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Asymptomatic Leishmaniosis in Dogs

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Introduction

When Bayer HealthCare, Animal Health Division, called for the 1st International CVBD Symposium in 2006, this was our first step to address the global threat of parasite-borne diseases in dogs (canine vector-borne diseases, CVBD). This was based on the belief that vector-borne diseases should be treated as one topic and dealt with on a global level and in an interdisciplinary way. Nowadays with increasing international travel and emerging climate change, vector-borne diseases have become a global issue and even reached public interest. Many of the parasite-transmitted diseases affect humans as well as animals. However, the dog as man's best friend plays an important role – being affected to a high extend and serving as a host for some of the zoonotic pathogens.

Nevertheless, it was open if leading experts in natural sciences, veterinary and human medicine from Europe, North America, Australia and Asia would follow the invitation to a CVBD meeting. But they did. The participants enjoyed working together and agreed to form a group, the CVBD World Forum. Since April 2006, the group meets at least once a year on a global basis to discuss current scientific findings as well as future trends and needs concerning the distribution, pathogenesis, clinical presentation, diagnosis and prevention of canine vector-borne diseases.

Besides gathering knowledge, the CVBD World Forum strives for raising awareness for the specific regional risks of CVBD and for fostering preventative measures. This was the reason to create a website (www.cvbd.org) to provide the veterinary practitioner with cutting-edge and clinically relevant scientific information on CVBD. This work is supported by Bayer HealthCare, Animal Health Division.

In the CVBD Digest, relevant findings from the CVBD symposia are presented periodically to veterinary practitioners. The first edition starts with leishmaniosis, one of the main topics in all three symposia so far. It is one of the major zoonotic diseases, being endemic in about 70 countries of the world (see page 7 for the distribution in Europe). In many other countries, the imported disease is a concern. Since the local situation can change quite rapidly, veterinarians all over the world should be aware of canine leishmaniosis and especially the implications of asymptomatic dogs.

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Asymptomatic Leishmaniosis in Dogs

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Often more than 50 % of dogs with a proven *Leishmania* infection are asymptomatic carriers. They are usually not presented to the veterinarian but can transmit the disease and therefore help maintaining a *Leishmania* infection in an endemic area. Infected dogs without clinical signs may be translocated to previously non-endemic regions. General protection of dogs by using a repellent parasiticide against sand flies could reduce the vector-host contact in infected symptomatic and asymptomatic carriers, and therefore will help to control this canine vector-borne disease (CVBD) as well as the corresponding zoonotic disease of visceral leishmaniosis.

Canine leishmaniosis (canL) is a severe, chronic, zoonotic, vector-borne disease with an endemic distribution in the Mediterranean basin, Asia and Latin America. The main agent for viscerocutaneous leishmaniosis in dogs is the protozoan *Leishmania (donovani) infantum*, syn. *L. chagasi* in the New World that also may cause visceral leishmaniosis (VL) in humans (Fig. 1). *L. infantum* is an (obligate) heteroxenous parasite, i.e. it needs two hosts to develop.

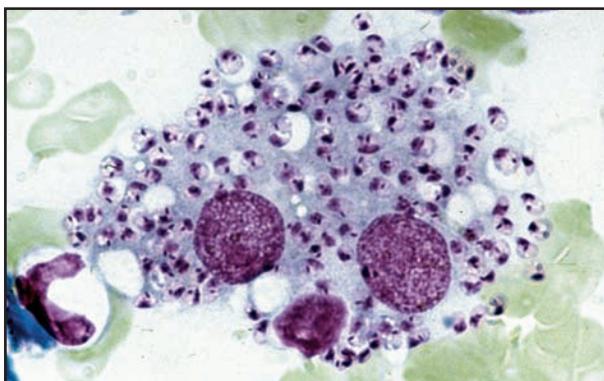


Fig. 1: Intracellular *Leishmania infantum* amastigotes within a dog's macrophage (bone marrow cytology; Giemsa-stained blood smear)
(© Photo by Roura X., Barcelona, Spain)

The insect hosts of *Leishmania* are phlebotomine sand flies of the genus *Phlebotomus* (Old World) and *Lutzomyia* (New World) (Fig. 2). Regarding the vertebrates, the principal hosts of *L. infantum* are dogs and other members of the Canidae family (foxes, jackals, wolves).



Fig. 2: Sand fly (*Phlebotomus* spp.) feeding on a human finger
(© Photo by Pospischil R., Monheim, Germany)

The prevalence of infection is highly dependent on the local environment. For the Mediterranean basin, canL is endemic and the seroprevalence of infections in dogs ranges from a few percent up to over 60 % (e.g. Mallorca, Malta) in selected populations^{1,2}.

The canine reservoir

The dog is both a natural host and a reservoir for *L. infantum*. According to CVBD World Forum member Dr. Gioia Capelli from Legnaro, Italy, this reservoir function is due to several reasons: a long pre-patent period, a high concentration of protozoan amastigotes in the skin, and a high percentage of relapses with uncertain parasitological sterilisation after treatment³. Living in close proximity to man, dogs are also the main reservoir for human VL. Other natural hosts as e.g. foxes have been implicated as additional sources for human VL, but it is unlikely that they maintain a transmission cycle independent of infectious dogs⁴.

Symptomatic and asymptomatic canL

Several surveys have shown that more than 50% of dogs with proven established infections of *L. infantum* seem apparently healthy on clinical diagnosis, that means asymptomatic^{5,6,7,8,9}. Influenced by a number of suspected factors (Tab. 1), the course of infection is mainly determined by the nature of the host's innate and adaptive immune response. On the one hand, there is the protective (self-healing or asymptomatic) phenotype, associated with the induction of Th1-regulated cell-mediated immunity. Contrary to this is the Th2-regulated humoral immune response that is associated with severe signs of the disease (Fig. 3–5).

Immune response (genetic determination; Th1 or Th2 response)

Concurrent infection and/or disease (e.g., ehrlichiosis, hepatozoonosis, demodicosis)

Immunosuppression or immunosuppressive therapy

Age (2–4 years, ≥ 7 years⁹)

Nutritional status

Repeated infections

Virulence of *Leishmania infantum* isolate

Tab. 1: Suspected influencing factors for the course of *Leishmania infantum* infection in dogs (modified after Baneth G., oral presentation on the 3rd Int. CVBD Symposium, 2008)

Thus, in endemic areas leishmaniotic dogs are usually classified into four groups: 1. asymptomatic, resistant dogs ("contacted dogs"), 2. asymptomatic dogs (preclinical), 3. oligosymptomatic dogs (with minimal signs of leishmaniosis), 4. symptomatic dogs (suffering from different forms of clinical leishmaniosis)¹⁰. Asymptomatic dogs are either progressing towards overt disease (pre-patent cases, group 2), remaining without signs for prolonged periods (even for life), or have gone through spontaneous

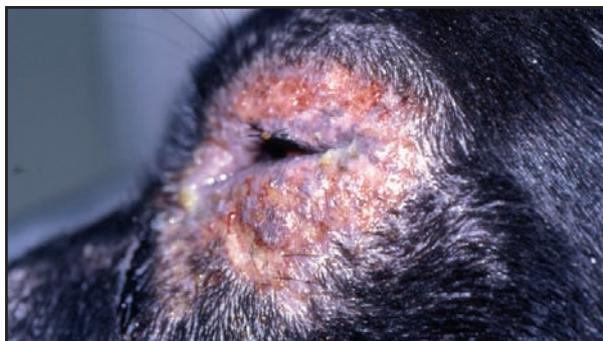


Fig. 3: Severe periocular inflammation with secondary bacterial infection
(© Photo by Miró G., Madrid, Spain)

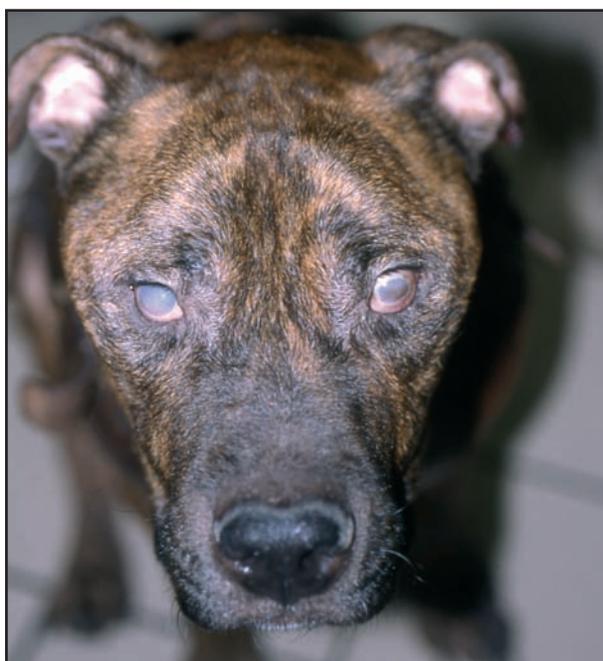


Fig. 4: Dog showing keratouveitis
(© Photo by Miró G., Madrid, Spain)



Fig. 5: Dog with ulcerative lesions around the eye
(© Photo by Miró G., Madrid, Spain)

remission – the latter two, belonging to group 1, are considered resistant (Fig. 6).

These different clinical presentations from subclinical/asymptomatic to the fully developed disease and the different and generally long periods of incubation between 2 and 12 months – with the extension to even a couple of years – cause a difficult situation for epidemiological studies. Due to massively differing sensitivities of diagnostic tests, epidemiological surveys may underestimate the prevalence of canL and the risk of parasite transmission¹¹. Numerous studies with various testing systems have been performed in order to improve the detection of asymptomatic carriers. To date, the combination of serology and highly sensitive PCR is recommended to be used for prevalence studies.

Risk of transmission

Both, asymptomatic and symptomatic dogs are able to infect sand flies. Epidemiologically, asymptomatic dogs play an extremely important part since they are considered healthy by their owners and are not examined resp. diagnosed as being infected or potentially infected. They represent a long living reservoir for *Leishmania* vectors, possibly carrying the disease into previously leishmaniosis-free areas, in case the vector is present³.

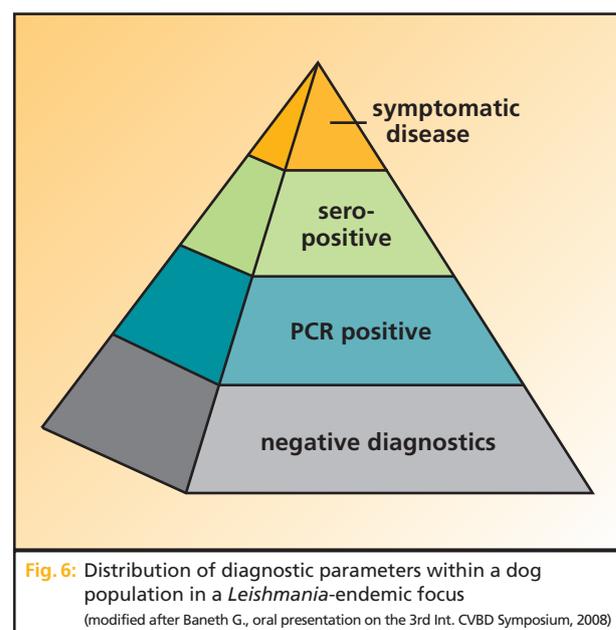
It is still questionable whether asymptomatic dogs have lower or equal capacity to infect the vector than symptomatic ones. Under experimental conditions symptomatic dogs proved to be four times more infective to sand fly vectors than oligo- or asymptomatic dogs¹². An additional risk of transmission is caused by a high percentage of relapses and an uncertain parasitological sterilisation after treatment.

Control of canL

Control of canL and consequently also of human VL is focused on the treatment of symptomatic dogs. However, complete elimination of *Leishmania*, cessation of infectivity to sand fly vectors, and prevention of relapse are not guaranteed. Consequently, control should also focus on the protection

of dogs against phlebotomines in general and therefore would affect asymptomatic dogs, as well. Protection can be achieved by avoidance of exposition and control of the vector. Apart from a vaccine, which is only registered in Brazil, in detail this implies a behaviour adapted to the circadian and seasonal activities of the vector (e.g. dogs should not be walked around sunset and sleep outside), and especially the protection of dogs using repellents. Besides the traditional shampoos and collars, repellents applied as spot-on on a monthly basis are a promising and innovative approach¹³.

In temperate climates, protection with repellents over the summer months may suffice to protect pet dogs. In tropical climates the transmission of *Leishmania* throughout the year and the involvement of often large numbers of stray dogs require a sustained repellent protection, which has to be monitored by public health authorities. In addition, the use of broad spectrum ectoparasiticides is preferred to minimize the risk for other CVBD transmitted by ticks, fleas or mosquitoes. Moreover, when travelling to endemic areas pet owners should place great importance on using repellents to prevent sand flies from feeding and consequently inhibit disease transmission.



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