia* species occurs in endemic areas.

Babesiosis (Piroplasmosis)

Canine babesiosis is caused by different strains of the intraerythrocytic protozoan parasite *Babesia canis*, and increasingly by *Babesia gibsoni*, which is extending its range in the USA and Europe. The relative importance of tick species in the transmission of canine babesiosis varies with geographical location.

The clinicopathogenesis of babesiosis caused by *B. canis canis*, the prevalent strain in Europe, and *B. gibsoni* involves progressive haemolytic anaemia. By contrast, the more severe disease caused by *B. canis rossi* in South Africa can involve hypoxic, hypotensive shock with disseminated intravascular coagulation (DIC), systemic inflammatory response syndrome and multiple organ dysfunction syndrome. The severity of disease also varies with the species of vector, and the age, breed and immune status of the dog.

Persistent infection with *B. canis* or *B. gibsoni* is common in endemic areas. Although these animals appear healthy unless subjected to stress, they provide a reservoir of infection for susceptible animals and have suboptimal athletic performance.

Ehrlichiosis

Canine ehrlichiosis is caused by tick-transmitted intracellular bacteria of the genus *Ehrlichia*, which, in dogs, have been identified parasitizing monocytes, granulocytes and platelets. Three genogroups of ehrlichiae have now been identified by 16S rRNA phylogenetic analysis. Genogroup III includes *E. canis*, which is responsible for widespread disease in tropical and temperate areas of the world. The geographical distribution of *E. canis* has expanded with the distribution of *R. sanguineus*.

Disease manifestations caused by members of the *E. canis* genogroup (genogroup III) infecting dogs can be indistinguishable, and there can be strain variation in pathogenicity.

Subclinical persistent infection owing to splenic sequestration of organisms is common. Severe life-threatening chronic ehrlichiosis can develop following persistent infection and can be associated with irreversible bone marrow destruction. Ehrlichiosis is more severe in certain breeds (e.g. German shepherd) and in younger animals. However, coinfection, immune status and strain variation could all play a role.

Anaplasmosis

Genogroup II *Ehrlichiae* of pathogenetic significance includes the *Anaplasma phagocytophila* group. Strains within the group are transmitted by *Ixodes* spp. ticks, and are the major causative agent of anaplasmosis in the Northern and Western USA and in Northern and Central Europe. Anaplasmosis is generally associated with less severe clinical signs than ehrlichiosis caused by *E. canis*. Coinfection with *Borrelia* in dogs is probable, as reported in humans.

Borreliosis (Lyme Disease)

Canine borreliosis is caused by a spirochete, *Borrelia burgdorferi sensu lato*, which is transmitted by ticks of the genus *Ixodes*. At least four genospecies, with geographical distribution primarily in the northern hemisphere, cause disease in humans. In northern Europe, the distribution of borreliosis is expanding, and infected *Ixodes ricinus* ticks are now commonly found in urban areas. In contrast to Europe with several *Borrelia* species, *B. burgdorferi sensu stricto* is the primary isolate in humans and dogs in the USA.

Although a high proportion of dogs are seropositive in endemic areas, relatively few develop clinical signs. Several mechanisms have been incriminated in causing joint damage. Persistent infection with *Borrelia* even after antibiotic therapy is reportedly

common in dogs. The organism is sequestered in the skin, connective tissue, joints and CNS. Reactivation of infection with recrudescence of disease can occur in immunocompromised individuals or in coinfection.

The Spotted Fever group

Rocky Mountain Spotted Fever (RMSF) is a potentially fatal rickettsial disease of dogs and humans caused by the intracellular bacterium *Rickettsia rickettsii*. It has been reported throughout the USA, Central and South America, and is transmitted by ticks of the *Dermacentor*, *Rhipicephalus* and *Amblyomma* genera, respectively. *Rickettsia conorii*, the agent of boutonneuse fever in humans in Southern Europe, the Middle East and Southern Africa is reported to infect also dogs.

The major pathogenic mechanism involved in canine RMSF is rickettsial invasion of, and damage to, endothelial cells of small arteries and venules. Although platelet consumption is considered the primary cause of the thrombocytopenia in clinical cases, anti-platelet antibodies have also been identified in infected dogs. A tendency towards more fulminant disease has been reported in Springer spaniels with phosphofructokinase deficiency and in German shepherds.

Diagnosis of tick-transmitted diseases requires a combination of compatible clinical and laboratory findings, direct microscopic visualization or immunodetection of infective organisms in blood or infected tissue, microbial culture, serological testing, immunoblotting and PCR.

The treatment of tick-transmitted diseases is a challenge for a variety of reasons. Many of the target organisms are intracellular and sequestration limits drug penetration and, consequently, drug efficacy. Therapy with a single chemotherapeutic agent might not be sufficient to eliminate infection. Poor or partial responses to single-agent chemotherapy might also reflect the presence of coinfection.

Reference: Shaw, S.E. et al. (2001) Tick-borne infectious diseases of dogs. *TRENDS in Parasitology* 117/2, 74-80

2. Insect-transmitted infectious diseases of dogs

Leishmaniosis

Infections in dogs with the protozoan parasite *Leishmania* are widespread in Mediterranean countries. Furthermore, canine leishmanioses have a worldwide distribution and can be found in Asia, Africa and America. First reports on canine leishmaniosis were recently published also from the US, it remains unclear until now whether the disease was imported from abroad, or has already established within the country.

Leishmanioses are vector-borne diseases: the promastigote stage of the parasite is transmitted to the host during the blood feeding of an insect vector, the sand fly. The causative agents of canine leishmaniosis are *Leishmania infantum* in the Mediterranean Basin and the Middle East and *L. chagasi* in South and Central America. Initially, *L. chagasi* was considered to be distinct from *L. infantum*, however, recent molecular studies indicate that they are indistinguishable.

L. infantum/chagasi is also an important human health problem and dogs serve as the main reservoir animal. Several studies showed that the prevalence of human leishmaniosis could be significantly decreased with control of leishmaniosis in dogs.

The Old World sand flies belong to genus *Phlebotomus*, the New World ones to the genus *Lutzomyia*. Both these genera are important vectors of *Leishmania* parasites.

Sand flies are nocturnal blood feeders, resting over the hot day away from sunlight in relatively cool and humid places, like cellars, stables, crevices or rodent holes. Once landed on the potential host, the dog or other mammal, they hop over the coat aiming for less hairy place; in the head region they like to bite around the muzzle, eye or mouth. Similarly to other bloodsucking insects, the sand fly saliva contains anticoagulants, vasodilatory peptides and enzymes with antiinflammatory, antihemostatic and anaesthetic properties. These components of saliva are important for transmission and serve as enhancing factors of the parasite infection.

Clinical features of canine leishmaniosis vary widely, while skin lesions are the most usual manifestation. The incubation period is 4 weeks to several years. The pathomechanism of the infection is a combination of chronic inflammation of skin, liver, GI-tract, kidneys, eyes and bones and an immune mediated polyarthritis,

glomerulonephritis, arthritis and uveitis. In most cases weight loss is common. Circulating immunocomplexes causing glomerulonephritis, proteinuria and subsequently renal failure is a common cause of death in affected animals.

While in endemic areas most dogs have contact with the parasite, the prevalence of the disease is usually up to 20%. Several treatment regimes are recommended but once a dog got ill the parasites will never been completely eliminated.

Reference: Mencke, N. et al. (2003) Repellent efficacy of a combination containing imidacloprid and permethrin against sand flies (*Phlebotomus papatasi*) on dogs. *Parasitol Res* 90, 108-111
Further information: <http://www.advantix.info>

Heartworm disease (Dirofilariosis)

Heartworm disease is caused by the nematode *Dirofilaria immitis* and is transmitted by mosquitoes of many species. Heartworm disease is common in Southern Europe, USA, Canada, Australia and Southeastern and Eastern Asia, including Japan. In Europe, it is prevalent in Portugal, Spain, Southern France, Italy, Greece and other peri-Mediterranean countries.

The dog is the primary host for *Dirofilaria immitis*. The microscopic larval parasites are transmitted by mosquitoes into the skin and from there they migrate slowly through the body to the right pulmonary artery. Here they may reach adult size (up to 30 cms). The onset of disease is usually slow (months to years) unless a dog has been exposed to a large number of infected mosquitoes at the same time.

Clinical signs include exercise intolerance, coughing, weight loss, and occasionally death. Diagnosis is by demonstrating worms in the pulmonary artery using ultrasound, characteristic heart and lung changes on radiography and use of serological testing. Treatment of heartworm infection in dogs is complex and potentially dangerous. As they are killed, the worms are washed into the pulmonary vasculature where they can cause thromboembolism.

Heartworm can affect humans but it is extremely rare and usually only occurs in areas of extremely high prevalence.

Subcutaneous Dirofilariosis

Subcutaneous dirofilariosis is caused by the nematode *Dirofilaria repens*, and, similar to *D. immitis*, is transmitted by mosquitoes of many species. The disease is restricted

to Europe, the Middle East, Asia and Africa. In Europe, subcutaneous dirofilariosis has been reported in France, Spain, Italy, Czech Republic, Slovakia, Switzerland, Greece, Bulgaria and the Balkan States. In Italy, *Dirofilaria repens* is reported with increasing prevalence from northern to southern regions, often clustering in coastal regions.

The dog is the primary host, but also cats and foxes are reservoirs of the nematode. Mosquitoes are infected when they ingest microfilariae of *D. repens* as they feed on the dog. Within the mosquito, the nematode develops to a larval parasite which infects a new host as the mosquito feeds.

Dirofilaria repens is considered to be of less pathogenicity than *D. immitis*. Clinical signs include a small, subcutaneous nodule caused by the presence of an adult worm. The location of the swelling may vary over time as the worms can move through subcutaneous tissue. In addition, they may be found in connective tissues between muscles during surgery.

Although infection cannot occur directly from dog to man, *D. repens* is considered to be an important and emergent zoonosis. In Italy, more than 100 human cases have been reported, with the majority from Piedmont, but also from Emilia-Romagna, Sardinia, Sicily, Tuscany, Apulia, Lombardy and the Central Region. Infection in man usually results in a subcutaneous nodule, with worms occasionally reaching deeper locations into the lungs. Both subcutaneous and pulmonary lesions must be differentiated from neoplasia. When the nodule's location is ocular, the worms are situated in the conjunctiva.

References: Shaw, E.S. (2005) Imported diseases of travelling dogs with reference to the United Kingdom. Proceedings of the 6th Bayer Ectoparasite Symposium, BSAVA Congress 2005, Birmingham, UK
Fisher, M., McGarry J.W. (2006) Focus on Small Animal Parasitology. Bayer HealthCare AG, Animal Health Division

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