doi: 10.5123/S2176-62232010000200002

The Neotropical *Leishmania* species: a brief historical review of their discovery, ecology and taxonomy

Espécies neotropicais de *Leishmania*: uma breve revisão histórica sobre sua descoberta, ecologia e taxonomia

Especies neotropicales de *Leishmania*: una breve revisión histórica sobre su descubrimiento, ecología y taxonomía

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ABSTRACT

This paper is a review of the major historical events leading to our present classification of the Neotropical *Leishmania* species, and apart from indicating the basic type of disease these different parasites may cause in humans, it does not discuss the clinical or epidemiological features of the leishmaniases. For each of these species, information is given on the known geographical distribution, recorded phlebotomine sand fly host(s) and the secondary, wild or domestic mammalian hosts. Reasons are given for regarding the parasite referred to as *Leishmania* (*L.*) *infantum chagasi*, the causative agent of American visceral leishmaniasis, as most probably indigenous to the Neotropics rather than imported during the Iberian colonisation.

Keywords: *Leishmania*; Neotropics; Ecology; Taxonomy.

INTRODUCTION

American cutaneous leishmaniasis (ACL) would appear to be an ancient disease afflicting humans in the tropical and sub-tropical areas of the New World, as suggested by early ceramics from Peru and Ecuador (*huacos*), which often depict human faces with ugly disfigurations very similar to those caused by mucocutaneous leishmaniasis. In addition, historians at the time of the Iberian colonisation often mentioned the frequency of indigenous inhabitants with cutaneous lesions. As long ago as 1571, Pedro Pizarro[83] described the destruction of the nose and lips of coca growers working on the lower eastern slopes of the Andes; because mucocutaneous leishmaniasis is now well known to be endemic in this area, it is highly likely that he was giving an early description of this disease.

It slowly became apparent that the skin lesions referred to by the Peruvian Indians as *uta* and the mucocutaneous disease known as *espundia* were both widespread throughout most of the Latin American continent, where they were given various names. For the less destructive skin lesions: *uta seco*, *úlcera de Velez*, *ulcer de los chicleros*, *buba*, *úlcera de Baurú*, *ferida brava*, *botão do oriente*, forest yaws, Bay-sore, *pian-bois* and bosch-yaws. For the highly destructive mucocutaneous leishmaniasis: *espundia*, *llaga corrosiva*, *cancro espúndico*, *nariz de tapir*, *tiacaraña*, *gangosa*, *ferida esponjosa*, and *cancro fagendênico*. The aetiology of these lesions, however, long remained unknown.

American visceral leishmaniasis (AVL) may have an equally ancient history in Latin America, but would clearly offer less visual evidence of its existence. However, the condition known in Brazil as *barriga d'água* (an abnormally distended abdomen), which is associated with fever and general malaise, was well known, and many such cases in the past were likely to have been undiagnosed AVL.

The following key chronological events in the history of ACL and AVL in the Neotropics, and in particular Brazil, will perhaps help to more readily see how the present classification of their causal agents took shape.

EARLY BEGINNINGS

For many years, Peruvian *uta* and similar skin lesions in other countries of Latin America were considered to be identical with "oriental sore" in Mediterranean and Asian countries, the aetiology of which was, at that time, also in doubt.

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1909-1911

The causative agent of Old World oriental sore was discovered in 1903[115] and named *Leishmania tropica* in 1906[62]. Similar skin lesions in the Neotropics were not associated with a leishmanial parasite until 1909, when Lindenberg[60] and Carini and Paranhos[6] independently demonstrated "Leishman-Donovan bodies" (amastigotes) in the skin lesions of individuals with "Baurú ulcer" from the State of São Paulo, Brazil. Curiously, Lindenberg (Figure 1) first published his discovery in a newspaper, *O Estado de São Paulo*, on 30th March 1909, and Carini and Paranhos recorded their findings the next day – in the same newspaper! Finally, in 1911, Splendore[105] demonstrated the presence of the parasite in mucocutaneous lesions of espundia.

Photograph donated by the late Professor C.S. Lacaz. Reproduced, with permission, from Lainson R. New World Leishmaniasis. In: Cox FEG, editor. The Wellcome Trust Illustrated History of Tropical Diseases. London: Wellcome Trust; 1996. p. 218-29.

Figure 1 – Adolpho Lindenberg (1872-1944): The first person to show that various skin lesions of humans in Latin America were due to species of *Leishmania*

At first it was thought that the causative parasite should be referred to as *Leishmania tropica* (Wright, 1903) Lühe, 1906, but the Brazilian clinician and parasitologist Gaspar Vianna[111] (Figure 2) studied amastigotes in the skin lesion of a patient in Além Paraíba, Minas Gerais State, Brazil, and concluded (erroneously, as it was later shown) that their morphology differed from that of *L. tropica* amastigotes. He therefore named the parasite *Leishmania brazilienses*, later amended to *L. braziliensis* by Matta[69], in 1916.

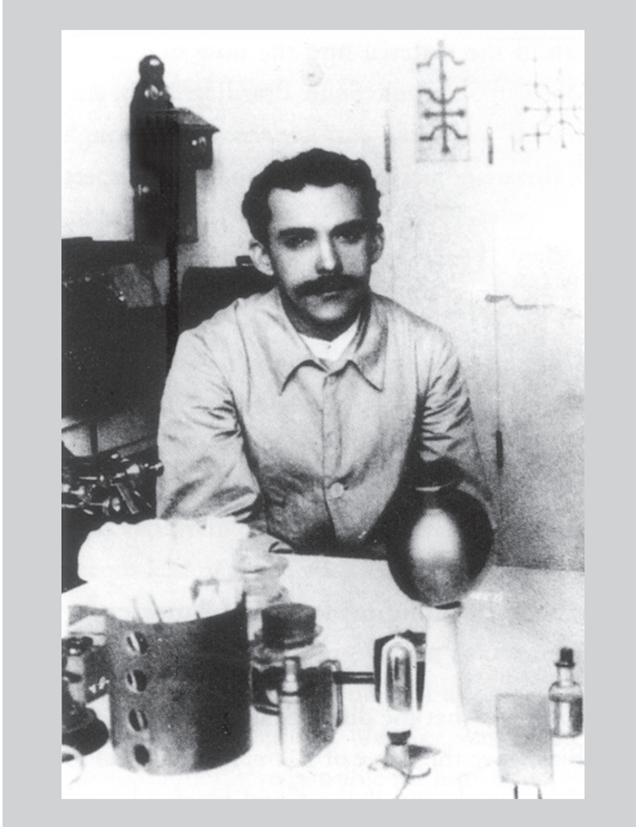

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Figure 2 – Gaspar Vianna (1885-1914): the Brazilian clinician and scientist who described *Leishmania* (*V.*) *braziliensis* and introduced the use of tartar emetic for the treatment of leishmaniasis

1913

For several years, there was a general opinion that all American cutaneous and mucocutaneous leishmaniasis was due to the single parasite, *L. braziliensis*. Nevertheless, Velez[110] decided, if only for patriotic reasons, that the parasite causing Peruvian uta was neither *L. tropica* nor *L. braziliensis* and thus named it *Leishmania peruviana*.

The first report of AVL in the Americas was probably that of Migone[74] in 1913, who saw what he considered to be amastigotes in the blood of a patient in Paraguay. The man's symptoms were highly indicative of AVL, and after failing to respond to treatment for malaria, he died. Before his illness, he had worked on the construction of the notorious São Paulo-Corumbá railway in Brazil, where it was thought he probably acquired his infection.

1934-1937

Although sporadic cases of AVL had begun to appear in a number of other South and Central American countries, some time elapsed before definitive proof of the existence of the disease was obtained in Brazil. In 1934, however, 41 cases were diagnosed following the examination of liver tissue removed by viscerotome[80] (Figure 3). Three of these were from the State of Pará and represented the first record of Amazonian AVL.

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Figure 3 – Henrique Penna (second from the left), who revealed the extent of visceral leishmaniasis in Brazil following the examination of viscerotome liver samples

Both *L. donovani* and *L. infantum*, the causative agents of Old World visceral leishmaniasis, were known to readily infect laboratory animals. Therefore, in 1937, when Cunha and Chagas[12] were, for some reason, unable to infect similar hosts with the parasite from Brazilian cases of AVL, it prompted them to name the parasite *Leishmania chagasi*.

1945-1948

A notable event in Brazil was the discovery by Medina[71] of an enigmatic parasite causing lesions in the skin of the domestic guinea pig (*Cavia porcellus*) in 1946; this parasite was later named *Leishmania enriettii* Muniz & Medina, 1948. This discovery was a clear indication that dermotropic species of *Leishmania* other than *L. braziliensis* might be infecting humans in Brazil. Until the 1960s, it was still thought that all cases of human ACL in this country were due to *L. braziliensis*. This general opinion persisted despite the fact that the causative agent of the disease in the confluent forest of neighbouring French Guyana had been named *L. guyanensis* Floch, 1954.

In 1946, Convit and Lapenta[9] described a strange form of cutaneous leishmaniasis in some patients in Venezuela that was characterised by a large number of nodular lesions scattered over the body and containing enormous numbers of large amastigotes. The patients showed a negative Montenegro skin test and did not respond to the usual antimonial drug treatment. The condition was referred to as diffuse cutaneous leishmaniasis (DCL) and the causative agent in Venezuela was later named *Leishmania pifanoi*[73].

1953-1961

In 1957, researchers in Panama[107,106] demonstrated the presence of a *Leishmania* species in the forest rodent *Proechimys semispinosus*, and other infections were recorded in forest rodents in the State of São Paulo, Brazil by Forattini[20] in 1960. In neither case, however, was it conclusively shown that the organism was identical to the parasite commonly infecting humans in the same locality.

By now it was becoming clear that different dermotropic leishmanial parasites were probably responsible for cutaneous leishmaniasis in different parts of the Neotropics. That causing "chiclero's ulcer" in the Yucatan, Guatemala and Belize was named *Leishmania tropica mexicana* by Biagi[3], in 1953, and in French Guyana, Floch[19] adopted this same trinomial nomenclature by referring to the cause of "pian-bois" as *L. tropica guyanensis* in 1954. Similarly, in other parts of South America, he regarded cutaneous leishmaniasis as being due to *L. tropica braziliensis*. However, in 1959, Medina and Romero[73], together with several other researchers, rightly disapproved of the specific name "tropica" for these parasites and instead gave the name *Leishmania braziliensis pifanoi* to the parasite associated with DCL in Venezuela. The Brazilian parasitologist Pessôa[81] followed suit in 1961 by listing the known *Leishmania* species in the Americas as *L. braziliensis braziliensis*, *L. b. guyanensis*, *L. b. peruviana*, *L. b. pifanoi*, and *L. b. mexicana*.

1962-1965

In 1962, Garnham[23] raised the parasite causing chiclero's ulcer in Belize, Central America, to specific rank as *Leishmania mexicana*. Additionally, in 1962 and 1964, during studies on the epidemiology of this disease, Lainson and Strangways-Dixon[56,57] established that forest rodents were reservoir hosts of the parasite and frequently showed visible lesions, rich in amastigotes, on their tails. A volunteer was successfully infected with the rodent parasite, and a biological and biochemical comparison of the organism with that from cases of ACL showed them to be identical. This represented the first conclusive association of a Neotropical leishmanial parasite known to infect man with a sylvatic reservoir in wild animals.

It was natural to suspect that a similar rodent reservoir of *L. braziliensis* probably existed in the forests of Brazil. Thus, during a visit to the Instituto Evandro Chagas (IEC) in 1963, the present author discussed the possibility of a collaborative programme on the eco-epidemiology of ACL in the Amazon Region with the late Director, Dr. Orlando Costa, and the late Dr. Otis Causey, at that time head of the IEC's arbovirus programme.

Causey was impressed by the similarity of the tail lesions caused by *L. mexicana* to similar lesions on the tails of rodents he had noted among animals captured in the Utinga forest in Belém, Brazil. He had, however, thought they were due to bacterial infections of damaged tails, and he promised to examine them more carefully in the future. A few weeks later, he presented the author with a Giemsa-stained smear from a lesion on the tail of a specimen of *Oryzomys capito*, a common forest rodent in his capture area, and it was rich in leishmanial amastigotes. This unexpectedly rapid discovery prompted a discussion with the Wellcome Trust in

London, who agreed to the establishment of the Wellcome Parasitology Unit (WPU) in the Department of Parasitology of the IEC for a provisional period of three years, with the promise of further support should the results of the research warrant it. The IEC/WPU programme lasted until 1992.

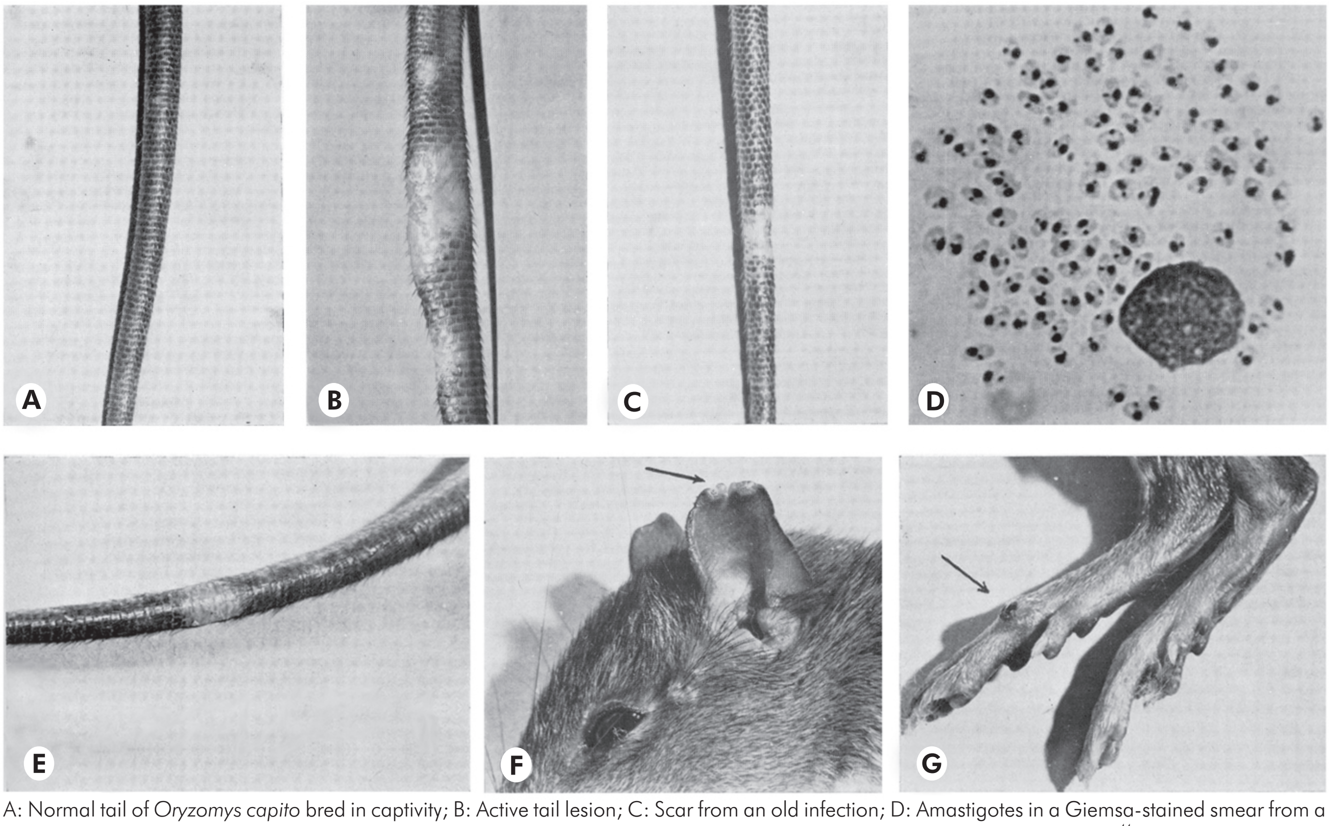
1965-1967

Although the parasite of *Oryzomys* was at first assumed to be *L. braziliensis* by Nery-Guimarães and Costa[77] in 1964, this conclusion was not supported by the WPU's comparison of the rodent parasite with that from cases of human cutaneous and mucocutaneous leishmaniasis. First, the amastigotes of the rodent parasite were clearly much larger than those of *L. braziliensis* and, when inoculated into the skin of laboratory hamsters and mice, rapidly produced huge tumour-like lesions packed with amastigotes. In contrast, *L. braziliensis* produced a small nodule that often required several months to become visible and only contained a small number of relatively tiny amastigotes. In addition, the rodent parasite – by now found to infect a variety of forest rodents (Figure 4) and marsupials – grew luxuriantly in a very simple blood-agar culture medium (NNN), whereas *L. braziliensis* struggled to survive in the same medium, with successful isolates often dying out after several sub-cultures. In 1969 and 1970, Lainson and Shaw[49,45] referred to these differences as the behaviour of "fast and slow strains" of *Leishmania*.

The continued examination of *Leishmania* isolates from patients coming to the IEC soon showed that a small number of the parasites were the same as those from *Oryzomys* and other rodents. Importantly, this identification indicated that the parasite was a causal agent of the condition known as DCL or, more correctly, anergic diffuse cutaneous leishmaniasis (ADCL), a very disfiguring infection produced in immunologically incompetent individuals that resists the usual treatment by anti-leishmanial drugs. Because the parasite's biological features closely resembled those of *L. mexicana* of Central America, it was given the name *L. mexicana amazonensis* Lainson and Shaw, 1972.

1968

This year saw the first incrimination of the fox *Cerdocyon thous* as an important reservoir host of the parasite responsible for Amazonian canine and human visceral leishmaniasis, variously referred to as *L. chagasi* or *L. donovani*. Three infected foxes[52,54] were found near Utinga, on the outskirts of Belém, and ten infected animals, a surprisingly high number, were later found among 25 examined (40%) on the island of Marajó, Pará[54]. None of these infected animals showed outward signs of disease.



A: Normal tail of *Oryzomys capito* bred in captivity; B: Active tail lesion; C: Scar from an old infection; D: Amastigotes in a Giemsa-stained smear from a tail lesion; E-G: Natural infection of *Proechimys* sp. ear, tail and foot lesions. Reproduced, with permission, from Lainson and Shaw[44].

Figure 4 – Rodent hosts of *Leishmania* (*L.*) *amazonensis* in the Brazilian Amazon Region

1977

Smears of liver and spleen tissue from a porcupine *Coendou prehensilis*, captured in a forested area of Pará, revealed the presence of amastigotes measuring up to 6.8 x 4.5 m[43], an unusually large size even when compared with *L. m. amazonensis* amastigotes. In 1971, Herrer[27] had given the name *Leishmania hertigi* to a parasite of Panamanian porcupines; therefore, the Brazilian *Coendou* parasite was given the subspecific name *Leishmania hertigi deanei* in honour of Leonidas Deane. Deane had encountered what was probably the same parasite in porcupines from the State of Piauí, Brazil, but, unsure of its nature, had refrained from naming it. The leishmanial nature of this strange parasite was indicated by its production (albeit only transitory) of amastigotes in the skin of experimentally inoculated hamsters and its formation of typical promastigote stages in blood-agar culture medium. In 1980, Miles et al[76] differentiated the parasite from *L.* (*L.*) *hertigi hertigi* and *L. mexicana amazonensis* by comparative isoenzyme profiles.

1979

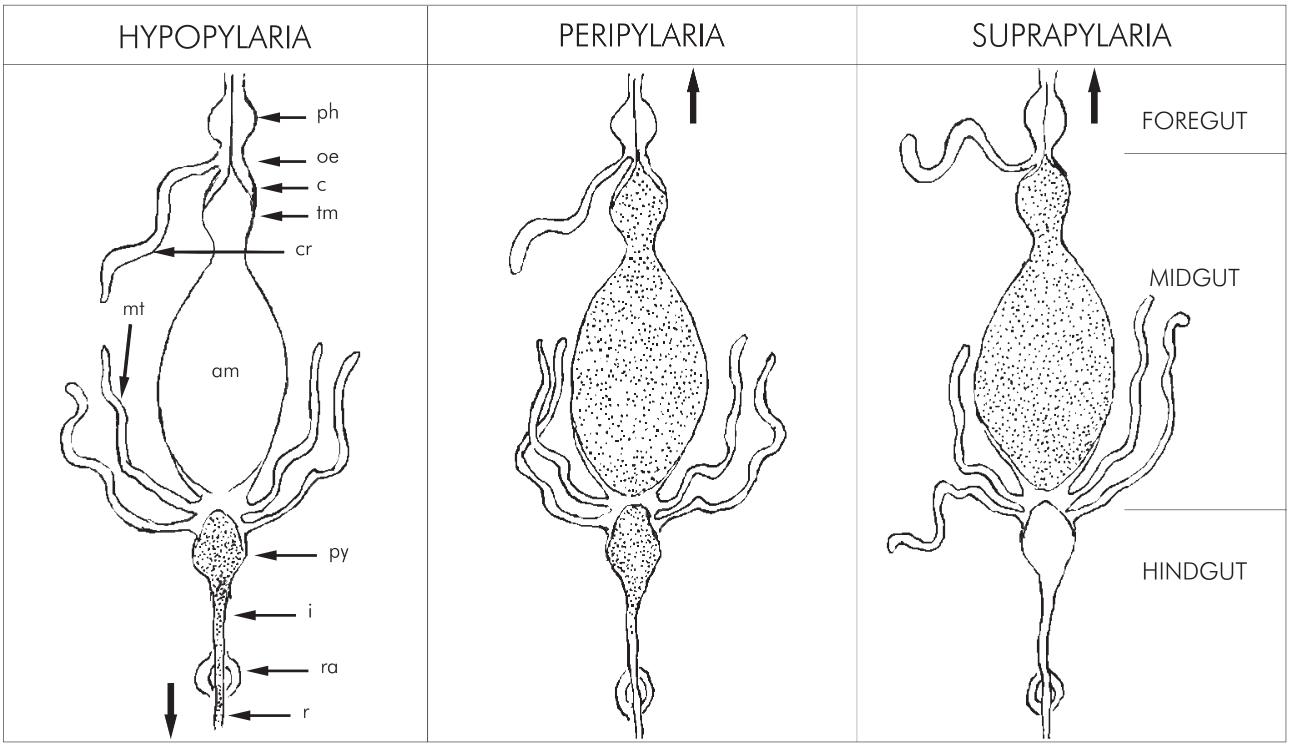
A species of *Leishmania* was isolated from the liver and spleen of a nine-banded armadillo, *Dasypus novemcinctus*, from the Monte Dourado (Jari) area of northern Pará, Brazil[51].

Biological features and the development of biochemical and immunological techniques gradually laid the foundation for preliminary attempts to classify the increasing number of accepted species of the genus *Leishmania*[46,50,42,117,51]. Particularly important were observations on the mode of development of these species in their phlebotomine vectors, which enabled the division of the parasites into three distinct groups referred to as Sections (Figure 5).

AN EARLY CLASSIFICATION OF THE *LEISHMANIA* SPECIES[51]

SECTION HYPOPYLARIA (from *hypo* = under, and *pyl* = gate)

The parasites included in this group were considered the most primitive species, and their development is limited to a posterior position in the pylorus, ileum and rectum of the sand fly gut. The reservoir hosts are apparently restricted to certain lizards of the Old World, in which the parasite may be in the promastigote and/or amastigote form in the viscera or blood. Listed species included *Leishmania agamae* David, 1929, and *L. ceramodactyli* Adler & Theodor, 1928. Transmission presumably follows the ingestion of an infected sand fly by the lizard. Some[35], including the present author, consider that these parasites are better placed in the genus *Sauroleishmania* Ranque, 1973.



ph = pharynx; oe = oesophagus; c = cardia; tm = thoracic midgut; cr = crop; mt = Malpighian tubules; am = abdominal midgut; py = pylorus; i = ileum; ra = rectal ampullae; r = rectum. Modified from Lainson and Shaw[51].

Section HYPOPYLARIA: The development of these primitive parasites, found only in lizards of the Old World, is restricted to the hindgut of the sand fly vector. Transmission occurs when the infected insect is eaten by the lizard.
Section PERIPYLARIA: Hindgut development is retained, but parasites also migrate to the midgut and foregut. Transmission occurs by the bite of the infected sand fly. Found in some lizards of the Old World. Also includes species of leishmanial parasites within the subgenus *Viannia*, which are restricted to mammals of the New World.
Section SUPRAPYLARIA: Hindgut development is completely lost, with parasites restricted to the midgut and foregut. Transmission occurs by the bite of the infected sand fly. Found in both Old World and New World mammals. Parasite distribution is shown by stippling, and the large arrows indicate the migratory direction of the promastigotes.

Figure 5 – Basic classification of the *Leishmania* species as determined by their developmental pattern in the sand fly hosts

SECTION PERIPYLARIA (from *peri* = on all sides, and *pyl* = gate)

These *Leishmania* species have maintained an obligate hindgut development in the sand fly, but, in addition, have now developed a migration to the foregut. Included here are the following parasites of Old World lizards: *Leishmania adleri* Heisch, 1958, and *Leishmania tarentolae* Wenyon, 1921. The parasite can now be transmitted by the bite of an infected sand fly or when the fly is eaten. This Section, however, was dominated by what Lainson and Shaw referred to as the *L. braziliensis* complex[51] of the New World. At that time, this complex included the following parasites, all of which infect humans: *L. braziliensis* Vianna, 1911; *L. peruviana* Velez, 1913; *L. guyanensis* Floch, 1954; and *L. panamensis* Lainson & Shaw, 1972.

SECTION SUPRAPYLARIA (from *supra* = above, and *pyl* = gate)

These *Leishmania* species were considered to have lost the primitive hindgut development in the sand fly, with the parasites now restricted to the midgut and foregut. They are found in the skin, viscera or blood of both Old World and Neotropical mammals, and transmission is by the bite of the infected sand fly vector. The Section was divided into four complexes, as follows:

The *L. donovani* complex

Leishmania donovani (Laveran & Mesnil, 1902) Ross, 1903 (Old World); *Leishmania infantum* Nicolle, 1908 (Old World); *Leishmania chagasi* Cunha & Chagas, 1937 (New World).

The *L. mexicana* complex

L. mexicana mexicana (Biagi, 1953) Lainson & Shaw, 1979; *L. mexicana amazonensis* Lainson & Shaw, 1972; *L. mexicana pifanoi* (Medina & Romero 1959) Medina & Romero, 1962; *L. mexicana aristidesi* Lainson & Shaw, 1979; *L. mexicana enriettii* Muniz & Medina, 1948 (All in the New World).

The *L. hertigi* complex

L. hertigi hertigi Herrer, 1971; *L. hertigi deanei* Lainson & Shaw, 1977 (New World).

The *L. tropica* complex

Leishmania tropica (Wright, 1903) Lühe,1906; *Leishmania major* Yakimov & Schockov, 1914; *Leishmania aethiopica* Bray, Ashford & Bray, 1973 (All in the Old World).

In 1982, the Russian researcher Saf'janova[91] separated the leishmanias of lizards from the true *Leishmania* species of mammals by the subgeneric use of the names *Sauroleishmania* Ranque, 1973, and *Leishmania* Ross, 1903, respectively. Within the subgenus *Leishmania*, she considered the *L. donovani* complex to consist of *Leishmania* (*L.*) *donovani*, *L.* (*L.*) *infantum* (Old World) and *L.* (*L.*) *chagasi* (New World). She did not consider the development of *L. braziliensis* and related Neotropical leishmanias in the sand fly's hindgut (members of the Peripylaria[51]) to be of taxonomic importance, however, and grouped all the Neotropical parasites together as *L.* (*L.*) *amazonensis*; *L.* (*L.*) *mexicana*; *L.* (*L.*) *braziliensis* and *L.* (*L.*) *panamensis* (dermal leishmaniases); and *L.* (*L.*) *chagasi* (visceral leishmaniasis). Furthermore, Saf'janova was of the opinion that there were insufficient taxonomic criteria to include *L. braziliensis peruviana* and *L. braziliensis guyanensis* in her classification. The exclusion of the latter two parasites was most likely due to the unavailability of recent literature that had clearly indicated specific characterisation on biological, biochemical and serological evidence[40,70,75].

1987 A REVISED CLASSIFICATION OF THE NEOTROPICAL *LEISHMANIA* SPECIES

Extensive studies of the ecology and epidemiology of cutaneous leishmaniasis in the Brazilian Amazon Region revealed a steadily increasing number of *Leishmania* species that were now more adequately characterised by their isoenzyme profiles[76], and this prompted a taxonomic revision[41].

In 1977, Lainson et al[58] had stressed the importance of using the presence or absence of hindgut development in the sand fly to distinguish parasites of the *L. braziliensis* complex (hindgut development present) from those of the *L. mexicana* complex (hindgut development absent)[58]. Accordingly, in the revised classification, all species with hindgut development were placed in the new subgenus *Viannia*, which was named in honour of Gaspar Vianna, who had described *L.* (*V.*) *braziliensis*, now the type species of the subgenus. It followed that all species lacking hindgut development were housed in the subgenus *Leishmania* Ross, 1903 used by Saf'janova[91] in 1982. In addition, while commenting on "the cumbersome combination of geographic names of parasites, which at times entered into absurd conflict with each other" (e.g., *L. braziliensis guyanensis* and *L. mexicana venezuelensis*), it was also proposed to raise the subspecific names to specific level. With these modifications, the following classification was given for *Leishmania* species of the Neotropics[41].

SUBGENUS *LEISHMANIA* ROSS, 1903

Definition: With the characters of the genus *Leishmania*. Life cycle in the insect host limited to the midgut and foregut. Type species: *Leishmania* (*Leishmania*) *donovani* (Laveran & Mesnil, 1903) Ross, 1903. It contained the following Neotropical parasites: *Leishmania* (*L.*) *chagasi* Cunha & Chagas, 1937; *L.* (*L.*) *enriettii* Muniz & Medina, 1948; *L.* (*L.*) *mexicana* Biagi, 1953 emend. Garnham, 1962; *L.* (*L.*) *amazonensis* Lainson & Shaw, 1972; *L.* (*L.*) *aristidesi* Lainson & Shaw, 1979; *L.* (*L.*) *venezuelensis* Bonfante-Garrido, 1980; *L.* (*L.*) *garnhami* Scorza et al, 1979; *L.* (*L.*) *pifanoi* (Medina & Romero, 1959) Medina & Romero, 1962; *L.* (*L.*) *hertigi* Herrer, 1971; *L.* (*L.*) *deanei* Lainson & Shaw, 1977.

SUBGENUS *VIANNIA* LAINSON & SHAW, 1987

Definition: With the characters of the genus *Leishmania*. Life cycle in the insect host including a prolific phase of development as rounded or stumpy paramastigotes and promastigotes attached to the wall of the hindgut (pylorus and/or ileum) by flagellar hemidesmosomes, but with later migration of the parasites to the midgut and foregut. Type species: *Leishmania* (*Viannia*) *braziliensis*.

Species of this subgenus are known only in the New World and were listed as follows: *L.* (*V.*) *braziliensis* Vianna, 1911, emend Matta, 1916; *L.* (*V.*) *peruviana* Velez, 1913; *L.* (*V.*) *guyanensis* Floch, 1954; *L.* (*V.*) *panamensis* Lainson & Shaw, 1972.

CONTINUING RESEARCH ON NEOTROPICAL *LEISHMANIA* SPECIES

1987

The use of monoclonal antibodies became an established method for the identification of *Leishmania* (*Viannia*) *braziliensis* in infected sand flies[97].

1988-1989

A new species of the subgenus *Viannia* was isolated from a sloth, a procyonid and two species of monkeys in lowland forest at the foot of the Carajás hills, Pará State, Brazil[38]. This parasite was named *Leishmania* (*Viannia*) *shawi* Lainson et al, 1989.

The parasite that had been isolated from the nine-banded armadillo (*Dasypus novemcinctus*) in 1979 was characterised and finally named as *Leishmania* (*Viannia*) *naiffi* Lainson & Shaw, 1989.

1991

Kreutzer et al[36] described a new species of *Leishmania* infecting humans in Colombia and Panama and named it *L.* (*Viannia*) *colombiensis*.

1992

Grimaldi et al[26] isolated another previously undescribed parasite from the sloth *Choloepus hoffmanni* and the squirrel *Sciurus granatensis* in Ecuador and gave it the name *L.* (*V.*) *equatorensis*.

2002

A parasite isolated from cases of ACL in soldiers engaged in manoeuvres in degraded forest in Belém, Pará State, Brazil, was found to differ from all previous *Leishmania* species in the Amazon region[99] and was given the name *Leishmania* (*Viannia*) *lindenbergi* Silveira et al, 2002.

2003

In 1977, a *Leishmania* of the subgenus *Viannia* was isolated from a single specimen of the sand fly *Lutzomyia tuberculata* taken from the trunk of a large tree in the Utinga forest. It remained for a long period in the IEC cryobank until it was finally characterised and named[4] *Leishmania* (*Viannia*) *utingensis* Braga et al, 2003.

1998/2005

The establishment of the subgenus *Viannia* and characterisation of additional leishmanial parasites isolated from sand flies, wild mammals and patients with ACL necessitated two further publications that updated and modified the classification[48,47].

A major change to the previous listing of parasites in the subgenus *Leishmania* was the proposal of the authors Lainson and Shaw[47], in 2005, to divide *Leishmania* (*L.*) *infantum* into two subspecies: *L.* (*L.*) *infantum infantum* (Old World) and *L.* (*L.*) *infantum chagasi* (New World). In addition, the new classification included *Leishmania* (*L.*) *forattinii* Yoshida et al, 1993, a parasite found in Brazil in an opossum, *Didelphis marsupialis aurita*, and a rodent, *Proechimys iheringi denigratus*.

All the presently recognised Neotropical species of *Leishmania*, their recorded geographical distribution, proven or suspected sand fly hosts, recorded mammalian reservoir hosts, and clinical data concerning those known to infect humans are given below.

PRESENT CLASSIFICATION OF THE NEOTROPICAL *LEISHMANIA* SPECIES

Adapted from Cox[11] and Lainson and Shaw[47].

Kingdom: **Protozoa** Goldfuss, 1818

Phylum: **Euglenozoa** Cavalier-Smith, 1998

Class: **Kinetoplastea**: Honigberg, 1963

Order: **Trypanosomatida** Kent, 1880

Family: **Trypanosomatidae** Doflein, 1901

Genus: ***Leishmania*** Ross, 1903

Subgenus: ***Leishmania*** Ross, 1903

Subgenus: ***Viannia*** Lainson & Shaw, 1987

SUBGENUS *LEISHMANIA*

LEISHMANIA (*LEISHMANIA*) *INFANTUM CHAGASI* (CUNHA & CHAGAS, 1937) SHAW, 2002

Known geographical distribution

Most of the Latin American continent, including Argentina, Bolivia, Brazil, Colombia, Ecuador, El Salvador, Guadeloupe, Guatemala, Honduras, Martinique, Mexico, Nicaragua, Paraguay, Surinam and Venezuela.

Known sand fly hosts

Lutzomyia (*Lutzomyia*) *longipalpis* is the principal vector throughout the range of AVL[14,37], but *Lu. evansi* has also been incriminated in Colombia and Venezuela[109,17]. *Lu.* (*Lu.*) *cruzi* became highly suspected as an alternative vector in the State of Mato Grosso do Sul, Brazil, when *L.* (*L.*) *infantum chagasi* was isolated from 14 specimens[93]. The females of *Lu. cruzi*, however, are indistinguishable from those of *Lu. longipalpis*, and even the males of the two species can only be separated based on small differences. The authors concluded that because *Lu. longipalpis* males were apparently absent at the time of their study, the infected females were *Lu. cruzi*. Although the presence of *Lu. longipalpis* in the same area has since been established[94], there now seems to be little doubt that *Lu.* (*Lu.*) *cruzi* may be an alternative vector of *Leishmania* (*L.*) *infantum chagasi* in the State of Mato Gosso do Sul.

Recorded mammalian hosts

The sylvatic canids *Cerdocyon thous* ("crab-eating fox")[52,54] and *Speothos venaticus* ("bush-dog")[18]; the felids *Panthera onca* (jaguar) and *Felis concolor* (puma)[13]; the opossums *Didelphis marsupialis*[10,108] and *D. albiventris*[98]; the domestic dog; and humans.

Human infection

L. (*L.*) *chagasi* predominantly produces visceral leishmaniasis, which is often fatal unless adequately treated, but infection can be asymptomatic in some individuals. In Costa Rica, infection is largely in the form of non-ulcerative cutaneous lesions[116], and in Honduras and Nicaragua, infection is both visceral and cutaneous[84,2].

Opinions have been divided as to whether the parasite named *L.* (*L.*) *chagasi* is indigenous to the American tropics or if the disease in the New World is due to *L.* (*L.*) *infantum*, which was introduced by Iberian immigrants, or their dogs, as recently as about 500 years ago. Arguments favouring the indigenous hypothesis have been given as follows[37,54,48,47]:

1. In terms of geological time, 500 years is a very short period for the parasite to have achieved such a wide distribution throughout the Latin American continent, from Mexico to Argentina.

2. The host-specificity of the *Leishmania* species in nature is most pronounced in the sand fly, which is generally regarded as the primary host of *Leishmania* species. Therefore, it seems unlikely that introduced *L.* (*L.*) *infantum* could have made a sudden jump from the genus *Phlebotomus* in the Old World to the genus *Lutzomyia* in the Americas. *Lutzomyia* (*Lutzomyia*) *longipalpis* is the principal vector of *L.* (*L.*) *infantum chagasi* throughout the geographical range[14,37], and it is not known to naturally transmit any other species of *Leishmania*.

3. Based on molecular data, it is frequently stated that the parasites referred to as *L.* (*L.*) *infantum* and *L.* (*L.*) *chagasi* are identical. There have been, however, a few publications (conveniently disregarded) claiming the demonstration of some differences between the two organisms. These, it has been claimed, have been demonstrated by restriction endonuclease digestion and hybridisation of kinetoplast DNA[33,32] and in radiorespirometry profiles of the two parasites[16,15]; finally, antigenic differences have been claimed for their respective promastigotes[92]. Unless these findings are disproved, it would therefore seem necessary to consider them in any discussion on the taxonomy of the two organisms.

4. In the transmission cycle of *L.* (*L.*) *infantum chagasi* among wild animals by the sylvatic population of *Lutzomyia longipalpis*, there is a high prevalence of infection in the native fox *Cerdocyon thous* in Brazil[54] and in the opossum *Didelphis marsupialis* in Colombia[10,108]. Infections have also been sporadically reported in other wild animals, including the opossum *Didelphis albiventris*[98] the "bush dog" *Speothos venaticus*[18], the jaguar *Panthera onca* and the puma *Felis concolor*[13]. All of the infections recorded in these wild animals have consistently been of a benign inapparent nature, which is more suggestive of a very ancient host-parasite relationship rather than infection with a strange and recently introduced parasite.

The great diversity of *Leishmania* species in the New World has prompted the suggestion that leishmanial parasites originated in the American tropics[78,79], and that the genus *Leishmania* gained entrance to the Old World via the Bering land bridge. Other authors[63], while agreeing with this hypothesis, have postulated that, following the introduction of the ancestral leishmanial parasite into the Old World and the evolution of *Leishmania donovani* and *Leishmania infantum* (an estimated 14-24 million years ago), the latter parasite gained entrance to the New World by way of the Iberian colonists.

To the present author, it seems equally reasonable to suggest that while this evolution of the ancestral parasite was taking place in the Old World, giving rise not only to the viscerotropic parasites *L.* (*L.*) *donovani* and *L.* (*L.*) *infantum*, but also to the dermotropic members of the *L.* (*L.*) *tropica* complex, another such evolutionary process of the ancestral parasite continued in the New World, producing the viscerotropic parasite named as *L. chagasi* and dermotropic parasites of the subgenus *Leishmania* (e.g., those of the *L. mexicana* and *L. hertigi* complexes). At the same time, another ancient line diverged to form the subgenus *Viannia*, the members of which retained the primitive characteristic of hindgut development in the sand fly gut. This group of leishmanial parasites is unknown in the Old World, possibly because their ancestral form never gained entrance via the Bering land bridge due to a restricted locomotor capacity of the mammalian reservoir hosts.

The name *L.* (*L.*) *infantum* Nicolle, 1908 clearly has chronological priority over the name *L.* (*L.*) *chagasi* Cunha & Chagas, 1937, and we are obliged to accept the specific name of *infantum* for the parasite in both hemispheres. The prolonged geographical separation might explain the above-mentioned recorded differences between the two populations, leading to the view that it is best to now regard them as the subspecies *L.* (*L.*) *infantum chagasi* and *L.* (*L.*) *infantum infantum*[95,39,47,11].

Some confusion has occurred regarding the authorship of this proposal. It was first made by Lainson and Shaw[47] when their chapter "New World Leishmaniasis" was submitted for publication in the 10th edition of "Topley & Wilson's Microbiology and Microbial Infections". There was an unusually long delay, however, before this edition finally appeared in print in 2005, and during this time, both Shaw[95], in 2002, and Lainson and Rangel[39], in 2003 used the new subspecific names in other publications. Chronologically, therefore, the correct subspecific names of *L. infantum* should be written as *L.* (*L.*) *infantum infantum* (Nicolle, 1908) Shaw, 2002 and *L.* (*L.*) *infantum chagasi* (Cunha & Chagas, 1937) Shaw, 2002.

LEISHMANIA (*L.*) *ENRIETTII* MUNIZ & MEDINA, 1948

Known geographical distribution

Known only in the States of Paraná[71] and São Paulo[65], Brazil.

Known sand fly hosts

Lu. monticola and *Lu. correalimai* are suspected, the former having been experimentally infected when fed on the lesions of guinea pigs[64].

Recorded mammalian hosts

Natural infections only recorded in the domestic guinea pig (*Cavia porcellus*).

Human infection

Not yet reported, and attempts to infect volunteers failed.

LEISHMANIA (*L.*) *MEXICANA* (BIAGI, 1953) GARNHAM, 1962

Known geographical distribution

Belize, Guatemala, Honduras, Costa Rica, southern USA. Reports in geographically widely separated South American countries must be viewed with caution.

Known sand fly hosts

Lutzomyia olmeca olmeca is a proven vector. *Lu. diabolica* is suspected in northern Mexico and southern Texas, and *Lu. anthophora* is suspected in Arizona.

Recorded mammalian hosts

The forest rodents *Ototylomys phyllotis*, *Nyctomys sumichrasti*, *Heteromys desmarestianus* and *Sigmodon hispidus*, and *Neotoma albigula* in the southern USA (Arizona); humans.

Human infection

Cutaneous leishmaniasis, with a pronounced tendency to cause lesions of the external ear ("chiclero's ulcer" or "chiclero's ear"). Occasional cases of ADCL.

LEISHMANIA (*L.*) *PIFANOI* (MEDINA & ROMERO, 1959) MEDINA & ROMERO, 1962

Known geographic distribution

Apparently limited to Venezuela, particularly in the States of Yaracuy, Lara and Miranda.

Known sand fly hosts

Uncertain, but possibly *Lutzomyia flaviscutellata*.

Recorded mammalian hosts

Humans. Although the wild animal reservoir hosts of *L.* (*L.*) *pifanoi* remain unknown, Lima et al[59] suggested that the rodents *Sigmodon hispidus* and *Rattus rattus* could be reservoirs of various *Leishmania* spp., including, presumably, *L.* (*L.*) *pifanoi*.

Human infection

So far, all cases recorded have been ADCL.

LEISHMANIA (*LEISHMANIA*) *AMAZONENSIS* LAINSON & SHAW, 1972

Known geographical distribution

Bolivia, Brazil, Colombia, French Guyana and Paraguay. Probably occurs in other Neotropical countries where the sand fly vector exists.

Known sand fly hosts

Lutzomyia (*Nyssomyia*) *flaviscutellata* is the major vector[44,96,113,112], with occasional infections reported in the closely related *Lu.* (*N.*) *olmeca olmeca* and *Lu.* (*N.*) *reducta*. A parasite identified as *L.* (*L.*) *amazonensis* was isolated from 16 of 1,715 specimens of *Lu. nuneztovari*[68] in Bolivia.

Recorded mammalian hosts

The terrestrial forest rodents *Proechimys* spp., *Oryzomys* spp., *Nectomys*, *Neacomys*, and *Dasyprocta*; the marsupials *Marmosa*, *Metachirus*, *Didelphis* and *Philander*; the fox *Cerdocyon thous*; humans.

Human infection

Localised single-sore cutaneous leishmaniasis and, in patients with a defective cell-mediated immune system, ADCL. Rare cases of visceral leishmaniasis have been attributed to this parasite in the State of Bahia, Brazil[1], but not elsewhere. The clinical and immunopathological spectrum of American cutaneous leishmaniasis, with particular reference to the disseminated form of the disease due to *L.* (*L.*) *amazonensis* and *L.* (*V.*) *braziliensis* and illustrating the extreme pathogenicity at the poles of ADCL and mucocutaneous leishmaniasis, has been described elsewhere[100].

LEISHMANIA (*LEISHMANIA*) *ARISTIDESI* (LAINSON & SHAW, 1979) EMEND LAINSON & SHAW, 1987

Known geographical distribution

Sasardi forest in the San Blas Territory of Eastern Panama.

Known sand fly hosts

A putative vector is *Lutzomyia* (*Nyssomyia*) *olmeca bicolor* based on its predominance in rodent and marsupial-baited Disney traps in areas where infected animals were also obtained[7].

Recorded mammalian hosts

The opossum *Marmosa robinsoni* and the rodents *Proechimys semispinosus* and *Dasyprocta punctata*[29,30].

Human infection

Not known, although *Lu. olmeca bicolor* has occasionally been found to feed on humans.

LEISHMANIA (*LEISHMANIA*) *GARNHAMI* SCORZA ET AL, 1979

Known geographical distribution

The Venezuelan Andes.

Known sand fly hosts

The most suspected vector is *Lu. youngi*. A parasite found in an infected specimen produced amastigotes in the skin of an inoculated hamster that were thought to be *L.* (*L.*) *garnhami*, but the parasite was not definitively identified[66].

Recorded mammalian hosts

The opossum *Didelphis marsupialis* and humans.

Human infection

ACL, of the simple localised lesion type.

LEISHMANIA (*LEISHMANIA*) *VENEZUELENSIS* BONFANTE-GARRIDO, 1980

Known geographical distribution

Venezuela, in the States of Lara and Yaracuy.

Known sand fly hosts

A definite vector has not been identified, but *Lu. olmeca bicolor* and *Lu. rangeliana* are suspected to be involved.

Recorded mammalian hosts

The wild mammalian hosts remain uncertain, but the parasite has been recorded in the domestic cat and humans. It has been suggested that the rodents *Sigmodon hispidus* and *Rattus rattus* are potential reservoir hosts of various *Leishmania* spp.[59], including, presumably, *L.* (*L.*) *venezuelensis*.

Human infection

Single or multiple skin lesions. Sometimes disseminated nodules that can be confused with ADCL, but the infection responds well to antimonial treatment.

LEISHMANIA (*LEISHMANIA*) *FORATTINII* YOSHIDA ET AL, 1993

Known geographical distribution

Brazil, in the States of São Paulo, Bahia and Espírito Santo.

Known sand fly hosts

Not yet identified, but *Lu.* (*Psychodopygus*) *ayrozai* and *Lu. yuilli* have been experimentally infected.

Recorded mammalian hosts

The rodent *Proechimys iheringi* and the marsupial *Didelphis marsupialis* in the State of São Paulo.

Human infection

Not yet recorded, but as the suspected vectors are known to feed on humans, infections might be found in the future.

LEISHMANIA (*LEISHMANIA*) *HERTIGI* HERRER, 1971

Known geographical distribution

Panama and Costa Rica.

Known sand fly hosts

The sand fly vector has yet to be discovered. The high rate of infection in the mammalian host suggests that it lives in close proximity to the vector(s), possibly in hollow trees.

Recorded mammalian hosts

The tropical porcupine *Coendou rothschildi*. Extensive examinations of other wild animals have revealed no other mammalian reservoir host.

Human infection

Unrecorded, possibly due to the inability of the parasite to survive in human tissues or because the vector never bites humans.

LEISHMANIA (*LEISHMANIA*) *DEANEI* LAINSON & SHAW, 1977

Known geographical distribution

To date, only recorded in the Brazilian Amazon Region.

Known sand fly hosts

The invertebrate host remains unknown. Tree-inhabiting sand flies of the species *Lutzomyia* (*Viannamyia*) *furcata* were taken from a hollow tree inhabited by an infected porcupine in Utinga forest, Belém, Pará, Brazil, and were shown to contain promastigotes in their undigested bloodmeals. However, there was no evidence that the parasites had migrated to the foregut, and they disappeared with the complete digestion of the blood[41].

Recorded mammalian hosts

The tree porcupine *Coendou p. prehensilis*. Like *L.* (*L.*) *hertigi*, *L.* (*L.*) *deanei* has a very high infection rate in this porcupine, and an exhaustive examination of other wild animals suggests that it is the sole mammalian reservoir host of the parasite.

Human infection

Unrecorded. Again, as is the case with *L.* (*L.*) *hertigi*, this may be because the organism cannot survive in human tissues or simply because the vector never bites humans.

In the 2005 classification[47] these two enigmatic parasites were placed under the heading of "*Leishmania*-like parasites of uncertain taxonomic position", largely because molecular studies[79] had suggested them to be more closely related to *Endotrypanum* (an endoerythrocytic flagellate of sloths) than to *Leishmania*. However, their present names were retained[47] until further information could be obtained, and, for this reason, I am grouping them here with members of the subgenus *Leishmania*. Based on the absence of attached hindgut forms of *L.* (*L.*) *deanei* in *Lutzomyia furcata*, albeit in transitory infections, this parasite certainly does not appear to be a member of the subgenus *Viannia*. Knowledge of the complete life cycles of these two organisms in their natural invertebrate hosts will hopefully indicate their exact taxonomic status.

Although both members of the *L. hertigi* complex appear to be peculiar to porcupines, they are easily distinguished by isoenzyme profiles and a marked difference in the morphology of their amastigotes: those of *L.* (*L.*) *hertigi* are strangely elongated and measure only from 3.5 x 1.2 to 4.8 x 2.5 m, while those of *L.* (*L.*) *deanei* are rounded in form and, at 5.1 x 3.1 to 6.8 x 3.7 m, are the largest of all recorded species of *Leishmania*.

THE SUBGENUS *VIANNIA*

LEISHMANIA (*VIANNIA*) *BRAZILIENSIS* (VIANNA, 1911) EMEND MATTA, 1916

Known geographical distribution

Although parasites variously referred to as *L. braziliensis* or *L. braziliensis sensu lato* have been reported in almost all Latin American countries from Argentina to Mexico, doubt remains as to the true nature of many records due to inadequate methods of identification in the past. Some may be simple zymodemes of *L.* (*V.*) *braziliensis*, but others may prove to be different, unidentified species of the subgenus *Viannia*.

Known sand fly hosts

The existing uncertainties regarding the exact geographical distribution of *L.* (*V.*) *braziliensis* make it difficult to identify all of its vectors. However, at least in Brazil, where the parasite has been recorded in every State, it is clear that there are numerous sand fly species involved in its transmission. These include *Lutzomyia* (*Nyssomyia*) *intermedia*, *Lu.* (*N.*) *whitmani sensu stricto*, *Lu.* (*Psychodopygus*) *wellcomei*, *Lu. migonei*[85] and *Lu.* (*N.*) *neivae* (Pinto, 1926) (for reference, see "Concluding Remarks").

In a recent study in the Salobo area of the Serra dos Carajás, Pará, Brazil, promastigotes from four specimens of *Lu.* (*Psychodopygus*) *davisi* were identified as *L.* (*V.*) *braziliensis*, while others from specimens of *Lu.* (*Psychodopygus*) *hirsuta* (3 infected), *Lu.* (*Nyssomyia*) *umbratilis* (3), *Lu.* (*N.*) *richardwardi* (2), *Lu.* (*Trichophoromyia*) *brachipyga* (2), *Lu.* (*T.*) *ubiquitalis* (2), *Lu. trinidadensis* (1) and *Lu. migonei* (1) remain to be identified[104]. *Lu.* (*P.*) *davisi* has previously been indicated as an important vector of zoonotic cutaneous leishmaniasis in the State of Rondônia[25].

In Pará State (near Paragominas), a parasite identified as *L.* (*V.*) *braziliensis* was isolated from a sand fly with the dual female morphology of *Lu.* (*P.*) *complexa* and *Lu.* (*P.*) *wellcomei*[103]. The females of these two species are morphologically indistinguishable, but it was concluded that the infected specimen was *Lu.* (*P.*) *complexa* due to the apparent absence of any males of *Lu.* (*P.*) *wellcomei*.

Recorded mammalian hosts

The low-level flight and high attraction to rodent-baited traps of the sand fly *Lu.* (*Psychodopygus*) *wellcomei*, an important vector of *L.* (*V.*) *braziliensis* in the Serra dos Carajás, Pará[55], led to early suspicions that terrestrial rodents and some marsupials might be the reservoir hosts of this parasite[114,55].

Before the development of biochemical, serological and molecular techniques for the characterisation and identification of *Leishmania* isolates, it was only possible to use biological ("extrinsic") characters of the parasites, such as the size of amastigotes and their behaviour in a standardised culture medium and in inoculated laboratory animals. Using such characters together with the pattern of development of parasites in experimentally infected sand flies (to indicate members of the subgenus *Viannia*), early researchers could at least say that isolates made from wild animals in an area highly endemic for human ACL due to *L.* (*V.*) *braziliensis* were probably this parasite. These records include the following wild animals.

Oryzomys concolor, *O. capito*, *O. nigripes*, *Akodon arviculoides*, *Proechimys* spp., *Rattus rattus*, *Rhipidomys leucodactylus* (Rodentia) and *Didelphis marsupialis* (Marsupialia)[21,22,45,51,53,88], all in Brazil; in Venezuela, *Rattus rattus* and *Sigmodon hispidus* (Rodentia)[59]. Finally, parasites from the Brazilian rodents *Bolomys lasiurus* and *Rattus rattus* were conclusively shown to be *L.* (*V.*) *braziliensis* by multilocus enzyme electrophoresis[5].

Domestic animals, including equines, dogs and cats, have been found with skin lesions due to *L.* (*V.*) *braziliensis* in areas that suggest a peridomestic transmission cycle. These reports have come primarily from Argentina, Bolivia, Brazil, Colombia and Venezuela. Humans are commonly infected.

Human infection

Cutaneous leishmaniasis, usually with one or a few lesions. Infection commonly leads to mucocutaneous disease. The clinical and immunopathological spectrum of American cutaneous leishmaniasis, with particular reference to the disseminated and mucocutaneous diseases, has been described elsewhere[100].

LEISHMANIA (*VIANNIA*) *PERUVIANA* VELEZ, 1913

Known geographical distribution

Peru, on the western side of the Andes, in areas with scant vegetation and a restricted population of wild animals. Could extend into the Argentinean highlands and other Andean countries.

Known sand fly hosts

Lutzomyia (*Helcocyrtomyia*) *peruensis* and *Lutzomyia verrucarum* are highly suspected, and a parasite with biological features similar to those obtained from humans and dogs has been isolated from the former[28].

Recorded mammalian hosts

Dogs and humans. A recent study reported the isolation of this parasite from the rodent *Phyllotis andinum* and the opossum *Didelphis marsupialis*[61].

Human infection

Simple cutaneous leishmaniasis with one or few lesions. The parasite is not known to produce the mucocutaneous disease.

LEISHMANIA (*VIANNIA*) *GUYANENSIS* FLOCH, 1954

Known geographical distribution

This sylvatic species commonly infects humans in Brazil, particularly north of the Amazon River, and in the neighbouring countries of French Guyana and Surinam. Also reported in Colombia, Ecuador, Venezuela and the lowland forest of Peru.

Known sand fly hosts

The principal vector is *Lutzomyia* (*Nyssomyia*) *umbratilis*, with relatively infrequent infections recorded in *Lu*. (*N*.) *anduzei* (Reviews[47,85]). Some early reports of infection in *Lu*. (*N*.) *whitmani s.l*. may have actually been *Leishmania* (*Viannia*) *shawi*.

Recorded mammalian hosts

Major sylvatic hosts are the sloth *Choloepus didactylus* and the lesser anteater *Tamandua tetradactyla*[53,24], with occasional infections in rodents and opossums. Infection in wild animals is benign and inapparent.

Human infection

Cutaneous leishmaniasis with one or multiple lesions. The latter may arise from multiple bites of infected sand flies or metastatic lymphatic spread. Rare cases of mucocutaneous involvement have been reported.

LEISHMANIA (*VIANNIA*) *PANAMENSIS* LAINSON & SHAW, 1972

Known geographical distribution

Canal Zone, Panama; also recorded in Colombia, Costa Rica, Ecuador, Honduras, Nicaragua and Venezuela.

Known sand fly hosts

The major vector is considered to be *Lutzomyia* (*N*.) *trapidoi*. A number of other species are thought to act as secondary vectors, including *Lu*. (*N*.) *ylephiletor*, *Lu*. (*Lu*.) *gomez* and *Lu*. (*Psychodopygus*) *panamensis*[34,8].

Recorded mammalian hosts

The sloth *Choloepus hoffmanni* is the major host, with occasional infections reported in the sloths *Bradypus infuscatus* and *B. griseus*. This parasite has also been reported in a number of other arboreal animals, including *Bassaricyon gabbi*, *Nasua nasua* and *Potos flavus* (Procyonidae), the monkeys *Aotus trivirgatus* and *Saguinus geoffroyi* and the terrestrial rodent *Heteromys* sp.[29,30]. Hunting dogs, like humans, often become "victim hosts" with visible skin lesions.

Human infection

Cutaneous leishmaniasis, with one to several lesions; rare cases of the mucocutaneous disease have been reported.

LEISHMANIA (*VIANNIA*) *LAINSONI* SILVEIRA ET AL, 1987

Known geographical distribution

Forested areas of Brazil, Peru and Bolivia.

Known sand fly hosts

To date, the only known vector is *Lutzomyia* (*Trichophoromyia*) *ubiquitalis*[102]. This insect is the first representative of the subgenus *Trichophoromyia* to be incriminated as a vector of a *Leishmania* species. *Lu*. (*T*.) *velascoi* is highly suspected as a vector in Bolivia[67].

Recorded mammalian hosts

So far, only the large rodent *Agouti paca*[101] and humans have been identified as hosts.

Human infection

Infection by this parasite usually presents as a single lesion, and no case of the mucocutaneous disease has yet been recorded.

LEISHMANIA (*VIANNIA*) *NAIFFI* LAINSON & SHAW, 1989

Known geographical distribution

This species has been isolated in the States of Pará and Amazonas, Brazil, and in French Guyana. However, it will almost certainly be reported in other parts of Latin America where the mammalian reservoir host and sand fly vectors coexist.

Known sand fly hosts

The principal vector of infection among the armadillo reservoir hosts appears to be *Lutzomyia* (*Psychodopygus*) *ayrozai*. This sand fly is not greatly anthropophilic, however, which probably accounts for the low rate of human infection. Rare infections have been recorded in *Lu*. (*P*.) *paraensis* and *Lu*. (*P*.) *squamiventris*, which are highly anthropophilic and are therefore likely vectors of the parasite to humans.

Recorded mammalian hosts

The only wild animal host known at present is the nine-banded armadillo *Dasypus novemcinctus*, in which infection is very common in apparently normal skin and viscera.

Human infection

Cutaneous leishmaniasis, usually in the form of a single lesion. Unlike most Neotropical *Leishmania* species, *L*. (*V*.) *naiffi* rarely produces a visible lesion in the skin of the laboratory hamster. If this parasite also produces occult infection in the skin of humans, it is possible that transmission to man is much more frequent than is generally thought.

LEISHMANIA (*VIANNIA*) *SHAWI* LAINSON ET AL, 1989

Known geographic distribution

Various areas of the Brazilian Amazon Region.

Known sand fly hosts

Lutzomyia (*N*.) *whitmani sensu lato*. Morphometric differences have been recorded between *Lu*. (*N*.) *whitmani* *sensu stricto* from the type locality in Bahia State, northeast Brazil, and the vector of *L.* (*V.*) *shawi* in the State of Pará, Brazilian Amazon[86]. These differences, together with separation of the two populations by DNA probes[87], suggest that the vector of *L.* (*V.*) *shawi* might be a "cryptic species" of a *Lu*. (*N.*) *whitmani* complex. This suggestion has been disputed, however, following a phylogenetic analysis of the mitochondrial (cytochrome b) haplotypes of *Lu*. (*N.*) *whitmani*, which led to the conclusion that clades of haplotypes and a continuum of interbreeding populations of this sand fly exist in the forests of Brazil[31]. Nevertheless, the behaviours of the type species of the sand fly in Bahia and of *Lu*. (*N.*) *whitmani s.l*. in the State of Pará are very different. In the former locality, the insect is highly anthropophilic, is commonly found in houses and is a vector of *L.* (*V.*) *braziliensis*. In the primary forest of Pará, however, the fly very rarely bites humans, has not been found to enter houses even when they are close to the forest, and is a vector of *L.* (*V.*) *shawi*.

Recorded mammalian hosts

The monkeys *Cebus apella* and *Chiropotes satanas* (Cebidae), the sloths *Choloepus didactylus* and *Bradypus tridactylus* (Xenarthra), the coatimundi *Nasua nasua* (Procyonidae), and humans.

Human infection

The parasite is responsible for cutaneous leishmaniasis, usually of the single lesion type, but cases of multiple lesions, clearly due to metastases, are occasionally seen. Mucocutaneous disease due to *L.* (*V.*) *shawi* has not yet been reported.

LEISHMANIA (*VIANNIA*) *COLOMBIENSIS* KREUTZER ET AL, 1991

Known geographical distribution

First recorded in Colombia and Panama, this parasite was also subsequently found in Venezuela. Its distribution likely extends into the forests of Brazil and of the Peruvian lowlands, as well as into other Latin American countries where the sylvatic mammalian and sand fly hosts coexist.

Known sand fly hosts

Lutzomyia (*Helcocyrtomyia*) *hartmanni* in Colombia; *Lu*. (*Lu.*) *gomezi* and *Lu*. (*Psychodopygus*) *panamensis* in Panama.

Recorded mammalian hosts

The sloth *Choloepus hoffmanni* and humans (Panama).

Human infection

Single or multiple cutaneous lesions. No case of the mucocutaneous disease due to this parasite has been reported.

LEISHMANIA (*VIANNIA*) *EQUATORENSIS* GRIMALDI ET AL, 1992

Known geographical distribution

To date, this parasite appears to be limited to the Pacific coast of Ecuador.

Known sand fly hosts

Lutzomyia (*N.*) *hartmanni*.

Recorded mammalian hosts

The sloth *Choloepus hoffmanni* and the squirrel *Sciurus granatensis*.

Human infection

Not yet recorded.

LEISHMANIA (*VIANNIA*) *LINDENBERGI* SILVEIRA ET AL, 2002

Known geographic distribution

This parasite has only been found in degraded forest in Belém, Pará, Brazil.

Known sand fly hosts

The vector is currently unknown, but *Lutzomyia* (*N.*) *antunesi* is highly suspected. This insect was shown to be the predominant anthropophilic sand fly in an area where a number of soldiers acquired *L.* (*V.*) *lindenbergi* infections while carrying out manoeuvres in the forest. In addition, the low-level flight of *Lu*. (*N.*) *antunesi* would explain why the skin lesions of these men were mostly on their faces and arms. Because the men spent most of their time standing in trenches, these parts of the body would be the most exposed to the bites of a low-flying sand fly. An unidentified *Leishmania* species was found in specimens of *Lu*. (*N.*) *antunesi* on the island of Marajó, Pará[90], but its development in the sand fly was suprapylarian. In contrast, in experimentally infected sand flies, the development of *L. lindenbergi* is peripylarian, which is typical of parasites in the subgenus *Viannia*.

Recorded mammalian hosts

To date, humans are the only known hosts. It is suspected that the wild animal reservoirs are probably terrestrial.

Human infection

Localised cutaneous lesions: to date, no case of the mucocutaneous disease has been reported.

LEISHMANIA (*VIANNIA*) *UTINGENSIS* BRAGA ET AL, 2003

Known geographic distribution

Belém, Pará, Brazil.

Known sand fly hosts

Only recorded from a single specimen of the sand fly *Lutzomyia* (*Viannamyia*) *tuberculata* that was taken from the trunk of a large tree in the Utinga forest, Belém, Pará, Brazil.

Recorded mammalian hosts

Currently unknown.

Human infection

The parasite has not been recorded in humans.

"HYBRIDS" OF *LEISHMANIA* SPECIES WITHIN THE SUBGENUS *VIANNIA*

These include *L.* (*V.*) *braziliensis / L.* (*V.*) *panamensis*; *L.* (*V.*) *braziliensis / L.* (*V.*) *guyanensis*; and *L.* (*V.*) *braziliensis / L.* (*V.*) *peruviana*, all of which have only been isolated from cases of human ACL. Only the latter "hybrid" has been associated with the mucocutaneous disease. It has been suggested that these "hybrids" are the result of genetic exchange. For more details and references, consult Lainson and Shaw[47].

CONCLUDING REMARKS

Since preparing this paper, I have been informed that the sand fly *Lutzomyia* (*Nyssomyia*) *neivae* (Pinto, 1926) has now been found to be naturally infected by *Leishmania* (*V.*) *braziliensis* in southern Brazil[82]. I am indebted to the reviewer of my paper for this information.

The difficulties in obtaining irrefutable proof of the participation of *Lutzomyia cruzi* in the transmission of *Leishmania* (*L.*) *infantum chagasi*, due to the fact that the females of this sand fly cannot be morphologically distinguished from those of *Lu.* (*Lu.*) *longipalpis*, is paralleled by a similar problem that arose during the search for the vector(s) of *Leishmania* (*V.*) *braziliensis* in the Serra dos Carajás, Pará, Brazil. The two predominant anthropophilic sand fly species in the area were found to be *Lutzomyia* (*Psychodopygus*) *wellcomei* and *Lu.* (*P.*) *complexa*, the females of which are also morphologically indistinguishable. Numerous infected females were found to be infected by *L.* (*V.*) *braziliensis*, and the problem was in deciding to which species they belonged. This dilemma was eventually solved by breeding out the adult flies from the eggs of infected females; this strategy provided the all-important males and conclusively showed the infected flies to be *Lu.* (*P.*) *welcomei*[89]. This method could perhaps also be used to identify infected *Lu. cruzi / Lu. longipalpis* in the State of Mato Grosso do Sul.

Considering the remarkable number of *Leishmania* species that have now been recorded in the Neotropics, and particularly in the Amazon region, this area might well be the birthplace of this genus. This hypothesis is supported by the observation that many of these parasites (species of the subgenus *Viannia*) have retained a hindgut development in the sand fly host, which is reminiscent of the life cycle of the monoxenous flagellates of insects from which *Leishmania* is thought to have evolved.

The existence of species of *Leishmania* that are known only in the sand fly host (e.g., *L.* (*V.*) *utingensis* in *Lutzomyia tuberculata*) suggests that others remain undetected among the numerous sand fly species that are non-anthropophilic. The continued search for these parasites and their wild mammalian reservoir hosts will be essential in generating an even more complete picture of the ecology of this fascinating group of parasites.

ACKNOWLEDGEMENTS

The author is indebted to the Wellcome Trust, London, for their continued support of the Wellcome Parasitology Unit over nearly 30 years, and to the succession of Directors of the Instituto Evandro Chagas, Secretaria de Vigilância em Saúde, Ministério da Saúde, Brazil, where this work was carried out. There is not enough space to list all the participants during this long period, but thanks must be given to the following: to Prof. Jeffrey J. Shaw, old friend and colleague who worked with the author from the date of the establishment of the WPU in 1965 until it was disbanded in 1992. To those who pioneered the biochemical, serological and molecular techniques for the identification of *Leishmania* species and enabled their installation in the IEC/WPU Leishmaniasis Programme, including Drs. M. L. Chance, P. J. Gardener, Prof. M. A. Miles, Prof. D. C. Barker, Dr. Diane McMahon-Pratt and Dr. J. David; and to Drs. Marinete M. Póvoa, Roseli R. Braga and Edna A. Y. Ishikawa, who so effectively used them. To our highly productive line of entomologists, Dr. Habib Fraiha, Prof. Richard Ward, Drs. Paul Ready, Adelson A. A. Souza, and Lee Ryan, and to clinician and parasitologist Fernando T. Silveira who, as the present head of the IEC's Leishmaniasis Programme, is using his long experience in the field and laboratory, with past members of the WPU, to ensure that it continues to flourish. Finally, to all past and present technical staff, in particular Maria das Graças S. da Silva, Sued Freitas Silva, Manoel C. de Souza, Roberto D. Naiff and Maricleide Naiff, Antonio Julio Monteiro, Deocleciano G. Primo, José Aprígio N. de Lima, João B. P. da Luz, António F. P. Martins, Nonato B. Pires, Iorlando da Rocha Barata and João A. Brandão.

Espécies neotropicais de *Leishmania*: uma breve revisão histórica sobre sua descoberta, ecologia e taxonomia

RESUMO

Este artigo apresenta uma revisão dos mais importantes eventos históricos que levaram à atual classificação das espécies neotropicais de *Leishmania* e indica as doenças básicas causadas em seres humanos por estes diferentes parasitos, sem discutir os aspectos clínicos e epidemiológicos das leishmanioses. Para cada uma das espécies descritas, são fornecidas informações a respeito de sua conhecida distribuição geográfica, dos flebotomíneos hospedeiros registrados e de seus reservatórios mamíferos secundários, selvagens ou domésticos. Os dados apresentados levam à conclusão de que o parasito *Leishmania* (*L.*) *infantum chagasi*, agente causador da leishmaniose visceral americana, é provavelmente autóctone da região neotropical, e não importada durante a colonização ibérica.

Palavras-chave: *Leishmania*; Neotrópico; Ecologia; Taxonomia.

Especies neotropicales de *Leishmania*: una breve revisión histórica sobre su descubrimiento, ecología y taxonomía

RESUMEN

Este artículo presenta una revisión sobre los más importantes eventos históricos que llevaron a la actual clasificación de las especies neotropicales de *Leishmania* e indica las enfermedades básicas causadas a humanos por estos diferentes parásitos, sin discutir los aspectos clínicos y epidemiológicos de las leishmaniasis. Para cada una de las especies descritas, se suministran informaciones a respecto de su conocida distribución geográfica, de los flebótomos hospederos registrados y de sus reservatorios mamíferos secundarios, salvajes o domésticos. Los datos presentados llevan a la conclusión que el parásito *Leishmania* (*L.*) *infantum chagasi*, agente causador de la leishmaniasis visceral americana, es probablemente autóctono de la región neotropical, y no importado durante la colonización ibérica.

Palabras clave: *Leishmania*; Neotrópico; Ecología; Taxonomía.

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Recebido em / Received / Recibido en: 16/4/2010
Aceito em / Accepted / Aceito en: 28/5/2010