EMERGENCE OF CANINE LEISHMANIOSIS IN NEW REGIONS: THE IMPORTANCE OF VERTICAL TRANSMISSION

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INTRODUCTION

- The most important and widely distributed Leishmania parasite in dogs is L. infantum, (= L. chagasi in south America). This parasite may be responsible of a very severe and often fatal disease in dogs that in general combines systemic signs to skin lesions. Although suspected long time ago, the infection of dogs due to other Leishmania species in the old world has been only recently completely validated by molecular identification (i.e. L. major, L. tropica). During the last 25 years, the knowledge on the disease and infection in dogs considerably changed. One the most important progress was to understand that most of infected dogs do not (and likely will not) exhibit a disease. Consequently the population of asymptomatic carriers exceeds by far the visible prevalence. This fact may be of high importance in non-endemic areas where incidence of clinical cases is low thus visible emergence is late as compared to presence of the parasite in the canine population.

- It is classically considered that Canine Leishmaniosis is a typical example of vectorial disease. The vector normally drives the epidemiology of a vectorial disease in endemic areas. Phlebotomine (not all but specifically adapted species) have been demonstrated to be the only group of insects regularly involved as “biological vectors” (Trypanosomids are typically primarily parasites of arthropods). Thus the distribution of enzootic areas normally overlaps the distribution of established populations of demonstrated competent species of sand flies. In Europe phlebotomine sand flies have not been found, so far, in most northern and eastern continental countries and British Islands.

- Canine leishmaniosis (CanGL = L.infantum) is endemic/encezootic in more than 70 countries, being highly prevalent in southern Europe, Africa, Asia, South and Central America. It becomes now also a concern in an increasing number of non-endemic/encezootic countries where imported infected dogs may create a veterinary and public health problem with potential consequences in the future. The other questions are the risks and the possible ways of dissemination of canine infection in such areas where known vectors are considered absent through other modalities for transmission.

1 FACTORS FOR INTRODUCTION OF LEISHMANIA IN NON-ENDEMIC AREAS

- Since last decades in Europe probably hundreds of thousands of dogs have freely travelled to endemic areas in Europe and a number of them been infected.

11 Adoption:
An important aspect is the adoption of dogs originating from endemic areas. A high proportion of these dogs is infected (detectable or not).

12 Fringe areas:
Another major question is the progressive peripheral extension of endemicity from endemic zones to contiguous areas by a “wave effect”. Several studies have shown the progressive extension of endemicity to adjacent new areas: i.e. Italy (Maroli et al 2008), France (Bourdeau et al 2014).

13 Climatic changes and Expansion of vectors
Extension of vectors has been demonstrated in the northern of Italy. Similarly the climatic changes help the sand flies to extend to higher altitudes. It is considered an evidence of an increasing risk of establishment by sand fly species, for the Atlantic Coast, inland parts of Germany, Switzerland, and Austria (Joylyon 2014). However, as the vectors are not reservoir and very slowly disseminate, their direct role is unclear. In return the progressive settlement by infected animals from the border of endemic areas could induce the infection of resident sand flies. These animals could be infected dogs but also infected wild fauna as well.
14 New vectors:
Also the question of other species of sand flies, present in non-endemic areas, that could be candidate vectors, is raised. *P. mascitii* is one of these species and its potential role is under consideration.

15 A diversified reservoir:
The concept of *reservoir* has also to be reviewed. The development of molecular techniques allowed the detection of *Leishmania DNA* in an increasing number of non-domestic asymptomatic mammals belonging to a variety of unrelated groups (rodents, carnivores ...) (Millan et al 2014). The possibility to transfer *Leishmania* to sand flies has been shown in tested species. Wild fauna could transfer progressively *Leishmania* in new areas to already present sand flies. An example is given by foxes or jackals that could play a role in the expansion. Moreover the "re"-discovery of the infection (and sometimes disease) in cats in endemic areas raises the question on the wide circulation of *Leishmania* in multiple animal species. It is now clear that, zoologically speaking, *L. infantum* is not associated to one specific host but actively develops in a multi-species reservoir. The evidence of potential role of many wild mammals as reservoirs has been illustrated by the episode of Human leishmaniasis in the Fuenlenbrada area in Madrid some years ago, involving lagomorphs and not dogs as reservoir and source.

16 Stability of foci:
Several descriptions have been made since a long time of foci of leishmaniosis in kennels in non-endemic areas. These foci may persist for years.

2 HOW *LEISHMANIA* MAY MAINTAIN IF NOT BY VECTORIAL TRANSMISSION ?
- Several descriptions have been made of autochthonous CanGL cases in non endemic areas in the absence of sand flies vectors.
Several non-vectorial ways of transmission between dogs have been observed and demonstrated. These original modalities are evident in non-endemic but also exist in endemic areas as well even if more difficult to demonstrate because masked by the dominance and pressure of vectorial transmission.

21 Direct horizontal:
Direct dog-to-dog transmission by *bite wounds* in kennel dogs has been suggested (Karmako et al 2014, Naucke et al 2016...). *Blood transfusion* is also a possible way as *Leish*-DNA has been detected in clinically healthy dogs (and human) blood donors (Ownes et al 2001, De freitas et al 2006). *Venereal horizontal* transmission from males to females has been shown. (Silva et al 2009, Baskari et al 2013, Silva et al 2014)

23 Vertical transplacental:
The vertical transfer of infection is now well accepted and such transmission is not rare and of importance in kennels or individual dogs (Roszal et al 2005, Boggiatto et al 2011, Naucke et and Lorentz 2012, Basjkari et al 2013, Ben slimane et al 2014 ± 15 other publications). Congenital transplacental transmission is the most likely the route of infection for most of autochthonous cases. It is not rare in susceptible dog breeds or lineage as shown in Foxhounds in the USA and Shar Pei in France. The Boxer breed, known since many years to be particularly susceptible to the disease, has a marked genetic predisposition (Miranda et al 2008, Quilez et al 2012). Vertical transmission in non-endemic areas was mostly described in kennels of Boxers: Finland (Karkamo et al. 2014) Germany (Naucke and Lorentz 2012), Czech republic (Svobodova et al 2017). The vertical transmission to the embryo could be very rapid, within the first weeks of pregnancy (Oliveira et al 2017) although not observed in all experiments (Latrofa et al 2016). Moreover the vertical transmission has been shown to persist for several generations, resulting in long term and stable foci with dissemination of infected dogs.

24 Other risks:
The role of transmission by various haematophagous arthropods such as fleas or ticks has been suspected long time ago but never really proven except in "artificial experimental situations" (Coutinho 2005, 2007). This hypothesis originate before the discovery of the true biological vectors (sand flies). The retrieval of *DNA of Leishmania* in ticks, fleas or any other blood-feeding arthropods (midges) does not imply that these arthropods act as vectors at a significant epidemiological level (except in confined population like kennels?). Experimental transmission to hammers by forced feeding of ticks engorged on infected dogs could support also the accidental transmission by ingestion. Iatrogenic transmission could be also a risk as it was shown the blood from infected blood donors may contain a non negligible parasitic load (indirectly measured by PCR).
CONCLUSION

Many questions on these aspects remain in non-endemic areas: exact distribution of potential vectors, number of infected dogs, role of the breed in the risk of vertical or horizontal transmission, frequency and detection of vertical transmission.

The reduction of the risk of non-vectorial transmission requires collaboration between dog owners, breed associations and veterinarians. Owners of travelling dogs should be informed and the use of adapted topical insecticides is a rule.

It could be recommended also to test (several times?) every dog before introduction into a non-endemic area. Testing dogs that travelled for a short period, before their re-introduction into a non-endemic area is of limited value because it takes several months for a test to give a positive result after exposure. Dogs confirmed to be infected should not be recommended for transfer from endemic areas into non-endemic areas. The most useful diagnostic should be firstly detection by quantitative serological techniques then, if negative, possibly molecular techniques (however PCR will detect only an undetermined proportion of infected dogs). Every infected dog should be discarded from possible reproduction. In addition, in case of risk of competent vectors in a free area, the use of insecticides in infected dogs in non-endemic areas could be strongly recommended.

References
- Kasbari M. et al. 2013. Importance of transplacental and venereal for canine leishmaniasis emergence, persistence and spreading in non endemic areas in France: Strong evidence form the field to the lab. Proceed Worleish 5 porto de Galhinhas.
- Latrofa M.S. et al. 2016. Vertical transmission of Anaplasma platys and Leishmania infantum in dogs during the first half of gestation. Parasites and Vectors;
- Menn B. et al. 2010. Imported and travelling dogs as carriers of canine vector-borne pathogens in Germany. Parasites and vectors.
- Oliveira, V. V. G. de et al. 2017: Molecular evidence of early vertical transmission of *Leishmania* (*Leishmania*) *infantum* in a dog. Ciência Rural.