The role of dogs as reservoirs of *Leishmania* parasites, with emphasis on *Leishmania (Leishmania) infantum* and *Leishmania (Viannia) braziliensis*

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Abstract

*Leishmania* parasites cause a group of diseases collectively known as leishmaniases. The primary hosts of *Leishmania* are sylvatic mammals of several orders (Rodentia, Marsupialia, Carnivora, etc.). Under certain circumstances, particularly in peridomestic and domestic transmission foci, synanthropic and domestic animals can act as source of infection for phlebotomine sand fly vectors. Dogs have long been implicated as the main domestic reservoirs of *Leishmania (Leishmania) infantum*, the aetiological agent of zoonotic visceral leishmaniasis, and there exists an increasing trend to regard dogs as the main domestic reservoirs of *Leishmania (Viannia) braziliensis*, the most widespread aetiological agent of American tegumentary leishmaniasis. However, insights derived from recent research indicate that not dogs but humans are probably the most important domestic reservoirs of *L. (V.) braziliensis*. In the present article, the role of dogs as reservoirs of *Leishmania* parasites, with emphasis on *L. (L.) infantum* and *L. (V.) braziliensis*, is reviewed.

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1. Introduction

*Leishmania* (Kinetoplastida: Trypanosomatidae) are protozoan parasites of great medical and veterinary significance (Dantas-Torres, 2006b), which are transmitted to a susceptible host by phlebotomine sand flies (Diptera: Psychodidae) of the genera *Phlebotomus* and *Lutzomyia* in the Old and New Worlds, respectively. The genus *Leishmania* is divided into two subgenera, *Leishmania* and *Viannia*, based on the pattern of development of the parasites in the sand fly gut (Lainson and Shaw, 1987). Of some 30 species of *Leishmania* known at present, ~20 are pathogenic for humans. About 30 species of phlebotomine sand flies are proven vectors (Ashford, 2000; Desjeux, 2004).

*Leishmania* parasites cause leishmaniases, a group of diseases with diverse epidemiological and clinical patterns (from self-healing skin ulcers to severe, life-threatening visceral disease). With some exceptions, the leishmaniases are zoonoses and the human infection is incidental. Natural vertebrate hosts of *Leishmania* parasites are mammals of the orders: Edentata (e.g., armadillos, sloths), Carnivora (e.g., dogs, cats), Hyracoidea (e.g., hyraxes), Rodentia (e.g., rats, gerbils), Primates (e.g., humans, monkeys), Marsupialia (e.g., opossums), and Perissodactyla (e.g., horses) (Ashford, 1996; Saliba and Oumeish, 1999; Gramiccia and Gradoni, 2005). The primary reservoir hosts of *Leishmania* are sylvatic mammals, such as forest rodents and wild canids. With the increasing process of domiciliation of the zoonotic cycle of transmission of leishmaniases, synanthropic and domestic animals have assumed an important role as reservoirs of infection.

Dogs have been found naturally infected by different species of *Leishmania*, such as *Leishmania (Leishmania) major* (Elbihari et al., 1987), although their role as reservoirs of some of these parasites is probably negligible; that is, they are more likely to be victims rather than reservoirs. In a recently published paper, Gomes et al. (2007) emphasize the utility of PCR in discriminating the species of *Leishmania* infecting dogs, particularly in areas where both visceral and cutaneous leishmaniases are endemic. Indeed, PCR-based methods have been proven to be powerful tools for the detection — in different clinical specimens — and discrimination of *Leishmania* species infecting a wide range of vertebrate (Brandão-Filho et al., 2003; Oliveira et al., 2005; Silva et al., 2005; Andrade et al., 2006) and invertebrate hosts (e.g., phlebotomine sand flies, ticks) (Coutinho et al., 2005; Parvizi et al., 2005). In the aforementioned paper, Gomes et al. (2007) released the following statement: “...domestic dogs are known to be the main visceral leishmaniasis and cutaneous leishmaniasis reservoirs”. And this is an issue of ongoing debate in the scientific literature.

As far it is known, the dog is not the main reservoir host of the aetiological agents of zoonotic cutaneous leishmaniasis (Ashford, 1996; Alvar et al., 2004; Desjeux, 2004; Gramiccia and Gradoni, 2005); except for *Leishmania (Viannia) peruviana*, the aetiological agent of uta, a typical localized ulcerative cutaneous leishmaniasis whose geographical distribution is restricted to the Peruvian Andes. For some authors (Llanos-Cuentas et al., 1999), dogs are believed to be reservoir hosts of *L. (V.) peruviana*. But even in this case, the incrimination is based on circumstantial evidence; that is, the finding of dogs naturally infected by *L. (V.) peruviana* and a relatively high dog blood index (i.e., the proportion of blood meals taken from dogs) among specimens of *Lu. peruensis*, a known vector of *L. (V.) peruviana* (Llanos-Cuentas et al., 1999). So, the status of dogs as reservoir hosts of *L. (V.) peruviana* is still uncertain (Reithinger and Davies, 1999).

In this article, the role of dogs as reservoirs of *Leishmania* parasites, with emphasis on *Leishmania (Leishmania) infantum* [syn. *Leishmania (Leishmania) chagasi*; Dantas-Torres, 2006a] and *L. (V.) braziliensis*, is reviewed in the light of epidemiological and experimental evidence as well as based on the author’s personal experience.

2. What does define a reservoir of infection?

Many researchers have tried to define what the term ‘reservoir’ — treated here as synonymous with ‘reservoir host’ and ‘reservoir of infection’ — actually means (Ashford, 1996, 2003; Haydon et al., 2002; Silva et al., 2005). On the contrary to what one might think, to define what is a reservoir is not an easy task. In a practical point of view, however, this term can be used to define a host that fulfills some attributes that favor the maintenance and dissemination of a given disease agent. Although this definition is less elaborate than some others (e.g., Ashford, 2003), it is the one used here, as it provides a practical and applicable view of the importance of reservoirs of infection for maintenance of the transmission cycle of the pathogens they carry. It is worthwhile to note that the importance of each animal host as reservoir of a given disease agent can obviously vary widely from region to region. Results from local studies cannot be extrapolated to other regions, without strong ecological evidence.
Perhaps it would be opportune to mention here that it is common to see in the scientific literature the following statement: *dogs are the main reservoirs of visceral leishmaniasis*. This should be avoided. Dogs are not reservoirs of visceral leishmaniasis; that is, they are reservoirs of the aetiological agent of visceral leishmaniasis. When taking its blood meal from an infected dog, a phlebotomine sand fly can become infected by *Leishmania* parasites (and not by leishmaniasis). In a subsequent blood meal, the phlebotomine sand fly can transmit *Leishmania* parasites to a naïve, susceptible human host. Note that the vector transmits the parasite to the human host, which can develop leishmaniasis or not, depending on several factors related to the host (e.g., age, nutritional status, genetics) and the parasite (e.g., species, strain).

3. Dogs as reservoir hosts of *L. (L.) infantum*

Not only domestic dogs, but canids in general, fulfill the required attributes to be efficient reservoirs of *L. (L.) infantum* (Alvar et al., 2004; Dantas-Torres and Brandão-Filho, 2006). Due to its close relationship with humans, the domestic dog has long been implicated as the main reservoir of *L. (L.) infantum* in China, the Mediterranean basin and the Americas (Ashford, 1996; Moreno and Alvar, 2002; Desjeux, 2004; Gramiccia and Gradoni, 2005; Lainson and Rangel, 2005; Dantas-Torres and Brandão-Filho, 2006). And there are some reasons for this:

- Although some dog breeds – e.g., Ibizian hounds (Solano-Gallego et al., 2000) – appear to be more resistant than others, dogs are often susceptible to *L. (L.) infantum* infection (Moreno and Alvar, 2002).
- In areas where zoonotic visceral leishmaniasis is endemic, the prevalence of *L. (L.) infantum* infection in dogs is often high, with a large proportion of asymptomatic ones (Dantas-Torres et al., 2006).
- Dogs may present an intense cutaneous parasitism by *Leishmania* amastigotes (intracellular forms), increasing the possibility of transmission (Ashford, 1996; Dantas-Torres and Brandão-Filho, 2006).
- Dogs are usually in or next to human houses, which favors the maintenance of the domestic transmission cycle of *L. (L.) infantum* (Dantas-Torres and Brandão-Filho, 2006).
- Dogs can remain infected by *L. (L.) infantum* without displaying apparent clinical signs of visceral leishmaniasis for years and even for their entire life (Moreno and Alvar, 2002).

- The *L. (L.) infantum* zymodeme MON-1, which is responsible for most of the cases of visceral leishmaniasis around the Mediterranean basin, is also the predominant zymodeme isolated from dogs (Pratlong et al., 2004).

It has been proven that infected dogs are sources of infection for phlebotomine sand flies of species *Lu. longipalpis* (Deane and Deane, 1955) and *P. perniciosus* (Molina et al., 1994), the main vectors of the aetiological agent of zoonotic visceral leishmaniasis in the New and Old Worlds, respectively. These phlebotomine sand flies can easily adapt to the peri-domestic environment or human dwellings and feed frequently on dogs (Colmenares et al., 1995; Killick-Kendrick, 1999; Feliciangeli, 2004; Lainson and Rangel, 2005).

There is sufficient epidemiological and experimental evidence supporting dogs as the main reservoir hosts of *L. (L.) infantum* for human infection. Therefore, it is plausible to conclude that the domestic dog plays an important role in the epidemiology of zoonotic visceral leishmaniasis. So, why cannot dog-culling programs control human visceral leishmaniasis? The definitive answer for this question is still unknown. The possible participation of other reservoir hosts, including asymptomatic infected persons (Costa et al., 2002) and cats (Maroli et al., 2007), in the transmission cycle of *L. (L.) infantum* cannot be excluded. Other possible reasons for the failure of dog-culling programs have been extensively discussed elsewhere (Reithinger and Davies, 1999; Courtenay et al., 2002; Moreira et al., 2004; Dantas-Torres, 2006b,c; Dantas-Torres and Brandão-Filho, 2006).

4. Dogs as reservoir hosts of *L. (V.) braziliensis*

There exists an increasing trend to regard dogs as the main domestic reservoirs of *L. (V.) braziliensis*, the most widespread aetiological agent of American tegumentary leishmaniasis (Falqueto et al., 1991; Reithinger and Davies, 1999; Davies et al., 2000; Reithinger et al., 2000, 2003; Padilla et al., 2002; Gomes et al., 2007). Attempts to control American tegumentary leishmaniasis by treating (Sessa et al., 1994) or culling (Costa et al., 2004) infected dogs have been proposed, although there is little evidence to demonstrate its effectiveness either in theory or in practice. There are many reports of natural infection of dogs by *L. (V.) braziliensis* (Aguilar et al., 1989; Reithinger and Davies, 1999; Madeira et al., 2003, 2006; Ryan et al., 2003; Castro et al., 2007), which is expected for the following reasons:
Dogs are susceptible to infection by *L. (V) braziliensis*, as demonstrated by experimental studies (Pimentel et al., 1988; Genaro et al., 1990).

Dogs appear to be relatively attractive for some proven or suspected vectors of *L. (V) braziliensis* (Campbell-Lendrum et al., 1999; Afonso et al., 2005).

Dogs are often present in areas where the peridomestic and domestic transmission cycles of *L. (V) braziliensis* occur, which is obviously expected because dogs are among the most popular domestic animals around the world; that is, they are almost invariably present anywhere where humans are.

Despite the relative attractiveness of dogs for some vectors of *L. (V) braziliensis*, some species such as *Lu. whitmani* appear to be significantly more attracted to humans than to dogs (Campbell-Lendrum et al., 1999). Cases of natural infection by *L. (V) braziliensis* have been reported in dogs, but also in cats, equines, rodents and opossums (Grimaldi and Tesh, 1993; Ashford, 1996; Gramiccia and Gradoni, 2005). So, are domestic dogs the main reservoirs of *L. (V) braziliensis*?

It has been experimentally demonstrated that *Lu. whitmani* can become infected by feeding on dogs infected by *L. (V) braziliensis* (Vexenat et al., 1986). However, the results of this study cannot be extrapolated, mainly because the phlebotomine sand flies were fed artificially on lesions; that is, the insects were allowed to feed directly on ulcerated lesions. In the same study, 180 females of *Lu. whitmani* were allowed to feed on non-ulcerated regions of an infected dog and none of them became infected (Vexenat et al., 1986). In a study carried out in Venezuela, Hernandez et al. (2006) found *Leishmania* promastigotes (flagellate forms) in only 0.88% (4 out of 455) of the dissected specimens of *Lu. youngi* that were allowed to feed on two dogs. It is also worthwhile to note that the xenodiagnosis was performed with wild-caught phlebotomine sand flies. As a consequence, the possibility that the phlebotomine sand flies could have been already infected (i.e., prior to feed on the dogs) cannot be excluded, even though they were collected from an area considered free of American tegumentary leishmaniasis.

The results of a study recently carried out in Colombia indicate that although dogs are susceptible to *L. (V) braziliensis*, their reservoir competence could be low. Travi et al. (2006) tested the competence of two naturally infected dogs to transmit *L. (V) braziliensis* to phlebotomine sand flies – both colonized and wild-caught – of the following species: *Lu. trapidoi*, *Lu. gomezi*, *Lu. longipalpis*, and *Lu. youngi*. Phlebotomine sand flies were allowed to feed on the lesion borders, but no infection was detected upon dissection of engorged specimens. The results of this study should also be interpreted with caution. The number of phlebotomine sand flies fed on dogs per xenodiagnosis was relatively low; that is, fewer than 50 per dog. Perhaps, this number was insufficient to detect truly infective individuals (Travi et al., 2006).

To incriminate an animal host as a reservoir of *Leishmania*, the parasites isolated from the animals must be indistinguishable from those of man. In a study carried out in Argentina, Marco et al. (2005) identified a *Leishmania* stock from a dog as *L. (V) braziliensis*. However, the zymodeme (KMS 3) found in the dog was not expressed in any of the 15 isolates from humans. Further studies, with a larger number of stocks from humans, dogs and, if possible, vectors are needed.

In areas where the human infection has been clearly acquired under certain specific situations, such as ecological tourism, road building, agricultural and military activities (Brandão-Filho et al., 1999; Ashford, 2000; Desjeux, 2001, 2004; Andrade et al., 2005; Alvar et al., 2006), the importance of dogs as reservoir hosts of *L. (V) braziliensis* is certainly negligible. In peridomestic and domestic transmission foci (Campbell-Lendrum et al., 2001; Yadon et al., 2003), dogs can probably serve only as a minor source of infection for phlebotomine sand flies. It is important to note that it is not known whether the dog is an essential piece in the peridomestic and domestic transmission of *L. (V) braziliensis* or not. Therefore, caution must be exercised to avoid mistaken conclusions on the role of dogs in the epidemiology of American tegumentary leishmaniasis.

The natural (i.e., primary) reservoir hosts of *L. (V) braziliensis* are largely unknown or unproven. As its cycle of transmission is primarily rural and often associated with human penetration of forested or wooded areas, it is suspected that sylvatic mammals may be natural reservoir hosts of *L. (V) braziliensis* (Grimaldi and Tesh, 1993; Gramiccia and Gradoni, 2005). Results of a study conducted in northeastern Brazil strongly indicate that, at least there, some small rodents are involved in the maintenance of the parasite in nature (Brandão-Filho et al., 2003).

Castro et al. (2007) have recently carried out a study in Paraná state, southern Brazil, to access the possible role of dogs as reservoirs of *L. (V) braziliensis*. Their results also suggest that dogs are not good reservoirs of this species of *Leishmania*.
5. Dogs as reservoir hosts of other Leishmania species

Cases of natural infection of dogs by L. arabica (Peters et al., 1986), L. (L.) major (Elbihari et al., 1987; Morsy et al., 1987), Leishmania (Leishmania) tropica, (Dereure et al., 1991; Guessous-Idrissi et al., 1997), L. (V.) peruviana (Llanos-Cuentas et al., 1999), and Leishmania (Leishmania) donovani (Dereure et al., 2003) have been documented. Although dogs have been found naturally infected by several species of Leishmania, their role as reservoir hosts of these parasites is probably negligible. In some instance [e.g., L. (L.) tropica in central to southwest Asia and L. (L.) donovani in northeast India], the man is the sole source of infection for the vector (Ashford, 2000). As previously mentioned (see Section 1), there is only circumstantial evidence about the role of dogs in the epidemiology of uta. Thus, the status of the dog as a reservoir host of L. (V.) peruviana is still uncertain.

6. General conclusions

The epidemiology of leishmaniasis involves a dynamic network of highly complex interactions among Leishmania parasites, phlebotomine sand fly vectors, and susceptible hosts. These, in a given moment in their life cycle, are linked by chance, by necessity, or both. For most of the species of Leishmania, humans and domestic dogs are merely accidental hosts, which are unfortunate enough to be exposed to an infected female phlebotomine sand fly. The increasing domestication of the transmission cycle of some Leishmania species has caused dramatic changes in the epidemiology of leishmaniasis, such as changes in transmission patterns due to the adaptation of these parasites to new vectors and hosts.

It is well known that the dog plays an important role in the zoonotic cycle of transmission of L. (L.) infantum. For L. (V.) braziliensis, however, the dog is most likely to be an incidental host and its role in the zoonotic cycle of transmission is probably negligible; except in peridomestic and domestic transmission foci, where not only dogs but domestic and synanthropic animals in general are likely to have a role in the epidemiology of American tegumentary leishmaniasis. Not necessarily acting as reservoirs of infection, but attracting vectors to human dwellings, for example.

For most Leishmania species, people are typical incidental hosts, but in some cases can also act as important reservoirs of infection (Ashford, 1996; Desjeux, 2004). It has been suggested that some New World leishmaniaises could become anthroponoses (Rotureau, 2006); that is, man is the sole source of infection for the vector. Insights derived from recent research strongly support this hypothesis. It is well established now that American tegumentary leishmaniasis patients may remain infected for several years, even after treatment completion and clinical cure (Schubach et al., 1998; Coutinho et al., 2002; Mendonça et al., 2004). Leishmania DNA has also been detected in blood of individuals with a positive leishmanin skin test but no past or present history of leishmaniasis (Coutinho et al., 2002). In Brazil, Ampuero et al. (2005) carried out a matched case–control study to identify risk factors for cutaneous leishmaniasis in children under 5 years of age. The most important risk factor was the presence of a family member with a history of cutaneous leishmaniasis in the year prior to the appearance of the disease in the child.

Based on the remarkable anthropophily (i.e., tendency towards human biting) of certain proven vectors of L. (V.) braziliensis (Killick-Kendrick, 1990; Campbell-Lendrum et al., 1999), the ability of American tegumentary leishmaniasis patients to remain infected for several years, and their infectivity to laboratory-reared sand flies (Rojas and Scorza, 1989; Vergel et al., 2006), one may obviously ask: are humans the main domestic reservoirs of L. (V.) braziliensis? The extensive available epidemiological and experimental data supports this hypothesis, which, however, remains to be proven. It is not known whether infected humans can solely maintain the domestic transmission cycle without the need of animals. Further studies aimed at determining whether American tegumentary leishmaniasis patients are infectious to phlebotomine sand flies, prior and after treatment, are advocated.

7. Final comment

Considering the current scenery of the leishmaniasises around the world, it seems to be clear that the control of these diseases is more complex than previously supposed. The control of reservoirs, particularly dogs, has been ethically rejected, mainly due its low impact on the incidence of leishmaniasises in humans. The leishmaniasises are intimately linked with poverty (Alvar et al., 2006). The control of the leishmaniasises is quite complex but is possible with a strong commitment from all parts involved. Future attempts to control the leishmaniasises must include measures not only to cut out the transmission cycle but also to improve housing conditions and environment sanitation as well as to ensure water and food supply among the poorest. It is
also fundamental to emphasize the importance of personal protective measures, such as the use of insecticide-treated bed nets and curtains, and to provide rapid diagnosis and treatment of the affected persons.

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