Feline Leishmaniasis: uncommon or unknown?

Leishmaniose Felina: rara ou desconhecida?

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Summary: Although feline leishmaniasis (FL) is considered to be a rare occurrence, in the past few years there has been an increase in the number of cases reported around the world. Current advances in diagnostic techniques as well as greater pet care, mainly in developed countries, have probably led to the larger number of cases reported. Nonetheless, FL is still poorly studied in terms of several aspects such as prevalence, clinical manifestations, parasite transmission to the vector, and protozoan species involved. In addition, there is little information about the real susceptibility and importance of cats in the transmission of Leishmania spp. All of these factors may contribute to the idea that FL is uncommon. Thus, the objective of the present study was to discuss the infection of domestic cats with Leishmania spp by reviewing case reports and epidemiological investigations, as well as experimental infection, and the attraction and host-feeding preference of some phlebotomines for cats.

Keywords: Leishmania, Leishmaniasis, Leishmanioses, cat, phlebotomine sand flies, epidemiology, serology, parasitology, experimental infection

Resumo: Apesar da Leishmaniose Felina (LF) ser considerada de rara ocorrência, nos últimos anos, houve um aumento no número de casos relatados em todo o mundo. Actualmente, o avanço nas técnicas de diagnóstico bem como a maior preocupação com a saúde dos animais de companhia, principalmente em países desenvolvidos, devem ter favorecido este aumento. No entanto, a LF é ainda pouco estudada em vários aspectos tais como prevalência, manifestações clínicas, transmissão do parasita ao vetor e espécies dos protozoários envolvidos. Ademais disso, há pouca informação sobre a real suscetibilidade e importância dos gatos na transmissão de Leishmania spp. Todos estes fortes factores podem levar a acreditar que a LF não seja comum. Assim, a presente revisão tem por objetivo discorrer sobre a infecção de gatos domésticos por Leishmania spp, incluindo relatos de casos clínicos e inquéritos epidemiológicos, bem como infecção experimental, e atratividade e preferência alimentar de alguns phlebotomíneos com relação aos gatos.

Palavras-chave: Leishmania, Leishmaníase, Leishmaniose, gato, flebotomíneo, epidemiologia, serologia, parasitologia, infecção experimental

Introduction

Leishmaniasis are a group of diseases of great impact on public health which are endemic in 88 countries around the world (WHO, 2004). They are caused by several species of Leishmania protozoa and transmitted to humans and animals by the bite of phlebotomine sand flies (Diptera: Psychodidae). In human beings, the clinical disease can occur in the visceral, cutaneous and mucosal forms. Several mammals are implicated as host reservoirs of the protozoa in the Leishmania spp cycle, including wild and domestic animals. Among domestic animals, dogs are involved in the domestic transmission to human beings, mainly in cases of visceral leishmaniasis by L. chagasi infection (sin. L. infantum – Mauricio et al., 1999). However, due to the marked urbanization of the leishmaniasis (Franke, 1999; Desjeux, 2002), together with the fact that canine leishmaniasis can be significantly controlled with deltamethrin collars (Killick-Kendrick et al., 1997; David et al., 2001; Davies et al., 2002; Maroli et al., 2002; Oliveira-Lima et al., 2002a; Oliveira-Lima et al., 2002b), other domestic species may become infected and sick, and may even be included in the epidemiology of the disease in endemic foci (Killick-Kendrick, 2002; Pennisi, 2002; Simões-Mattos, 2002).

In a historical context, the leishmaniasis have been extensively investigated since the beginning of 20th century. At that time, the role of some host mammals as Leishmania reservoirs was poorly known. When the first cases of feline leishmaniasis (FL) were reported, among other animal species, some researchers speculated that domestic cats (Felis catus) might play a role in the epidemiology of the leishmaniasis. Thus,
epidemiological investigations (Sergent et al., 1912; Gimeno Ondovilla, 1933; Giordano, 1933; Chagas et al., 1938) and experimental reproduction of the disease (Laveran, 1913; Nicole and Blaizot, 1912 cited by Marrechal, 1993; Giordano, 1933; Mello, 1940) were carried out in cats. However, uncertain findings led investigators to rule out this hypothesis and the studies were abandoned. Nonetheless, by the end of the 20th century, the larger number of FL cases diagnosed, mainly by molecular biology techniques, as well as the improved knowledge concerning the host/parasite/vector relationship, led some researchers to speculate again about the role of cats as Leishmania-reservoir hosts in endemic foci (Johnson et al., 1993; Pennisi, 2002; Simões-Mattos, 2002). However, the studies are still few and insufficient and this and other questions have not been elucidated. On the other hand, FL is a real fact and we speculate that it is still under-diagnosed.

Although Leishmania infection has been already detected in wild felids (Hoogstral and Dietlein, 1964; Morsy et al., 1999), the aim of this review was to consider only the infection of domestic cats (Felis catus), and to discuss the case reports and epidemiological investigations, as well as the experimental infection, the feeding preference and engorgement rate of some phlebotomine sand flies for feline species.

**Leishmania spp infection in domestic cats**

**Clinical case reports**

Clinical cases were considered to be cats who exhibited to a greater or lesser extent some signs of systemic or cutaneous manifestations of different diseases. In most of these cases, the cats’ owners sought professional care to obtain a conclusive diagnosis of the disease that affected their animals and Leishmania protozoa were demonstrated by different techniques. In this respect, up to now, it seems that 28 clinical cases of FL have been reported around the world (Figure 1). Eleven of them (39.3%) occurred in the New World, and 17 (60.7%) in the Old World. Among the cases detected in the New World, ten were diagnosed in South America.

In 1927, Salvador Mazza (Brumpt, 1949) reported in Argentina what was probably the first clinical case in the world of a cat infected with *L. braziliensis* that showed an ulcer in the orbital region. In Venezuela, Bonfante-Garro et al. (1991, 1996) isolated *L. (L.) venezuelensis* from large nose and ear nodules of four cats. Still in South America, five clinical cases were reported in Brazil. The first report mentioned a cat with cutaneous ulcerations in the ears and nose without identification of *Leishmania* species (Mello, 1940). The second one occurred in a queen infected with *Leishmania (Viannia)* sp that presented a vegetative lesion in the pelvic limb (Passos et al., 1996). Savani et al. (2002) recorded the third case of a cat with a nodular lesion in the nose whose scratches were found to be positive for *Leishmania* organisms. On the other hand, culture medium was negative for spleen and liver samples. Polymerase chain reaction (PCR) analysis of spleen material permitted to conclude that this was a *L. (L.) infantum* chagasi infection (Savani et al., 2004).

To our knowledge, still in Brazil, Schubach et al. (2004) reported the two most recent clinical cases of FL in the world. Both cats lived with two dogs and one man with cutaneous leishmaniasis. The first case, a queen, showed a cutaneous ulcer on the nose that had been present for six months and two additional small ulcers on the face. The other case, another female cat, had been showing a papule on the nose and a vegetative lesion on the nasal mucosa for the last three months. A *Leishmania* diagnosis by histopathology and culture was positive, and the protozoa were characterized by isoenzyme electrophoresis as *L. (V.) braziliensis*.

Only one North American FL case was diagnosed in the state of Texas (Craig et al., 1986). Interestingly, the animal was evaluated by Barnes et al. (1993) for seven years. This cat had several nodules on the ear with aspirations showing protozoa morphologically compatible with *L. mexicana*, and later characterized by isoenzyme analysis. After radical pinnectomy, the animal had lesion recurrence in both the pinnectomized ear and in the nose. A survey for feline leukemia virus (FeLV) and feline immunodeficiency virus (FIV) and a skin test (i.e. Montenegro test) for *Leishmania* were negative. The cat was euthanatized when it was 13 years old due to a mediastinal lymphoblastic lymphosarcoma. Histological examination of tissues did not reveal *Leishmania* dissemination to the viscera.

Of 17 FL cases reported in the Old World, three were diagnosed in Asia, two in Africa and twelve in Europe. In Asia, the first case occurred in Vietnam in a cat that showed an ulcer on the thorax (Bergeon, 1927). Later, in Iraq, culture material and smears from papules, nodules and ulcers on the nose and ears of two cats revealed organisms morphologically compatible with *L. tropica* (Machattie et al., 1931).

In Africa, at the end of the 1940 decade, microscopic examination of material collected from lip and ear ulcers confirmed a case of FL in Algeria (Bosselut, 1948). Another one occurred on Reunion Island in 1976. This cat had only swelling of lymph nodes whose aspirates showed protozoal organisms (Denuzière, 1977).

Europe has the largest number of clinical cases of FL reported in the world. The first European case occurred in Switzerland in 1977 in an animal that presented cutaneous lesions all over its body (Schwalder, 1977). Nonetheless, according to author, the infection supposedly had occurred in Spain. France has three cases recorded. The first had developed over a period of five months and was characterized by pruriginous erythema and pustules on the elbow, skull and lumbar area. Later, the cat showed weight loss and emesis when it was euthanatized. The first clinical suspicion was eosinophilic granuloma, but *Leishmania* infection was confirmed by...
microscopy (Dunan et al., 1989). In the second case, an old queen showed crusty and pruriginous dermatitis, diffuse alopecia in the ears and ulcerative periocular lesions, in addition to a nodule on the nose. FIV and FeLV surveys were negative, but serology and parasitology tests on smears and culture medium as well as the PCR applied to bone marrow were positive for *Leishmania* infection (Laruelle-Magalon and Toga, 1996). The most recent French case occurred in a cat that showed lesions throughout the body, alopecia, seborrheic-ulcer-crusty dermatitis and evident emaciation. FIV, FeLV and feline infectious peritonitis (FIP) exams showed negative results. The FL diagnosis was confirmed by histology of a cutaneous biopsy, smears from bone marrow aspirates, direct agglutination, and Western Blot. The protozoa were characterized as *L. infantum* by electrophoresis technique (Ozon et al., 1998).

Only one FL case has been reported in Portugal, involving a queen with a cutaneous nodule in the orbital area. A clinical picture of asymmetric and non-pruriginous alopecia was reported before the emergence of this lesion. Histopathological findings of the extirpated nodule confirmed *Leishmania* infection, and lesion recurrence was observed above the other eye (Costa Duarte et al., 1994).

In Spain, one case of feline visceral leishmaniasis (VL) and one case of cutaneous leishmaniasis (CL) were diagnosed by Hervás et al. (1999). The visceral form affected a queen with severe jaundice and emesis which died after hospitalization. Post-mortem examination revealed enlargement of spleen and liver. Classic histology and electron microscopy showed *Leishmania* spp forms in the liver, spleen, stomach and large intestine. The second form occurred in another queen with a history of abortions and recurrent alopecia of the abdomen and head, together with ulcerations of bone protrusions and enlargement of popliteal lymph nodes. Aspirates from these lymph nodes as well as indirect fluorescent antibody test (IFAT) were found to be positive for *Leishmania* infection. Nonetheless, FIV and FeLV showed negative results.

Italy recorded five cases of European FL. The first two cases occurred in a male cat and a female cat. The former showed a small crusty ulcer on the nose and a cystic lesion in the parietal region. Serological assays for FeLV and coronavirus were negative, in contrast to FIV and *Leishmania*. Protozoal amastigotes were seen on smears from both lesions. Seven months before the diagnosis of leishmaniasis, the adult male had presented bleeding lesions on the neck, cachexia and generalized alopecia. Later, it showed submandibular lymphadenia and diarrhea. FIV, FeLV and coronavirus tests showed negative results, but anti-*Leishmania* antibodies were positive. *Leishmania* were detected by microscopy, culture and PCR of aspirates of submandibular lymph nodes (Pennisi, 1999; Pennisi, 2002). Two more cases of FL reported by Pennisi (2002) occurred in a male cat and a female cat. The physical examination of the male cat with abscesses due to fight with other cats showed also popliteal lymphadenopathy. Survey for anti-FIV and anti-*Leishmania* antibodies, as well as PCR of blood and lymph node, showed positive results. Three years later, this cat showed a small bloody cyst on the edge of the ear, and the popliteal lymph nodes were still enlarged. *Leishmania* amastigotes were observed in smears from aspirates of the cyst and the lymph node. In addition, the isolation of the protozoa in culture medium was obtained only from the lymph node, but PCR carried out on blood, lymph node and lesion was positive. The other case occurred in a female cat who had no skin lesions but showed nonspecific signs of leishmaniasis such as anorexia, weight loss, depression, ocular complications, generalized lymphadenopathy and hepatomegaly. Positive titers were found for FIV, *Toxoplasma* and *Leishmania*. In addition, cytology and culture medium of the mate-

![Figure 1 - Worldwide distribution of feline leishmaniases reported from 1927 to 2004.](image-url)
cral isolated from lymph nodes permitted the visualization of *Leishmania* organisms. In these four FL cases, the *Leishmania* species was not identified. Finally, the fifth Italian case was of an animal with an ulcerated nodule on the eyelid as well as a history of lethargy. In addition, the cat showed weight loss, dysorexia, severe ulcerative stomatitis, lymphadenopathy, and spleen enlargement. Serological assays for FIV, FeLV and *Leishmania* were positive. Smears of material from lesions and lymph nodes raised the suspicion of *Leishmania* infection. Electron microscopy, immunohistochemistry and culture revealed the presence of *Leishmania* organisms. Finally, PCR allowed the identification of the protozoa as *L. infantum* (Poli et al., 2002).

Of all countries that presented FL cases, Vietnam and Reunion Island were the only two exceptions of endemic regions for leishmaniasis. Thus, the feline leishmaniasis reported in these two countries were probably not autochthonous.

In summary, of 28 clinical cases of FL, 92.8% exhibited cutaneous manifestations which were the only sign in 57.7% of them. On the other hand, a 17.4% rate of lymphadenopathy and a 4.3% rate of visceromegaly were cited in association with the cutaneous manifestations. In addition, very few cases presented lymphadenopathy (7.7%) and visceromegaly (3.8%) as the single disease manifestation. Interestingly, cutaneous manifestations were observed in most cases of infection with the viscerotropic *Leishmania* strain.

Concerning to the type of cutaneous lesions, nodules and ulcers were predominant (Figure 2). These lesion types reported in FL cases are similar to those occurring in human and canine leishmaniasis. In addition, the head, and the nose in particular, was the most affected area in the body (Figure 3). This affected region seems to be coherent with the ability of phlebotomines to bite areas with little hair.

Several diagnostic techniques, alone or in combination, have been applied for *Leishmania* spp surveys in clinical FL cases. The presence of amastigotes, by cytology and/or histology, was assayed in 82% of all clinical cases, with 95.6% of positivity. On the other hand, culture medium was cited in 71.43% of cases, with 95.6% of positivity. The infrequent use of culture medium may with successful promastigote isolation in 85% of the cases reported. Smears of material from lesions and lymph nodes raised the suspicion of *Leishmania* infection. Electron microscopy, immunohistochemistry and culture revealed the presence of *Leishmania* organisms. Finally, PCR allowed the identification of the protozoa as *L. infantum* (Poli et al., 2002).

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Since the FL report by Barnes et al. (1993), isoenzymes, electrophoresis, indirect radioimmune assay (RIA) and PCR have been performed to identify *Leishmania* organisms. Thus, in 15 of 28 clinical cases for which molecular biology techniques were used for *Leishmania* identification, it was possible to obtain species classification in 11 (73.3%), subgenus classification in one (6.7%), and genus classification in three (20%) cases. These techniques allowed to diagnose in the New World one cat infected with *L. chagasi*, four with *L. venezuelensis*, one with *L. mexicana*, two with *L. braziliensis* and another with the subgenus *Viannia*. In the Old World, three cats were classified as being infected with *L. infantum* and three with *Leishmania* sp. The remaining FL cases were diagnosed by conventional methods, and the classification attributed to *Leishmania* species may be due to epidemiological findings and geographical localization.

**Parasitological and serological epidemic investigations**

Parasitological and serological investigations have been conducted after the emergence of some clinical cases of FL, or even in endemic regions for leishmaniasis. Thus, to our knowledge, since 1912, twenty-four epidemiological investigations were carried out in the Old World and the New World, and *Leishmania* parasites and specific-*Leishmania* antibody surveys were conducted using several techniques (Tables 1 and 2).

Of all epidemiological investigations, those carried out by Pennisi et al. (1998 and 2000) are particularly important not only because of the techniques employed, but also because of the nature of the findings. In these studies it was possible to establish a correlation between PCR and IFAT, as well as between *Leishmania* and FIV co-infection. Although there was no significant difference between the two diagnostic methods, FIV infection had a significant positive influence on anti-*Leishmania* antibodies.

In all epidemiological studies, none of the animals that harbored *Leishmania* parasites showed any sign or symptom suggestive of leishmaniasis. Similarly, among cats with positive serology only two (0.95%) were sick. The parasite rates (5.5%) and the serological (16.6%) surveys lead us to ask which role these infected cats may play in the transmission of disease in endemic areas. Since they were infected but showed no sign or symptom of leishmaniasis, they may represent the condition of a healthy carrier, or of a healed case. To test this assumption, in a study involving experimental infection of cats with *L. braziliensis*, we observed that anti-*Leishmania* antibody titers appeared later than lesions, showing that serology was not a good marker of clinical disease (Simões-Mattos et al., in press).
Experimental infection of domestic cats with *Leishmania* spp

In an attempt to explain the occurrence of natural cases of FL, some investigators have evaluated the susceptibility of cats experimentally infected with *Leishmania* spp. Different routes and undetermined amount of inoculum were used in the first studies. Hepatic pulp from a dog with VL (Laveran, 1913), a culture of *L. infantum* (Nicolle and Blaizot, 1912 cited by Marechal, 1993), material from the spleen of a child with VL (Giordano, 1933), material from ulcers of cat with natural FL (Mello, 1940), and a visceral emulsion from a dog with VL (Deane, 1958) were inoculated in cats without successful reproduction of the disease.

In 1984, Kirkpatrick et al. established an infection protocol with *L. donovani* and *L. chagasi* for cats. *Leishmania* organisms were detected at different times in blood, liver, spleen and bone marrow up to the 16th week post-infection (w.p.i.). In Brazil, Barbosa-Santos et al. (1988) inoculated 10⁶ *L. braziliensis* promastigotes on the nose of cats, half of which had been previously injected intraperitoneally with 10³ antigens of the same *Leishmania* species. Without apparent lesion in either group, a new challenge with 10⁶ *L. amazonensis* promastigotes was performed at the same site of infection. *Leishmania* isolation in culture medium was obtained from the lesions of animals that had not been injected with *L. braziliensis* antigens by the intraperitoneal route. On the other hand, dissemination and visceralization were not observed. Nonetheless, the protocol used by Anjili and Githure (1993) with 10⁶ promastigotes of *L. donovani* did not lead to the detection of parasites over a period of six months.

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**Table 1** - Epidemiological investigation of domestic cats by parasitological methods in different countries from 1912 to 2000.

<table>
<thead>
<tr>
<th>Country</th>
<th>Technique/source</th>
<th>Positive/examined (%)</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Algeria</td>
<td>Undefined/bone marrow</td>
<td>1/1 (100)</td>
<td>Sergent et al. (1912)</td>
</tr>
<tr>
<td>Brazil</td>
<td>Cytology/liver</td>
<td>1/202 (0.5)</td>
<td>Chagas et al. (1938)</td>
</tr>
<tr>
<td></td>
<td>Cytology/liver</td>
<td>0/142 (0.0)</td>
<td>Deane (1956)</td>
</tr>
<tr>
<td></td>
<td>Cytology/liver</td>
<td>0/214 (0.0)</td>
<td>Alencar et al. (1955)</td>
</tr>
<tr>
<td></td>
<td>Cytology*/ear</td>
<td>1/53 (1.9)</td>
<td>Sherlock (1996)</td>
</tr>
<tr>
<td>Italy</td>
<td>Cytology and histology/spleen, liver and bone marrow</td>
<td>0/120 (0.0)</td>
<td>Giordano (1933)</td>
</tr>
<tr>
<td></td>
<td>PCR*/blood</td>
<td>54/89 (60.6)</td>
<td>Pennisi et al. (2000)</td>
</tr>
<tr>
<td>Jordan</td>
<td>Cytology/spleen and liver</td>
<td>16/78 (20.5)</td>
<td>Morsy et al. (1980)</td>
</tr>
<tr>
<td>Spain</td>
<td>Undefined/undefined</td>
<td>1/495 (0.2)</td>
<td>Gimeno Ondovilla (1933)</td>
</tr>
<tr>
<td>Total</td>
<td></td>
<td>74/1394 (5.3)</td>
<td></td>
</tr>
</tbody>
</table>

* associated with IFAT.

**Table 2** - Epidemiological investigation of domestic cats by serological methods in different countries from 1982 to 2002.

<table>
<thead>
<tr>
<th>Country</th>
<th>Technique</th>
<th>Positive/examined (%)</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Brazil</td>
<td>IFAT</td>
<td>0/53 (0.0)</td>
<td>Sherlock (1996)</td>
</tr>
<tr>
<td></td>
<td>ELISA</td>
<td>9/84 (10.7)</td>
<td>Simões-Mattos et al. (2001a)</td>
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<tr>
<td></td>
<td>ELISA</td>
<td>43/106 (40.5)</td>
<td>Simões-Mattos (2002)</td>
</tr>
<tr>
<td></td>
<td>IFAT</td>
<td>45/89 (50.5)</td>
<td>Oliveira (2002)</td>
</tr>
<tr>
<td>Egypt</td>
<td>IHA</td>
<td>3/80 (3.7)</td>
<td>Michael et al. (1982)</td>
</tr>
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<td></td>
<td>IHA</td>
<td>1/28 (3.6)</td>
<td>Morsy et al. (1988)</td>
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<tr>
<td></td>
<td>IHA</td>
<td>2/60 (3.3)</td>
<td>Morsy and Aboul el Seoud (1994)</td>
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<td>France</td>
<td>IFAT</td>
<td>1/174 (0.6)</td>
<td>Bez (1992)</td>
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<td></td>
<td>WB</td>
<td>14/110 (12.7)</td>
<td>Marechal (1993)</td>
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<td></td>
<td>WB</td>
<td>12/97 (12.4)</td>
<td>Oxn (1999)</td>
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<td>Italy</td>
<td>IFAT</td>
<td>55/93 (59.1)</td>
<td>Pennisi et al. (1998)</td>
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<td></td>
<td>IFAT</td>
<td>1/110 (0.9)</td>
<td>Poli et al. (2002)</td>
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<tr>
<td>Spain</td>
<td>DAT</td>
<td>21/50 (42.0)</td>
<td>Ramos et al. (2002)</td>
</tr>
<tr>
<td></td>
<td>ELISA</td>
<td>2*117 (1.7)</td>
<td>Portús et al. (2002)</td>
</tr>
<tr>
<td>USA</td>
<td>DAT</td>
<td>1/10 (10.0)</td>
<td>Mac Vean cited by Kirkpatrick et al. (1984)</td>
</tr>
<tr>
<td>Total</td>
<td></td>
<td>210/1261 (16.6)</td>
<td></td>
</tr>
</tbody>
</table>

IHA = indirect hemagglutination assay; DAT= direct agglutination test; IFAT= indirect fluorescent antibody test; WB=western blot; ELISA=enzyme-linked immunosorbent assay. * Low antibody titers.

**Figure 2** - Frequency of lesion type in case reports of feline leishmaniasis from 1927 to 2004. *Dry or humid, pruriginous or non-pruriginous, cluster, alopecic, erythematous and/or pustular.

**Experimental infection of domestic cats with *Leishmania* spp**

In an attempt to explain the occurrence of natural cases of FL, some investigators have evaluated the susceptibility of cats experimentally infected with *Leishmania* spp. Different routes and undetermined amount of inoculum were used in the first studies. Hepatic pulp from a dog with VL (Laveran, 1913), a culture of *L. infantum* (Nicolle and Blaizot, 1912 cited by Marechal, 1993), material from the spleen of a child with VL (Giordano, 1933), material from ulcers of cat with natural FL (Mello, 1940), and a visceral emulsion from a dog with VL (Deane, 1958) were inoculated in cats without successful reproduction of the disease.

In 1984, Kirkpatrick et al. established an infection protocol with *L. donovani* and *L. chagasi* for cats. *Leishmania* organisms were detected at different times in blood, liver, spleen and bone marrow up to the 16th week post-infection (w.p.i.). In Brazil, Barbosa-Santos et al. (1988) inoculated 10⁶ *L. braziliensis* promastigotes on the nose of cats, half of which had been previously injected intraperitoneally with 10⁴ antigens of the same *Leishmania* species. Without apparent lesion in either group, a new challenge with 10⁶ *L. amazonensis* promastigotes was performed at the same site of infection. *Leishmania* isolation in culture medium was obtained from the lesions of animals that had not been injected with *L. braziliensis* antigens by the intraperitoneal route. On the other hand, dissemination and visceralization were not observed. Nonetheless, the protocol used by Anjili and Githure (1993) with 10⁶ promastigotes of *L. donovani* did not lead to the detection of parasites over a period of six months.
As previously mentioned, we carried out an experimental infection with 10⁷ promastigotes of *L. braziliensis* simultaneously inoculated on the ear and nose of cats and followed up the animals for two years and three months. The animals showed lesions similar to those observed in human beings with cutaneous leishmaniasis, which fully regressed by about 32 and 40 weeks post-infection in the ear and nose, respectively (Simões-Mattos et al., 2001b). Concerning the immune response, antibody titers formation occurred later than lesion formation, and even after self-healing some cats still remained serologically positive at the end of the study. Thus, we concluded that domestic cats were partially susceptible to experimental infection with *L. braziliensis*, showing chronic clinical manifestations, anti-*Leishmania* antibody titers, lesions harboring parasites, and spontaneous healing of the lesions (Simões-Mattos et al., in press).

**Attractiveness/host feeding preference and engorgement rate of phlebotomine sand flies**

In view of the occurrence of FL, cats seem to be attractive for some phlebotomines species. However, there are still few experimental studies on the attractiveness or host feeding preference and engorgement rate of different phlebotomines in which cats were included.

In Brazil, Deane (1956) studied the attractiveness of several animal species for *Lutzomyia longipalpis*, the vector of *L. chagasi*-agent of VL, and observed that the cat was the only mammalian species not used by phlebotomines as a blood meal source. Nonetheless, the author commented that he had seen a sandfly feeding on a cat inside the house. On the other hand, in Kenya, *Phlebotomus guggisbergi* was much more attracted by cats than by dogs (Johnson et al., 1993).

Supporting Deane’s findings (1956), more recently Dias et al. (2003) also evaluated the cat among other domestic and wild animals as blood meal sources for same phlebotomine. In the cited study, the use of the precipitin test applied to the gut of *L. longipalpis* also led to the conclusion that this sand fly had not fed on cats. In Egypt, El Sawaf et al. (1989) studied by immunoelectrophoresis blood meals from *P. papatasii* and *P. langeroni* collected indoors and outdoors. Both phlebotomines fed predominantly more on humans than on dogs, cats or rats. On the other hand, similar studies were carried out in Peru using bloodmeal analysis by precipitin in *L. verrucarum* and *L. peruvensis* sandflies (Ogosuku et al., 1994). The findings of this study are quite interesting, mainly regarding the mixed bloods detected in these sandflies both when collected indoors and outdoors, which showed that they had fed on at least two different hosts. In indoor collections, the most common multiple feeding involved human and cat blood detected in *L. verrucarum*. Although for the sandflies collected outdoors cows and cats were the most frequent sources of the same phlebotomine, cat blood was the most frequent for *L. peruvensis* (Ogosuku et al., 1994). Colmenares et al. (1995) tested host-feeding patterns of *P. perniciosus* by the competitive ELISA biotin/avidin method at four sites in Spain. At least in Barcelona, the blood meals of these phlebotomines were found to originate from dogs (33%), humans (25%), cats (25%) and mice (17%).

Some studies have determined the rate of engorgement of female sandflies after contact only with cats. In the Mediterranean, Sánchez et al. (2000) exposed one cat to the bite of *P. perniciosus*, and observed a 93% rate of engorged females of these sandflies. In a similar study using *L. migonei*, one of the main vectors of *L. braziliensis* protozoa in Brazil, we detected a 90% rate of engorged female sandflies after contact with a cat in a cage (unpublished data).

**Final considerations**

Even though FL is considered to be a rare occurrence, cases have been reported in America, Europe, Asia and Africa, and more frequently since the 90’s. This may be due in part to the boom of this disease in the past few years, to the advances of diagnostic techniques, to the increased breeding of cats, mainly in developed countries, and/or partly to the greater health care devoted to pets. However, in spite of the increased numbers of FL cases, we believe that they are still under-diagnosed possibly because of the difficulties in clinically distinguishing leishmaniasis from other diseases that affect cats. In addition, veterinarians may be unaware that cats can be infected with *Leishmania* spp and can develop leishmaniasis. Furthermore, cats are
less frequent visitors than dogs to veterinary clinics, at least in developing countries where leishmaniases are common. Also, the clinical manifestations of FL are still unclear, so that the disease may be easily confused with neoplasms and mainly with infectious diseases caused by viruses, bacteria, protozoa and fungi. Fungal infections are the most dangerous, mainly in cases of histoplasmosis, sporotrichosis and cryptococcosis. It is important to keep in mind that when a clinical diagnosis of fungal infection rather than of Leishmania infection is made, treatment with antifungal drugs may result in temporary healing, since these drugs have some effect against Leishmania spp. All of these factors contribute to the lack of FL diagnoses, falsely leading to the belief that FL is uncommon. Thus, laboratory techniques may help prevent misdiagnosis, mainly in endemic areas for leishmaniases.

In summary, it is clear that domestic cats are truly infected with several Leishmania species, that they may or may not become ill, that they harbor the protozoa and that they are also attractive as a blood meal source to some phlebotomines. Thus, from an epidemiological point of view, it is important to elucidate several questions. Are the cats occasionally infected or are they reservoir hosts of these protozoa? Are they frequently healthy carriers of Leishmania spp and potential transmitters of protozoa to the vectors? Does FIV and/or FeLV co-infection promote FL? The answers to these questions will permit us to understand the consequences of this disease for feline health and to determine the risk factors of human populations exposed to cats infected with Leishmania spp.

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