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CUTANEOUS LEISHMANIASIS IN FRENCH GUIANA: A REVIEW

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Abstract. A review of a 10 year investigation carried out by various institutions on cutaneous leishmaniasis in French Guiana is presented, with emphasis on epidemiology, clinical aspects, and therapy.

Located at the very top of South America, French Guiana is a 90,000 km² territory belonging to the Northern part of the Amazonian region. Its weather is equatorial with a long rainy season (December–July) alternating with a dry season (August–November). The rainfall is abundant throughout the country, ranging from 3,750 mm/year in the Northeast to 2,250–2,500 mm/year in other parts of the territory. With the exception of a narrow coastal fringe of savanna <30 km deep, the territory is covered with primary rain forest. The country is sparsely populated (73,022 people at the 1982 census) and the developed areas are along the sea coast and the banks of the main rivers.

Cutaneous leishmaniasis is a nosological entity well known among the primitive populations of French Guiana, Amerindians, and Bush Negroes, who have specific names for the disease in their languages.[1] The disease was locally called "pian bois" by the creole population and was well known at the time of the gold seekers. The first parasitologically confirmed case was described in 1943 by Floch[2] and the parasite called *Leishmania guyanensis*.[3] Human cases have been recorded regularly; 83 cases were diagnosed between 1943 and 1951, half of them parasitologically confirmed. Since 1977, the number of cases diagnosed has increased and the disease has become a public health problem among people in contact with the forest.

A joint research program was begun in 1978 by the Institut Pasteur de la Guyane française, the Centre ORSTOM, and the Dermatology Department of the Hospital Jean Martial of Cayenne. It continued until 1988 and dealt with the epidemiological features of the disease and its transmission, clinical characteristics, and therapeutic aspects. This collaborative program has yielded numerous publications. Our knowledge has matured to the point where a synthesis of these data is desirable in order to provide a comprehensive review of cutaneous leishmaniasis in French Guiana.

ECOLOGY OF THE PATHOGENIC COMPLEXES

Parasites

Two species of *Leishmania* have been isolated in French Guiana, parasitizing distinct natural hosts: *L. braziliensis guyanensis* and *L. mexicana amazonensis*. They belong to 2 different complexes, according to the Lainson and Shaw classification,[4] and can be distinguished by several phenotypic characters (main diameter of amastigotes, culture growth, behavior in hamster) and isoenzyme characterization. Of 112 *Leishmania* isolates obtained in French Guiana from human lesions (91 with multiple geographic contamination sites), phlebotomine sand flies (11), and wild mammals (10), Desjeux and Dedet[5] found 103 isolates related to *L. b. guyanensis*; of these, 88 were from human cases. Only 7 related to *L. m. amazonensis*: 3 from patients, 3 from *Proechimys,* and 1 from *Lutzomyia flaviscutellata*. Two isolates obtained from the sand fly *Lu. umbratilis* differed from the reference strains used. Three distinct zymodemes were distinguished within the *L. b. guyanensis* taxon by variations of 2 enzymes.[5]

Vectors

Seventy-four different sand fly species have been found in French Guiana, mainly in the *Lutzomyia* genus (71 species), but the *Brumptomyia* and *Warileya* genus are also present. A list of species has been established and a computer aided identification program of sand flies of French Guiana has recently been published.[6] Only 4 species (all belonging to the *Nyssomyia* sub-genus) have been found to harbor *Leishmania* promastigotes. These remain unidentified in the case

of *Lu. gomezi* and *Lu. yuilli pajoti*. *Lu. umbratilis* has been regularly found naturally infected by promastigotes (93 infected females out of 5,083 collected in a single sylvatic site in the Montsinery vicinity and then dissected [1.83%]), characterized by isoenzyme electrophoresis as *L. b. guyanensis* in 8 cases.[5,7] A single specimen of *Lu. flaviscutellata* out of 254 dissected has been found infected by *L. m. amazonensis*.[8]

Lu. umbratilis is the most common species found on human beings[7,9] and on tree trunks[10] in French Guiana. It is an arboreal sand fly, more abundant in the canopy than at ground level,[9] but it is present at ground level all year round, with seasonal and inter-annual fluctuations.[7] Infected aggressive females were collected at ground level all year round, but especially at the end of the dry season.[7] *Lu. umbratilis* is an opportunistic sand fly attracted by various species of mammals, including humans, on which it feeds. Le Pont and Pajot showed that 100% of the females in contact with the sloth *Choloepus didactylus* fed rapidly and heavily.[9]

Reservoirs

The 2-toed sloth, *C. didactylus,* has been found infected by *L. b. guyanensis* in French Guiana[11] and in the Pará State of Brazil.[12] From a sample of 486 wild mammals collected at 13 different sites and examined between 1981 and 1987, including marsupials, edentates, and rodents, the following species were found to harbor *L. b. guyanensis*: *C. didactylus* (11/31), the marsupial *Didelphis marsupialis* (2/122), and the rodent *Proechimys* sp. (2/89).[13] From these observations, *C. didactylus* appears as a primary reservoir of *L. b. guyanensis* in French Guiana as in other parts of the northern Amazonian Basin. In the Pará State of Brazil, *Tamandua tetradactyla* was found acting as reservoir of *L. b. guyanensis*.[12] *D. marsupialis* and *Proechimys* act in French Guiana as occasional hosts of *L. b. guyanensis,* as they do in the Pará State of Brazil.[14] In the central amazon region of Brazil, *D. marsupialis* is assumed to be the main reservoir.[15]

L. m. amazonensis was isolated from normal skin of 3 *Proechimys* out of 95 examined, 2 of which were identified as *Proechimys cuvieri*.[13]

Epidemiological synthesis

There exist in French Guiana at least 2 distinct cycles of leishmaniasis. Both occur in the rain forest, but at 2 different altitudinal levels. There is a *L. b. guyanensis* cycle, located in the canopy with the arboreal sand fly *Lu. umbratilis* as the vector and at least 1 mammal of the canopy, the sloth, as a reservoir, and a *L. m. amazonensis* cycle, which occurs at ground level with *Lu. flaviscutellata* as the vector and *P. cuvieri* as the reservoir.

TRANSMISSION CONDITIONS

The parasite life cycles develop in the forest and a human infection in French Guiana results from incursions into the forest. In a sample of 219 patients, Dedet and others[1] determined that those infected were young male adults (mean age 28.8 ± 9.2 years) who enter the forest for professional (84.2%) or leisure (15.8%) activities.

Exposure occurs throughout the territory, with a higher density of cases in an area located inside the 3,500 mm isohyet. This is also the most regularly visited part of the country, due to the proximity of the main town, Cayenne.[1]

Deforestation appears to be a favorable factor for the multiplication of sand flies, especially of the *Nyssomyia* sub-genus, which includes the 2 leishmaniasis vectors of French Guiana.[16] Infection resulting from bites occurs at dusk or during the night and corresponds to the activity period of *Lu. umbratilis*.[9] However, cutting down the trees lead to immediate aggression by sandflies and diurnal contamination.

The major transmission periods occur during periods of low rainfall, i.e., October–December, and represent the high-risk season in French Guiana.[1] The establishment of human settlements in the forest has given rise to specific transmission process, with intradomiciliary contamination[17] occurring by infected sand flies flying at night from the neighboring forest to human housing.[18]

HUMAN DISEASE

The yearly registration of cutaneous leishmaniasis cases obtained from the files of the Institut Pasteur de Guyane française and the dermatology department of the hospital of Cayenne showed a remarkably constant annual incidence of ~2.3/1,000 inhabitants (statistics for 8 years, 1979–1986).[1] The disease has an important socio-economic impact on the development of the country due to its direct cost (0.13% of the gen-

eral budget in 1979–1980) and to its influence on the productive sector of the local economy (unpublished data).

The human disease results from penetration of the parasite through the bite of an infected sand fly. The sand flies bite exclusively on parts of the body not protected by clothing.[19] Factors which could explain individual susceptibility to leishmania infection were investigated, but neither cutaneous factors[20] nor blood group types[21] appeared to be important.

All the cases seen in French Guiana were lesions of the skin, without any mucous secondary involvement. A reference from 1965[22] reports a case from French Guiana with coexistence of cutaneous and mucous *Leishmania* lesions, but no strain was isolated at that time and the responsible species remains unknown. To our knowledge, there is no documented case of mucous involvement due to *L. b. guyanensis* either in French Guiana or in neighboring countries (in contrast to infections with *L. b. panamensis* sp.). The lesions are generally of the classic ulcerative wet type (92.1%). The ulcer is covered with a scab in 30.9% of the cases and surrounded by small peripheral papulae in 19.8%. In ~30% of the cases, subcutaneous lymphangitic extension occurs and manifests as a chain of small subcutaneous nodules located on the draining territory of the cutaneous lesion.[1] The lesions are preferentially located on the legs and forearms (20.7% and 19.8% of cases, respectively). Patients may harbor both simple (40.8%) or multiple lesions. The mean number of lesions/patient was 3.6 in a sample of 211 patients.[1]

Of 91 isolates obtained from human lesions, 88 were characterized as *L. b. guyanensis* by isoenzyme characterization and only 3 as *L. m. amazonensis.*[5] Cases due to *L. m. amazonensis* exhibited limited cutaneous lesions, of ulcerative or nodular type, without any tendency to disseminate.[23] Spontaneous evolution is difficult to follow in French Guiana, where cases are systematically treated. In 1 case, we had the opportunity of following a spontaneous evolution with self cure appearing at 30 months.[1]

The majority of the cases were treated with meglumine antimoniate with doses of 30 mg Sb^{+5}/kg body weight/day for 12–15 days. With this treatment, Pradinaud[24] reported ~100% recovery with few benign side effects, particularly the absence of fatal alteration of cardiac rhythm or cardiac arrest.

Since 1980, the treatment has been changed by local physicians and meglumine antimoniate replaced by pentamidine mesylate administered im with a variable regimen.[25] The most common and efficient regimen (99.3% of recovery) consists of 3.5 mg base/kg/day on successive days 3 times (total dose of 720 mg base/series). The most serious side effect observed was diabetes mellitus (2 cases in 416 observations; E. Drillaud, Faculté de Médecine, 3ter place de la Victoire, 33000 Bordeaux, France, personal communication). The therapeutic change gives comparable efficacy with a 70% reduction in the total cost of leishmaniasis in French Guiana. After a cure by either product, relapses (i.e., recurrence of an active lesion at the site of one previously cured) occurred in ~7% of the cases 2 months–3 years after the cure.[1]

Clinical trials of imidazoles were conducted in French Guiana. Ketoconazole was ineffective in *L. b. guyanensis* cutaneous leishmaniasis.[26,27] Metronidazole also was without effect.[24] Individual antimalarial prophylaxis with chloroquine or amodiaquine did not prevent leishmanial infection by *L. b. guyanensis*.[28]

Insect repellents are of limited efficacy, due to the very high humidity in the forest, but wearing thin clothing is recommended as an individual prophylactic measure.[19] In human settlements established in the forest, a preventive measure consisting of a 400 m forest-free belt around the settlements has been proposed by Esterre and others.[29]

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REFERENCES

1. Dedet JP, Pradinaud R, Gay F, 1989. Epidemiological aspects of human cutaneous leishmaniasis in French Guiana. *Trans R Soc Trop Med Hyg 83:* 616–620.
2. Floch H, 1943. Rapport sur le fonctionnement technique de l'Institut Pasteur de la Guyane francaise et du territoire de l'Inini pendant l'annee 1943. *Inst Pasteur Guyane frse Terr Inini 75:* 79.
3. Floch H, 1954. Leishmania tropica guyanensis n. sp. agent de la leishmaniose tegumentaire des Guyanes et de l'Amerique centrale. *Ann Parasitol Hum Comp 38:* 784–787.

4. Lainson R, Shaw JJ, 1979. The role of animals in the epidemiology of South American leishmaniasis. Lumsden WHR, Evans DA, eds. *Biology of the Kinetoplastida.* New York: Academic Press, 1–116. UI:7700171
5. Desjeux P, Dedet JP, 1989. Isoenzyme characterization of 112 Leishmania isolates obtained in French Guiana. *Trans R Soc Trop Med Hyg 83:* 610–612.
6. Lebbe J, Vignes R, Dedet JP, 1987. *Identification assisted par ordinateur des phlebotomes de Guyane francaise/Computer aided identification of phlebotomine sandflies of french Guiana (Diptera: Psychodidae).* France: Inst Pasteur de Guyane francaise Ed.
7. Pajot FX, Chippaux JP, Geoffroy B, Dedet JP, 1986. La leishmaniose en Guyane francaise. 6. Fluctuations saisonnieres de la densite et du taux d'infection naturelle de Lutzomyia (Nyssomyia) umbratilis Ward et Fraiha, 1977 en foret degradee. *Cah ORSTOM ser Ent Med Parsitol 24:* 191–198.
8. Dedet JP, Pajot FX, Desjeux P, Goyot P, Chippaux JP, Geoffroy B, 1985. Natural hosts of Leishmania mexicana amazonensis Lainson and Shaw, 1972 (Kinetoplastida: Trypanosomatidae) in French Guiana. *Trans R Soc Trop Med Hyg 79:* 302–305. UI:85301387
9. Le Pont F, Pajot FX, 1980. La leishmaniose en Guyane francaise. 1. Etude de l'ecologie et du taux d'infection naturelle du vecteur Lutzomyia (Nyssomyia) umbratilis en saison seche. Considerations epidemiologiques. *Cah ORSTOM ser Ent Med Parasitol 18:* 359–382.
10. Geoffroy B, Dedet JP, Lebbe J, Esterre P, Trape JF, 1986. [Note on the relations between vectors of leishmaniasis and forest trees in French Guiana]. *Ann Parasitol Hum Comp 61:* 483–490. UI:87126520
11. Gentile B, Le Pont F, Pajot FX, Besnard R, 1981. Dermal leishmaniasis in French Guiana: the sloth (Choloepus didactylus) as a reservoir host. *Trans R Soc Trop Med Hyg 75:* 612–613. UI:82108710
12. Lainson R, Shaw JJ, Povoa M, 1981. The importance of edentates (sloths and anteaters) as primary reservoirs of Leishmania braziliensis guyanensis, causative agent of "pianbois" in north Brazil. *Trans R Soc Trop Med Hyg 75(4):* 611–612. UI:82108709
13. Dedet JP, Gay F, Chatenay G, 1989. Isolation of Leishmania species from wild mammals in French Guiana. *Trans R Soc Trop Med Hyg 83:* 613–615.
14. Lainson R, Shaw JJ, Ready PD, Miles MA, Povoa M, 1981. Leishmaniasis in Brazil: XVI. Isolation and identification of Leishmania species from sandflies, wild mammals and man in north Para State, with particular reference to L. braziliensis guyanensis causative agent of "pianbois." *Trans R Soc Trop Med Hyg 75:* 530–536. UI:82108685
15. Arias JR, Naiff RD, 1981. The principal reservoir host of cutaneous leishmaniasis in the urban areas of Manaus, Central Amazon of Brazil. *Mem Inst Oswaldo Cruz 76:* 279–286. UI:83088038
16. Alexandre DY, Dedet JP, Esterre P, 1987. La leishmaniose en Guyane francaise. 7. Caracteristiques structurales de quelques sites de contamination humaine en foret. *Cah ORSTOM ser Ent Med Parasitol 25:* 101–109.
17. Le Pont F, Pajot FX, 1981. La leishmaniose en Guyane francaise. 2. Modalites de la transmission dans un village forestier: Cacao. *Cah ORSTOM ser Ent Med Parasitol 19:* 223–231.
18. Chippaux JP, Pajot FX, Barbier D, 1984. La leishmaniose en Guyane francaise. 5. Note complementaire sur l'ecologie du vecteur dans le village forestier de Cacao. *Cah ORSTOM ser Ent Med Parasitol 22:* 213–218.
19. Dedet JP, Esterre P, Pradinaud R, 1987. Individual clothing prophylaxis of cutaneous leishmaniasis in the Amazonian area. *Trans R Soc Trop Med Hyg 81:* 748. UI:88219099
20. Esterre P, Ridel PR, Jamet P, Dedet JP, 1987. Cutaneous factors in susceptibility to American cutaneous leishmaniasis. *Trans R Soc Trop Med Hyg 81:* 160. UI:88178906
21. Esterre P, Dedet JP, 1989. Relationships of American cutaneous leishmaniasis to blood group types. *Ann Trop Med Parasitol 83:* 345–348.
22. Chalchat P, Colas-Belcour J, Destombes P, Drouhet E, Fromentin H, Martin L, Ravisse P, Silverie J, 1965. A propos d'un cas guyanais de leishmaniose cutaneo-muqueuse resistant aux antimoniaux et gueri par l'Amphotericine B. *Bull Soc Path Exot 58:* 73–80.
23. Dedet JP, Pradinaud R, Desjeux P, Jacquet-Viallet P, Girardeau I, Esterre P, Gotz W, 1985. [The 2 first cases of cutaneous leishmaniasis due to Leishmania mexicana amazonensis in French Guiana]. *Bull Soc Pathol Exot Filiales 48:* 64–70. UI:85177216
24. Pradinaud R, 1979. Le risque de leishmaniose chez le touriste en Guyane. *Med Afr Noire 26:* 283–286.
25. Pradinaud R, Girardeau I, Sainte-Marie D, 1985. A pentamidina, excelente terapeutica da leishmaniose cutanea. Esquema de tratamento idealizado na Guiana Francesa em dose unica. *An Bras Dermatol 60:* 385–387.
26. Dedet JP, Jamet P, Esterre P, Ghipponi PM, Genin C, Lalande G, 1986. Failure to cure Leishmania braziliensis guyanensis cutaneous leishmaniasis with oral ketoconazole. *Trans R Soc Trop Med Hyg 80:* 176. UI:86262709
27. Dedet JP, Jamet P, Esterre P, Ghipponi PM, Genin C, Lalande G, Gay F, 1987. Echec du ketoconazole dans le traitement de la leishmaniose cutanee a Leishmania braziliensis guyanensis en Guyane francaise. *Med Mal Infect 17:* 4–8.
28. Dedet JP, Esterre P, 1986. Lack of effect of antimalarial prophylaxis with chloroquine or amodiaquine in cutaneous leishmaniasis in French Guiana. *Trans R Soc Trop Med Hyg 80:* 490. UI:87095233
29. Esterre P, Chippaux JP, Lefait JF, Dedet JP, 1986. [Evaluation of a cutaneous leishmaniasis control program in a forest village of French Guyana]. *Bull World Health Organ 64:* 559–565. UI: 87051978