

5 Control of Vector-Borne Diseases in Dogs and Cats

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INTRODUCTION

Vector-borne diseases are caused by a wide range of infectious agents including viruses, bacteria and parasites (protozoa and helminths), which are transmitted by a variety of arthropod vectors such as ticks, lice, fleas and Diptera (mosquitoes, phlebotomine sand flies¹, muscid flies).

Vector-borne pathogens or diseases are important because:

- They may be highly pathogenic in dogs and cats.
- Their transmission is often unpredictable.
- Their diagnosis and control are difficult.
- Variable clinical signs can develop after long incubation periods and these are rarely pathognomonic.
- Animals may have persistent infections and thus act as reservoirs.
- Several are important zoonoses, such as leishmaniosis, borreliosis, rickettsiosis, bartonellosis, anaplasmosis and dirofilariosis.

Climatic and ecological changes, national regulations on the management of stray dogs and cats together with an increase in pet travel and translocation of pet animals can influence the epidemiological situation of vector-borne diseases in Europe. Rare diseases may increase in frequency in certain areas, either due to the increased importation of infected animals or because the causative agents and their vectors spread to and establish in previously non-endemic areas. Such an expansion of endemic areas has been recorded for various parasitic diseases such as dirofilariosis, babesiosis and leishmaniosis. Babesiosis, for example, has been observed across central Europe in the past few years, emerging from previous endemic regions in Europe. Another important feature of these diseases is their increasing occurrence in wild animals, which could act as reservoirs.

The effective control of vector-borne diseases requires a thorough knowledge of the infectious agents, their vectors and major hosts. Besides giving an overview of the majority of vector-borne diseases of dogs and cats, this guideline focuses on the following important infections/diseases: leishmaniosis, dirofilariosis, bartonellosis, babesiosis, ehrlichiosis, anaplasmosis and vector-borne viral diseases.

The following vector-borne diseases are not presented in detail in this guideline, but are mentioned here and in the tables:

- Haemoplasmosis (formerly haemobartonellosis) is caused by small Gram-negative bacteria, mycoplasmas or haemoplasmas, that attach to the surface of red blood cells, e.g. *Mycoplasma haemocanis* and *M. haemofelis*, in dogs and cats, respectively. Other less pathogenic species have been described mainly in cats: *Candidatus Mycoplasma haemominutum* and *Candidatus Mycoplasma turicensis*, but also in dogs: *Candidatus Mycoplasma haematoparvum*. Although their mode of natural transmission is still not known, ticks and fleas could be implicated and direct transmission may also be possible.
- Rickettsiosis (induced by e.g. *Rickettsia conorii*, *R. slovaca*, *R. felis*) is caused by small intracellular Gram-negative bacteria that typically cause fever in the acute phase in susceptible hosts. They are transmitted by many arthropods.
- Cytauxzoonosis is an emerging tick-borne disease of domestic and wild felids (other non-vectorial routes of transmission are under discussion). *Cytauxzoon felis* induces severe and often fatal disease in domestic cats. In Europe, several clinical and subclinical infections caused by *Cytauxzoon* sp. have been reported. It is generally considered less virulent in domestic cats than *C. felis* but its clinical significance and mode of transmission in domestic cats in Europe remains unclear.

- Hepatozoonosis (induced by e.g. *Hepatozoon canis*) is caused by protozoal pathogens of dogs transmitted by the ingestion of an infected tick.
- Onchocercosis (*Onchocerca lupi*) is an ocular disease of varying severity in dogs. This filarioid has also been recognised as a zoonotic agent, though the information about the biology and epidemiology of this infection is largely unknown.
- Thelaziosis (*Thelazia callipaeda*) is caused by a nematode located in the conjunctival sac which is transmitted by drosophilid flies.

¹ phlebotomine sand flies – within Europe Psychodid sand flies of the genus *Phlebotomus* are responsible for the transmission of *Leishmania infantum*. These will be referred to throughout the text as phlebotomes.

Table 1: Arthropod-borne infections of dogs and cats in Europe

Disease or infection	Causative agents	Vector	Host	Geographical distribution	Severity of clinical signs
DISEASES CAUSED BY PROTOZOA					
Leishmaniosis	<i>Leishmania infantum</i>	Phlebotomes	Dogs, cats, foxes, hares, humans, other mammals	Southern Europe	Subclinical–severe
Cytauxzoonosis	<i>Cytauxzoon</i> sp.	Ticks (species unknown)	Cats	Italy, Spain, Switzerland, Portugal, Romania	Subclinical–severe
DISEASES CAUSED BY HELMINTHS					
Dipylidiosis Filariosis	<i>Dipylidium caninum</i>	Fleas, lice	Dogs, cats, foxes, humans	Europe	Subclinical
	<i>Dirofilaria immitis</i>	Culicidae	Dogs, cats, foxes, humans	Southern and parts of central Europe	Subclinical–severe
	<i>D. repens</i>	Culicidae	Dogs, cats, foxes, humans	Southern, central and eastern Europe	Minor–moderate
	<i>Acanthocheilonema dracunculooides</i> & <i>A. reconditum</i>	Fleas (<i>A. reconditum</i>), louse flies, Culicidae and <i>Rhipicephalus sanguineus</i> (<i>A. dracunculooides</i>)	Dogs, foxes	Spain, France, Italy, Portugal, Greece	Minor
Thelaziosis	<i>Thelazia callipaeda</i>	Drosophilid flies (<i>Phortica</i> spp.)	Dogs, cats, foxes, wolves, humans, other mammals	Italy, France, Switzerland, Spain, Portugal, Romania, Germany	Minor–moderate
BACTERIAL INFECTIONS OR DISEASES					
Rickettsiosis	<i>Rickettsia felis</i> Other	Fleas	Dogs, cats, hedgehogs, humans	Europe	Subclinical–moderate
Bartonellosis (cat scratch disease)	<i>Bartonella henselae</i>	Fleas, (ticks)	Cats (reservoir host), humans	Europe	Subclinical–minor
Bartonellosis (dog endocarditis)	<i>Bartonella vinsonii</i> and others	Arthropod vectors	Dogs	Europe	Moderate–severe
Haemoplasmosis	<i>Mycoplasma haemofelis</i> (cats), <i>M. haemocanis</i> (dogs) and others	Fleas (ticks) suspected	Cats, dogs	Europe	Cats: minor–severe Dogs: subclinical
Tularaemia	<i>Francisella tularensis</i>	Ticks, mosquitoes, Tabanidae	Cats (dogs), other mammals, humans	Europe	Subclinical–severe
VIRAL INFECTION					
West Nile virus infection	West Nile virus (WNV), Flavivirus	<i>Culex</i> spp. and other mosquitoes	Horses, humans, (dogs, cats); reservoir: birds	Romania, Czech Republic, Italy, France, Portugal, Greece, Spain	Subclinical–severe

Table 2: Tick-borne infectious agents of dogs and cats in Europe

Disease	Causative agents	Vectors	Hosts	Geographical distribution	Severity of clinical signs
DISEASES CAUSED BY PROTOZOA					
Babesiosis (piroplasmosis)	<i>Babesia canis</i>	<i>Dermacentor reticulatus</i>	Dogs, wolves	Western, southern and central Europe up to the Baltic following distribution of vector	Moderate–severe
	<i>B. vogeli</i>	<i>Rhipicephalus sanguineus</i>	Dogs	Southern Europe following distribution of vector	Mild–moderate
	<i>B. gibsoni</i> and <i>B. gibsoni</i> -like	<i>Haemaphysalis</i> spp., <i>Dermacentor</i> spp.	Dogs, wolves	Sporadic and rare in Europe	Moderate–severe
	<i>Babesia microti</i> -like/ <i>Babesia vulpes</i>	<i>Ixodes hexagonus</i> ¹	Dogs, foxes	Northwestern Spain, Portugal, Italy, Croatia, France, Sweden	Moderate–severe
Hepatozoonosis	<i>Hepatozoon canis</i> ²	<i>Rhipicephalus sanguineus</i>	Dogs, foxes	Mainly southern Europe	Mostly mild infection; subclinical
	<i>Hepatozoon felis</i> , <i>Hepatozoon</i> spp.	Unknown	Cats	Spain, Portugal, Switzerland, Austria	Subclinical–severe
DISEASES CAUSED BY NEMATODES					
Filariosis	<i>Acanthocheilonema (Dipetalonema) dracunculoides</i> , <i>Acanthocheilonema (D.) reconditum</i> , <i>Cercopitiphilaria</i> spp.	<i>Rhipicephalus sanguineus</i> ³	Dogs, cats	Southern Europe	Minor
DISEASES CAUSED BY BACTERIA					
Bartonellosis	<i>Bartonella henselae</i> , <i>Bartonella vinsoni</i> , <i>Bartonella</i> spp.	Fleas suspected ³ , organism found in <i>Ixodes</i> spp. ticks	Many animals, dogs, cats, humans	Throughout Europe	Commonly subclinical infection
Borreliosis (Lyme disease)	<i>Borrelia burgdorferi</i> complex (especially <i>B. garinii</i> and <i>B. afzelii</i> in Europe)	<i>Ixodes ricinus</i> , <i>I. hexagonus</i> , <i>I. trianguliceps</i> , <i>I. persulcatus</i>	Many animals especially rodents, dogs, cats, humans	Throughout Europe	Mostly subclinical
Ehrlichiosis (monocytic)	<i>Ehrlichia canis</i>	<i>Rhipicephalus sanguineus</i>	Dogs (cats)	Southern Europe following distribution of vector	Moderate–severe
Neoehrlichiosis	<i>Candidatus, Neoehrlichia mikurensis</i>	<i>Ixodes ricinus</i>	Rodents, humans, dogs	Europe	Unknown
Anaplasmosis (granulocytic ehrlichiosis)	<i>Anaplasma phagocytophilum</i>	<i>Ixodes ricinus</i> , <i>I. trianguliceps</i>	Many animals, dogs, cats, humans	Throughout Europe	Mild and subclinical infections common
Anaplasmosis (infectious cyclic thrombocytopenia)	<i>Anaplasma platys</i>	<i>Rhipicephalus sanguineus</i>	Dogs	Southern Europe following distribution of vector	Commonly subclinical infections
Rickettsial infections (Mediterranean spotted fever/MSF)	<i>Rickettsia conorii</i>	<i>Rhipicephalus sanguineus</i>	Dogs	Southern Europe following distribution of vector	Commonly subclinical infection
Coxiellosis (Q Fever)	<i>Coxiella burnetii</i>	<i>Ixodes</i> spp., ³ <i>Dermacentor</i> spp.	Ruminants, dogs, cats, humans	Throughout Europe	Subclinical infection
Tularaemia	<i>Francisella tularensis</i>	<i>Ixodes</i> spp., ³ <i>Dermacentor</i> spp., <i>Haemaphysalis</i> spp., <i>Rhipicephalus sanguineus</i>	Lagomorphs, cats	Southern Europe	Subclinical infection, occasionally moderate–severe in young cats
DISEASES CAUSED BY VIRUSES					
European tick-borne encephalitis	Tick-borne encephalitis virus (TBEV) (Flavivirus)	<i>Ixodes ricinus</i> , <i>I. trianguliceps</i> , <i>I. persulcatus</i>	Many animals, rodents, dogs	Central, eastern and northern Europe	Can be moderate–severe but not commonly reported
Louping-ill infection	Louping-ill virus, (Flavivirus)	<i>Ixodes ricinus</i> , <i>I. trianguliceps</i>	Many animals, mainly sheep, dogs	UK, Ireland	Can be moderate–severe but not commonly reported

¹ Potential competent vector but not yet experimentally demonstrated.

² Transmission of *Hepatozoon* spp. is by ingestion of an infected tick and not a tick bite.

³ Ticks are not the sole arthropod vectors for these diseases.

1. CONSIDERATION OF PET HEALTH AND LIFESTYLE FACTORS

Animals require care tailored to their individual needs. Certain factors may dictate more intensive monitoring and/or treatment, while others may warrant a less aggressive approach.

Animal

The age and health status of the animal are important, including its history and origin. Some breeds or individuals have a genetically-determined susceptibility to some diseases such as leishmaniosis, while other concomitant infections may predispose to, or aggravate, vector-borne diseases.

Environment

Dogs and cats housed in kennels and catteries or animals living outdoors may be at greater risk of acquiring vector-borne diseases compared to individual animals living indoors. Fleas and *R. sanguineus* however, frequently live and may establish infestations indoors.

The risk of transmission may also depend on various local conditions such as (micro-) climate and local topography.

Nutrition

Poor nutrition may increase susceptibility to many diseases including vector-borne diseases.

Location and travel

Dogs and cats living in, or travelling to, specific geographical areas endemic in certain vector-borne diseases are at a higher risk of infection. The following situations could present a higher risk:

- animals travelling with their owners on holiday,
- animals being rehomed,
- animals going to boarding facilities,
- animals attending dog and cat shows,
- animals taken into fields for countryside walks,
- animals taking part in hunting activities.

Guests visiting with their pets can also bring parasites into environments, causing infestations in pets that don't travel.

Transmission by blood transfusion

Veterinary surgeons should be aware that most of these infections may be present in the blood of animals that appear healthy. It is especially important to avoid causing iatrogenic infection from these individuals. In particular, animals that are to act as blood donors should be screened and demonstrated to be seronegative/ polymerase chain reaction (PCR) negative (depending on the screened pathogen) for relevant infections prior to donating blood.

2. PREVENTION AND CONTROL OF VECTOR-BORNE DISEASES

2.1. Insect-borne diseases

2.1.1. Canine leishmaniosis

2.1.1.a. Agents and vectors

In Europe, canine leishmaniosis is predominantly caused by *Leishmania infantum* which comprises various enzymatic types (zymodemes). Other species (*L. tropica*, *L. major*) have rarely been diagnosed (Table 3). The vectors are several species of blood-sucking flies of the genus *Phlebotomus* (Phlebotominae subfamily; phlebotomes = sand flies).

Dogs are considered the main reservoir of *L. infantum* infection but cats can also be hosts. Many other mammalian species can become infected including humans and this parasite has been isolated from various mammals such as rodents (e.g. rats and squirrels), hares and rabbits. Horses, goats, sheep, cats and wild canids including foxes, wolves and jackals can become infected but the epidemiological role of these hosts has not yet been clearly established.

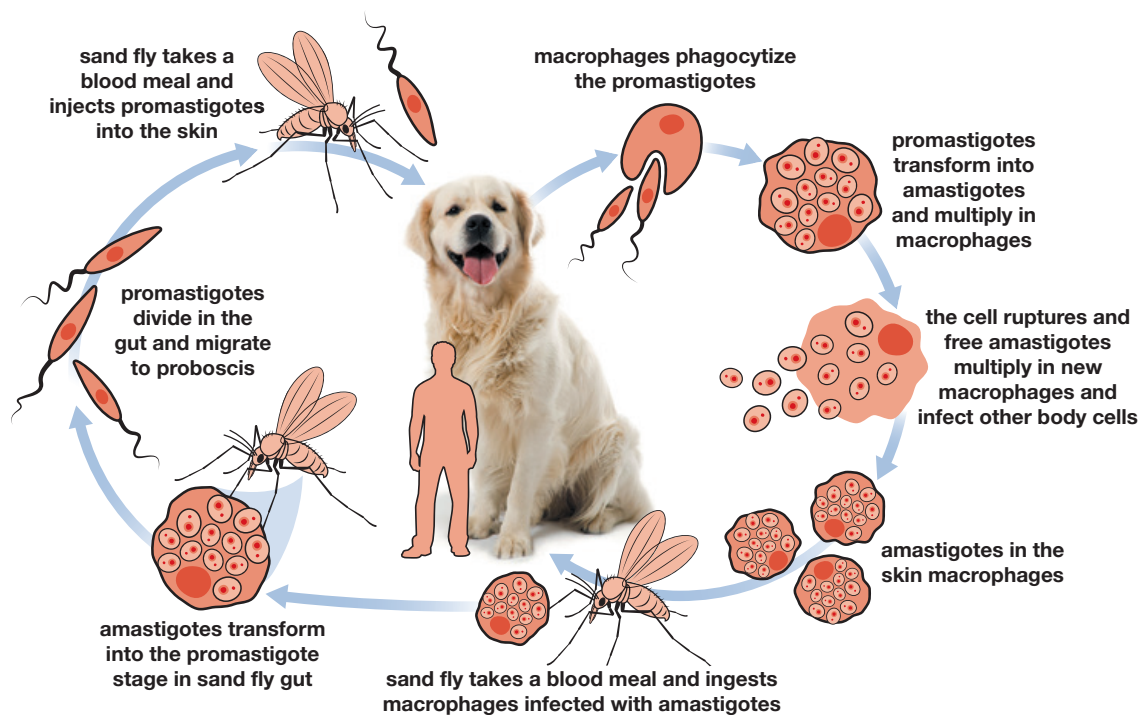


Figure 1: *Leishmania* life cycle

The development of phlebotomes takes place in terrestrial habitats. Eggs are laid in soil rich in organic matter and the larvae develop through four instars before they pupate and the adults emerge (Figure 1). The seasonal dynamics of phlebotomes have not been fully explored; however, it is known that some palaeartic species overwinter as 4th stage larvae. Phlebotomes have a nocturnal circadian activity with most species seeking their hosts after sunset. Activities vary from species to species and within their habitat. During the day, adult phlebotomes rest in dark, humid places especially cracks and holes in stone walls, wood piles, animal stables and basements or dark cellars of houses.

Phlebotomes are widespread in the Mediterranean region, Africa and the Middle East. They are well adapted, depending on the species, to tropical or subtropical climates and even to arid habitats. Furthermore, it has been known for decades that the *Phlebotomus perniciosus* endemic area extends up to northern France, and this species was found in localised areas in southern Germany and southern Switzerland.

Table 3: *Leishmania* species infecting dogs and cats in Europe

Causative agent	Vector	Hosts
<i>Leishmania infantum</i> (variety of zymodemes)	<i>Phlebotomus</i> spp. (sand flies) e.g. <i>P. perniciosus</i> , <i>P. ariasi</i> , <i>P. perfiliewi</i> , <i>P. neglectus</i> , <i>P. tobbi</i> , <i>P. langeroni</i>	Dogs, foxes, jackals, hares, rabbits, rodents, cats, various other mammals, humans
<i>L. tropica</i>	<i>P. sergenti</i> , <i>P. arabicus</i>	Dogs, humans, hyraxes
<i>L. major</i>	<i>P. papatasi</i>	Rodents, dogs, humans

2.1.1.b. Biology and transmission

- *Leishmania* spp. occur and multiply in two well-differentiated forms: intracellular amastigote stages infecting cells of the vertebrate host and extracellular flagellated promastigote stages in the gut of phlebotomes.
- *Leishmania* spp. are highly vector-specific and are transmitted by the blood-sucking females of several *Phlebotomus* species while feeding on their hosts. Vector activity is linked to a minimum temperature of 15°C.
- The parasite development in the vector is temperature dependent and lasts around 7–14 days at temperatures above 18°C.
- Other ways of transmitting *Leishmania* not dependent on phlebotomes have been reported: intra-uterine from mother to offspring, via infected blood donors or through venereal transmission. However, their epidemiological significance is still unknown. In non-endemic areas, these alternative transmission routes might explain infections occurring in the absence of a competent vector. Furthermore, direct transmission through biting, wounds or transmission via other hematophagous arthropods (e.g. ticks, fleas) have been postulated, but remain unproven.
- There is some evidence of resistance in certain dog breeds (e.g. the Ibiza hound) as well as susceptibility of other breeds to disease development (e.g. German Shepherds, Rottweilers, Cocker Spaniels and Boxers) but no sex- or age-dependent risks have been described. Infected but clinically healthy dogs, including those which have undergone successful chemotherapy, may represent potential parasite carriers.
- The incubation period can vary between three months to years and is dependent on the individual immune response of the infected dogs.
- After local multiplication of parasites in dendritic cells and macrophages in the skin, dissemination primarily occurs via the lymphatic system and blood. Parasites can be found mainly in the skin, lymph nodes, spleen, liver, bone marrow and many other organs or body fluids (e.g. intestine, saliva, semen, conjunctiva and urine).
- Clinical signs are only observed in a low proportion of infected dogs. Infected but clinically healthy dogs represent an important reservoir of infection for phlebotomes.
- The main risks in endemic areas are related to vector exposure and abundance of reservoir hosts which include dogs living outdoors, stray dogs, hunting dogs and dogs adopted from animal shelters in endemic areas being rehomed in non-endemic areas. Different studies suggest that cats might act as alternative reservoir hosts of *L. infantum* based on the PCR detection of infections in peripheral blood in up to 20% of cats in Portugal and 60% in Sicily; however, few of them had shown clinical disease. Further investigations are required to confirm the possible role of cats in *L. infantum* transmission.

2.1.1.c. Distribution in Europe

Canine leishmaniosis is endemic in southern Europe with prevalence rates of infection of up to 60% in exposed populations. Figure 2 shows the approximate northern limit of the endemic area. Outside this area, many imported cases of canine leishmaniosis and a few cases in cats have been diagnosed and treated. However, there are a few reports of isolated cases in dogs which did not travel through or reside in endemic areas. Most probably, focal transmission can occur for a limited period of time if there is sufficient infection pressure from imported infected dogs and competent vectors.

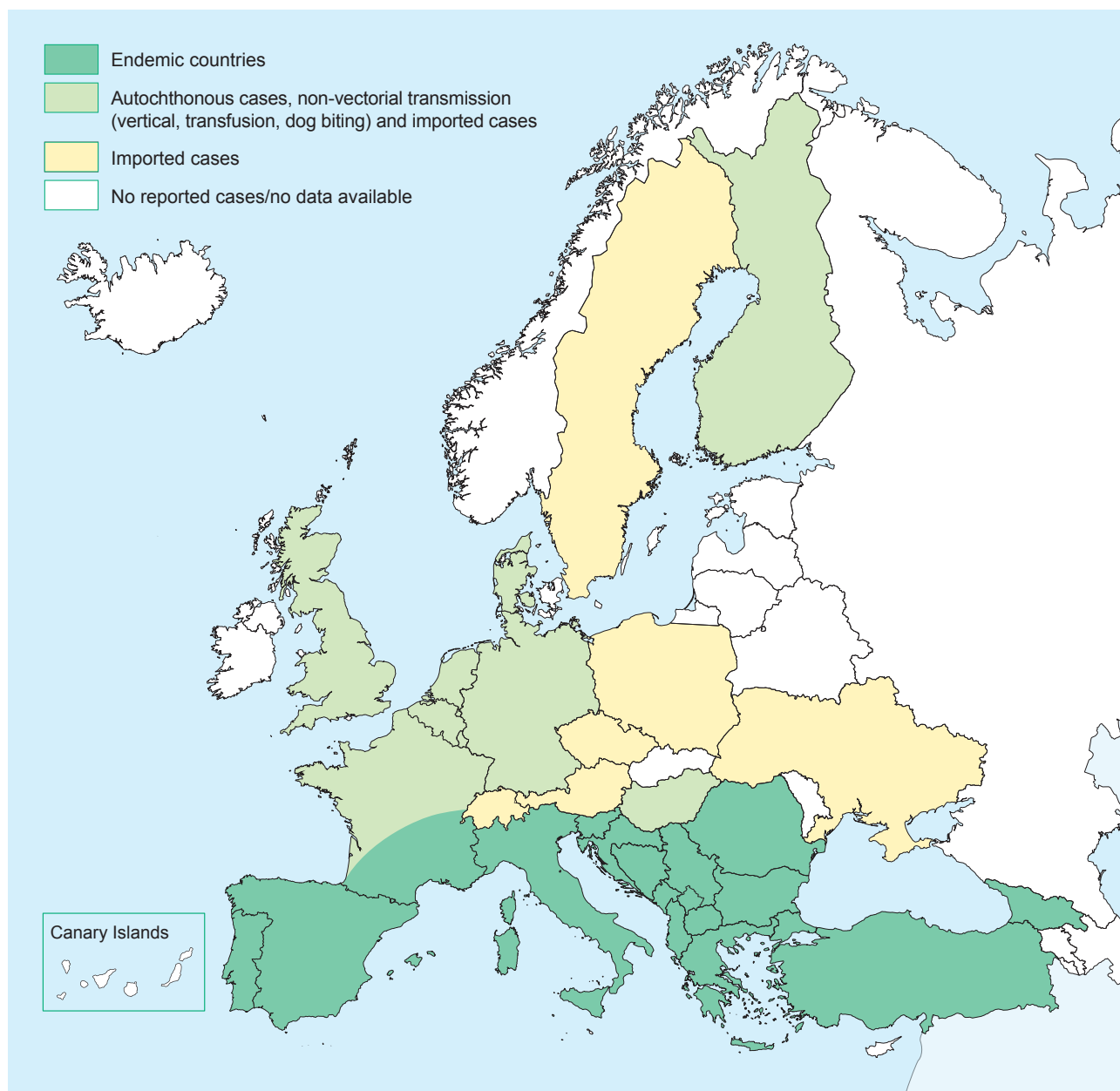


Figure 2: Approximate distribution of canine leishmaniosis in Europe

This map depicts approximate prevalence and is for informational and illustrative purposes only. ESCCAP cannot guarantee the map's completeness since the data are only collected from ESCCAP member countries. All of ESCCAP's maps are dynamic and in a constant state of maintenance, correction and revision. For the most up-to-date version, please visit www.esccap.org/guidelines-maps/. This map does not express any opinion on the part of ESCCAP concerning the legal status of any country or territory or concerning the delimitation of frontiers or boundaries.

2.1.1.d. Clinical signs/laboratory abnormalities

In endemic areas, a large number of infected dogs may be clinically healthy.

Clinical signs are highly variable depending on immune responses, disease history and possibly many other, as yet unknown, factors. Local cutaneous lesions at the site of the initial phlebotome bites are often the first signs observed before disseminated infection occurs. Typical *Phlebotomus* bite sites include the ear pinnae, nose and abdomen. The localised lesions sometimes go unnoticed or are misdiagnosed as tick or simply insect bites. They consist of single or several specific papular to ulcerative lesions, called chancres or “chancres d’inoculation”. They last several weeks but are self-limiting. During this period, infected dogs may remain seronegative but later around 25% seroconvert and the disease becomes generalised. In affected dogs, enlargement of single or multiple lymph nodes may be evident accompanied by weight loss, anorexia and weakness.

More severe clinical signs may develop and the disease can be fatal if therapy is not instituted. Severe clinical signs include skin lesions like alopecia, nodules, ulcers, hyperkeratosis, intense exfoliative dermatitis, mucocutaneous lesions and onychogryphosis (nail hyperplasia). Generalised cutaneous forms of the disease are normally non-pruritic and are most often keratoseborrhoeic but may also be ulcerative, papular or pustular or, less frequently, nodular. General signs might include loss of body weight, asthenia (weakness), pallor of mucous membranes, muscular atrophy, splenomegaly, epistaxis and haematuria. Other clinical signs may include gastrointestinal disorders (vomiting, diarrhoea and chronic colitis), lameness (polyarthritis, osteomyelitis, polymyositis), vascular disorders (systemic vasculitis, arterial thromboembolism), glomerulonephritis (polyuria and polydipsia), ocular lesions (blepharitis, conjunctivitis, keratoconjunctivitis, anterior uveitis). Even uncommon but already reported cardiorespiratory and neurological disorders may occur in some cases.

Although the clinicopathological abnormalities may be variable, there are many common findings such as a normocytic normochromic non-regenerative anaemia and, less frequently, thrombocytopenia and leucopenia. Plasma protein changes with hyperglobulinaemia and hypoalbuminaemia are particularly common. Proteinuria and variable azotaemia with an increase in the urine protein/creatinine ratio, due essentially to immune-mediated glomerulonephritis, are present in some sick dogs and are considered an indicator of poor clinical prognosis.

2.1.1.e. Diagnosis

To reduce the potential for transmission of *Leishmania* from dogs to vectors, the diagnosis should be confirmed and treatment instituted as early as possible. Clinical signs, together with relevant epidemiological information and various laboratory test abnormalities strongly indicate a tentative diagnosis. CBC, biochemical profile and urinalysis including a urine protein/creatinine ratio (only in proteinuric dogs) should always be performed.

Direct diagnosis is possible by detecting the amastigote stages in Giemsa or Diff-Quik stained smears obtained from superficial lymph nodes or bone marrow aspirates or by observing the promastigotes after in vitro culturing of samples (Figure 3). The sensitivity of parasite detection is lower with skin biopsies and is generally reduced in clinically healthy, infected dogs, but can be increased by molecular or immunohistochemical techniques.

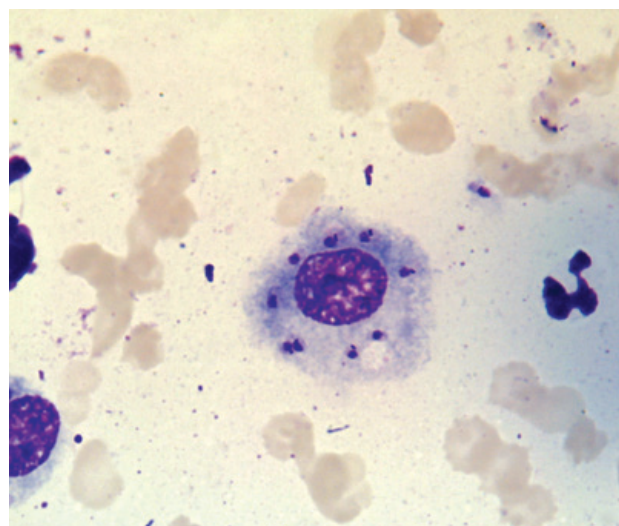


Figure 3: *Leishmania infantum* amastigotes in a macrophage from a lymph node aspirate

Polymerase chain reactions (PCRs), mostly targeting repetitive sequences, have proven to be highly sensitive compared with laborious in vitro cultivation, combined with the fact that they are not impaired by microbial contamination. However, the diagnostic sensitivity is dependent on the quality of the clinical samples. Lymph node aspirates, especially from animals with lymphadenopathy, are most convenient while bone marrow sampling is more invasive but may be indicated for special cases such as suspect but clinically unremarkable animals. Blood samples and conjunctival swabs can be used in clinical cases but the diagnostic sensitivity is low while skin biopsies have been shown to be a useful alternative for sensitive molecular diagnosis. Quantitative PCR allows the parasitic load to be estimated in comparable tissues, which could be useful for follow-up during treatment although this approach needs to be thoroughly evaluated.

Serology is the most commonly used first step allowing the detection of a specific antibody response in dogs around 3–5 months after initial infection. In subclinical infections, this period may extend to years. Different laboratory-based methods have been used to detect anti-*Leishmania* antibodies such as the indirect fluorescent antibody test (IFAT), enzyme linked immunosorbent assays (ELISA) and Western blot (WB). Both the sensitivity and specificity of these tests vary according to the defined cut-off values in different laboratories. Point-of-care tests (“rapid tests”) based on immunochromatographic methods have been developed and many commercial in-house kits are now available for practitioners for a qualitative diagnosis in the clinic or for use in epidemiological field studies. These tests have a reasonable sensitivity for the initial detection of seropositive dogs. However, for the confirmation of clinical cases and for clinical management post chemotherapy, especially in animals with low specific antibody reactions, methods allowing quantitative estimations (e.g. IFAT, ELISA) are required. IFAT, ELISA and rapid test results based on whole antigens have to be carefully interpreted in non-DIVA vaccinated dogs (differentiating infected from vaccinated animals) because recently-immunised dogs may remain positive for up to 6 months.

2.1.1.f. Control

Treatment

Before initiating chemotherapy, animal owners should be informed about the prognosis, treatment cost and the fact that the dog remains infected even when a clinical cure is achieved. Furthermore, there are certain country-specific veterinary public health regulations that have to be respected. Although euthanasia of infected dogs is not mandatory in any European country, there is an obligation for practitioners to communicate all new cases to the appropriate authorities in some countries such as Portugal, Italy and Greece.

Indications for treatment

Indication for treatment includes dogs with clinical signs and clinicopathological abnormalities associated with a positive serology and/or the evidence of the parasite in target organs. The drugs which are mostly used for the treatment of canine leishmaniosis are listed in Table 4 (see www.esccap.org for links to approved products for specific countries). Generally, meglumine antimoniate or miltefosine have been used successfully in combination with allopurinol. In most cases, allopurinol as monotherapy is administered on a daily basis over several weeks or months after the leishmanicide cycle. In European endemic areas with a high seasonal infection pressure, combined therapy is recommended (see Table 4).

Besides specific therapy, supportive treatment together with an appropriate diet is recommended. A commercially available diet for clinically affected dogs without signs of renal disease is available containing moderate protein levels supplemented with omega acids, zinc sulphate and antioxidants.

An improvement may be observed within a few weeks after beginning chemotherapy but clinical cure is only achieved after several months. As the *Leishmania* infection is not eliminated by treatment with currently available compounds, relapses are common. First indicators of relapse are clinical signs and/or clinicopathological abnormalities associated with the disease, together with a significant rise in specific antibody reactions by ELISA or by IFAT (a 2–4 fold increase in titre) when examined by the same laboratory.

If there is no clinical improvement following a course of treatment, an alternative drug or a different dosage should be considered. Alternatively, the diagnosis should be queried or the animal should be examined for the presence of concomitant vector-borne diseases such as ehrlichiosis, anaplasmosis, babesiosis, hepatozoonosis, or other diseases such as endocrinopathies, neoplasias, or immune-mediated diseases, all of which may affect the response to treatment.

Table 4: Chemotherapy of canine leishmaniosis

Drugs*	Dosage	Route of administration
Meglumine antimoniate	50 mg/kg (BID) for 4–6 weeks	Subcutaneous injection
Allopurinol**	10 mg/kg (BID) for 6–18 months	Oral
Miltefosine	2 mg/kg once daily for 4 weeks (with food)	Oral
Meglumine antimoniate + allopurinol**	see above for both compounds	Subcutaneous injection + oral
Miltefosine + allopurinol**	see above for both compounds	Both oral

* Most cytotoxic drugs are teratogenic in humans therefore gloves must be worn when administering.

** Not registered for veterinary use in Europe.

Numerous pharmacokinetic studies have shown that administration of meglumine antimoniate by intramuscular or subcutaneous injection is more effective in maintaining sustained drug plasma concentrations than intravenous injections. After intravenous administration, plasma concentrations fall within two hours whereas they fall within four hours after intramuscular administration. When injected subcutaneously, plasma concentrations rise after five hours and remain at therapeutic levels for at least 12 hours. It must be stressed that repeated intramuscular injections frequently lead to the development of painful oedematous reactions and myositis and are therefore not recommended; subcutaneous injections, being safer and painless, are preferred, although some side effects may be presented (potential nephrotoxicity and panniculitis at the injection site). Different dosages of meglumine antimoniate have been tested but the most widely accepted regimen is indicated in Table 4.

Allopurinol is commonly administered twice daily in a whole dose of 10 mg/kg bodyweight orally for 6–18 months with generally satisfactory results, a clinical cure being observed in most dogs within 6–12 months of treatment. After a clinical cure has been achieved, it is advisable to stop treatment and monitor the dog for possible relapses after three months and subsequently at six-monthly intervals. As with all other drugs, relapses are relatively common but animals can generally be re-treated with the same compound. Some side effects have been reported including the development of xanthine nephrolithiasis (few reports) and dogs on long-term therapy with allopurinol should be checked using urinalysis and/or abdominal ultrasonography. Usually, xanthinuria has a good prognosis and this side effect disappears shortly after reducing the dosage or the cessation of treatment (if this is deemed necessary).

Moreover, miltefosine, an alkylphospholipid molecule, has shown therapeutic effectiveness comparable with that of antimonial compounds. Side effects including vomiting, diarrhoea and anorexia of varying severity have been reported but these are quick to resolve if the drug is administered with food.

Several clinical trials, combining two compounds, e.g. antimonials or miltefosine plus allopurinol, have shown that they induce a clinical remission in most cases and partial reduction of the parasitic burden (see Table 4).

The use of non-specific immune modulatory drugs has been reported as potentiating the immune system of sick dogs to control the infection and to prevent development of clinical disease in uninfected dogs. Recently, domperidone, which has been launched in several European countries, has shown to manage the early stages of the disease or to prevent development of clinical disease as part of an integrated control programme. Further results, however, are needed in order to better evaluate these therapies.

The curative effects of some other drugs, either used alone or in combination, have been reported for the treatment of canine leishmaniosis, with varying efficacy (aminosidine, furazolidone, marbofloxacin, perifosine, oleylphosphocholine). None are currently recommended for use as first-line therapy but some would be helpful as complementary drugs in some clinical cases (e.g. antibiotics). Amphotericin B, once recommended for cases refractory to antimonials, is not well accepted due to its nephrotoxicity and the invasive intravenous route of administration. Furthermore, it is a first-line drug for visceral leishmaniosis in humans and the World Health Organization (WHO) and several public health committees have argued for restricted use of Amphotericin B (liposomal formulations) in dogs to avoid selection for resistance.

Resistance to drugs used for the chemotherapy of *Leishmania infantum* in dogs

To date, resistance has been observed against meglumine antimoniate in vitro. Moreover, disease relapse in dogs with leishmaniosis during allopurinol treatment has recently been described and associated with allopurinol resistance of *L. infantum* isolated from relapsed animals. Further studies are needed to better evaluate this fact.

Control strategies

Some control strategies used in the past, such as the culling of seropositive dogs in endemic areas, have been shown to be ineffective in reducing *Leishmania* transmission.

Prevention of phlebotome bites by the application of repellents/insecticides in the form of impregnated collars, spot-on and spray formulations is currently the most promising strategy; spray preparations have a short duration of effect. The basic objective is to interrupt parasite transmission and thus control the disease. The phlebotome season in endemic areas may vary from year to year and from region to region. As a general rule, in endemic areas, the season starts in April and continues until November. In some areas it may be necessary to protect dogs all year round (e.g. in southern Spain, Italy, Portugal and Greece).

Numerous studies have assessed the efficacy of synthetic pyrethroids in preventing phlebotome bites. For example, it has been observed that dog collars impregnated with 4% deltamethrin possess a repellent effect against phlebotomes lasting from one week after application to over six months, thereby resulting in a significant decrease in the incidence of disease in endemic areas such as Italy or Spain over a period of 2–3 years. Applications of permethrin alone, or in combination with other insecticides as a spot-on, have also been shown to protect dogs against phlebotome bites within hours (i.e. after 24 hours) and for up to 3–4 weeks thus decreasing the incidence of canine leishmaniosis in endemic areas.

Data of two clinical field studies performed in *Leishmania infantum* endemic areas using a slow-release imidacloprid (10%)/flumethrin (4.5%) collar indicate a significant reduction in the risk of *Leishmania* infection in treated dogs compared to non-treated dogs, while the efficacy of the product in the prevention of sand fly bites has not been established.

These studies show that the interruption of *Leishmania* transmission through the external application of synthetic pyrethroids to dogs could be a major tool if incorporated into future disease control programmes in regions where pet dogs are the main reservoir of *L. infantum*.

Finally, other control measures to reduce disease transmission include keeping dogs indoors during dusk and dawn throughout the whole risk season, the use of insecticidal room sprays, protective nets at windows and doors (mesh size <math><0.4\text{ mm}^2</math>), and mosquito bed nets treated with synthetic pyrethroids. Wherever they have been implemented, these measures have brought about a dramatic reduction in phlebotome populations. Moreover, reducing the breeding sites of phlebotomes by removing garbage and deposits of organic matter is also recommended in the vicinity of houses and places where dogs are present.

Vaccination is another prevention strategy and to date, the application of synthetic pyrethroids in combination with vaccination represents the best way of controlling the disease.

A vaccine, based on a native antigen purified from medium supernatant of *L. infantum* cultures, was available in some EU countries for use in non-infected dogs between 2011 and 2020 however, the vaccine is no longer available.

Moreover, in 2016 the European Commission approved the marketing of a new vaccine composed of Protein Q, a recombinant protein constructed from the union of five antigenic fragments of four proteins of the parasite *Leishmania infantum*. This vaccine can be given to seronegative dogs over six months of age as an initial single injection followed by annual revaccination. The vaccine is indicated to reduce the risk of developing an active infection, clinical disease or both, following exposure to *L. infantum*. This new vaccine does not interfere with the detection of anti-*L. infantum* antibodies and thus allows the discrimination of vaccinated from naturally infected dogs.

Resistance to repellents and insecticides: There are no reports of resistance of phlebotomes to synthetic pyrethroids.

2.1.1.g. Public health considerations

Human leishmaniosis caused by *L. infantum* is an important vector-borne zoonotic disease in southern Europe. Clinical cases of human leishmaniosis generally prove fatal without therapy, especially in children and immunocompromised patients.

Evidence points to the spread and (re-)emergence of this disease in humans in some endemic areas. In Madrid, there were more than 700 new clinical cases (visceral and cutaneous) reported between 2009 and 2016. The epidemiological and molecular typing-based studies of this outbreak suggest different genotypes circulating among sand flies, dogs and other alternative hosts (mainly hares and rabbits). These scientific studies have contributed to a better understanding of this important zoonosis.

The responsibility of veterinary practitioners must be to adequately manage the disease in dogs to reduce parasite transmission since dogs are the main reservoir of infection.

The following principles must be stressed:

- A thorough diagnostic procedure should be established to identify infected and/or sick dogs.
- The best treatment for sick dogs should be chosen, bearing in mind the potential risks for the development of resistance to “first line” drugs used in humans.
- The use of topical insecticides should be recommended for all dogs at risk and especially for infected clinically healthy or sick dogs even after successful chemotherapy; these should be applied throughout the risk season which depends on climatic conditions. In the southern European endemic areas, the risk season is between April and November. In warmer areas all year round use of repellents is strongly recommended.
- In endemic areas, kennels housing stray, hunting or breeding dogs should maintain a strict vector-borne disease monitoring programme; this should be combined with measures designed to prevent disease transmission by phlebotomes and thus avoid the risk of focal, highly endemic transmission.
- To avoid an extension of endemic areas, *Leishmania*-infected dogs should not be translocated to non-endemic areas where phlebotomes may be present.

2.1.1.h. Feline leishmaniosis

Despite the high prevalence of canine leishmaniosis in endemic areas, feline leishmaniosis is frequently subclinical. Over 80 clinical cases in cats have been described in literature in Europe, South America and Texas, USA. These cases were characterised by cutaneous lesions (nodular and ulcerative lesions), enlarged lymph nodes, weight loss and ocular lesions. Weight loss, reduced appetite, dehydration and lethargy are the most frequent non-specific signs. The pathogenesis of feline leishmaniosis is not currently known and the pattern of immune response to *L. infantum* infection has never been investigated in cats.

Xenodiagnoses studies performed in two chronically infected cats have shown that a cat can be infectious to *Phlebotomus*, the competent *L. infantum* vector. However, the role of the cat in the transmission cycle of leishmaniosis is not clear.

The diagnosis protocol is exactly the same as for the dog including parasitological, molecular and serological techniques. The diagnostic evaluation should always be completed with CBC, a biochemical profile, urinalysis with a quantitative evaluation of proteinuria and any other tests recommended for excluding other compatible or concurrent diagnoses. Regarding therapy, a few leishmanicide drugs have been tested on cats but there is no specific information on pharmacokinetic and pharmacodynamic studies of these compounds in cats. Allopurinol is the most frequently used oral drug at a dosage of 10–15 mg/kg bodyweight twice a day for several months.

Finally, in terms of prevention, there are currently no drugs available for cats to avoid phlebotomine bites and to prevent *Leishmania* transmission. Permethrin cannot be used as a preventative in cats due to its toxicity for this species. Flumethrin collars have sand fly repellency properties and may be an off-label option.

Further information about canine and feline leishmaniosis can be found on the LeishVet website at www.leishvet.org

2.1.2. Dirofilariosis and other filarial infections

2.1.2.a. Agents and vectors

Filarial worms are nematodes infecting the connective tissues and vascular system of dogs and cats. Mosquitoes, but also fleas and ticks, act as vectors for the different species (Table 5). *Dirofilaria immitis*, the canine and feline heartworm, is the most pathogenic species, while *D. repens*, which causes subcutaneous dirofilariosis, is the most important species responsible for zoonotic infections in Europe.

Table 5: Filarial species infecting dogs and cats in Europe (see Table 6 for morphology of microfilariae)

Filarial parasite	Vectors	Prepatent period	Length of adult worms	Location of adult worms
<i>Dirofilaria immitis</i>	Mosquitoes (Culicidae)	120–180 days	M: 12–18 cm F: 25–30 cm	Pulmonary arteries/ right heart
<i>Dirofilaria repens</i>	Mosquitoes (Culicidae)	189–259 days	M: 5–7 cm F: 10–17 cm	Subcutaneous tissue/ muscular fasciae
<i>Acanthocheilonema</i> (formerly <i>Dipetalonema</i>) <i>reconditum</i>	Fleas and ticks	427–476 days	M: 9–17 mm F: 21–25 mm	Subcutaneous tissue/ muscular fasciae, peritoneal cavity, kidney
<i>Acanthocheilonema</i> (formerly <i>Dipetalonema</i>) <i>dracunculoides</i>	Fleas and ticks (<i>R. sanguineus</i>)	120 days	M: 15–31 mm F: 33–55 mm	Peritoneal cavity
<i>Cercopithifilaria</i> spp.	Ticks (<i>R. sanguineus</i>)	Unknown	M: unknown F: 23–24 mm	Subcutaneous tissue/ muscular fasciae

M: male; F: female

2.1.2.b. Biology and transmission

Filarial nematodes are parasites of domestic and wild carnivores, mainly canids. However, due to the low host specificity of their arthropod vectors, many mammalian hosts can be infected, including humans. In such hosts, the parasites generally do not develop to the adult stage.

■ *Dirofilaria immitis* and *D. repens* microfilariae are released by female worms into the blood stream where they become available to blood-sucking mosquitoes. Microfilariae develop to the infective stage (L3) and are transmitted via saliva during feeding. *Dirofilaria immitis* larvae undertake an extensive migration to reach the pulmonary arteries and the right heart where they develop into the adult stages and mate. In dogs, adult worms have a lifespan of up to seven years (although survival in cats is shorter), and microfilariae survive 2–18 months in the bloodstream. The infective larvae of *D. repens* migrate into the subcutaneous connective tissues where they reach maturity. Adult worms are found between subcutaneous and deep connective tissue layers in most parts of the body. Adults can live for several years (Figures 4 and 5).

■ *Acanthocheilonema* (syn. *Dipetalonema*) *reconditum* is found in subcutaneous tissues and fasciae, the peritoneal cavity and the kidneys of canids, *Cercopithifilaria grassii* is a parasite of the subcutaneous tissues and fasciae of canids and *A. dracunculooides* is a parasite of the peritoneal cavity. For treatment and prevention purposes, circulating microfilariae of these species must be differentiated from those of *D. immitis* and *D. repens*.

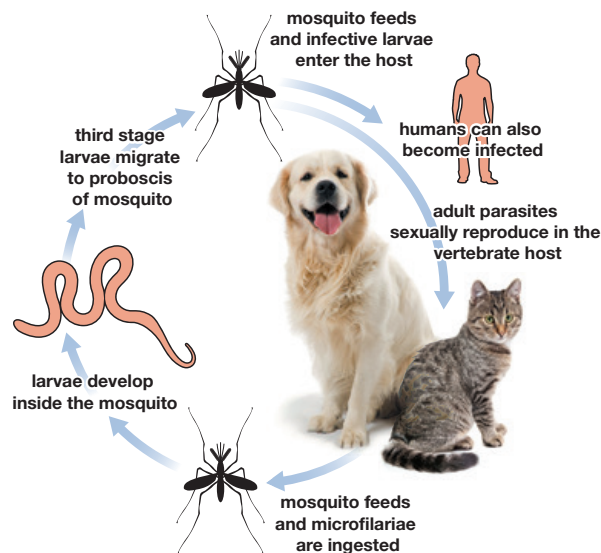


Figure 4: *Dirofilaria immitis* life cycle

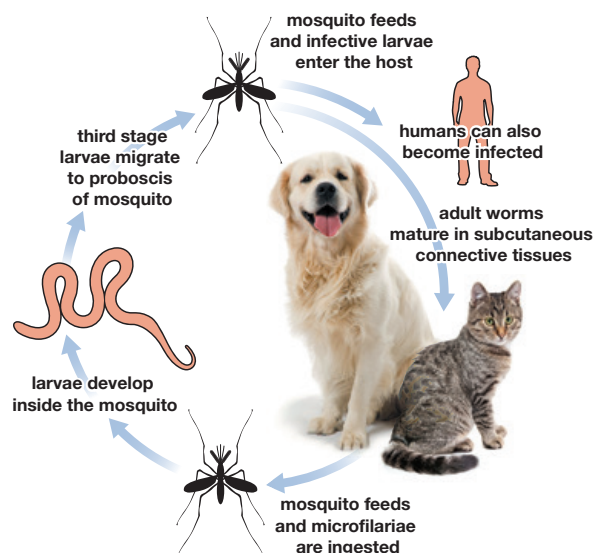


Figure 5: *Dirofilaria repens* life cycle

2.1.2.c. Distribution in Europe

The frequency of transmission and the spread of *Dirofilaria* spp. infections depend upon environmental factors such as temperature, the density of vector populations and the presence of microfilaraemic dogs, which are the main reservoirs of infections. Due to tourism and animal adoption, infected dogs are increasingly being moved from endemic areas such as Portugal, Spain, Italy and Greece to non-endemic areas.

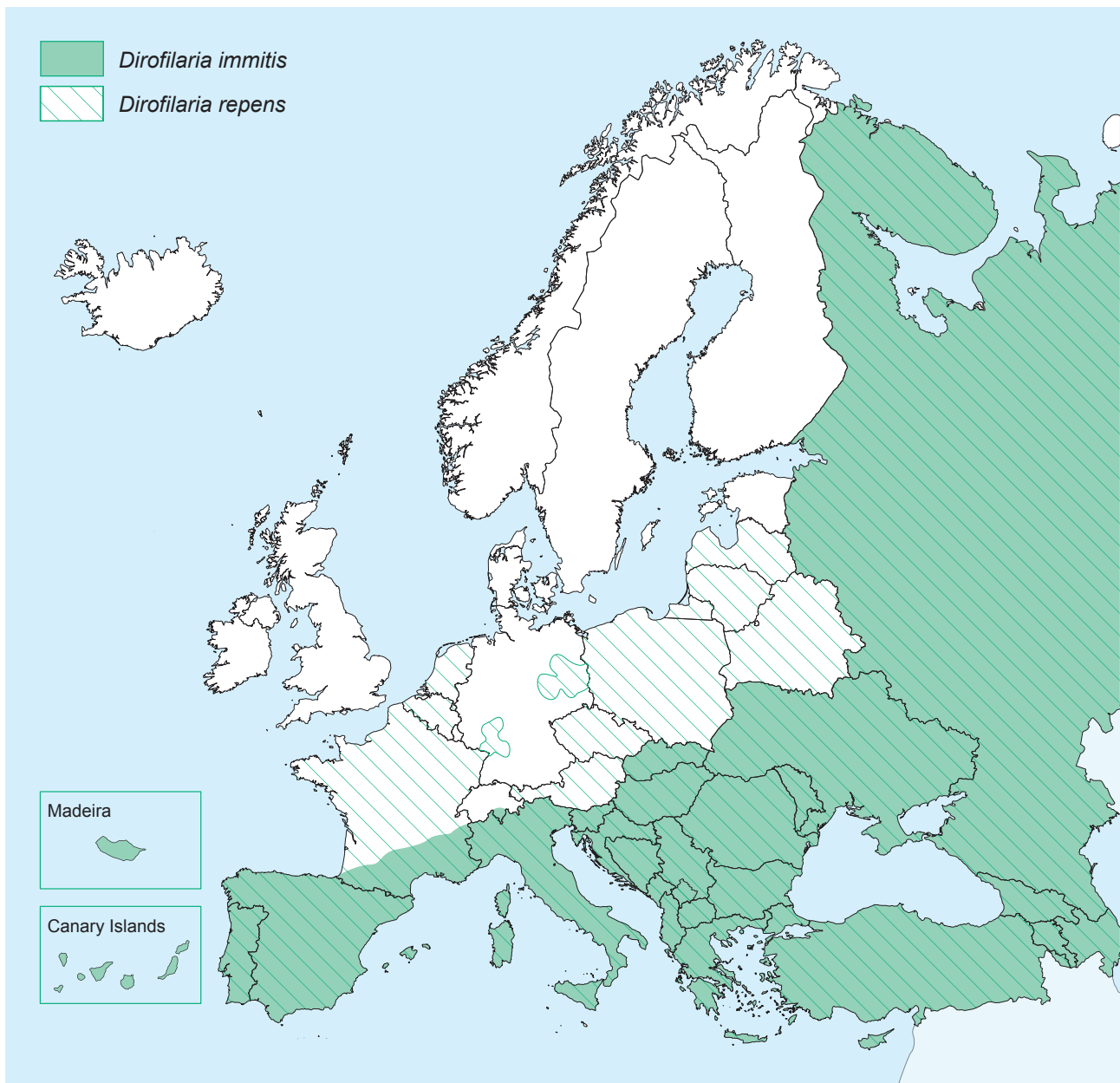


Figure 6: Approximate distribution of *Dirofilaria immitis* and *Dirofilaria repens* in Europe (© ESCCAP)

This map depicts approximate prevalence and is for informational and illustrative purposes only. ESCCAP cannot guarantee the map's completeness since the data are only collected from ESCCAP member countries. All of ESCCAP's maps are dynamic and in a constant state of maintenance, correction and revision. For the most up-to-date version, please visit www.esccap.org/guidelines-maps/. This map does not express any opinion on the part of ESCCAP concerning the legal status of any country or territory or concerning the delimitation of frontiers or boundaries.

Dirofilaria immitis is endemic across southern Europe and in Slovenia, Romania and Bulgaria (Figure 6). The endemic areas of *D. immitis* and *D. repens* overlap in many regions. Recently, *D. repens* infections in dogs that had never left Germany, Austria, Italy, Czech Republic or Poland have been documented.

Feline *Dirofilaria* infections occur in areas where canine infections are highly prevalent; the prevalence in cats, however, is generally only a tenth of that in dogs.

Acanthocheilonema dracunculoides infections have prevalence rates of up to 14% in hunting dogs and dogs living outdoors in some countries and regions of Europe such as Spain and southern Italy (Sicily).

2.1.2.d. Clinical signs

Infections with *D. immitis* may cause severe and potentially fatal disease in dogs and cats. Despite its name, heartworm disease is essentially a pulmonary disease because the worms are predominantly located in the pulmonary arteries and the right heart is involved only in the later stages.

DOG

Clinical signs of the disease caused by *Dirofilaria immitis* develop gradually and may begin with a chronic cough which may be followed by moderate to severe dyspnoea, weakness and sometimes syncope after exercise or excitement. At this stage, auscultation may reveal abnormal pulmonary sounds (crackles) over the caudal lung lobes and a split second heart sound can often be heard. Later, when right congestive heart failure is developing, ascites, and less often oedema in the limbs, may be observed together with anorexia, weight loss and dehydration. Arterial damage is usually more severe in dogs that perform intensive physical exercise. Sudden death is rare and usually occurs following respiratory distress or progressive emaciation.

During the chronic stages of the disease, there may be a sudden onset of acute signs. For example, after severe spontaneous thromboembolism following the natural death of many heartworms, dogs may show acute life-threatening dyspnoea and haemoptysis.

In small dogs, the displacement of adult worms from the pulmonary arteries to the right heart, due to pulmonary hypertension and a sudden decrease in right cardiac output, is a common event. In such cases, affected dogs present the so-called “caval syndrome”. Dyspnoea, a tricuspid cardiac murmur and haemoglobinuria, due to mechanical haemolysis in the right cardiac chambers, are the most typical signs and the outcome is usually fatal.

CAT

Most cats show no clinical signs of the presence of *Dirofilaria immitis* for a long time after initial infection and may spontaneously self-cure. In most cases, the onset of clinical signs seems to be related to the natural death of parasites or to the arrival of pre-adult heartworms (L5) in the pulmonary arteries. Feline heartworm disease is now recognised as a significant pulmonary syndrome defined as “Heartworm Associated Respiratory Disease” (HARD). Clinical signs associated with HARD include anorexia, lethargy, weight loss, coughing, haemoptysis, dyspnoea, rapid heart rate, vomiting, diarrhoea, blindness, convulsions. Collapse and sudden death in apparently healthy cats is not an infrequent consequence of infection.

Dirofilaria repens is the most frequent species associated with subcutaneous filariasis of dogs and cats. In some cases, subcutaneous, non-inflammatory nodules containing adult parasites or immature stages can be observed. These “cold” nodules are not painful and appear free within the skin. The parasite may also be observed during surgery in the perimuscular fasciae, perirenal fat or abdominal cavity or may migrate to the ocular conjunctiva. Rarely, in cases of heavy infection and sensitised patients, pruritus, pustules, ulcerative lesions and exfoliative dermatitis may be seen, associated with microfilariae in the skin.

Infections with *A. reconditum*, *A. dracunculoides* and *C. grassii* are mostly subclinical. Differentiation of all species that produce microfilariae in the bloodstream is necessary for treatment and prevention purposes.

2.1.2.e. *Wolbachia* species and filarial worm symbiosis

Gram-negative bacteria of the genus *Wolbachia* are obligate endosymbionts of both *D. immitis* and *D. repens*. These bacteria play an important role in the pathogenesis and immunology of heartworm infection. *Wolbachia* can be eliminated from filarial worms through antibiotic therapy of the infected host (e.g. doxycycline). Such depletion of *Wolbachia* is often followed by clear anti-inflammatory effects, thus, antibiotic treatment may be used concomitantly with the use of adulticidal therapeutic agents.

2.1.2.f. Diagnosis

DOG

Heartworm infection in dogs can be detected with blood tests which demonstrate the presence of circulating microfilariae or adult antigens in serum or plasma samples. Further diagnostic procedures are required to determine the severity of disease and possible treatment options.

Blood examination for microfilariae

Blood samples should be examined after concentration by the Knott or the filtration test and morphological identification carried out (Table 6). NB Wet blood smears do not allow species identification and have a very low sensitivity. Furthermore, negative test results for microfilariae cannot rule out infection as they are not always present (occult infection). Molecular testing (PCR) is available in some laboratories to differentiate species of filarial worms.

Table 6: Morphological features of blood microfilariae¹ from filarial worms of dogs and cats

Species	Length (μ)	Width (μ)	Features
<i>Dirofilaria immitis</i>	301.77 ± 6.29 290–330	5–7	No sheath, cephalic end pointed, tail straight with the end pointed. APh-S: two activity spots located around the anal and the excretory pores.
<i>D. repens</i>	369.44 ± 10.76 300–370	6–8	No sheath, cephalic end obtuse, tail sharp and filiform often ending like an umbrella handle. APh-S: one spot around the anal pore.
<i>Acanthocheilonema reconditum</i>	264.83 ± 5.47 260–283	4	No sheath, cephalic end obtuse with a prominent cephalic hook, tail button hooked and curved. APh-S: activity throughout the body.
<i>A. dracunculoides</i>	259.43 ± 6.69 190–247	4–6.5	Sheath, cephalic end obtuse, caudal end sharp and extended. APh-S: three spots which include an additional spot in the medium body.

¹ Microfilariae (n=10) measured after concentration by the Knott test; when using the Difil® test, lengths are shorter. APh-S: acid phosphatase stain.

Blood/serological tests for adult female antigens

Antigens from adult female heartworms are present approximately 6–8 months post infection. Point-of-care immunoassays are considered highly specific and some of them can be used in-house for a quick diagnosis.

Radiographs, electrocardiography and echocardiography

Auxiliary evaluations are often useful in determining the extent of pulmonary and cardiac pathological changes in infected dogs; mainly thorax X-ray and echocardiography.

CAT

Blood examination for microfilariae

Detection of microfilariae in the blood of infected cats is unlikely to be successful, therefore the sensitivity is very low.

Blood/serological tests for adult female antigens

Tests detecting adult female heartworm antigens have a very high specificity and can thus provide definitive proof of infection. In many cases, however, these tests yield false-negative results because of low worm burdens or the presence of only male or immature worms. A negative test therefore does not rule out infection. Heat treatment of serum prior to antigen testing may increase the sensitivity of antigen testing in cats.

Diagnostic imaging

Thorax radiographic alterations and echocardiography are very useful for the diagnosis of the disease in cats. Cardiac ultrasound allows direct visualisation of the parasites in the right atrium and ventricle, in the main pulmonary artery and in the origin of both its main branches.

The specificity is virtually 100%, and the sensitivity in cats is very high as only a short portion of the caudal pulmonary arteries cannot be examined. Cardiac ultrasonography should always be performed when feline heartworm infection is suspected.

2.1.2.g. Control

Treatment

Adulticidal therapy (*D. immitis*) in dogs:

I. The organic arsenical compound melarsomine dihydrochloride is the only effective drug available for treating adult heartworm infections in dogs. The currently-accepted regimen is a two-step treatment to reduce the risk of pulmonary thromboembolism: after one initial treatment of 2.5 mg/kg bodyweight, given by deep intramuscular injection in the lumbar muscles, the recommended follow-up treatment is administered 30–60 days later (2.5 mg/kg bodyweight twice at an interval of 24 hours). Complications, due to pulmonary thromboembolism, should be reduced by the restriction of exercise following treatment and by the administration of a corticosteroid (e.g. prednisone at 0.5 mg/kg BID 1st week, 0.5 mg/kg SID 2nd week, 0.5 mg/kg EOD 3rd and 4th weeks) after melarsomine dihydrochloride injections.

Wolbachia (obligate, intracellular, gram-negative, endo-symbiotic bacteria) has been implicated as crucial in the pathogenesis of filarial diseases. Doxycycline reduces the *Wolbachia* burden in all stages of heartworms. Thus, administration of doxycycline at 10 mg/kg daily for 4 weeks before the administration of melarsomine dihydrochloride is strongly recommended.

II. Surgical intervention is advised when multiple worms have been displaced into the right cardiac chambers producing sudden onset of caval syndrome.

Adulticidal therapy (*D. immitis*) in cats:

There is no registered, safe and effective adulticide for cats. Decreasing doses of prednisolone are advised in cats in order to relieve respiratory distress with an initial dose of 2 mg/kg bodyweight per day. If a cat presents with severe signs of HARD, high doses of oral prednisolone (1–2 mg/kg bodyweight 3 times a day) are recommended.

Adulticidal therapy in canine and feline *D. repens* infection:

Spot-on moxidectin is licenced in all European countries as an effective adulticide therapy for *D. repens* infection and for the reduction of microfilaremia in dogs. Because of the zoonotic potential of *D. repens*, microfilaraemic dogs should be treated monthly for 12 months with preventative drugs able to kill microfilariae (see below).

Control strategies for dogs

Topical or oral macrocyclic lactones administered monthly throughout the transmission season are effective against *D. immitis* third stage larvae (L3) and L4 which have developed within the previous 30 days, thus preventing disease caused by adult worms. Several compounds alone, or in combination with other parasiticides, are available for oral administration or topical application (Table 7); for links to approved compounds in individual countries see www.esccap.org. An injectable, sustained-release macrocyclic lactone has been approved in some European countries for use only in dogs older than six months and is registered to give protection for one year.

Prevention, through monthly administration of macrocyclic lactones, should start before the mosquito season in spring and continue until late autumn. Recently, topical administration of permethrin with dinotefuran has shown repellent efficacy against mosquitoes on dogs for at least 4 weeks. In southern Europe, protection against heartworm should be carried out from May until the end of November. In hyperendemic areas, a year-round preventive therapy is recommended.

Table 7: Prevention of dirofilariasis in dogs and cats in Europe: minimal and maximal dosages of macrocyclic lactones

Compound	Presentation	Dog (min.–max. dosage)	Cat (min.–max. dosage)
Ivermectin	Tablets/chewable tablets	6–12 µg/kg	24–71 µg/kg
Milbemycin oxime	Flavoured tablets	0.5–2.5 mg/kg	2–4 mg/kg
Moxidectin	Tablets Injectable Topical	3–6 µg/kg 0.17 mg/kg 2.5–6.25 mg/kg	1–2 mg/kg
Selamectin	Topical	6–12 mg/kg	6–12 mg/kg

Currently, preventative drugs are fully effective against *D. immitis* larvae but reports from the USA suggest that drug resistance is emerging. Even though there have been no reports of resistance in Europe, in view of the fact that the maintenance of macrocyclic lactone efficacy is critical for *Dirofilaria* control, there are some recommendations which may assist in decreasing the risk of resistance selection.

1. Dogs should be checked for both circulating antigens and blood microfilariae (Knott test) at the beginning of each preventative annual treatment.
2. Although *Dirofilaria* does not appear to be entirely dependent on its bacterial symbiont *Wolbachia*, which can be killed by prolonged antibiotic treatment, the clearing of bacteria from circulating microfilariae seems to prevent the onset of infective larvae which may develop in mosquitoes afterwards.
3. The combination of heartworm preventatives with products designed to prevent mosquito blood-feeding activity (repellents) during the heartworm transmission season could be useful in protecting dogs from infection and from ectoparasite infestations that often occur in the same season.

Control strategies for cats

Prophylactic larval treatments in cats follow the same regimen as in dogs with monthly dosing regimens (see www.esccap.org for links to tables of approved compounds in individual countries).

Control strategies for canine and feline *D. repens* infections

Monthly treatments with macrocyclic lactones (oral or spot-on formulations) or an annual treatment with an injectable, sustained-release formulation at the same dosages used against *D. immitis* L3–L4, i.e. once at the beginning of the risk season, have been found to be effective in preventing subcutaneous infection in dogs naturally exposed to *D. repens* transmitting mosquitoes.

Control strategies for travelling dogs and cats

Before travelling from endemic areas to non-endemic areas, dogs should be examined for dirofilarial infections, treated against adult heartworms and cleared of both *D. immitis* and *D. repens* microfilariae. Furthermore, animals with unknown history should receive prophylactic treatment for two months to kill potential migrating L3–L4 and be tested for circulating antigens and microfilariae six and twelve months later.

Dogs and cats travelling from non-endemic to endemic areas should be protected against adult filarial infections. They should be treated within 30 days of arriving in the risk areas with macrocyclic lactone preventative drugs. For pets spending no more than one month in endemic areas, a single treatment, usually administered soon after returning home, is sufficient to assure complete protection. In the case of longer visits, a monthly regimen should be administered with the first treatment being given within 30 days of entering the risk area and the last within one month of leaving.

2.1.2.h. Public health considerations

In Europe, *D. repens* is the most important cause of human filarial infection. Most human cases are asymptomatic and infections are often diagnosed after the surgical removal of a nodule containing worms. Pre-adult worms are also often observed in the conjunctiva and even in the vitreous of the eye. Furthermore, visceral localisation of both *D. repens* and *D. immitis*, such as in the lung, mesentery and dura mater, may mimic neoplasia. The infection in humans is probably underdiagnosed due to lack of awareness by physicians.

Further information about heartworm can be found on the following websites:
European Society of Dirofilariosis and Angiostrongylosis (ESDA): www.esda.vet
American Heartworm Society: www.heartwormsociety.org

2.1.3. Bartonellosis

2.1.3.a. Agents and vectors

The most important species involved in bartonellosis is the bacterium *Bartonella henselae* which is of relevance mainly as the causative agent of cat scratch disease (CSD) in humans. Cats are considered the main reservoirs of, amongst others, *B. henselae* and *B. clarridgeiae*. The vectors of many *Bartonella* species, especially *B. henselae*, are fleas, mainly the cat flea *Ctenocephalides felis felis*. *Bartonella* spp. have also been found in other blood-sucking arthropods such as ticks and flies but the role of these vectors in the transmission of infection is still ill-defined. In the vast majority of humans with cat scratch disease, bacillary peliosis hepatitis (multiple, randomly distributed, blood-filled cavities throughout the liver) or bacillary angiomatosis (vascular proliferation that occurs primarily in immunocompromised individuals), *B. henselae* or *B. quintana* have been isolated as the agents. On the basis of serological tests, *B. clarridgeiae* has been suspected to be the cause of diseases similar to cat scratch disease.

2.1.3.b. Biology and transmission

Bartonella are haemotrophic bacteria which are facultative intracellular parasites of red blood cells and endothelial cells. They can be detected in samples of cat blood as well as in specimens from claws and in saliva. How *B. henselae* is transmitted has not been clearly defined. Infection occurs through contact with fleas and their faeces (Figure 7). The agent can survive and remains infectious for up to nine days in the faeces of infected fleas. For the infection of humans, scratches and bites from cats play a crucial role. It is assumed that the oral cavity and the claws of infected cats are contaminated with bacteria-containing flea faeces during grooming and that the agent is transmitted to humans through skin wounds. Another possibility is iatrogenic transmission during blood transfusions.

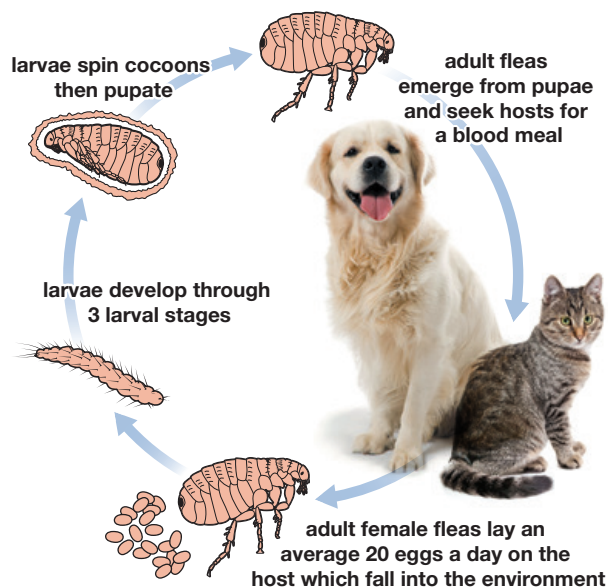


Figure 7: Flea life cycle

2.1.3.c. Distribution in Europe

The agent *B. henselae* and the primary vector *Ctenocephalides felis felis* are distributed worldwide.

Bartonella infection most probably occurs in cats less than two years of age, cats with access to outdoor areas, stray cats and animals in multi-cat households. The observed prevalence of *Bartonella* infection varies between cat populations and is often dependent on the detection method used.

2.1.3.d. Clinical signs

Most infections with *Bartonella* spp. in cats remain subclinical. Generally, a bacteraemia develops within 1–3 weeks of the initial infection with chronic recrudescence for up to 21 months. Clinical signs are observed only in immunosuppressed cats which may present fever, lymphadenopathy, gingivitis, uveitis, and endocarditis; transient anaemia and persistent eosinophilia have also been described. Infection has also been associated with diseases of the urinary tract as well as with reduced reproductive performance.

In dogs, more than eight species of *Bartonella* have been associated with endocarditis, myocarditis, hepatitis and rhinitis, but *Bartonella*-associated disease is probably underdiagnosed.

2.1.3.e. Diagnosis

The following diagnostic procedure is recommended:

1. Identification of clinical signs that may be associated with bartonellosis.
2. Exclusion of other causes that might explain the clinical picture.
3. Laboratory tests:
 - a. The gold standard for the diagnosis of bartonellosis is blood culture. It is also possible to detect *Bartonella* DNA in samples of blood, tissue, cerebrospinal fluid or aqueous humour.
 - b. Antibodies can be detected serologically from approximately 10–14 days after infection. A positive serological finding only shows cat or dog exposure to *Bartonella* spp. For the diagnosis of clinical bartonellosis, repeated testing of serum samples should show a rising antibody titre.
4. Response to treatment with an antibiotic effective against *Bartonella* spp. However, this may be complicated by the fact that the drugs effective against *Bartonella* spp. are broad spectrum antibiotics which are also effective against other possible infections which may have been included in the differential diagnosis. Despite following this procedure, a definitive diagnosis of bartonellosis is not always possible.

2.1.3.f. Control

Treatment

The therapy of bartonellosis with currently available drugs only reduces the bacteraemia but does not eliminate the pathogen. Treatment is therefore only recommended for animals that show clinical signs and/or have contact with immunocompromised persons.

Possible therapies include:

- Amoxicillin/clavulanic acid at a dose of 22 mg/kg bodyweight orally every 12 hours for seven days.
- Doxycycline at a dose of 10 mg/kg bodyweight every 12 or 24 hours for 2–4 weeks.
- Enrofloxacin at a dose of 5 mg/kg bodyweight once daily for 2–4 weeks.

If the cat or dog responds to the therapy, it should be continued for at least 28 days or two weeks after remission of the clinical signs.

Should the animal still show clinical signs after seven days:

- Azithromycin 10 mg/kg bodyweight orally once daily for approximately 10 days.

As above, the treatment should be continued for up to two weeks after the signs have subsided.

Prevention

The primary measure for the prevention of *Bartonella* spp. infection is effective protection against flea infestations. This includes the prompt use of an anti-flea treatment on infected animals and good hygiene to minimise the presence of flea faeces both on the animal and in its environment (see ESCCAP Guideline 3: Control of Ectoparasites in Dogs and Cats). In households with immunocompromised persons, special precautions must be taken.

- New cats should only be introduced into the household if they are older than one year, confirmed to be free of fleas and preferably have also tested negative for *Bartonella* spp.
- The cats should be kept indoors.
- Wounds caused by cat scratches or bites should be immediately washed and disinfected.

2.1.3.g. Public health considerations

Transmission to humans occurs through contact with subclinically-infected cats usually by being scratched or bitten. Transmission can also occur by flea faeces contaminating skin lesions. It is unclear whether humans can become infected by being bitten directly by the cat flea.

Also in humans, infection with *B. henselae* does not always cause disease. Disease characteristics are significantly different in immunocompetent and immunosuppressed patients.

Immunocompetent patients usually suffer from the classical form of cat scratch disease (CSD) with pustule formation at the infection site, regional lymphadenopathy, abscess formation and possibly fever. Most cases of uncomplicated CSD are self-limiting but may last for months until complete resolution. This disease syndrome responds only minimally or not at all to antimicrobial therapy.

The course of disease is much more complicated in immunocompromised patients. Bacillary peliosis, bacillary angiomatosis, endocarditis, retinitis and encephalopathies can develop. In such cases, antimicrobial therapy is indicated and generally effective.

2.1.4. Viral infections

The reader is referred to section 2.3.

2.2. Tick-borne diseases

2.2.1. Babesiosis (piroplasmosis)

2.2.1.a. Agents and vectors

Babesia spp. (Table 8) are haemoprotozoa that exclusively infect erythrocytes and are transmitted by hard ticks.

Table 8: *Babesia* species of dogs and cats and their vectors in Europe

Causative agent	Size	Hosts	Tick vector
<i>Babesia canis</i>	Large ¹	Dogs	<i>Dermacentor reticulatus</i>
<i>B. vogeli</i>	Large	Dogs	<i>Rhipicephalus sanguineus</i>
<i>B. microti</i> -like/ <i>B. vulpes</i> ²	Small	Dogs ³	<i>Ixodes hexagonus</i> ⁴
<i>B. gibsoni</i> and <i>gibsoni</i> -like	Small ⁵	Dogs ³	<i>Rhipicephalus sanguineus</i> ⁴ <i>Haemaphysalis</i> spp. <i>Dermacentor</i> spp.
<i>Babesia</i> spp.	Small/large	Cats ³	<i>Rhipicephalus</i> spp. ⁴

¹ larger than half the diameter of an erythrocyte.

² synonym: *Theileria annae*-*Babesia annae*.

³ other species may also be important, like the fox (*Vulpes vulpes*) and the European wolf (*Canis lupus*).

⁴ role as vectors is suspected but has not been experimentally demonstrated.

⁵ smaller than half the diameter of an erythrocyte.

2.2.1.b. Biology and transmission

Babesia spp. are generally highly host-specific with regard to both the transmitting tick species and the mammalian host.

After being ingested with a blood meal, *Babesia* stages penetrate the gut epithelium of the tick, multiply and migrate to different organs including the tick ovary and salivary glands. Transovarial transmission from infected adult female ticks to their progeny occurs with large *Babesia* spp. and thus their larvae (“seed ticks”) can be an important source of infection (Figure 8).

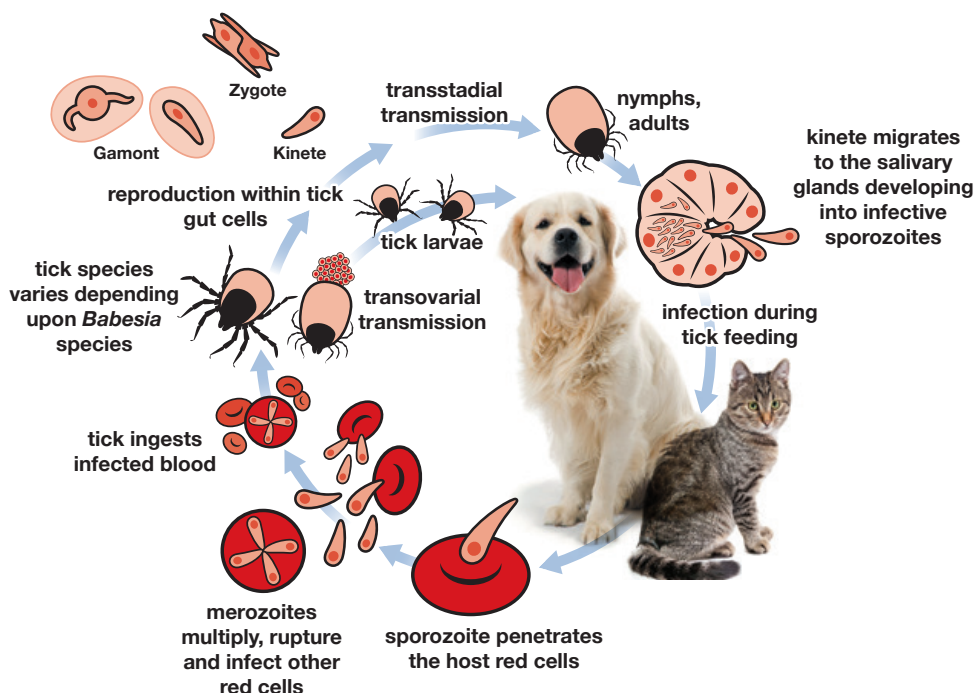


Figure 8: *Babesia* spp. life cycle

Females of different species of Ixodidae, generally require a period of initial feeding (24–48 hours) before *Babesia* sporozoites are available for transmission within their saliva to the dog. In male ticks, transmission may be more rapid as they repeatedly feed taking only small amounts of blood, and they perform co-feeding with females and possibly feed from several different hosts.

Sporozoites infect erythrocytes, differentiate into merozoites and divide by binary fission eventually causing cell lysis.

2.2.1.c. Distribution in Europe

Endemic areas of canine babesiosis (Table 9) are related to the distribution of the tick vector (for details see ESCCAP Guideline 3: Control of Ectoparasites in Dogs and Cats). In central Europe, canine babesiosis appears to be one of the most frequently imported diseases and the endemic area of *B. canis* seems to have expanded in central Europe up to the Baltic region in recent years. Besides *B. canis* (large *Babesia* species), small *Babesia* spp. can sporadically occur in Europe. Babesiosis in cats has only occasionally been observed in Europe and the species and vectors are still unknown.

Table 9: Currently recognised distribution of canine *Babesia* spp. in Europe

<i>Babesia</i> spp. in dogs	Distribution
<i>B. canis</i>	Endemic in northern Spain, Portugal, France, The Netherlands, Italy, focally in central and eastern Europe up to the Baltic region associated with the distribution of <i>Dermacentor</i> spp. At least one endemic focus in the UK.
<i>B. vogeli</i>	Southern Europe, associated with the distribution of <i>Rhipicephalus sanguineus</i> .
<i>B. gibsoni</i> or <i>B. gibsoni</i> -like spp.	Sporadic and rare in Europe, imported from Asia.
<i>B. microti</i> -like (<i>B. vulpes</i>)	Northwest Spain and Portugal (in foxes found in Croatia, Italy, Germany). Recently found in ticks from UK dogs.

2.2.1.d. Clinical signs

Babesiosis may be subclinical or may follow a peracute, acute or chronic course. Furthermore, different species and subspecies or strains differ with regard to their pathogenicity. Several species or strains may be found in the same host, namely in overlapping areas of *Babesia* distribution, which makes diagnosis based on clinical signs rather difficult (Table 10).

Table 10: Clinical manifestations of canine babesiosis

Causative agent	Clinical presentation
<i>B. canis</i>	Acute disease: incubation period 1–3 weeks. Moderate to severe clinical signs, depending on the age and immune status of the dog: medium–high fever, lethargy, anorexia, jaundice, vomiting and in some cases, red-coloured urine (“rusty urine”). Common clinicopathological findings are haemolytic anaemia, thrombocytopenia, neutropenia and sporadic haemoglobinuria. If untreated, a long recovery period may be followed by relapses which may lead to shock, icterus and severe or even fatal renal failure. Atypical forms may be associated with haemorrhage and disseminated intravascular coagulation with severe locomotor, cerebral, ocular, gastrointestinal and vascular disturbances. Chronic disease: clinical signs may include moderate depression, intermittent fever, anaemia, myositis and arthritis.
<i>B. vogeli</i>	Mild to moderate clinical signs; often subclinical but severe forms have been observed in puppies.
<i>B. gibsoni</i>	Moderate to severe clinical signs.
<i>B. microti</i> -like (<i>B. vulpes</i>)	Moderate to severe clinical signs including apathy, anorexia, fever, severe anaemia, haemoglobinuria and thrombocytopenia; a low parasitaemia may be present which is not related to the severity of the clinical signs.

Babesiosis in cats

Several *Babesia* spp. or subspecies have been reported in domestic cats from various parts of the world, particularly South Africa. Relatively few reports originate from Europe, and clarification of the species infecting cats in Europe is currently under investigation. Clinical cases of feline babesiosis reported are characterised by lethargy, anorexia, weakness and diarrhoea. Fever with icterus is uncommon, but signs may not be apparent until later stages of the disease.

In cats, co-infection with other pathogens such as retroviruses and haemotropic mycoplasmas are suspected to increase susceptibility to *Babesia* infections via immunosuppression.

2.2.1.e. Diagnosis

Blood smears: A diagnosis of acute babesiosis can be confirmed with high sensitivity by the examination of thin blood smears (Giemsa-stain or Diff-Quik) to detect large or small *Babesia* spp. Freshly-prepared blood smears can be used. For *B. canis*, peripheral capillary blood taken from the ear pinna or the tip of the tail may yield higher numbers of parasitised cells, and a rapid diagnosis of the acute disease is therefore possible when a sick animal is first presented. *Babesia canis* are large, piriform organisms found singly or in pairs in erythrocytes (Figure 9). *Babesia gibsoni* and *B. vulpes* are generally single, rounded intracellular organisms, but can occasionally be seen as four linked organisms within single red cells (forming a “Maltese cross” shape); parasitaemia is normally low. The diagnosis of chronic infections or carrier dogs is a challenge under clinical settings, due to very low and often intermittent parasitaemia.

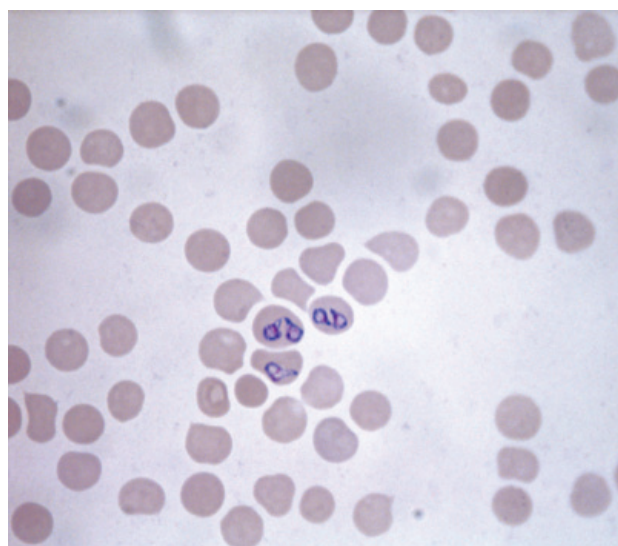


Figure 9: *Babesia canis* piroplasm in red blood cells

Serology: Specific antibodies can only be detected from two weeks after the first infection and acute infections will therefore be missed if relying on serology for diagnosis. For canine babesiosis, the indirect fluorescent antibody test (IFAT) using infected red blood cells either from infected dogs or from cell cultures, is the most common laboratory-based test, and also an ELISA is available in some European Countries. In endemic areas, seropositivity may not be synonymous with disease and may be detected in a high number of dogs which have been in contact with the parasite but did not become ill.

Molecular diagnosis: Species- or subspecies-specific PCRs (including real-time PCRs) have been described and are being increasingly used in routine laboratory diagnosis. The sensitivity of the PCR has been proven to be higher than blood smear examination especially for the diagnosis of chronically infected dogs but false-negative results cannot be completely excluded. Identification of species and subspecies can be important in terms of treatment options and prognosis.

2.2.1.f. Control

Treatment

Chemotherapy should be initiated immediately after confirmation of a babesiosis diagnosis. Imidocarb dipropionate, and in some countries phenamidine, are the drugs commonly used for the therapy of *B. canis* infection and in many cases, treatment with these drugs improves the clinical status, even though parasitological cure is likely never achieved. However, in endemic areas, treated dogs do not develop a specific immune response capable of protecting against re-infection. In all cases, adequate supportive therapy is strongly recommended including blood transfusion and, if appropriate, rehydration.

There is little information on the therapy of babesiosis caused by small *Babesia* spp. in dogs and by *Babesia* spp. in cats. However, currently available chemotherapeutic agents used at the recommended dosage can reduce both the clinical severity and mortality rate (Table 11).

Table 11: Chemotherapy of babesiosis in dogs

Drug	Dose	Efficiency and side effects
Imidocarb dipropionate ¹	5–6 mg/kg bodyweight, i.m. or s.c., administered 2 weeks apart are recommended	<i>B. canis</i> : clinical improvement within 48 hours in the absence of hepatic, renal and vascular complications. Side effects: related to an anticholinesterase effect include hypersalivation, tachycardia, dyspnoea, vomiting and diarrhoea. <i>B. gibsoni</i> : less effective, <i>B. microti</i> -like/ <i>B. vulpes</i> : not effective.
Phenamidine ²	15–20 mg/kg bodyweight, s.c., a second administration after 48 hours is sometimes recommended	<i>B. canis</i> : clinical improvement within 48 hours in the absence of hepatic, renal and vascular involvement. Side effects: injection site pain, hypotension, tachycardia and vomiting.
Pentamidine ²	16.5 mg/kg bodyweight, i.m. once or twice 24 hours apart	Side effects: vomiting, hypotension and local irritation and pain at injection site.
Atovaquone ²	13 mg/kg bodyweight orally every 8 hrs for 10 days	High efficacy against <i>B. microti</i> -like/ <i>B. vulpes</i> infections (in combination with azithromycin).
Buparvaquone ²	5 mg/kg bodyweight i.m. 2 doses with an interval of 48 hours	Recent evidence of its efficacy against <i>B. microti</i> -like/ <i>B. vulpes</i> species (in combination with azithromycin).
Azithromycin ²	10 mg/kg bodyweight orally, once daily for 10 days	High efficacy against <i>B. gibsoni</i> infections (in combination with atovaquone).
Diminazene aceturate ^{2,3}	3.5–7 mg/kg bodyweight i.m. as a single dose	High efficacy against <i>B. gibsoni</i> .
Clindamycin ²	12.5 mg/kg bodyweight, orally every 12 hours	Indicated for <i>B. gibsoni</i> infections in combination with diminazene aceturate and imidocarb dipropionate.

¹ To prevent or mitigate adverse reactions, atropine (0.05 mg/kg bodyweight) can be administered before or within 30 minutes of administration of imidocarb dipropionate.

² Not registered for veterinary use in Europe.

³ Caution must be taken due to its neurological side effects.

Resistance against compounds used for chemotherapy or prophylaxis of canine babesiosis has not yet been recorded.

Prevention

So far, no strategic control programmes have been developed for canine/feline babesiosis. The risk of infection with *Babesia* spp. for individual dogs in endemic areas or for dogs travelling to, or through, such areas can be significantly reduced by effective tick control (see ESCCAP Guideline 3: Control of Ectoparasites in Dogs and Cats).

Immunity resulting from repeated infection is incomplete and can be adversely affected by drug treatment. Chemoprophylaxis with oral doxycycline can be considered for splenectomised or immunocompromised dogs with a history of *Babesia* infection. It is also an alternative in cases where vaccination or tick control is contraindicated or for countries where vaccines are not available. Chemoprophylaxis can be administered hours before entering an endemic area.

One vaccine which can prevent severe disease, but not infection, is available in some European countries. The level of immune-protection may vary depending on the species, subspecies and the antigenic structure of the strains, and this has to be considered in different endemic areas. Re-vaccination every six months in highly endemic areas is advised. Vaccination of pregnant or lactating bitches is not recommended.

Post-vaccination side effects are diffuse swelling and/or hard painful nodules at the site of injection but these generally disappear within four days. Rarely, reactions following the second dose of vaccination may persist for up to 14 days. Vaccinated dogs may develop a stiff gait and reduced appetite for 2–3 days after vaccination.

2.2.1.g. Public health considerations

Infections with *Babesia* spp. of dogs and cats have not been reported in humans.

2.2.2. Ehrlichiosis

2.2.2.a. Agents and vectors

Ehrlichia are vector-borne, Gram-negative, obligate intracellular bacteria. In Europe, *Ehrlichia canis* is the aetiological agent of canine monocytic ehrlichiosis (CME). This pathogen infects mainly lymphocytes and monocytes wherein the typical, microscopically visible microcolonies (morulae) develop. The main host of *E. canis* is the dog (other canids can serve as reservoirs of infection); the vector is the tick *Rhipicephalus sanguineus*. *Ehrlichia canis* or a closely-related species has been described in cats but has no veterinary relevance.

2.2.2.b. Biology and transmission

All stages (larvae, nymphs, adults) of *R. sanguineus* preferentially feed on canids and may acquire *E. canis* from bacteraemic animals. The pathogen may overwinter in infected ticks. Transstadial (from larva to nymph to adult), but probably no transovarial, transmission occurs. During the incubation period of 8–20 days, the pathogens multiply by binary fission in leucocytes of the dog, forming morulae within circulating mononuclear cells. Subsequently, they spread via the mononuclear phagocytic system to the liver, spleen and lymph nodes. This may lead to impairment of platelet function, sequestration and destruction.

Transmission of *E. canis* by blood transfusion has also been described, therefore screening of canine blood products is strongly recommended in endemic areas.

2.2.2.c. Distribution in Europe

The geographical distribution of *E. canis* generally corresponds to the distribution of its vector *R. sanguineus*. Countries with reported infections in dogs are France, Italy, Portugal, Greece, Switzerland, Germany, UK and Spain (also in cats).

2.2.2.d. Clinical signs

DOG

During the acute phase of canine monocytic ehrlichiosis, which lasts around 1–3 weeks, dogs show apathy, weakness, lethargy, anorexia, dyspnoea, fever, lymphadenopathy, splenomegaly, weight loss and vomiting.

The clinical signs associated with haematological abnormalities are pale mucous membranes, petechiae, ecchymoses, epistaxis, prolonged bleeding during oestrus, haematuria and melaena. The clinicopathological abnormalities include thrombocytopenia, leucopenia and mild to moderate normocytic, normochromic, and non-regenerative anaemia. In the subclinical phase, which may last for weeks or months, the dogs appear clinically normal. Typical laboratory abnormalities include anaemia, thrombocytopenia and hypergammaglobulinaemia. Chronic canine monocytic ehrlichiosis is characterised by a very complex clinical picture. Noticeable signs are weakness, apathy, sustained weight loss, fever, lymphadenopathy, splenomegaly, peripheral oedema in the hind limbs and scrotum, pale mucous membranes, a predisposition for bleeding with haemorrhages in the skin and mucous membranes, mucopurulent ocular and nasal discharges, epistaxis, and haematuria. In addition, interstitial pneumonia with dyspnoea, renal dysfunction, glomerulonephritis, arthritis, polyomyositis and lameness may, less commonly, occur.

Typical ocular signs can include anterior uveitis, corneal opacity, hyphaema, subretinal haemorrhage, retinal detachment and blindness. With the involvement of the CNS and secondary to meningitis, cervical pain, hyperesthesia, nystagmus, signs of meningoencephalomyelitis, paresis, ataxia and convulsions appear.

Typical laboratory abnormalities are an increase in liver enzyme activities (alanine aminotransferase (ALT) and alkaline phosphatase), as well as hyperproteinaemia, hypergammaglobulinaemia, moderate hypoalbuminaemia, proteinuria, thrombocytopenia, leucopenia, anaemia and less commonly pancytopenia. Cases of chronic severe CME in dogs, associated with pancytopenia, have a poor prognosis.

CAT

Reports of *E. canis* infections in cats are rare. Clinical manifestations are still not very well described.

2.2.2.e. Diagnosis

The diagnosis of *Ehrlichia* infections in dogs is generally based on the combination of a thorough anamnesis to assess the possibility of an exposure to ticks, the assessment of clinical signs, laboratory abnormalities (CBC and biochemical profile) and serology and/or PCR.

- Morphological diagnosis: A diagnosis is confirmed if the microscopic examination of blood smears reveals morulae in lymphocytes and/or monocytes.

During the course of canine monocytic ehrlichiosis, morulae are rarely found, in contrast to infections with *A. phagocytophilum* (see section 2.2.3.). Lymphocytes and monocytes (4% in the acute phase) are infected but not granulocytes.

In order to increase diagnostic sensitivity, buffy coat smears or thin blood smears of blood or lymph node aspirates should be performed. The diagnostic sensitivity of buffy coat and lymph node cytology may increase to 60–66%.

- Serology: Antibodies may be detected by an indirect immunofluorescence test (IFAT) in the laboratory using *E. canis* antigens. Seroconversion may occur 1–4 weeks after exposure to infection, thus, dogs and cats with acute infections can be serologically negative. IFAT or ELISA results must be interpreted with caution due to cross-reactivity with different species of *Ehrlichia* and *Anaplasma*. Moreover, the antibodies for *E. canis* can present for months or years therefore seropositivity does not necessarily indicate current disease. In other cases, seropositivity can indicate exposure but not infection.

In endemic areas, positive IFAT results may be due to a previous infection and may not necessarily indicate a current acute infection. A repeat of IFAT after several weeks (3–4 weeks) is recommended for patients from endemic areas and a rising titre is indicative of a current infection. Point-of-care tests (“rapid tests”) based on immunochromatographic or ELISA methods have also been developed and many point-of-care immunoassays are now available in general practice.

- PCR: A positive PCR result generally confirms the presence of an infection. However, a negative PCR result does not exclude the presence of an infection.

2.2.2.f. Control

Treatment

The treatment of cases of canine ehrlichiosis consists of the administration of antirickettsial agents together with supportive therapy. Tetracyclines are the most commonly used compounds, with doxycycline at a dosage of 10 mg/kg bodyweight per day over 4 weeks being the most commonly used treatment scheme. Chloramphenicol has been used in dogs under one year of age, but its use is not recommended when doxycycline is available. Other antibiotics such as rifampicin have shown that, in experimental infections, they may be an alternative treatment and contributed to improving laboratory findings, but they were not effective in eliminating the infection of *E. canis* in dogs.

Prevention

The primary measure for the prevention of *Ehrlichia* infections is an effective protection against tick infestation (see ESCCAP Guideline 3: Control of Ectoparasites in Dogs and Cats).

2.2.2.g. Public health considerations

E. canis is not considered a zoonotic agent.

2.2.3. Anaplasmosis

2.2.3.a. Agents and vectors

Anaplasma spp. are vector-transmitted, Gram-negative, obligate intracellular bacteria. In Europe, *A. phagocytophilum* (formerly *Ehrlichia phagocytophila*) and *A. platys* (formerly *E. platys*) have been reported in domestic dogs and cats. They infect predominantly neutrophil and rarely eosinophil granulocytes (*A. phagocytophilum*) or platelets (*A. platys*) respectively and develop into typical microcolonies (morulae) that are observable by light microscopy. An overview of the biological features of the two important species is given in Table 12.

Table 12: *Anaplasma* spp. affecting dogs and cats in Europe

Causative agent	Disease	Hosts	Reservoir	Tick vector
<i>Anaplasma phagocytophilum</i>	Canine granulocytic anaplasmosis (CGA)	Dogs, cats, humans, horses, sheep, goats, cattle, llamas	Roe deer, red deer, small rodents, lynx ¹	<i>Ixodes ricinus</i> , (<i>I. trianguliceps</i>) ²
<i>Anaplasma platys</i>	Canine cyclic thrombocytopenia (CCT)	Dogs	Unknown	<i>Rhipicephalus sanguineus</i> ³

¹ Partial list; additional species tested positive in serology and PCR.

² *A. phagocytophilum* has been demonstrated in *I. trianguliceps* in the UK.

³ Role as a tick vector suspected but not proven.

2.2.3.b. Biology and transmission

Anaplasma phagocytophilum

Transstadial but not transovarial transmission of *A. phagocytophilum* occurs in the *Ixodes* vector. Usually, tick feeding for 24–48 hours is required for the transmission of this agent to susceptible dogs.

The incubation period in the mammalian host is 1–2 weeks. After endocytosis, *A. phagocytophilum* develops by binary fission into morulae in the phagosomes predominantly of neutrophils and rarely eosinophils. Cells infected with *A. phagocytophilum* are found in the circulating blood as well as in the tissues of the mononuclear phagocytic system, such as the spleen, liver and bone marrow.

Anaplasma platys

The natural mode of transmission has not been definitely established, but ticks and other arthropod vectors are likely to be involved. In experimental infections, the incubation period ranges from 8–15 days. Infections lead to cyclic thrombocytopenia, and the highest bacterial load is found during the initial peak. In subsequent cycles, only around 1% of the platelets are affected while thrombocytopenic episodes remain approximately the same. Over time, the severity of the thrombocytopenic response diminishes.

2.2.3.c. Distribution in Europe

The geographical distribution of infections with *A. phagocytophilum* and *A. platys* generally corresponds to the distribution of their respective (or supposed) tick vectors (Table 13). With dog travel on the increase, infections must also be expected to occur in previously non-endemic areas.

Table 13: Distribution of pathogenic *Anaplasma* spp. in Europe

Causative agent	Location	Countries with reported cases
<i>Anaplasma phagocytophilum</i>	Europe-wide	Austria ¹ , Belgium ² , Bulgaria ² , Czech Republic ² , Denmark ³ , France ² , Germany ^{1,3} , Hungary ¹ , Ireland ³ , Italy ^{1,3} , Latvia ¹ , Netherlands ² , Norway ² , Poland ¹ , Portugal ^{1,2,4} , Slovenia ¹ , Spain ^{1,3} , Sweden ^{1,3} , Switzerland ^{1,3} , UK ^{1,3}
<i>Anaplasma platys</i>	Countries with Mediterranean climate ⁵	France ¹ , Greece ¹ , Italy ¹ , Portugal ¹ , Spain ¹

¹ Reported in dogs.

² Infection demonstrated in ticks.

³ Reported in cats.

⁴ Infection demonstrated in wild rodents.

⁵ In many European countries with cold or temperate climates, cases are seen only in animals imported from areas with a Mediterranean climate.

2.2.3.d. Clinical signs

Table 14: Clinical manifestations and laboratory findings of pathogenic *Anaplasma* infections in dogs

Causative agent (disease)	Clinical signs	Laboratory findings
<i>Anaplasma phagocytophilum</i> (CGA)	Non-specific clinical signs ¹ such as sudden onset of lethargy, inappetence/anorexia and fever; surface bleeding (petechiae, melaena, epistaxis), lameness (polyarthritis), pale mucous membranes, diarrhoea, vomiting, tachypnoea, splenomegaly, enlarged lymph nodes. Rare signs are cough, uveitis, limb oedema, polydipsia/polyuria.	Most common laboratory abnormalities are thrombocytopenia, non-regenerative normocytic normochromic anaemia, lymphopenia, monocytosis, leucopenia, and leucocytosis, hyperglobulinaemia, hypoalbuminaemia, increased liver enzymes (ALP). Rare: hyperbilirubinaemia, renal azotaemia.
<i>Anaplasma platys</i> (CCT)	Fever, lethargy, anorexia, pale mucous membranes, petechiae, nasal discharge and lymphadenomegaly.	Cyclic thrombocytopenia ² , non-regenerative normocytic normochromic anaemia, hyperglobulinaemia, hypoalbuminaemia.

¹ Have been observed but are not always present.

² Cyclic bacteraemia and cyclic thrombocytopenia (< 20,000/μl) at 1–2 week intervals.

The clinical manifestations following *A. platys* infection (Table 14) may vary depending on the geographical region: in the USA it is considered to lead mainly to subclinical infections while distinct clinical syndromes have been reported in some countries of the Mediterranean basin. Concurrent infections, with *E. canis* or *Babesia* spp., have been reported which makes it difficult or almost impossible to attribute specific clinical signs to a single pathogen.

Reports of *Anaplasma* spp. infections in cats are rare. Cats with *A. phagocytophilum* infections suffer from lethargy, anorexia, fever, lymphadenopathy, anaemia and thrombocytopenia.

2.2.3.e. Diagnosis

The diagnosis of *Anaplasma* spp. infections in dogs is generally based on the combination of a thorough anamnesis to assess the possibility of a previous tick infestation, the clinical signs, haematological and clinical chemistry findings, serology and PCR results.

- Serology: Antibodies may be detected by indirect immunofluorescent assay (IFA) using *A. phagocytophilum* or *A. platys* antigens. Seroconversion may occur 1–4 weeks after exposure and, thus, dogs and cats with acute infections can be serologically negative.
- Point-of-care tests (“rapid tests”) based on immunochromatographic or ELISA methods have also been developed and commercial kits are now available for practitioners.

Additionally, in endemic areas, positive IFA results may result from a previous infection and may not necessarily be indicative of an acute infection.

Generally, two serological tests at an interval of 3–4 weeks need to be carried out to monitor if seroconversion has occurred. A positive result of a single serological test combined with clinical signs is not sufficient evidence for a diagnosis of anaplasmosis. It is important to remark that *A. phagocytophilum* might cross react with other bacteria such as *A. platys* and *Coxiella burnetii*.

- PCR: Specific assays for the detection of *A. phagocytophilum* and *A. platys* are performed by specialised laboratories. A PCR-positive result generally confirms an infection. A PCR-negative result does not exclude the possibility of an infection.
- Morphological diagnosis: A definitive diagnosis is made when morulae can be observed in neutrophil (and more rarely eosinophil) granulocytes (*A. phagocytophilum*) or platelets (*A. platys*) on microscopic examination of blood smears.

To increase the diagnostic sensitivity, buffy coat smears should be examined. Positive results should be confirmed by PCR analysis.

2.2.3.f. Control

Treatment

The treatment of anaplasmosis consists of the administration of antirickettsial agents and complementary treatment. Tetracyclines are the most commonly used compounds, with doxycycline at a dosage of 10 mg/kg bodyweight per day over 3–4 weeks being the most commonly used treatment scheme. With correct treatment, the prognosis of *A. phagocytophilum* infections is fairly good. Dogs that do not have a good clinical response within a few days of commencing doxycycline therapy should be tested for other vector-borne diseases associated with the geographical area or travel history taken.

Prevention

The primary measure for the prevention of *Anaplasma* infections is an effective protection against tick infestations (see ESCCAP Guideline 3: Control of Ectoparasites in Dogs and Cats).

2.2.3.g. Public health considerations

Infections with *A. phagocytophilum* have been reported in humans. The transmission of the agent in all cases was by ticks; direct transmission from infected dogs to humans has not been reported. Dogs may also carry infected ticks to human beings. Blood from infected dogs should be handled with caution.

2.2.4. Borreliosis (Lyme disease)

2.2.4.a. Agents and vectors

There are currently 11 known species/genotypes of the *Borrelia burgdorferi* complex (= sensu lato) which are spirochaetes that infect many mammals and birds. They are transmitted by ticks (*Ixodes ricinus*, *I. hexagonus*, and *I. persulcatus*). Human infections are of major public health importance and although infections have been demonstrated in dogs, they are not of major clinical importance. Humans, as well as dogs, acquire *Borrelia* infection when exposed to infected ticks but there is no interdependency between dogs and humans in terms of transmission. Positive serology in cats has also been reported but disease in cats, if it occurs at all, is poorly understood and there is therefore little data concerning the prevalence of infection, clinical appearance and treatment options for cats.

2.2.4.b. Biology and transmission

- Currently, ticks of the family Ixodidae and mostly of the genus *Ixodes* are recognised vectors of *B. burgdorferi* s.l.
- Larval, nymph and adult female tick vectors can acquire *Borrelia* when feeding on an infected “reservoir host”, which is an animal harbouring the pathogen as a long-term infection. It is also the case that ticks can become infected with the spirochaetes when feeding next to infected ticks (co-feeding transmission).
- Several animal species have been identified as reservoirs of *Borrelia* in Europe, including many mammals and birds.

Borrelia in ticks disseminates to the salivary glands and is transmitted transstadially but there is no transovarial transmission. The tick must be attached for at least 16–24 hours before pathogen transmission to a new host occurs. *Borrelia* remains in the skin of a host before disseminating to other tissues. In some cases, it can take up to four weeks before a systemic infection develops.

2.2.4.c. Distribution in Europe

As one would expect, endemic areas of borreliosis are related to the distribution of the tick vectors. Over the past twenty years, a number of studies have been published on the prevalence and genetic variability within the *B. burgdorferi* complex in Europe. Lyme borreliosis is present all over Europe, except in extremely hot southern or cold northern areas.

2.2.4.d. Clinical signs

Borreliosis is a well-recognised disease in humans but, as yet, is not clearly defined in dogs. Most infected dogs have subclinical status and it is difficult to correlate naturally acquired *B. burgdorferi* infection with clinical signs in dogs such as fever, lameness, myalgia and lethargy. “Lyme arthropathy” which is lameness in one or more joints has been described; puppies may be at higher risk of polyarthrititis. The term “Lyme nephropathy” has been used for a syndrome of protein losing immune complex nephropathy that occurs in 2% of seropositive dogs. However, renal invasion of this spirochaete does not appear to be responsible for the histopathological and functional changes in the kidneys of affected dogs. It is estimated that less than 5% of dogs with suspected Lyme disease actually have the disease due to *B. burgdorferi*.

Clinical manifestations in naturally-infected cats are uncommon.

2.2.4.e. Diagnosis

Direct diagnosis: Detection of *Borrelia* by culture, cytology or PCR may be difficult because some studies suggest that *B. burgdorferi* invades the soft tissues of dogs after transmission by ticks and does not appear to be present in the bloodstream or urine of infected dogs. That is why the organism is rarely found in blood, urine, joint fluid or CSF.

Serology: Antibodies against *Borrelia* usually appear 3–5 weeks after infection and can be detected using several commercially available qualitative and quantitative immunochromatographic tests. However, positive results merely indicate exposure to the infection rather than an existing disease. If dogs suspected of having Lyme disease are seropositive, it is recommended that a Western Blot immunoassay is carried out to check for specific banding patterns. Additionally, specific antibody reactions to the C6 peptide are highly sensitive and specific for detection of antibodies against *B. burgdorferi* in the blood, serum or plasma of dogs and this C6 peptide is not found in sera of vaccinated dogs. Finally, it is remarkable that the serological cross-reactivity among *Borrelia* spp. as well as *Leptospira* spp. may occur with a conventional indirect fluorescent antibody test.

2.2.4.f. Control

Treatment

Treatment studies for Lyme disease in dogs have produced variable results but a response to antibiotic therapy should be evident within 1–2 days in the case of polyarthritis. Studies in experimentally-infected dogs have shown that antibiotic treatment does not clear the infection in all dogs. The drug of choice is doxycycline, 10 mg/kg bodyweight per day orally for a minimum of one month; or a penicillin such as amoxicillin.

Prevention

Prophylactic measures to reduce infestation by infected ticks and to prevent transmission of the pathogen have been shown to reduce the risk of infection and clinical disease.

Serological positivity in healthy dogs can lead to a misdiagnosis or the unnecessary treatment of many animals which will never develop Lyme disease.

Serological screening can, however, provide seroprevalence and sentinel data which may increase owner awareness about tick infestations and control.

The use of *Borrelia* vaccines is still a controversial issue due to the presence of several *Borrelia* spp. in the field and the fact that some vaccines protect only against *Borrelia burgdorferi sensu stricto*.

Tick control is currently the method of choice for disease prevention.

2.2.4.g. Public health considerations

Dogs and cats are not reservoirs of *Borrelia burgdorferi* and thus do not present a public health concern with regard to the transmission of this disease to humans. However, ticks collected from dogs or cats may carry the pathogen and have to be carefully disposed of after removal to prevent their transmission of *Borrelia* to new hosts including humans. Dogs may serve as an appropriate sentinel for the risk of human borreliosis because it has been reported that they are approximately six times as likely to be infected with *B. burgdorferi* as humans because of more frequent environmental exposure to ticks.

2.3. Vector-borne viral diseases

2.3.1.a. Agents and vectors

Vector-borne viral diseases, transmitted either by ticks or mosquitoes, can have one of three causative agents (Table 15).

Table 15: Vector-borne viruses which can affect dogs or cats in Europe

Disease	Causative agent	Hosts	Vector
European tick-borne encephalitis (TBEV) ¹	TBEV (Flavivirus)	Dogs, humans, horses; Reservoirs: rodents, birds, red foxes, ruminants; (not in cats).	<i>Ixodes ricinus</i>
Louping-ill infection	Louping-ill virus (LIV) ² , (Flavivirus)	Natural infection mainly in sheep and red grouse; occasionally also in dogs ³ , humans, horses, pigs, cattle, goats, farm-raised deer; (not in cats).	<i>Ixodes ricinus</i> (possibly other routes of transmission)
West Nile virus infection	West Nile virus (WNV) ⁴ , (Flavivirus)	Horses, humans, dogs and cats ⁵ ; reservoir: birds	<i>Culex</i> spp. and other mosquitoes (WNV also isolated from ticks)

¹ Also known as early summer meningoencephalitis.

² Closely related to TBEV.

³ Most frequently in working sheepdogs or hunting and gun dogs.

⁴ Belongs to the Japanese encephalitis virus complex.

⁵ WNV has been associated with sporadic disease in small numbers of other species including dogs and cats during intense periods of local viral activity.

2.3.1.b. Biology and transmission

Infections are usually initiated by the bite of an infected tick or mosquito (Table 15).

TBEV: *Ixodes ricinus* larvae, nymphs and adult ticks can be infected and transstadial and occasionally transovarial transmission occurs. Due to low host specificity of *I. ricinus*, the virus can be transmitted to a wide range of vertebrates but most infections remain subclinical. Infections in humans via unpasteurised milk have been reported.

LIV transmission through *I. ricinus* infestation but also by exposure to tissues of infected animals and by aerosols, for example in slaughterhouses or laboratories has been reported. Food-borne transmission is possible via unpasteurised milk, pig meat or carcasses. Ticks become infected by feeding on animals, usually sheep or grouse, with high blood virus loads. Transstadial but usually not transovarial transmission occurs.

For WNV, wild and domestic birds act as the main hosts but there is a great diversity of potential hosts and vectors. Humans and other mammalian species (mainly horses) are dead-end hosts. Infections, which are often subclinical, are seasonal in temperate climates and peak in early autumn in the northern hemisphere.

2.3.1.c. Distribution in Europe

European TBEV may occur in areas wherever its tick vector *I. ricinus* is present. Endemic regions have been documented within many European countries. WNV appears to be ubiquitous, existing in a variety of climatic zones. Presently, in Europe, the virus seems to be restricted to Mediterranean and eastern European countries (Table 16).

Table 16: Distribution of vector-borne viral infections affecting dogs and cats in Europe

Disease	Countries with reported cases
European tick-borne encephalitis (TBE)	Austria, Czech Republic, France (eastern), Germany, Greece, Italy (northeastern), Norway, Sweden, Switzerland
Louping-ill infection	Ireland ¹ , UK
West Nile Virus infection	No clinical cases reported in dogs and cats in Europe so far. Waves of outbreaks in other species have been reported over the past two decades in various European countries. ²

¹ A virus, presumably originating from a British Louping-ill virus isolate also caused disease in livestock and humans in Norway. Closely related but distinctly different viruses have also been found in diseased sheep or goats in other European countries, such as Spain, Turkey, Greece and Bulgaria.

² Romania (humans, 1996–97), Czech Republic (humans, 1997), Italy (horses, 1998), France (horses, 1962, 2000, 2006), Portugal (horses, 2010, 2015, 2018; human, 2015), Spain (horses, 2018).

2.3.1.d. Clinical signs

Clinical manifestations of vector-borne viral diseases are diverse and those reported in pets are almost exclusively from canine clinical cases.

Table 17: Clinical manifestations of vector-borne viral infections in dogs

Disease	Clinical presentation
European tick-borne encephalitis (TBE)	Peracute lethal (3–7 days), acute (1–3 weeks), chronic subclinical ¹ (months). Rottweiler dogs seem to be over represented in reported TBEV cases. Fever, apathy, weakness, anorexia, ² ± severe encephalitis: multifocal neurological signs including myoclonic convulsions, paresis, stupor, hyperesthesia, cranial nerve deficits and reduced spinal reflexes. Dogs are accidental hosts and seem to be much more resistant to clinical disease than humans.
Louping-ill infection (LIV)	Acute viral encephalomyelitis, but may also be subclinical. ¹ Muscle tremors, spasms, ataxia, fever, asthenia, weakness, paresis. Louping-ill viruses are primarily associated with disease in sheep, cattle or people but the disease has also been reported in horses in LIV areas. Infections of domestic animals have been mainly reported in the British Isles but could also be expected in other countries with areas endemic for <i>I. ricinus</i> .
West Nile Virus infection	Clinical disease in dogs appears to be rare with only few reported cases in the USA and Africa. Fever, apathy, anorexia, progressive neurological signs including stiff gate, ataxia, paresis, tremors, altered behaviour and conscious proprioceptive deficits.

¹ Infection with flaviviruses and seroconversion in the absence of apparent disease is common.

² In dogs, there is no biphasic course as described in humans.

2.3.1.e. Diagnosis

TBE is a seasonal disease which depends on the climate-related activity of *I. ricinus*. A possible diagnosis is based on clinical evidence and on the known risk of exposure to tick bites in virus endemic regions (Table 17). A rise in specific antibody titres in samples taken 2–3 weeks apart, or specific antibodies in the CSF, may confirm a diagnosis. Cross-reactivity among different flaviviruses has been reported. In contrast to other flaviviruses, viraemia in TBE is usually very short-lived and is not present at the time of clinical presentation. In cases with rapid disease progression, diagnosis is confirmed at necropsy examination by histopathology.

- In viral CNS infections with e.g. TBEV and WNV, mononuclear pleocytosis is found in the CSF of infected dogs.
- In LIV infection, there is an increase in serum antibody titres measured by the haemagglutination inhibition test.
- Immunohistochemistry, virus isolation and RT-PCR and serology are used to detect infection with WNV.
- Flaviviruses are usually eliminated by the immune system.

2.3.1.f. Control

Treatment

Clinically-apparent TBEV infections are treated using non-steroidal anti-inflammatory drugs (NSAIDs) and broad-spectrum antibiotics if accompanied by a secondary bacterial infection; adequate supportive therapy including rehydration is recommended. Treatment with glucocorticoids is controversial.

Prevention

- Safe and effective vaccines against TBEV are available for use in humans at risk of exposure but no vaccines or vaccination schedules are available for dogs or cats. Some dogs in endemic regions have been vaccinated, but vaccine efficacy was not assessed. The main control measure is based on prevention of exposure to ticks.
- Animals that survive a LIV infection and eliminate the virus by an effective humoral immune response remain seropositive and the protection is probably lifelong.
- Avoiding mosquito bites by the use of repellents is the most important way to prevent WNV infection. Vaccines are available for horses at risk and an experimental vaccine for dogs and cats is being evaluated.

For further details about the prevention and control of ectoparasites, see ESCCAP Guideline 3: Control of Ectoparasites in Dogs and Cats.

2.3.1.g. Public health considerations

Recently, there has been an increasing awareness of TBEV-related risk to humans and dogs.

Human cases of Louping-ill are very uncommon but are occasionally seen, mainly in slaughterhouse or laboratory workers.

There is a rising concern of the potential of WNV to further spread in Europe and there is an increased risk linked to possible virus transmission by blood transfusion and organ transplantations.

APPENDIX 1 - GLOSSARY

Adulticide	Compounds that act against adult insects.
Amastigote	Non-motile parasitic forms, in the life cycle of some protozoans, that usually develop in the cells of vertebrate hosts.
Antigen	A foreign substance which induces an immune response in the body, especially by producing antibodies.
Application	Like treatment, but describing the various forms of veterinary medicinal products which can be given (applied) to animals, such as spot-ons, pour-ons, oral products, injectables etc.
Asymptomatic	Capable of carrying and transmitting disease but exhibiting no symptoms or clinical signs.
Autochthonous	Native or indigenous rather than imported.
Binary fission	Asexual reproduction by means of a cell or organism dividing into two or more new cells or organisms.
CBC	Complete blood count.
Chemoprophylaxis	Disease prevention by the use of chemicals or drugs.
Chemotherapy	Disease treatment by use of chemicals.
Control	General term comprising 'therapy' (treatment) and 'prevention' (prophylaxis).
Cutaneous	Relating to or affecting the skin.
Dendritic cells	Cells with a probing, 'tree-like' shape, responsible for the initiation of adaptive immune responses.
Ectoparasiticide	Compound developed for the animal administered use as a therapeutic agent to eliminate any existing ectoparasite infestation and prevent reinfestation.
Efficacy	This is the ability of a drug to produce the desired therapeutic effect at the recommended dosage. In the field, faecal egg reduction counts are just one example of a wide range of tests used to demonstrate efficacy.
Endemic	Prevalent in, or restricted to, a particular region.
Endosymbiont	An organism living internally in symbiosis with another.
Epidemiology	Study of the causes, distribution and control of disease.
Erythrocyte	Red blood cell.
Filarial	Relating to nematode worms now classified as Onchocercidae.
Gamont	A particular life cycle stage of protozoa. Gamonts give rise to gametes which unite in pairs to form zygotes.
Gram-negative	A staining technique for the preliminary identification of bacteria, in which a violet dye is applied, followed by a decolourising agent and then a red dye. The cell walls of certain bacteria (denoted Gram-positive) retain the first dye and appear violet, while those that lose it (denoted Gram-negative) appear red.
Gram-positive	A staining technique for the preliminary identification of bacteria, in which a violet dye is applied, followed by a decolourising agent and then a red dye. The cell walls of certain bacteria (denoted Gram-positive) retain the first dye and appear violet, while those that lose it (denoted Gram-negative) appear red.
Haemoprotozoa	Single-celled protozoan parasites which inhabit the bloodstream of their living host, whether intracellular or extracellular.
Helminth	A parasitic worm such as a roundworm (ascarid, strongyle, pinworm), tapeworm or fluke.
Host	An organism that harbours parasites.
Incubation	In parasitology, the period of time from parasite exposure to the onset of clinical signs.
Infection	Invasion and multiplication of microorganisms in body tissues.
Infective	Capable of producing infection.

Infestation	In this context, the presence of parasites in the environment, on the skin, or in the hair of a host.
Ingestion	Taking into the body by mouth.
Insect-borne	Insect-borne diseases are infections transmitted by insects.
Insecticide (insecticidal compound)	Insecticides are compounds that act against ectoparasites belonging to the class Insecta by zoological nomenclature. In this guideline, fleas, mosquitoes, sand flies and chewing and sucking lice are insects.
Integrated control	The use of several measures to control different parasites or parasite stages present in the animal and stages present in the environment.
Kinete	A particular life cycle stage produced in the midgut cells of ticks or mosquitoes. They migrate directly to the tick's salivary glands or mosquito's mouthparts where they develop into infective sporozoites.
L1 – L2 – L3 – L4 – L5 or Pre-adult	This is the normal larval development sequence of nematodes, beginning with the first larval stage (L1) which moults four times to the pre-adult stage. Generally, the development of nematodes from first stage larvae (L1) to third stage larvae (L3) occurs in the environment or in an intermediate host and the fourth stage larvae (L4), L5 or pre-adult and adult within the host.
Larvae	The active immature form of an insect, especially one that differs greatly from the adult and forms the stage between egg and pupa.
Lymphocyte	A form of small leucocyte (white blood cell) with a single round nucleus, occurring especially in the lymphatic system, but also in the bloodstream.
Macrophage	Specialised cells involved in the detection and destruction of harmful organisms within the body.
Merozoite	A protozoan cell that may become either a meront or a gamont.
Microfilaria/microfilariae	An early stage (minute or pre larva) in the life cycle of certain parasitic nematode worms. Sometimes abbreviated to "mf". Plural: microfilariae.
Monocyte	A type of leukocyte or white blood cell with a simple oval nucleus and clear, greyish cytoplasm.
Monotherapy	Therapy that uses one type of treatment to treat a certain disease or condition.
Morphology	The form and structure of organisms.
Morulae	A solid ball of cells resulting from division of a fertilised ovum, and from which a blastula is formed (singular: morula).
Nematode	Roundworms, in this context parasitic.
Neutrophil	A type of granulocyte or white blood cell which forms an essential part of the innate immune system.
Palaeartic	A zoogeographical region consisting of Europe, Africa north of the Sahara, and most of Asia north of the Himalayas.
Parasiticide	A compound developed for killing parasites.
Pathogen	An agent capable of causing disease.
Pathogenesis	The manner of development of a disease.
Pathogenic	Relating to an agent that is capable of causing disease.
Phagocyte	A type of immune cell that has the ability to engulf and devour foreign particles.
Phagocytize	When a phagocyte cell engulfs and devours a foreign material.
Phlebotome	A sand fly. In Europe, Psychodid sand flies of the genus Phlebotomus are responsible for the transmission of leishmaniosis.
Piroplasm	Vector-borne intracellular haemoprotozoan parasites.
Prepatent period	This is the time interval between infection of a definitive host with a parasite species and the first detection of eggs or larval stages in the faeces.
Prevalence	A term describing the proportion (usually given as a percentage) of infected hosts within any group of animals.

Prevention	Measures taken prior to any infection/infestation of the pet animal with endoparasites/ectoparasites, to prevent the establishment of an infection/infestation. Prevention for an extended period may be achieved by the use of a product with persistent activity for certain periods of time following treatment.
Proboscis	In insects etc it is an elongated sucking mouthpart used for feeding.
Promastigote	Motile, elongated, extracellular form in the life cycle of some protozoans.
Prophylactic	Measures taken to prevent or reduce the risk of infection.
Protozoa	Single-celled microscopic organisms.
Pruritus	Severe itching.
Repellent	A compound, which makes a host unattractive to a parasite and thus can prevent attack or establishment.
Resistance	The capacity to withstand the effects of a harmful chemical agent.
Seroconversion	The change from a seronegative to a seropositive result owing to the development of specific antibodies in the blood serum as a result of infection or immunisation.
Serology	The scientific study or diagnostic examination of blood serum, especially with regard to the response of the immune system to pathogens or introduced substances.
Seronegative	Giving a negative result in a test of blood serum.
Seropositive	Giving a positive result in a test of blood serum.
Sporozoite	The cellular infective unit that emerges during excystation of oocysts and sporocysts.
Subclinical	Relating to a disease which is not severe enough to present definite or observable symptoms or clinical signs.
Subcutaneous	Under the skin.
Symbiosis	Interaction between two different organisms living in close physical association, typically to the advantage of both.
Therapy	Any medical intervention to cure a disease; this includes the use of veterinary medicinal products (treatment), to eliminate an existing parasite infection.
Tick-borne	Tick-borne diseases are infections transmitted by ticks.
Topical	Applied to the skin surface.
Transovarial transmission	Transovarial transmission occurs in certain arthropod vectors as they transmit pathogens from female parent to offspring.
Treatment	Administration of veterinary medicinal products (medication) as deemed necessary based on any given diagnosis.
Vector	An organism, typically a biting insect or tick, that transmits a pathogen or parasite from one animal or plant to another.
Vector-borne	Vector-borne diseases are infections transmitted by infected arthropod species such as a mosquito, tick or sand fly.
Vertical transmission	When the transmission of causative agents occurs from mothers to their offspring.
Viscera	Soft internal organs of the body.
Visceral	Relating to the viscera.
Zoonosis	Any infectious disease that can be transmitted between animals (usually vertebrates) and humans.
Zoonotic	Transmissible between animals (usually vertebrates) and humans.
Zygote	A diploid cell resulting from the fusion of two haploid gametes; a fertilized ovum.

APPENDIX 2 - BACKGROUND

ESCCAP (European Scientific Counsel Companion Animal Parasites) is an independent, not-for-profit organisation that develops guidelines based on up-to-date scientific information and promotes good practice for the control and treatment of parasites in companion animals. With application of the proper advice the risk of diseases and parasitic transmission between animals and humans can be minimised. ESCCAP aspires to see a Europe where companion animal parasites no longer threaten the health and wellbeing of animals and humans.

There is a great diversity in the range of parasites and their relative importance across Europe and the ESCCAP guidelines summarise and highlight important differences which exist in different parts of Europe and, where necessary, specific control measures are recommended.

ESCCAP believes that:

- Veterinarians and pet owners must take measures to protect their pets from parasitic infections.
- Veterinarians and pet owners must take measures to protect the pet population from risks associated with travel and its consequent potential to change local parasite epidemiological situations through the export or import of non-endemic parasite species.
- Veterinarians, pet owners and physicians should work together to reduce the risks associated with zoonotic transmission of parasitic diseases.
- Veterinarians should be able to give guidance to pet owners regarding risks of parasite infection and diseases and measures which can be taken to minimise these risks.
- Veterinarians should attempt to educate pet owners about parasites to enable them to act responsibly not only for their own pet's health but for the health of other pet animals and people in their communities.
- Veterinarians should wherever appropriate undertake diagnostic tests to establish parasite infection status in order to provide the best possible advice.

To achieve these objectives, ESCCAP produces:

- Detailed guidelines for veterinary surgeons and veterinary parasitologists.
- Translations, extracts, adaptations and summarised versions of guidelines which address the varied requirements of European countries and regions.

Versions of each guideline can be found at www.esccap.org.

Disclaimer:

Every effort has been taken to ensure that the information in the guideline, which is based on the authors' experience, is accurate. However, the authors and publishers take no responsibility for any consequence arising from the misinterpretation of the information herein nor is any condition or warranty implied. ESCCAP emphasises that national, regional and local regulations must be borne in mind at all times before following ESCCAP advice. All dosages and indications are provided for guidance. However, vets should consult individual data sheets for details of locally approved treatment regimens.



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5 Control of Vector-Borne Diseases in Dogs and Cats

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