LEISHMANIAS AND LEISHMANIASIS OF THE NEW WORLD, WITH PARTICULAR REFERENCE TO BRAZIL

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Problems in understanding leishmaniasis in the Americas stem partly from ignorance concerning the protozoan parasites (Leishmania) causing the disease. Until about 1960, relatively little was known of their epidemiology, their vectors, or their host species. Since that time, however, a good deal of research has been completed. On the basis of this, the authors have presented a revised classification of the major species and subspecies of leishmanias in the Western Hemisphere. This new taxonomy, given in the following article, is not intended to be rigid or restrictive; rather, it is designed to help stimulate interest in unearthing the large amount of significant information about these important organisms that still remains unknown.

Introduction

It is our intention here to discuss the parasites responsible for cutaneous and mucocutaneous leishmaniasis in the Americas, rather than the clinical manifestations of the diseases they may cause in man. Particular reference will be made to the taxonomy of the organism—and to the epidemiologic situation in Brazil—in the light of recent research.

Leishmaniasis remains a major problem in Brazil. There, as in most other parts of the New World, it is principally an occupational hazard of the forest worker. This makes it of particular economic importance, since the country is presently making major efforts to promote development by exploring and clearing large areas of virgin forest for farming or mining, and by constructing extensive new road systems.

Classification Problems

Clinical Classifications

Past emphasis on the clinical aspects of leishmaniasis has resulted in a bewildering array of terms but little progress in understanding the organisms causing the disease. Thus, textbooks refer to “Chiclero’s ulcer,” “Bay-sore,” “pianbois,” “framboesiform,” “verrucasal” or “nodular” leishmaniasis, “simple” and “mucocutaneous” leishmaniasis, “espundia,” “ulcera de Bauru,” “tuta,” and “diffuse cutaneous leishmaniasis.”

If infection with Leishmania were restricted to man, there might be some excuse for such classification; but the various forms of the disease in the Americas are zoonoses involving a wide variety of wild or domesticated animals. Man is more correctly regarded, therefore, as an accidental host who plays no important role in
maintaining the parasites in nature. It should be remembered, too, that while a given variety of *Leishmania* may produce a generally consistent clinical picture, individual persons may react differently to the same parasite.

Extreme examples of this are patients with diffuse cutaneous leishmaniasis. Due to their anergid condition, these unfortunate persons develop a particularly disfiguring and incurable infection in which large nodules may be scattered over most of the body. But when the same parasite infects immunologically competent subjects it produces a single ulcer or a limited number of lesions that are relatively easy to treat.

Moreover, the disease symptoms may vary greatly at different stages of infection. Thus the mucocutaneous disease starts with a primary lesion that can develop anywhere on the body; nasopharyngeal destruction may begin as much as 15 to 20 years later, after the initial ulcer has disappeared and been forgotten. Pian-bois may involve metastatic spread from the primary sore, particularly along the lymphatics, producing ulcers scattered all over the body.

In general, then, classifying leishmanias on a clinical basis is unsound. Unfortunately, however, classification on a firmer, biological basis has proved difficult in the past, because of the close similarity of both amastigote and promastigote stages of most of the parasites and our relative ignorance of their biology.

**Past Classification**

In the New World, leishmaniasis extends from Mexico’s Yucatan Peninsula in the north to Argentina in the south. Despite the immense geographic area involved and the obvious ecological differences existing within it, there was for a long time a tendency to attribute all the disease forms to a single parasite, *Leishmania braziliensis* (62). As consistently stressed by the late Saul Adler (1), “...use of one name *L. braziliensis* ... has been an important obstacle in the path of research.” Velez (61) established a separate name, *Leishmania peruviana*, for the parasite responsible for uta in the Peruvian Andes, but most authors still referred to it as *L. braziliensis*, even though each type of organism had a perfectly distinct ecology and epidemiology of its own.

The first serious attempts to separate the different leishmanias were made by Biagi (7) and Floch (15). The former author referred to *Leishmania tropica mexicana* as the cause of Chiclero’s ulcer in Mexico, Guatemala, and British Honduras, and the latter author referred to *L. tropica braziliensis* as the parasite associated with mucocutaneous leishmaniasis in Brazil. The organism responsible for pian-bois in the Guianas, uta in Peru, and cutaneous leishmaniasis generally in Panama and Costa Rica, was referred to simply as *L. tropica guyanensis*.

Pessôa, on the other hand (45) preferred to consider all these parasites as subspecies of *Leishmania braziliensis*, and called them *L. braziliensis mexicana*, *L. braziliensis guyanensis*, and *L. braziliensis peruviana*. He also gave the name *L. braziliensis pifanoi* to the organism isolated from a case of diffuse cutaneous leishmaniasis in Venezuela (39). A few years later Garnham (23) assigned the parasite responsible for Chiclero’s ulcer the rank of a separate species, *Leishmania mexicana*.

**The Need for Revised Classification of the Leishmanias**

Up to now, one of the major obstacles in the way of classifying the leishmanias of the Americas was our poor knowledge of their life cycles. Nor was much known about their comparative serologic and immunologic features. However, Adler (2) differentiated *L. tropica*, *L. mexicana*, and *L. braziliensis* by serologic techniques, and Lainson and Shaw (28) found that whereas a previous infection by *L. braziliensis panamensis* would protect humans against *L. mexicana mexicana*, the reverse did not apply. That is, a *L. m. mexicana* infection did not protect against *L. b. panamensis*.

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6 The amastigote (unflagellated) stage is found in the vertebrate hosts, including man; the promastigote (flagellated) stage is found in the sandfly vectors that transmit the organism to the vertebrate hosts.
During the 1960’s, efforts were largely devoted to the epidemiology of the various leishmanias of the Western Hemisphere in the hope that better understanding of their life cycles might throw some light on ways to control the diseases that they cause—and incidentally provide a basis for better classification.

**Isolation of Leishmanias from Rodents in Panama and Brazil**

In Panama (4), workers at the Gorgas Memorial Laboratories (using N.N.N. culture medium) isolated a leishmania from the heart-blood of forest rodents belonging to the genera *Proechimys* and *Hoplomys*. This leishmania was generally considered to be the same as that infecting man in Panama, but attempts to find the parasite in other animals of these genera failed, and the significance of the blood infections in *Proechimys* and *Hoplomys* remained obscure.

In Brazil Forattini (16), also using N.N.N. culture medium, tested the heart-blood of over 900 wild animals belonging to several different species. Amastigotes were observed in skin lesions of one agouti (*Dasyprocta* sp.) and one forest rat (*Kannabateomys*), and promastigotes were isolated in N.N.N. cultures of heart-blood taken from one paca (*Cuniculus paca*). As far as we know, however, the parasites were not studied further and their true nature is still unclear. In 1960 Alencar, et al. (3) reported the isolation of promastigotes from the heart-blood of a domestic rat in Ceará State, Brazil. Again, the exact nature of the infection is still uncertain.

**Isolation of L. mexicana from Rodent Tail-Lesions**

During 1959-1962, work was started in British Honduras in an effort to elucidate the life-cycle of *Leishmania mexicana* (34, 35, 36, 57, 58). These studies dealt primarily with skin samples from wild animals, because experimental *L. mexicana* infections in both wild and laboratory animals showed that the parasites were usually restricted to that tissue. Using this approach *L. mexicana* was finally isolated from numerous specimens of forest rodents, including members of the genera *Ototylomys*, *Heteromys*, and *Nyctomys*, the parasites being localized in discrete skin lesions on the rodents’ tails. Inoculation of the isolated parasites into volunteers produced *L. mexicana*-type lesions; the organisms were also successfully transmitted to another volunteer by the bite of an experimentally infected sandfly of the species *Lutzomyia pessoana*. Subsequent work in Belize and on the Yucatan Peninsula showed the natural vector of *L. mexicana* to be *Lutzomyia olmeca* (8, 14, 67).

**Similar Isolation of Other Leishmanias**

These observations served as a stimulus that quickly produced results elsewhere in the New World. In 1963 there arose an opportunity to discuss our Belize findings with Dr. Otis Causey in his arbovirus laboratory at the Evandro Chagas Institute in Belém, Brazil. He mentioned having seen skin lesions on the tails of some of the rodents captured during his work in the forests around Belém and promised to examine them for leishmanias at the next opportunity. Within 2 weeks he had uncovered a remarkably heavy focus of rodent leishmaniasis in the cricetid *Oryzomys capito* (41, 42, 43). Similar infections in spiny rats (*Proechimys*) and opossums (*Marmosa*) have since been found by Lainson and Shaw in this same region (29, 31).

These latter authors have also extended their observations (unpublished observations, 30) to the areas of new roads being built in the Mato Grosso and Amazon regions. They have found infections in *Oryzomys* in the State of Rio de Janeiro, Brazil (56); and in *Marmosa*, *Heteromys*, and *Oryzomys* from Trinidad (60, personal communication).
Leishmania mexicana mexicana, the Agent of Chiclero’s Ulcer, in Belize, Central America (Figures 1-4):

FIGURE 1—Tropical rain-forest endemic for Chiclero’s ulcer.

FIGURE 2—The “spiny mouse,” Heteromys desmarestianus, a natural host of L. m. mexicana.

FIGURE 3—The tail of a naturally infected rodent, Ototylomys phylloides, magnified to show lesions due to L. m. mexicana (arrows).

FIGURE 4—Typical erosion of the human ear due to L. m. mexicana.

Leishmania mexicana amazonensis in Brazil (Figures 5-16):

FIGURE 5—A typical igapó or swamp forest, where rodents and marsupials are commonly infected with L. m. amazonensis.

FIGURE 6—Oryzomys capito, a rodent commonly infected with L. m. amazonensis.

FIGURE 7—Proechimys guyannensis, one of the major reservoir hosts of L. m. amazonensis, showing a small lesion on the ear (arrow).

FIGURES 8 and 9—Lesions on the tail of Oryzomys capito (Pará State) and Neacomys spinosus (Mato Grosso State) due to L. m. amazonensis.

FIGURE 10—The murine opossum, Marmosa murina (Pará State) showing a lesion on the base of the tail (arrow).

FIGURE 11—Amastigotes of L. m. amazonensis in a smear from a tail lesion of Proechimys guyannensis.

FIGURE 12—Dissected stomach of the sandfly vector, Lutzomyia flaviscutellata, showing enormous numbers of promastigotes of L. m. amazonensis.

FIGURE 13—Stained preparation of the same promastigotes.

FIGURE 14—Histiocytomata produced by metastatic spread of L. m. amazonensis in a hamster inoculated with promastigotes from Lu. flaviscutellata.

FIGURES 15 and 16—Diffuse cutaneous leishmaniasis in an adult man and a 4-year-old girl caused by L. m. amazonensis in Pará State, northern Brazil.
**Leishmania braziliensis braziliensis** in Brazil (Figures 17-25):

FIGURE 17—A typical high, dry forest ("terra firme"), endemic for leishmaniasis caused by *L. b. braziliensis*, along the new Trans-Amazon Highway in Pará State, northern Brazil.

FIGURE 18—Men cutting timber in a densely forested region of the Serra dos Carajás, Pará State, northern Brazil. Such workers stand a high risk of contracting cutaneous or mucocutaneous leishmaniasis.

FIGURE 19—A tail lesion (arrow) caused by *L.b. braziliensis* in the rodent *Oryzomys concolor*, Mato Grosso State, Brazil.

FIGURE 20—*Psychodopygus* sandfly feeding on man (flash photograph, taken at night), Mato Grosso State, Brazil.

FIGURE 21—Rosettes of promastigotes of *L. b. braziliensis* in the hindgut triangle of an experimentally infected sandfly. Parasites of the *mexicana* complex do not develop in this part of the insect’s gut.

FIGURE 22—An early lesion due to *L. b. braziliensis* on the leg of a forest worker in Mato Grosso State, Brazil.

FIGURE 23—An extensive leg ulcer caused by *L. b. braziliensis*, Pará State, northern Brazil.

FIGURE 24—Advanced mucocutaneous leishmaniasis, with collapse of the septum and erosion of the upper lip, Pará State, northern Brazil.

FIGURE 25—A hamster's nose eight months after inoculation with *L. b. braziliensis* isolated from a mucocutaneous case. Compare this modest growth with the florid development of *L. mexicana amazonensis* in the hamster after only 5 months (Figure 14).

**Leishmania braziliensis guyanensis** (Figure 26):

FIGURE 26—A lesion of the human arm, showing initiation of metastatic spread along the lymph vessels (arrow points to secondary nodule).

**Leishmania peruviana** (Figures 27-29):

FIGURE 27—An area endemic for uta, caused by *L. peruviana*, in the Peruvian Andes. Compare this barren terrain with the heavily forested endemic areas of *L. mexicana* and *L. braziliensis*. The dry stone wall is a typical breeding place for the sandfly vectors.

FIGURE 28—A dog showing small lesions on the nose due to *L. peruviana*. The dog is the only known reservoir host of this parasite.

FIGURE 29—A young girl with a nose lesion caused by *L. peruviana*. 

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In Panama, workers at the Gorgas Memorial Laboratories have isolated *Leishmania* from sloths (*Bradypus infuscatus* and *Choloepus hoffmanni*), procyonids (*Potos flavus* and *Basaricyon gabbii*), and a marmoset (*Saguinus geoffroyi*) (5, 6, 59). These Panamanian parasites resemble those infecting man, and have generally been regarded as *L. braziliensis*. More recently in Panama, Herrer, et al. (26) have found a second type of *Leishmania*, very similar to *L. mexicana*, in rodents of the genera *Proechimys*, *Oryzomys*, *Diplomys*, and *Agouti*, and in the marsupial genus *Marmosa*.

**Discovery of L. mexicana amazonensis**

It was first thought that the very common leishmania of Brazilian rodents and marsupials was the one generally responsible for human cutaneous and mucocutaneous leishmaniasis. Some authors, indeed, referred to it as *L. braziliensis*. More recently, Lainson and Shaw (32, 33) concluded that the parasite was biologically quite different from *L. braziliensis* and named it *Leishmania mexicana amazonensis*. In fact this organism only rarely infects man because its vector, *Lutzomyia flaviscutellata*, is not an anthropophilic species (30, 53, 54).

**A Revised Classification System**

These and other studies made it clear that some revised system of classification would have to be found if utter confusion was to be avoided in subsequent literature on *Leishmania* and leishmaniasis. Lainson and Shaw (33) consequently divided the neotropical leishmanias into two major groups—the *mexicana* and *braziliensis* complexes. This classification is reorganized here into table form (see Appendix) and brought up to date with more recent information.

*L. enriettii*

The enigmatic *L. enriettii* (40) has been included in the *mexicana* complex (see Appendix, Table 6A). Discovered in a laboratory guinea pig in Curitiba, Paraná State, Brazil, the parasite has never been encountered again and its natural host and vector remain unknown. Although it does not normally infect the hamster, its behavior in the guinea pig is comparable to development of other *mexicana* types in the hamster, with relatively rapid metastasis to the extremities. The unusually large amastigote of *L. enriettii*, which is up to 6.0 μm x 4.0 μm, permits its ready differentiation from all other leishmanias, and this feature alone warrants its classification as a distinct species within the *mexicana* complex.

Because it was found in a laboratory guinea pig, it seems curious that *L. enriettii* will not infect the wild guinea pig, *Cavia aperea*, from the same region of Brazil. How the infection was transmitted to the laboratory animal remains a mystery. It seems difficult to imagine that it was by the bite of an infected sandfly, because of the circumstances described, and it remains possible that the infection originated in a guinea pig previously inoculated with material from a wild animal during some other study. No human infection with *L. enriettii* has yet been recorded, and attempts to infect volunteers with amastigotes and promastigotes have apparently been unsuccessful (40).

*L. mexicana pifanoi*

*Leishmania mexicana pifanoi* is known only from human cases of diffuse cutaneous leishmaniasis in Venezuela. It is very similar to *L. m. amazonensis*, and could indeed be identical to that parasite. If this is so, the subspecific name *pifanoi* will of course take preference over *amazonensis*, which would then become a synonym. Only future epidemiologic and other studies can resolve this point. In the meantime, it is convenient to refer to the parasite as *L. m. pifanoi* within the *mexicana* complex (Table 4A).

*L. peruviana*

*Leishmania peruviana* is another parasite de-
serving classification as a separate species, if only by virtue of its unique epidemiology. This organism is the Hemisphere’s only known causative agent of cutaneous leishmaniasis in man that is not associated with forests and does not appear to have any wild animal reservoirs. Uta, the local name of the disease produced by *L. peruviana* occurs up to almost 3,000 meters on the barren slopes of the Peruvian Andes; its only known reservoir is the domestic dog. The vector is thought to be *Lutzomyia verrucaram* or *Lu. peruensis* (24); the peridomestic nature of these sandflies has permitted efficient control of the disease by spraying with DDT. *L. peruviana* is rather hard to classify, as there is little available literature on its behavior in the laboratory. However, lack of available strains of the parasite in hamsters and difficulty in acquiring cultures suggest that *L. peruviana* certainly does not behave like an organism of the mexicana group. It has been placed, therefore, in the braziliensis complex (Table 1OA).

**Notes on Two Other Leishmanias**

Two other leishmanias have recently been discovered in Panama. One of these, as yet unnamed (Table 5A), is closely related to *L. m. amazonensis* and may even prove to be identical. It infects wild rodents and opossums and is probably transmitted by *Lutzomyia olmeca bicolor*, a sandfly closely related to *Lu. flaviscutellata* (26). No human infections have yet been reported; as in the case of *L. m. amazonensis*, however, such infections may be rare simply because the vector transmitting the parasite hardly ever bites man.

The other parasite has been classified as a separate species, *Leishmania hertigi*, because of its distinctive morphology (25). It appears to only infect the tree porcupine, *Coendou rothschildi*, producing an asymptomatic infection with parasites scattered throughout the dermis. The organism grows very poorly in hamster skin. It is not clear whether *L. hertigi* is capable of infecting man, and its vector is unknown. It has been included here with parasites of the braziliensis complex.

**Other Recent Observations on Leishmanias and Their Reservoir Hosts**

Several new observations, either very recently published or in the process of being published, should be mentioned because they have a bearing on the situation.

Chance, *et al.* (9) have studied the DNA from various leishmanias and concluded that “In terms of DNA buoyant density . . . representatives of the fast and slow-growing strains (33) are clearly separate species.” This observation has now been incorporated into Table 1A as one of the principal features differentiating parasites of the *L. mexicana* and *L. braziliensis* complexes.

Long-term studies on animals captured along the new Trans-Amazon Highway in Pará State, Brazil (Lainson and Shaw, unpublished observations), have indicated that, in some areas at least, the major host of *L. mexicana amazonensis* is the echimyid rodent *Proechimys guyannensis*, and not the cricetid *Oryzomys capito* as was previously thought. Furthermore, the most common type of infection is asymptomatic, with the parasites scattered throughout apparently normal dermis (see Table 1). Infections were transmitted by routine intradermal inoculation of hamsters with triturated skin taken from the nose, ears, and base of the tail of each *Proechimys*. Of 166 *Proechimys* tested, 26 (15.7 per cent) were infected, but only five showed visible skin lesions. An infection was also noted in a lone opossum, *Metachirus nudicaudatus*, from the same area; once again the parasite was isolated from apparently normal skin.

Information on the isolation of *L. braziliensis braziliensis* from wild animals appears limited to reports of infections among cricetid rodents (*Oryzomys concolor*) in Mato Grosso State, Brazil (30, 32), and among *Oryzomys nigripes*, *O. capito laticeps*, and *Akodon arviculoides* in São Paulo State, Brazil (19, 21). In most cases the animals showed inconspicuous lesions on their tails.

All other attempts to pinpoint wild animal hosts of *L. b. braziliensis* have produced disap-
pointing results and have been dogged by difficulties relating to the parasites' very poor growth in both hamster skin and N.N.N. culture medium. In this respect it should be mentioned that Lainson, et al. (37) previously reported an apparent failure to infect hamsters at all, following intradermal inoculation of the animals with material containing amastigotes from human lesions and with rich suspensions of promastigotes from infected sandflies. A single isolation of a parasite resembling *L. b. braziliensis* has been made in hamster skin, however, following hamster inoculation with a liver-and-spleen suspension from a *Proechimys* captured along the Trans-Amazon Highway. The isolated organism shows all the characteristics of the *L. braziliensis* group; further examinations concerning its true nature are in progress. The parasite's visceral location in the wild host is particularly interesting, especially since no isolation could be made from the animal's skin (Lainson and Shaw, unpublished observations).

Recently, another leishmania has recently been found in the viscera of an opossum, *Didelphis marsupialis*, also captured along the Trans-Amazon Highway (Lainson and Shaw, unpublished observations). This leishmania is morphologically distinct from both *L. mexicana* and *L. braziliensis*.

Yet another leishmania has recently been found in the viscera of the sloth, *Choloepus didactylus*, in various areas of Pará State in northern Brazil. However, this is almost certainly the same parasite originally noted by Deane (12) among these animals in the same region. Deane and Deane (13) were uncertain if its amastigotes, seen in smears of the viscera, were those of a *Leishmania* species or were some stage in the development of *Endotrypanum*—a strange endoerythrocytic hemoflagellate commonly found in *Choloepus didactylus*. Present studies (Shaw and Lainson, unpublished observations) indicate that the parasite is distinct from *L. braziliensis braziliensis*, although it clearly belongs to the *braziliensis* complex. In Panama, the leishmania commonly found in the sloths *Choloepus hoffmanni* and *Bradypus infuscatus* is considered to be the same as that infecting man, namely *L. braziliensis pana-mensis* (10).

**Transmission of New World Cutaneous and Mucocutaneous Leishmaniasis**

It is a remarkable fact that although some 504 natural flagellate infections have been reported among wild-caught sandflies in the Ame...
ricas, in only 18 instances have the parasites been positively identified as *Leishmania*.

Within the *L. mexicana* complex, *L. mexicana mexicana* is transmitted among wild rodents by *Lutzomyia olmeca* (14). Although Biagi, et al. (8) also regarded this fly as the principal human vector, some doubt about this remains. *Lu. olmeca* can by no means be regarded as a highly anthropophilic species, yet Chiclero's ulcer is very common in most of British Honduras, the Yucatan Peninsula, and Guatemala. Attempts have been made to explain this paradox by suggesting that an increased rate of biting occurs when *Lu. olmeca* is disturbed in leaf-litter in the early hours of the morning (66). The argument does not seem convincing, however, and it seems possible that some other more anthropophilic species of sandfly may be involved in the onward transmission of *L. m. mexicana* to man.

In Brazil, *L. mexicana amazonensis* parasitizes rodents and more rarely opossums, being transmitted among them by the sandfly *Lutzomyia flaviscutellata*, a close relative of *Lu. olmeca*. Lainson and Shaw (29) isolated the organism from six of eight infected flies; in subsequent work, *L. m. amazonensis* infections were found in 37 *Lu. flaviscutellata*, out of a total of 4,802 dissected (63). These flagellates have produced typical *L. m. amazonensis* infections when inoculated into hamsters. As previously noted, however, few infections are encountered in humans because *Lu. flaviscutellata* rarely bites man.

It is a sad fact that we know little about the vectors of parasites in the *L. braziliensis* complex, which are clearly of greater opossum, being transmitted among them by the sandfly *Lutzomyia flaviscutellata*, a close relative of *Lu. olmeca*. Lainson and Shaw (29) isolated the organism from six of eight infected flies; in subsequent work, *L. m. amazonensis* infections were found in 37 *Lu. flaviscutellata*, out of a total of 4,802 dissected (63). These flagellates have produced typical *L. m. amazonensis* infections when inoculated into hamsters. As previously noted, however, few infections are encountered in humans because *Lu. flaviscutellata* rarely bites man.

Information on the epidemiology of *L. braziliensis* guyanensis is scanty, and nothing at all is known about its reservoir hosts. Wijers and Linger (65) showed that *Lutzomyia squamiventris* was the most common man-biter in areas of Surinam where pian-bois was a problem, but no infections were found upon dissection of large numbers of this species. These authors did find flagellates in 12 specimens of *Lu. anduzei*, but inoculation of the promastigotes into hamsters produced no conclusive evidence that the parasites were in fact *Leishmania*.

Up to very recently there had been no direct isolation of *L. braziliensis braziliensis* from wild-caught sandflies, although promastigotes have been seen in *Lutzomyia migonei*, *Lu. whitmani*, and *Lu. pessoai* from the State of Säo Paulo, Brazil. (46, 47, 48). Forattini and Santos (18) described a similar infection in a single *Lu. intermedia* from Paraná State. In Venezuela, promastigotes have been seen in *Lu. migonei*, in *Lu. longipalpis*, and in a specimen tentatively identified as *Lu. anduzei* (16, 49, 50). In none of these cases, however, was the exact nature of the flagellates determined. It has also been suggested that *Ps. panamensis* may be the major vector of cutaneous leishmaniasis in Venezuela (49, 51), but evidence is still needed to support this view.

Recently, Ward, et al. (64) studied the phlebotomid fauna in forested areas of Pará State in northern Brazil where cutaneous and mucocutaneous leishmaniasis is very common. Among other things, they observed that one particularly common sandfly, *Psychodopygus wellcomei* (22), often attacked man vigorously in broad daylight. As this species was also highly attracted to wild rodents, it was strongly suspected of serving as a vector for transmission of *L. b. braziliensis* to man. Lainson, et al. (37) later found heavy promastigote infections in three *Psychodopygus wellcomei*, two *Ps. paraensis*, and one *Ps. amazonensis*. Inoculation of the flagellates from a *Ps. wellcomei* into hamster skin resulted in isolation of a *Leishmania* that was indistinguishable from *L. b. braziliensis* isolated from man in the same region.
Forattini et al. (20) also demonstrated the leishmanial nature of promastigotes found in *Lu. pessoi* and *Lu. intermedia* by infecting hamsters with these flagellates.

**The Epidemiologic Situation in Brazil**

We now know of three different leishmanias that are responsible for cutaneous or mucocutaneous leishmaniasis in Brazil.

The first, *L. mexicana amazonensis*, is widely distributed throughout the country among wild rodent and marsupial hosts. It extends through northern and central Brazil, and very likely into all parts of the country where forests prevail. The parasite rarely infects man, however, because its vector, *Lutzomyia flaviscutellata*, is not anthropophilic. The other two parasites, *L. braziliensis guyanensis* and *L. braziliensis braziliensis*, have highly anthropophilic vectors and often seriously affect man.

In the neighboring Guianas leishmaniasis is caused primarily by *L. b. guyanensis*, which produces pian-bois, the typically multilesion cutaneous infection, apparently without subsequent nasopharyngeal involvement. Rare cases of nasopharyngeal involvement in this region probably result from an overlapping of *L. b. braziliensis* infections.

Passing into the adjacent Brazilian Federal Territory of Amapá and the northern state of Pará, the admixture of the two parasites becomes more marked and cases of mucocutaneous leishmaniasis become more common; however, the major scourge of forest workers remains pian-bois.

Finally, as we move further south through Pará or westwards into Amazonas, pian-bois disappears and is replaced by the more typically single-lesion or limited-lesion disease caused by *L. b. braziliensis*, with its frequent nasopharyngeal sequelae.

**Concluding Remarks**

Few taxonomic systems are foolproof, and all require repeated modification as new facts and new organisms are discovered. The classification presented here is certainly no exception, but we hope that it will provide an effective groundwork, facilitating the comparison of known leishmania parasites and the naming of new ones.

Great strides have been made during the past 10 years in advancing our knowledge of the leishmanias, giving scientific workers a new awareness that these curious and important organisms are not simply a small group of dubious species, with monotonously identical morphologies and uninteresting natural histories. Much remains to be done, however, and only long and patient field studies will enable us to determine the extensiveness of the range of parasites within this actively speciating complex, the significance of the roles they play in human disease, and the important variations and complexities of their life cycles.

**SUMMARY**

One of the things that makes leishmaniasis of the Western Hemisphere a particularly enigmatic disease is lack of knowledge about its causative agents. All these agents are protozoans of the genus *Leishmania*, but while some may infect man little or not at all, others can cause serious disease.

Past efforts to classify the parasites on the basis of clinical symptoms have produced a good deal of confusion. There were several reasons for this: first, man should properly be regarded as an accidental host of these leishmanias, which are maintained in nature by a wide spectrum of animal species; second, different patients may develop different reactions to the same parasite for immunological reasons; and third, leishmaniasis can last many years and its symptoms vary greatly during the course of the infection.

Until fairly recently there was relatively little known about the hosts, vectors, and epidemiologies of the various leishmanias, and there
had been little opportunity to set up an effective system of classification on this basis. However, during the 1960's a considerable amount of such work was accomplished and a number of new leishmanial parasites were discovered. This showed the importance of revising the existing taxonomy and provided a basis by which such revision could be achieved.

The authors' revised classification of Western Hemisphere leishmanias is presented as part of this article. It is understood that few taxonomic systems are foolproof, and that all require repeated modification. The classification offered here is no exception to these rules. It is hoped, however, that it may help to orient our existing knowledge and help stimulate greater interest in the natural histories of these curious and important agents of human disease.

APPENDIX: Classification of New World leishmanias

TABLE 1A—Principal features distinguishing the *L. mexicana* complex from the *L. braziliensis* complex.

<table>
<thead>
<tr>
<th>Identifying criteria</th>
<th>Parasites of the <em>L. mexicana</em> complex</th>
<th>Parasites of the <em>L. braziliensis</em> complex</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sandfly vectors; behavior in sandfly</td>
<td>Sandflies of the <em>intermedia</em> group; no development in the hindgut triangle</td>
<td>Sandflies of the <em>Psychodopygus</em> and <em>intermedia</em> groups; development in hindgut triangle</td>
</tr>
<tr>
<td>Behavior in hamster skin</td>
<td>Rapid formation of histiocytoma very rich in amastigotes; spread by metastases</td>
<td>Very slow formation of small nodule or ulcer with scanty amastigotes; no metastatic spread</td>
</tr>
<tr>
<td>Behavior in N.N.N. culture medium</td>
<td>Luxuriant growth</td>
<td>Poor to moderate growth</td>
</tr>
<tr>
<td>Comparative study of DNA (See reference 9—Chance, Peters, and Griffiths, 1973.)</td>
<td>Distinguishable from parasites of <em>L. braziliensis</em> complex by buoyant density of DNA</td>
<td>Distinguishable from parasites of <em>L. mexicana</em> complex by buoyant density of DNA</td>
</tr>
</tbody>
</table>
I. The *L. mexicana* complex

**TABLE 2A—*Leishmania mexicana mexicana***

**Known geographic areas:**
The Yucatan, Mexico; Belize; Guatemala.

**Known natural hosts:**
Forest rodents—*Otoylomys phyllosis, Heteromys desmarestiani, Nyctomys sumichrasti, Sigmodon hispidus*

**Vectors:**
*Lutzomyia olmeca*

**Disease in man:**
Common in man, cause of Chiclero’s ulcer; single or limited number of skin lesions, with frequent involvement of ear tissue; no nasopharyngeal lesions or other metastases; rare cases reported of diffuse cutaneous leishmaniasis.

**TABLE 3A—*Leishmania mexicana amazonensis***

**Known geographic areas:**
The Amazon Basin and Mato Grosso, Brazil; the Island of Trinidad; probably extends throughout Brazil in areas where the vector occurs.

**Known natural hosts:**
Forest rodents and marsupials—*Oryzomys capito, O. concolor, O. macconnelli, Proechimys gypsianensis, Heteromys amalals, Neacomys spinosus, Nectomys squamipes, Dasyprocta spp., Marmosa murina, M. mitis, Caluromys philander, Metachiron medicaudatus*

**Vectors:**
*Lutzomyia flaviscutellata*

**Disease in man:**
Rarely infects man because the vector is not anthropophilic; single or limited number of skin lesions; no preference for ear tissue and no nasopharyngeal involvement; several cases of diffuse cutaneous leishmaniasis due to this parasite recorded in Pará State, Brazil.

**TABLE 4A—*Leishmania mexicana pifanoi***

**Known geographic areas:**
Venezuela

**Natural hosts:**
Probably forest rodents—*Zygodontomys microtinus and Proechimys guyannensis* have been found with tail lesions containing amastigotes

**Vectors:**
Unknown

**Disease in man:**
So far only reported to have caused a few cases of diffuse cutaneous leishmaniasis.

**TABLE 5A—*Leishmania mexicana subspecies***

**Known geographic areas:**
Panama

**Known natural hosts:**
Forest rodents and marsupials—*Oryzomys capito, Proechimys semispinosus, Diplomys labilis, Agouti paca, Marmosa robinsoni*

**Vectors:**
*Lutzomyia flaviscutellata*

**Disease in man:**
Rarely infects man because the vector is not anthropophilic; single or limited number of skin lesions; no preference for ear tissue and no nasopharyngeal involvement; several cases of diffuse cutaneous leishmaniasis due to this parasite recorded in Pará State, Brazil.

**TABLE 6A—*Leishmania enriettii***

**Known geographic areas:**
Curitiba, Paraná State, Brazil

**Known natural hosts:**
Unknown; discovered in a colony of laboratory guinea pigs (*Cavia porcellus*), but will not infect wild guinea pigs (*Cavia aperea*)

**Vectors:**
Unknown

**Disease in man:**
Not yet described
II. The *L. braziliensis* complex

**TABLE 7A—Leishmania braziliensis braziliensis**

**Known geographic areas:**
Brazil, eastern Peru, Ecuador, Bolivia, Venezuela, Paraguay, Colombia

**Known natural hosts:**
Poorly known. Forest rodents *Oryzomys concolor* (Mato Grosso); *O. nigripes*, *O. capito laticeps*, and *Akodon arviculoides* (São Paulo State, Brazil)

**Vectors:**
(a) Proven by isolation of *L. b. braziliensis* after inoculation of hamster with flagellates from sandflies: *Psychodopygus wellcomei* in Pará State, Brazil; and *Lutzomyia pessoai* and *Lu. intermedius* in São Paulo State, Brazil
(b) Indicated only by microscopic evidence of promastigotes: *Ps. paraensis*, *Ps. amazonensis* in Pará State; *Lutzomyia migonei*, *Lu. whitmani* in southern Brazil; *Lu. anduzei* in Venezuela

**Disease in man:**
Lesions are usually single or few in number, but frequently very large, persistent and disfiguring; metastases to nasopharyngeal tissues (espundia) is a common sequel

**TABLE 8A—Leishmania braziliensis guyanensis**

**Known geographic areas:**
The Guianas; Amapá, Roraima, Pará, and Amazonas in northern Brazil

**Natural hosts:**
Unknown

**Vectors:**
Promastigotes found in *Lutzomyia anduzei*, but not yet proven to be *L. b. guyanensis* by hamster inoculation

**Disease in man:**
Pian-bois; single skin lesions, frequently with metastatic spread along lymphatics producing ulcers all over the body; rare cases of mucocutaneous leishmaniasis were probably due to geographic overlap with *L. b. braziliensis*

**TABLE 9A—Leishmania braziliensis panamensis**

**Known geographic areas:**
Panama, possibly extending into Central America in the north and Colombia in the south

**Known natural hosts:**
Forested rodents—*Proechimys semispinosus* and *Hopomys gymnurus*; marmoset—*Saguinus geoffroyi*; procyonids—*Potos flavus* and *Bassaricyon gabbii*; sloths—*Choeloeopus hoffmani* and *Bradypus infuscatus*; it is not certain that all these species were infected with the same parasite

**Vectors:**
Proven by inoculation of hamsters with flagellates from infected sandflies: *Lutzomyia trapidoi*, *Lu. ylephiletrix*, *Lu. gomezi*, and *Psychodopygus panaensis*

**Disease in man:**
Usually causes a single ulcer, but may sometimes spread via lymphatics; nasal involvement is rarely reported and may be due to vector bite on the nose rather than metastatic spread

**TABLE 10A—Leishmania peruviana**

**Known geographic areas:**
Western Peruvian Andes; the only known form of New World cutaneous leishmaniasis not associated with forests

**Known natural hosts:**
Domestic dog; no wild hosts known

**Vectors:**
Uncertain; *Lutzomyia verrucarum* and *Lu. peruensis* are suspected

**Disease in man:**
Uta—single or limited skin lesions which are self-healing; no nasopharyngeal involvement

**TABLE 11A—Leishmania hertigi**

**Known geographic areas:**
Panama

**Known natural hosts:**
The procupine *Coendou rothschildi*

**Vectors:**
Unknown

**Disease in man:**
Not yet described
REFERENCES