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American cutaneous leishmaniasis in French Guiana: an epidemiological update and study of environmental risk factors

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Abstract

Background American cutaneous leishmaniasis (ACL) is endemic in French Guiana. Its epidemiology is evolving, notably because of immigration, anthropization of natural areas, and new microbiological methods. Our first objective was to update epidemiological data. Our second objective was to look for risk factors of ACL.

Methods This multicentric study was conducted from October 2017 to June 2018 in French Guiana. Patients with suspicion of mucocutaneous leishmaniasis were included in case of positive smear, culture, or PCR-RFLP on skin biopsy.

Results One hundred and twenty-three patients met the inclusion criteria. Among those patients, 59.3% were Brazilian, mostly gold miners. Most of them (58%) were between 16 and 40 years old, and 69% were male. A large proportion of patients lived in traditional wooden houses (51%). Patients living in coastal towns were usually infected during trips to the primary forest (60%) and had a shorter time to diagnosis than workers of the hinterland. Among environmental risk factors, the presence of a water spring (40%) and dogs around houses (40%) were frequently reported. *Leishmania guyanensis* represented 80% of cases, followed by *Leishmania braziliensis* (6%), *Leishmania naiffi* (2%), and *Leishmania amazonensis* (1%).

Conclusions Gold mining and trips to the primary forest represent high-risk situations for ACL in French Guiana, where the population of infected patients is dominated by Brazilian immigrants. Possible environmental risk factors such as the presence of dogs, water sources, and traditional wooden houses require further investigation.

Introduction

American cutaneous leishmaniasis (ACL) is endemic in many tropical countries around the world.[1,2] This neglected tropical disease involves a great range of species, hosts, and vectors across the continents. In the Americas, the World Health Organization (WHO) considers it as a major public health disease.[3] Mucocutaneous forms are characterized by an important severity, as they cause long-lasting and debilitating injuries.[4,5]

In French Guiana, five species have been incriminated, the two most frequent being *Leishmania* (*Vianna*) *guyanensis* and *Leishmania* (*Vianna*) *braziliensis.* However, a possible shift toward a greater prevalence of *Leishmania braziliensis* has been reported in previous studies[6] and needs to be followed up.

New species such as *Leishmania lainsoni* and *Leishmania naiffi* have been sporadically reported,[6–11] but the clinical data of these patients were not thoroughly studied. Epidemiological data are frequently updated with new techniques of species identification. Simon *et al* produced the last study on this subject in 2017,[6] establishing the utility of polymerase chain reaction-restriction fragment length polymorphism (PCR-RFLP), and describing a possible increase of *L. braziliensis* after Brazilian immigration. Since then, the introduction of Matrix-Assisted Laser Desorption/Ionization (MALDI-TOF) in French Guiana offers another tool for species identification.

French Guiana is divided into two different ecological regions. The hinterland is covered by primary rain forest, with few human settlements, mostly illegal gold mines. The coastal region covers the north of the territory and is more anthropized.[8,11,12] It has been suggested in previous studies that contamination occurred during professional activities in the hinterland and during leisure activities on the coast.[11] These data deserve update and confirmation. Several studies have looked for risk factors of ACL in the world[12–14] and in South America,[15–19] incriminating factors linked to agriculture, water sources, or animals closed to human settlements. However, such a work has never been conducted in French Guiana.

Therefore, our first objective was to update clinical and epidemiological data concerning ACL in French Guiana. Our second objective was to look for geographic and behavioral risk factors of the infection.

Materials and methods

This study was conducted in 10 health centers for remote areas and in the General Hospital of Cayenne from October 2017 to June 2018, as this period corresponds to the wet season during which most cases of ACL occur.[8,10,20] Information files with epidemiological and clinical data were filled in by nurses or physicians for each suspected case of ACL. Patients were included when one of the following tests was positive: smear, culture from skin biopsy, PCR-RFLP from skin biopsy.[6] Species isolation was made by MALDI-TOF from positive cultures or by PCR-RFLP from skin biopsy.

PCR-RFLP was performed using the technique first described by Simon *et al*[7] in 2009, using a 615-bp fragment of the RNA polymerase II gene. Since then, this technique has become the reference method for species identification in French Guiana.[6] Mass spectrometry was performed on positive parasite cultures as previously reported.[21]

The study was performed according to the Declaration of Helsinki protocols. Data were collected as part of the usual research and surveillance system of the National Reference Center for Cutaneous Leishmaniasis (associate laboratory), which was settled in the Hospital of Cayenne with the approval of the ethical board.

Results

During the study period, samples were collected among 168 patients with clinical suspicion of cutaneous leishmaniasis. One hundred and twenty-three patients (73.2%) had positive samples (38 women and 85 men, sex ratio 2.18) and constituted the study population. Concerning the country of birth, the most important group was formed by Brazilian patients (73, 59.3%), followed by patients born in French Guiana (35, 28.5%), mainland France (11, 8.9%), Laos (2, 1.6%), and Haiti (2, 1.6%). Mean time to diagnosis was 2 months; most patients (80%) were diagnosed within a month. Mean time to diagnosis was significantly longer ($P = 0.01$) for patients infected in the hinterland (2.3 months) than for patients infected on the coast (1.6 months). HIV serology was positive for two patients. Sociodemographic and clinical characteristics of patients are detailed in Table 1.

Leishmania guyanensis was the most frequent species involved (98, 80%), followed by *L. braziliensis* (7, 6%), *L. naiffi* (2, 2%), and *L. amazonensis* (1, 1%). In 15 cases, (12%) species identification was not achievable. Patients infected with *L. braziliensis* included three gold miners contaminated on their gold camps, two soldiers infected while on duty in the forest, one doctor hunting frogs in a swamp, and an agronomy student infected during field work in a secondary forest. One case of *L. amazonensis* was recorded as a single nodule in a gold miner. Two cases of *L. naiffi* were recorded. Both patients presented a single lesion of the arm and complained of very mild symptoms but were subsequently lost to follow-up.

Concerning clinical variability, *L. guyanensis* was more frequently responsible for multiple lesions (48 cases, 49%) than *L. braziliensis* (one case, 14%). There was no case of mucosal infection. The mean number of lesions for coastal forms of *L. guyanensis* was 2.5, significantly lower than the hinterland (mean number 3.4, $P = 0.01$). Another feature of the *L. braziliensis* infection was a higher male predominance (sex ratio 6) compared to *L. guyanensis* (sex ratio 1.72).

Concerning risk factors and environmental data, most contaminations occurred during professional activities for gold miners (91%), soldiers (75%), and farmers (100%). Infections occurred during leisure activities for most coastal citizen workers (57%). Many cases were recorded in people living in urban settings (50%) who were probably contaminated during trips in the primary forest (60% of them). On the other hand, patients living in the countryside were infected close to home in 70% of cases. One concomitant infection in two members of the same family was recorded in a mother and her son living on the coast. Other data on clinical, behavioral, and environmental risk factors of ACL are detailed in Table 2. Thirty patients (40%) had a water spring within 100 m of their houses. Thirty-three patients (45%) reported dogs around their houses; 42 (51%) lived in traditional wooden houses called *carbet*.

Table 1 Sociodemographic and clinical characteristics of 123 patients with confirmed Cutaneous Leishmaniasis in French Guiana, October 2017–June 2018

	Number of patients (%)
Mean age (year)	34
Age categories (year)	
	9 (7)
17–25	19 (16)
26–40	51 (42)
41–75	43 (36)
>75 years	1 (1)
Gender	
Female	38 (31)
Male	85 (69)
Gender ratio (M/F)	2.18
Profession	
Farmer	1/91 (1)
Own account workers	1/91 (1)
Higher professional occupation	7/91 (8)
Intermediate occupation	11/91 (12)
Employee	4/91 (4)
Worker	7/91 (8)
Retiree	2/91 (2)
Unemployed, student	11/91 (12)
Gold miners	44/91 (48)
Number of lesions	
Unique	63 (51)
Multiple	60 (49)
Mean number	3, 12
Lesion locations	
Head	15 (12)
Upper limbs	50 (41)
Trunk	23 (19)
Lower limbs	67 (55)
Clinical presentation	
Ulceration	110 (91)
Nodule	16 (13)
Ulcerations and nodules	13 (11)
Other	4 (3)
Average time to diagnosis (months)	6 (5)
HIV-seropositive	2 (2)

Five patients had disseminated leishmaniasis, four of them caused by *Leishmania guyanensis*. In the last case, the species could not be determined.

Table 2 Clinical, behavioral, and environmental risk factors of cutaneous leishmaniasis

	All species (%)
Previous history of LC	
Personal	12/97 (12)
Familial	14/96 (15)
Setting	
Urban	26/102 (25)
Rural	31/102 (30)
Gold mining camp	44/102 (43)
Agricultural activity	2/76 (3)
<100 m	18/77 (23)
>100 m	9/77 (12)
Water spring	
<100 m	30/75 (40)
>100 m	12/75 (16)
Animals inside houses	
Dogs	29/72 (40)
Cats	12/72 (17)
Others	9/72 (13)
Animals around houses	
Sloths	13/74 (18)
Dogs	33/74 (45)
Cats	20/74 (27)
Rats	30/74 (41)
Chicken	19/74 (26)
Others	3/74 (4)
Other people in house	45/65 (70)
Average number of people in house	3.3
Types of housing	
Townhouse	21/83 (25)
Creole house	17/83 (20)
Carbet	42/83 (51)
Township	3/83 (4)
House accessibility	
Accessible by car	33/64 (51)
Only by boat/walking	11/64 (17)

Discussion

This study offers new insight into the clinical and epidemiological features of ACL in French Guiana. Wet ulceration was the most frequent clinical presentation, therefore contrasting with the dry and crusty ulcers caused by *L. infantum*, *L. tropica*, or *L. major*[22] in North Africa. Most lesions were localized on the upper or lower limbs (Table 1), probably because of the preference of vectors for uncovered areas.[8,23] Peridomiciliary contamination, which is usually associated with lesions on covered areas,[24] was rare among our patients. The absence of mucosal involvement was concordant with the findings of Dedet *et al*[8] in 1989.

Concerning medical histories of our patients, 12% of them presented a personal history of ACL (Table 2). Similar figures have been described in other parts of the world.[13] Infection-induced immunity after ACL is known to be unstable and quite unpredictable.[25] This tendency to develop several infections in a lifetime probably reflects a continued exposition to risk factors in the same individual. Among our patients, only 15% had a familial history of ACL, which may be surprising as families share common risk factors. The establishment of human settlements in the forest may give rise to intradomiciliary contamination.[26] However, we reported only one case of concomitant infection in two members of the same family. Gold miners and soldiers do not bring their families with them on places of contamination, which could explain why familial clusters were so rare.

Our findings allow us to draw a profile of the typical person at risk of ACL as a male Brazilian in his 30s involved in outdoor occupational or leisure activities. Indeed, sex ratio (2.18) and mean age (34) in this study confirm previous findings and highlight young male adults as the typical targets of ACL.[8–11,27–,29] Brazilian patients represented more than half of the study population (59.3%), and 60% of them (44 patients) declared working as illegal gold miners. Though 21% of them did not declare any activity, probably by fear of legal pursuits, we might assume they also worked on gold camps as miners or sex workers. In 1989, Dedet *et al*[8] reported Europeans and Creoles as the most frequent ethnic groups infected with *Leishmania*, attributing this finding to an easier access to health care. However, the 1989 study was conducted before the rise of illegal gold mining in French Guiana, essentially performed by Brazilian immigrants. This study is an example of how population moves can influence the epidemiology of a neglected tropical disease.

Concerning the incidence of each species of *Leishmania*, our results confirm a trend which was observed in previous studies: a predominance of *L. guyanensis* but a significant presence of *L. braziliensis* (6%). Though *L. amazonensis*[6,7,9,11,30–32] was once the second most frequent species in French Guiana, we recorded only one case of this species. It has been incriminated in visceral and diffuse cutaneous forms and is known to be resistant to pentamidine.[33,34] Therefore, a close surveillance of its presence and epidemiology in French Guiana must be continued. Two cases of *L. naiffi* were reported. This species is still relatively unknown, and only a few cases have been described thus far.[35] The first reports described a benign clinical course and a good response to pentamidine.[35,36] However, recent reports suggested that *L. naiffi* could be the causative agent of more severe infections.[37] Our cases seem to confirm the first reports of *L. naiffi* and indicate a benign, pentamidine-sensitive disease. One explanation is that several strains of *L. naiffi*, with different clinical features, might be present throughout South America. Another hypothesis is that *L. naiffi* was unproperly identified in previous studies. *L. braziliensis* has been linked to small outbreaks in French Guiana and other countries of South America.[11,15,27,38] After an outbreak occurring in Saul in 2015, the emergence of *L. braziliensis* in French Guiana was given two possible explanations: a greater presence of humans in deep forest areas where transmission of *L. braziliensis* usually occurs, or the development of a peridomestic cycle with specific reservoirs and vectors.[38] Our results support the first hypothesis, as most patients infected with *L. braziliensis* seemed to be contaminated away from their homes, in less anthropized areas. Indeed, all seven cases of *L. braziliensis* occurred during occupational activities such as gold mining or soldiering, a trend already suggested in reports of *L. braziliensis* in soldiers.[27] We recorded no outbreak among our patients, and transmission of *L. braziliensis* seemed to remain stable during the rainy season.

Concerning the genetic variability of *L. guyanensis*, Rotureau *et al*[11] determined two genotypes within this species, distributed in the coastal region (Genotype 1) and the hinterland (Genotype 2). The latter was linked to chronic diseases and disseminated presentations. Our data seem to confirm this trend, as time to diagnosis (2.1 months) and number of lesions (3.4) were higher for patients infected in the hinterland. However, patients living on the coastal region benefit from a better access to healthcare, which might explain the shorter duration of disease.

In this study, people living in carbet (traditional, wooden, wall-less shelter) represented 51% of cases of ACL, though this type of housing represents only 20% of homes in French Guiana.[39] Quality of housing has been incriminated as a risk factor for several species of ACL in South America.[16,17,19,40] In Brazil, Membrive *et al*[16] showed that ACL was significantly associated with the absence of ceiling below the roof of the residence, as in Amerindian carbet. However, some authors argued that the vicinity of the forest, more than the building style, was to be incriminated in this kind of houses, which are mostly found in secondary forest areas.[17] A larger study including a multivariate analysis could determine if housing style remains a risk factor independently of the environmental setting.

Concerning the presence of animals around houses, sloths are usually considered as the main reservoir of *L. guyanensis* in French Guiana. However, they were spotted around houses in only 18% of cases. Dogs, on the other hand, were more frequent (40% of patients). Dogs have been suspected or incriminated as reservoirs for several *Leishmania* species,[16,30,41] and their role in the parasitic cycle still needs to be thoroughly established.

Studies of environmental risk factors in South America have linked the vicinity of streams with a higher risk of ACL.[16] Indeed, living within 100 m of a water source was a redundant feature in our patients (40%). Many reservoirs, such as water opossum (*Chironectes* sp.) or water rat (*Nectomys* spp.),[42] are known to roam around brooks and rivers. On the other hand, few of our patients (3%) were farmers, though 23% lived less than 100 m away from fields. These findings do not corroborate other studies which incriminated several cultures such as banana,[17] cacao,[18] and bamboo[40] as risk factors. The predominance of traditional polyculture in French Guiana[43] does not allow us to incriminate any specific crop. This traditional agriculture may have fewer consequences on the biodiversity of vectors and reservoirs than intensive monoculture.

There are some limitations to our study. The small number of patients and the even smaller number of *L. braziliensis* cases did not allow us to perform a complete statistical analysis. This ancillary research was not conceived as a case/control study, because of the lack of adequate controls. Missing data because of incomplete files as well as the exclusion from patients seen in the Hospital of Saint-Laurent (Lower Maroni) represented other bias. It would be interesting to perform a real case/control study over several years, to increase statistical power, by comparing households with and without ACL. However, such a study would require an improvement in logistical and safety issues in the isolated areas of French Guiana where environmental data would be collected. Although such a research might not be feasible in the near future, this study provides hints for interesting research in other settings of South America.

In conclusion, this study highlights the predominance of young male patients among cases of ACL in French Guiana. Brazilian gold miners seem particularly at risk of infection, though trips to the primary forest can trigger infections in people dwelling on the coastal region. Though *L. guyanensis* remains by far the most frequently detected species, the presence of several cases of *L. naiffi* and the clinical importance of *L. braziliensis* underline the necessity of regular epidemiological updates in French Guiana. Traditional housing and the presence of dogs and water sources around houses need to be thoroughly studied to establish their role as risk factors of ACL, as they are often reported in infected patients.

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