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Sand Fly Vectors of Leishmania in the Americas - A Mini Review

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Abstract

Phlebotominae sand flies are natural hosts of various microorganisms including etiological agents of diseases of medical and veterinary importance such as viruses, bacteria and protozoa. Parasites of the genus *Leishmania* is widely spread around the world and are pathogenic to man, wild and domestic animals with a variety of species and, in most cases, a specific vectors. In the Neotropical region nearly 530 species of sand flies are known and this current review updates the information on the vectors of leishmaniases in the Americas.

Introduction

Sand flies (Diptera: Psychodidae: Phlebotominae) are natural hosts of various microorganisms including etiological agents of diseases of medical and veterinary importance such as viruses, bacteria and protozoa. Four genera of trypanosomatid protozoa are found parasitizing this group of insect: *Endotrypanum*, *Trypanosoma*, *Sauroleishmania* and *Leishmania*. Only the latter genus is pathogenic for man who has sand flies as vectors, a fact that gives these insects great importance for the transmission of leishmaniases in various regions of the world including Americas [1,2]. Several countries in the New World have occasional to high incidence of skin and visceral leishmaniasis. The main risk factors for contracting this disease are increase human exposure to sand fly in sylvatic areas or intense urbanization of new areas with environmental changes of ecosystems and adaptation of sand flies to new environments [3-5].

Phlebotomine sand flies are a group of insects with a long evolutionary history that probably has appeared in the Lower Cretaceous [6,7]. This well-defined group is likely to have a monophyletic origin with adaptation to diverse environments and today they are found in temperate regions but most species presents tropical and subtropical distribution [8,9].

Adults, males and females, are recognized by their small size, hairy body, the wings held erect on the body when resting, and a bouncy flight. Females are blood feeders and, in general, tend to bite at night or in twilight, but also can sting during the day in forested areas.

Today, there are slightly 1.000 described species of sand flies in the world and near 530 species are found in the Neotropical region. Among these a little more than 20 species are considered proven vectors of leishmaniases in the New World. This relatively small number of vectors is in function of a number of physiological and biochemical factors inherent to both insects and parasites, these factors influence the survival of the parasites in the digestive tract of the insect, its multiplication and transformations that result in the development of infective forms, influencing the transmission to the vertebrate host [9-11].

The development of different species of *Leishmania* in the sand fly species possible varies on the location of the infection in the digestive tract of the insect, which allows dividing them into three different groups. This physiological characteristic of *Leishmania* served as the basis for the current classification of the genus *Leishmania* into two subgenera: *Leishmania* and *Viannia* and separating the genus *Sauroleishmania* which was subsequently confirmed to be a valid genus by biochemical and molecular studies. The latter genus includes species of lizards and parasites not pathogenic to humans but sand flies are their natural vectors. *Endotrypanum* is a blood parasite of sloth in South and Central America and natural infection of sand flies can often lead to a mistaken diagnosis for *Leishmania* [11,12].

The search of natural infection of sand flies by *Leishmania* is made by dissection of females and observing the flagellated forms in the digestive tract of the insect. Although laborious, this technique allows establishing the rate of infection, observing the activity, the development and location of flagellates in the insect, which aids the identification of the parasite to the subgenus level, and allows the isolation of the flagellate for further confirmation and comparison with human or non-human isolates [13,14].

In recent years, molecular techniques based on PCR have been applied in the detection of *Leishmania* in sand flies transmission in different regions [15,16]. Due to its high sensitivity, a high number of sand flies with "natural" infection has been observed, but in reality, in most cases, these findings do not meet the basic criteria to be determinant as vectors since the presence of DNA only indicates that the insect was fed on infected source with parasite DNA, without, however, indicate that there was adhesion or multiplication of the *Leishmania* in the digestive tract of the insect. Thus, the abdominal status of the female sand fly is a useful biological character for vector incrimination investigation and in an mature infected sand fly blood meal is fully digested [10,16].

Discussion

Visceral leishmaniasis

***Leishmania (Leishmania) infantum*:** Today there is no doubt that *Leishmania infantum*, responsible for visceral leishmaniasis (VL), was introduced to the South and Central America by infected dogs as companions of the new settlers from Portugal and Mediterranean region [17]. Visceral leishmaniasis is now an endemic disease in different regions of the continent and the primary vector is *Lutzomyia*

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longipalpis [5,18]. This sand fly has a geographic distribution from southern Mexico (20°N) to Uruguay (32°S). More recently *Lu. cruzi* a sibling species of the *Lu longipalpis* complex, has been incriminated as main vector in the western region of Brazil and possible some areas of Bolivia [19,20]. Another sand fly, *Pintomyia (Pifanomyia) evansi* is also the vector in certain regions of Venezuela and the Caribbean coast of Colombia [21]. The dispersion and presence of a domestic reservoir, such the dog, and the constant ecological change in natural habitats of sand flies may be responsible for the presence of new vectors of *L. infantum* in different regions of the Americas [22].

Cutaneous leishmaniasis

It´s well known that cutaneous leishmaniasis (CL) in the New World is an autochthonous disease caused by different species of Leishmania Ross, 1903. Under an epidemiological point of view CL is a zoonotic disease where sylvatic animals play an important role in the maintenance of the cycle. However in some specific situation, due to human modification of the environment and the constant presence of sinanthropic and domestic animals, CL becomes a zoo anthroponotic disease. Up to this moment, at least, twelve species of Leishmania are responsible for cutaneous leishmaniasis in the Americas, three belonging to the subgenus Leishmania, nine to the subgenus Viannia. Due to the variety of Leishmania species involved and a wide geographical distribution there are also a variable number of vectors and in some cases one species of Leishmania may have more than one vector (Table 1).

***Leishmania (Leishmania) mexicana*:** Also known as "ulcera de los chicleros" with a limited distribution in the southern United States, Mexico and Central American countries where Bichromomyia olmeca olmeca is a proven vector. Although this sand fly bites man frequently, it shows some preference for wild rodents. For this reason the characteristics the disease is typically a zoonosis and infection is commonly contracted in forests [23]. Another sand fly of importance is Lutzomyia (Tricholateralis) cruciata (Coquillett) which may be of epidemiological significance due to its anthropophilic behavior in the endemic regions of CL, but the role as vector still requires confirmation[1,24].

***Leishmania (Viannia) panamensis*:** This parasite is responsible for cutaneous leishmaniasis in northern South America and Central America showing a relatively wide geographical distribution being isolated in South America (Ecuador, Venezuela and Colombia) and Central America (Panama, Costa Rica and Nicaragua). Its transmission usually occurs in primary and secondary forests in those countries where several different sand fly species act as vectors such *Nyssomyia trapidoi* in Colombia, Panama and Costa Rica, *Nyssomyia ylephiletor* in Costa Rica and Panama, *Lutzomyia (Tricholateralis) gomezi* (Nitzulescu) in Panama and *Psychodopygus panamensis* Shannon, 1926 in Panama [25].

***Leishmania (V.) braziliensis*:** The exact geographical distribution of *L. braziliensis* sensu lato is still uncertain although the parasite has already been identified from Central America to Argentina. The parasite is responsible for the cutaneous form that can evolve to form muco-cutaneous leishmaniasis. In Brazil the parasite has been identified in virtually all states, with several sand fly species implicated in the transmission. The two major vectors are *Nyssomyia intermedia* and *Ny. whitmani* with a wide distribution in peri-urban and urban areas of the Northeast, Southeast, South and Central Brazil [15,22]. In some areas of Minas Gerais, São Paulo and southern Brazil, *Ny. intermedia* is sympatric with the sister species *Ny. neivai*. This later species is more common in some regions of southern Brazil and Argentina [22,26]. With respect to *Ny. whitmani* is possible that it is a species complex and its importance as a vector of *Leishmania* spp have to be re-evaluated in various regions of Brazil. There are strong indications that this is a sylvatic species, where primary forests would be their natural breeding sites. However, observations in several regions of Brazil indicate a tendency to inhabit secondary forest or areas already altered by man. Its importance as a vector of *Leishmania braziliensis* in the Northeast and Southeast and possibly other regions of Brazil [22,27] is irrefutable and maybe also an important vector in Argentina and Paraguay. Another possible vector of *L. braziliensis* is *Migonemyia (Migonemyia) migonei* a sand fly with a wide distribution throughout most of South America and well adaptated to most environments modified by man. It has been considered a suspected vector in Brazil and also in Venezuela where natural *Leishmania* infection had been frequently found [15].

In the North and Northeast of Brazil, *Psychodopygus wellcomei* Fraiha, Lainson and Shaw is an important vector of this parasite. This sand fly that has a preference for forested areas is highly anthropophilic and bites humans during the day and at night. Another sand fly of the same group is *Psychodopygus complexus* that is also considered vector *L. braziliensis* in some Amazonian areas [1,28].

***Leishmania (Leishmania) venezuelensis*:** To date, this parasite was identified in only a few isolated cases of cutaneous leishmaniasis

Leishmania spp.	Geographic distribution	Clinical Forms	Vectors
L.(Leishmania) infantum	South and Central America	Visceral	*Lu.longipalpis, Lu.cruzi,* *Lu.evansi*
L.(Viannia) braziliensis	South and Central America	CL/MUCL	*Ny. intermedia, Ny. neivai, Ny. whitmani, Mi. migonei, Psy. wellcomei,* *Psy. complexus*
L. (V.) guyanensis	North of Brazil, French Guiana & Suriname	CL/MUCL	*Ny. umbratilis*
L. (V.) panamensis	North of South and Central America	CL	*Ny. trapidoi, Ny. ylephiletor, Lu. gomezi, Psy. Panamensis*
L. (V.) peruviana	Peru	CL	*Lu. peruensis, Lu. verrucarum*
L. (V.) lainsoni	North of Brazil, Bolívia and Peru	CL	*Tr. ubiquitalis, Lu. nuneztovari , Tr. velascoi*
L. (V.) naiffi	North of Brazil and French Guiana	CL	*Psy. Ayrozai*
L. (V.) shawi	North of Brazil	CL	*Ny. whitmani*
L (V.) colombiensis	Colombia and Panamá	CL	*Lu. hartmanni, Lu. gomezi, Psy. panamensis*
L. (V.) lindenbergi	North of Brazil	CL	*Nyssomyia antunesi*
L.(L.) amazonensis	South and Central America	CL/DCL	*Bi. flaviscutellata, Pi. nuneztovari*
L. (L.) mexicana	South of USA, México and Central America	CL/DCL	*Bi. olmeca olmeca*
L.(L.) venezuelensis	Venezuela	CL	*Bi. olmeca bicolor*

Table 1: Vectors of *Leishmania* spp. responsible for human leishmaniases in the Americas. CL: Cutaneous Leishmaniasis; MUC: Mucous-cutanoeus Leishmaniasis; DCL: Diffuse Leishmaniasis.

in humans and domestic animals in Venezuela, and the possible vector is still unknown. There are strong indications that the *Bichromomyia olmeca bicolor* is the vector in Venezuela. This species has a fairly wide distribution in northern South America, including Brazil, Panama and Costa Rica showing a marked attraction to rodents but occasionally bites humans [1,9].

***Leishmania (L.) amazonensis*:** This parasite has a wide distribution in several countries in South and Central America and their life cycle is typically a zoonotic disease among wild rodents. Until 1975 human cases of cutaneous leishmaniasis associated with this species was restricted to the Amazon Basin, where the vector *Bichromomyia flaviscutellata* a fly with zoophilic habits, was considered the vector and the disease were restricted to the forest environment. Eventually, new cases of cutaneous leishamaniasis outside the Amazon confirmed that this parasite was not restricting to this region. Although uncommon in catches with light traps, its role as a vector of *Leishmania amazonensis* is undisputed in Brazil [1,22,29] and other countries of South America. *Pintomyia (Pifanomyia) nuneztovari* has been found naturally infected by *L. amazonensis* and is suspect of transmitting in the Sub Andean region of Bolivia [1,30].

***Leishmania (Viannia) guyanensis*:** This is quite common *Leishmania* infecting man in northern Brazil, mainly north of the Amazon River. It is also common in French Guiana and Suriname. The main vector of this species is *Nyssomyia umbratilis* that bites man with certain aggressiveness. In human cases of CL caused by this parasite is common a large number of skin lesions due to the large quantities of sand flies which bite man when disturbed by incursion into the forest. The attack of the females of *Ny. umbratilis* may occur during the day in the "shadow" of the forest hence giving the name of the species. Ny *umbratilis* is also vector of parasites of sloths *Endotrypanum* which often complicates the diagnosis of *Leishmania* [12].

***Leishmania (Viannia) peruviana*:** This parasite is responsible for "uta" a form of cutaneous leishmaniasis with single lesion that usually heals spontaneously. The parasite has been isolated from human cases and dogs mainly on the western slopes of the Peruvian Andes at 1300 meters above sea level. In this area *Lutzomyia (Helcocyrtomyia) peruensis* and *Lutzomyia verrucarum* are the suspect vectors. Both species can be found in intra or peridomicile but primarily in animal shelters and *Lu. verrucarum* is reasonably more anthropophilic than *Lu. peruensis*.

***Leishmania (Viannia) lainsoni*:** Until recently this species had only been isolated in the state of Pará where the rodent (*Agouti paca*) is the wild reservoir with occasional infection of man. The parasite has already been registered in Peru and Bolivia. In Pará and probably other area of the Amazon region *Trichophoromyia ubiquitalis* is the main vector, but his poor anthropophily certainly determines the existence of few human cases. Two other species may be responsible for transmission of *L. lainsoni* in the sub-Andean region of Bolivia: *Pintomyia (Pifanomyia) nuneztovari* and *Trichophoromyia velascoi* [30,31]. Recently, *Trichophoromyia auraensis* (Mangabeira,1942) has also found infected by *L. lainsoni* in Madre de Dios region of Peru [32] however, further studies are needed to determine actually the main vector in both regions of Bolivia and Peru.

***Leishmania (Viannia) naiffi*:** Rare cases of cutaneous leishmaniasis by this parasite have been recorded in the Brazilian Amazon region (Amazonas and Pará) and also in Guyana, but its distribution is likely to be broader. This species infects the armadillo (*Dasypus novemcintus*) with a few known human cases and a possible vector *Psychodopygus ayrozai* and two other species, *Psy. squamiventris* and *Pys. paraensis* that are quite anthropophilic, may be involved in the transmission of the parasite in the Amazon region [28].

***Leishmania (Viannia) shawi*:** This parasite occurs in the Amazon region which is responsible for skin infection in man and a variety of wild animals. The only sand fly so far incriminated as vector is *Nyssomyia whitmani* than in primary forests of the region is zoophilic and rarely bites humans.

***Leishmania (Viannia) colombiensis*:** This *Leishmania*, although uncommon, have been isolated from human cases in Colombia and Panama. The vectors are *Lutzomyia (Helcocyrtomyia) hartm*anni in Colombia, *Lutzomyia (Tricholateralis) gomezi* and *Psychodopygus panamensis* in Panama.

***Leishmania (Viannia) lindenbergi*:** This was isolated and described after an outbreak of cutaneous leishmaniasis among training soldiers in a secondary forest on the outskirts of Belem, Pará, Brazil. Although not know with certainty the vector, *Nyssomyia antunesi* is the primary suspect of transmitting parasite among the soldiers. This species is quite anthropophagic and with a wide distribution in the Amazon region.

Concluding Remarks

Despite the large number of researchers dedicated to the study of the complex problem of leishmaniases in the Americas a great deal is still to be studied with respect to this protozoan, particularly regarding the vector species. There are necessary studies on the biology of most of Neotropical sand flies, and laboratory studies that may prove their status as natural and primary vectors. Additionally satisfactory prophylactic measures in a disease transmitted by vectors implicated in vector control, or other strategies that will minimize contact of the parasite with humans and their livestock, thereby preventing transmission. The lack of resources for immunization of the population and their livestock in the prevention of leishmaniases give more importance to the study of species incriminated as vectors. Thus apart from ecological studies of the sand fly species, the observation on the biology of laboratory colonies could bring information that may clarify the role of different vector species. This can also, provide the studies of experimental infection and transmission, which may define, without doubt, when a suspect sand fly is a real vector.

With regard to research for natural infection, dissection of sand flies, although laborious, is still the only way to detect an active infection and allowing the observation of parasite development in the insect, and the isolation of the strain for comparisons and studies.

References

1. Young DG, Duncan MA (1994) Guide to the identification and geographic distribution of Lutzomyia sand flies in Mexico, West Indies, Central and South America. MemAmerEntSoc 54: 881.
2. Alvar J, Vélez ID, Bern C, Herrero M, Desjeux P, et al. (2012) Leishmaniasis worldwide and global estimates of its incidence. PLoS One 7: e35671.
3. Brandão-Filho SP, de Carvalho FG, de Brito ME, Almeida Fde A, Nascimento LA (1994) American cutaneous leishmaniasis in Pernambuco, Brazil: eco-epidemiological aspects in 'Zona da Mata' region. Mem Inst Oswaldo Cruz 89: 445-449.
4. Brazil RP (2013) The dispersion of Lutzomyia longipalpis in urban areas. Rev Soc Bras Med Trop 46: 263-264.
5. Grimaldi G Jr, Tesh RB, McMahon-Pratt D (1989) A review of the geographic distribution and epidemiology of leishmaniasis in the New World. Am J Trop Med Hyg 41: 687-725.
6. Azar D, Nel A (2003) Fossil psychodoid flies and their relation to parasitic diseases. Mem Inst Oswaldo Cruz 98 Suppl 1: 35-37.

7. Filho JD, Brazil RP (2003) Relationships of new world phlebotomine sand flies (Diptera: Psychodidae) based on fossil evidence. Mem Inst Oswaldo Cruz 98 Suppl 1: 145-149.

8. Aransay AM, Scoulica E, Tselentis Y, Ready PD (2000) Phylogenetic relationships of phlebotomine sandflies inferred from small subunit nuclear ribosomal DNA. Insect Mol Biol 9: 157-168.

9. Galati EAB (2003) Classificação de Phlebotominae. In Rangel E, Lainson R eds, Flebotomíneos do Brasil. Rio de Janeiro: Fiocruz, 23-175.

10. Bates PA, Rogers ME (2004) New insights into the developmental biology and transmission mechanisms of Leishmania. Curr Mol Med 4: 601-609.

11. Killick-Kendrick R (1990) The life-cycle of Leishmania in the sandfly with special reference to the form infective to the vertebrate host. Ann Parasitol Hum Comp 65 Suppl 1: 37-42.

12. Shaw JJ (1992) Endotrypanum, a unique intraerythrocytic flagellate of New World tree sloths, An evolutionary link or an evolutionary backwater?Ciência e Cultura. Rio de janeiro 44: 107-116.

13. Lainson R, Shaw JJ (1987) Evolution, classification and geographical distribution. Peters W, Killick-Kendrick R. The Leishmaniases in Biology and Medicine: Volume I Biology and Epidemiology, London: Academic Press Inc, 1-120.

14. Killick-Kendrick R (1990) The life-cycle of Leishmania in the sandfly with special reference to the form infective to the vertebrate host. Ann Parasitol Hum Comp 65 Suppl 1: 37-42.

15. Pita-Pereira D, Alves CR, Souza MB, Brazil RP, Bertho A, et al. (2005) Identification of naturally infected Lutzomyia intermedia and Lutzomyia migonei with Leishmania (Viannia) braziliensis in Rio de Janeiro Brazil revealed by a PCR multiplex non-isotopic hybridization assay. Trans R Soc Trop Med Hyg 99: 905-913.

16. Bakhshi H, Oshaghi MA, Abai MR, Rassi Y, Akhavan AA, et al. (2013) Molecular detection of Leishmania infection in sand flies in border line of Iran-Turkmenistan: restricted and permissive vectors. Exp Parasitol 135: 382-387.

17. Kuhls K, Alam MZ, Cupolillo E, Ferreira GE, Mauricio IL, et al. (2011) Comparative microsatellite typing of new world leishmania infantum reveals low heterogeneity among populations and its recent old world origin. PLoS Negl Trop Dis 5: e1155.

18. Deane LM, Grimaldi G (1985) Leishmaniasis in Brazil. In: Chang KP, Bray RS (eds.) Leishmaniasis, Elsevier, New York, pp. 247-275.

19. Brazil RP, Passos WL, Brazil BG, Temelj kovitch M (2010) Diptera, Psychodidae,Phlebotominae Rondani,1840:Range extension and new records from low land Bolivia. Check List: 567-588.

20. dos Santos SO, Arias J, Ribeiro AA, de Paiva Hoffmann M, de Freitas RA, et al. (1998) Incrimination of Lutzomyia cruzi as a vector of American visceral leishmaniasis. Med Vet Entomol 12: 315-317.

21. Travi BL, Vélez ID, Brutus L, Segura I, Jaramillo C, et al. (1990) Lutzomyia evansi, an alternate vector of Leishmania chagasi in a Colombian focus of visceral leishmaniasis. Trans R Soc Trop Med Hyg 84: 676-677.

22. Rangel EF, Lainson R (2009) Proven and putative vectors of American cutaneous leishmaniasis in Brazil: aspects of their biology and vectorial competence. Mem Inst Oswaldo Cruz 104: 937-954.

23. Biagi F (1972) Problems in the taxonomy of New World Leishmania species. Trans R Soc Trop Med Hyg 66: 943-944.

24. Pech-May A, Escobedo-Ortegón FJ, Berzunza-Cruz M, Rebollar-Téllez EA (2010) Incrimination of four sandfly species previously unrecognized as vectors of Leishmania parasites in Mexico. Med Vet Entomol 24: 150-161.

25. Christensen HA, Herrer A, Telford SR (1965) Leishmania braziliensis from Lutzomyia panamensis in Panama. J Parasitol 55: 1090-1091.

26. Córdoba-Lanús E, De Grosso ML, Piñero JE, Valladares B, Salomón OD (2006) Natural infection of Lutzomyia neivai with Leishmania spp. in northwestern Argentina. Acta Trop 98: 1-5.

27. Ready PD, Day JC, Souza AA, Rangel EF, Davies CR (1997) Mitochondrial DNA characterization of populations of Lutzomyia (Nysomyia) whitmani (Antunes & Coutinho,1939) sl. (Diptera: Psychodidae: Phlebotominae) in Brazil. Mem Inst Oswaldo Cruz 91: 43-50

28. Lainson R (2010) The neotropical Leishmania species: a brief historical review of their discovery, ecology and taxonomy. Rev Pan-Amaz Saude 1: 13-38.

29. Dorval ME, Alves TP, Cristaldo G, Rocha HC, Alves MA, et al. (2010) Sand fly captures with Disney traps in area of occurrence of Leishmania (Leishmania) amazonensis in the state of Mato Grosso do Sul, mid-western Brazil. Rev Soc Bras Med Trop 43: 491-495.

30. Martinez E, Le Pont F, Torrez M, Telleria J, Vargas F, et al. (1999) Lutzomyia nuneztovari anglesi (Le pont & Desjeux, 1984) as a vector of Leishmania amazonensis in a sub-Andean leishmaniasis focus of Bolivia. Am J Trop Med Hyg 61: 846-849.

31. Corrêa JR, Brazil RP, Soares MJ (2005) Leishmania (Viannia) lainsoni (Kinetoplastida: Trypanosomatidae), a divergent Leishmania of the Viannia subgenus--a mini review. Mem Inst Oswaldo Cruz 100: 587-592.

32. Valdivia HO, De Los Santos MB, Fernandez R, Baldeviano GC, Zorrilla VO, (2012) Natural Leishmania Infection of Lutzomyia auraensis in Madre de Dios, Peru, Detected by a Fluorescence Resonance Energy Transfer-Based Real-Time Polymerase Chain Reaction. Am J Trop Med Hyg : 87: 511-517