

VISCERAL LEISHMANIASIS IN BRAZIL: GEOGRAPHICAL DISTRIBUTION AND TRANSMISSION

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SUMMARY

After a brief historical account the Authors discuss the geographical distribution of the disease, which they correlate with the environmental conditions required by the vector, *Phlebotomus longipalpis*. They compare the importance of the known hosts of the etiological agent — man, dog and the fox *Lycalopex vetulus* — as reservoirs of the infection and refer to some aspects of the bionomics of *Phlebotomus longipalpis*. Finally, they discuss some of the distinctive epidemiological features of kala-azar in Brazil and their bearing on the prophylactic measures.

INTRODUCTION

In 1934 PENNA ⁴⁷ reported the finding of leishmania infection in liver sections of 41 people among 47,000 examined *post mortem* through viscerotomy, which was then routinely performed for the detection of yellow fever foci in Brazil. The positive samples were mostly from children and came from eight States in the Northern, Northeastern and Eastern regions. This was the first proof that visceral leishmaniasis was endemic and rather widely distributed in the Country. Interested by PENNA's report and oriented by the location of his cases, EVANDRO CHAGAS started field surveys and, in 1936, made the first *in vivo* diagnosis of a kala-azar case undoubtedly acquired in Brazil ¹³: a sixteen year old boy whose sister had been one of the viscerotomy cases. During the two subsequent years studies were made by CHAGAS and a group of co-workers ^{14, 15} (among whom the Authors of the present paper), chiefly within a limited area in the State of Pará where a few cases had been previously identified *post mortem*, and 8 new

patients were then found. The most important contributions by CHAGAS' group were the finding of infected domestic animals (7 dogs and 1 cat) and the first data indicating the possible role of *Phlebotomus longipalpis* as the vector. The fact that all infected humans and dogs dwelt within or close to the forest led to the assumption that there should exist some wild reservoir of the parasite. This, however, was not found among the several hundred mammals and other vertebrates then examined. For a while Brazilian workers assumed that the parasite was a new species, namely *Leishmania chagasi* ¹⁸, but this was later recognized as indistinguishable from *L. infantum* (= *L. donovani*) ¹⁷.

To CHAGAS the disease appeared to present singular features, which would make it differ from both the so called "Mediterranean" and "Indian" types. According to his hypothesis the parasite would have been present in the New World since pre-colum-

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bian times, dwelling in some indigenous mammal and only occasionally producing disease in man or dog living in the neighbourhood of wooded areas¹⁵.

For a long period afterwards, infection of man and dog seemed indeed occasional since few cases are to be found in medical literature for many years. Except for two small foci in the Northeastern region^{1, 48}, most of those were isolated cases found in widely distant localities or diagnosed among migrant laborers. Up to 1952, a total of 33 human infections detected *in vivo* had been reported for the whole country²⁰ — an average of less than 2 per year through the eighteen years following PENNA's report. Animal infections summed up to 8 dogs and 1 cat for the same period. Visceral leishmaniasis, thought to be of no public health importance, was all but forgotten.

In 1953, during a medical meeting in the State of Ceará, a local physician, T. C. ARACÃO⁷ reported that he had recently attended to 46 patients of visceral leishmaniasis, from the rural surroundings of his home town, Sobral. According to his statements, he and fellow physicians in the area (where malaria was known not to occur) had been for some time confronted with cases of febrile splenomegaly and anemia, with a fatal outcome. With a sudden increase of such cases, local doctors finally became aware of the nature of the disease which was confirmed through the finding of the parasite in spleen and bone marrow smears.

As scores of new cases continued to appear in the Sobral area and elsewhere, the Ministry of Health created a federal organism to reevaluate the problem, establish treatment centers and launch a control program. Between 1953 and 1961 the number of kala-azar cases in Brazilian medical journals reached a mark well above the two thousands* and many others remain unpublished since they are no longer considered a rarity.

Now, one may ask if the disease was ever such a rarity in the country. Through informations gathered among the local popula-

tion in Ceará's foci in 1953-1954, we came to the conclusion³⁴ that wala-azar was long endemic in the area and that an epidemic probably occurred about twenty years before. According to the informers — whose descriptions of the disease were surprisingly accurate — the epidemic was quite devastating for the age group under 5 years.

It was unfortunate that CHAGAS and co-workers made their studies in a region (the Amazon) which, as we presently realize, was far from typical. The importance of the problem went unrecognized and the idea widely spread that the disease was rare in Brazil. For rural doctors, who often cannot dispose of laboratories and other facilities, the identification of kala-azar was made more difficult by the frequent co-existence of endemic malaria, or schistosomiasis, or both. Finally, it must be emphasized that the endemic foci are mostly areas which only in recent years are being penetrated by roads and other items of progress. Even at the present moment it is difficult to estimate the actual distribution and prevalence of the disease, since extensive sections of the rural population are still deprived of any kind of medical assistance. However, it is worth mentioning that a recent report revealed that among 438,501 *post mortem* liver viscero-tomies performed throughout Brazil (all states), 340 leishmania infections were found, or 0.8 per thousand⁴⁵.

In 1953 an epidemiological investigation was confided to the Authors of the present paper. During 1953-1955, having studied the chief endemic area in the State of Ceará and visited other foci, we have been able to clarify some aspects of the epidemiology, mainly those concerning reservoirs and transmission.

GEOGRAPHICAL DISTRIBUTION

In Figure 1 the larger map (A) shows Brazil divided into States; the red dots correspond to counties where human cases of the disease have been identified either *post mortem* or *in vivo* during a period — 1934 to 1958 — for which complete data are available. The smaller map (B) shows the division of the country into five great regions — Northern, Northeastern, Eastern,

* For the State of Ceará alone, ALENCAR⁴ mentions 2,096 patients treated between 1953 and 1960, and also a number of cases have been reported from other States, mostly from Piauí and Bahia.

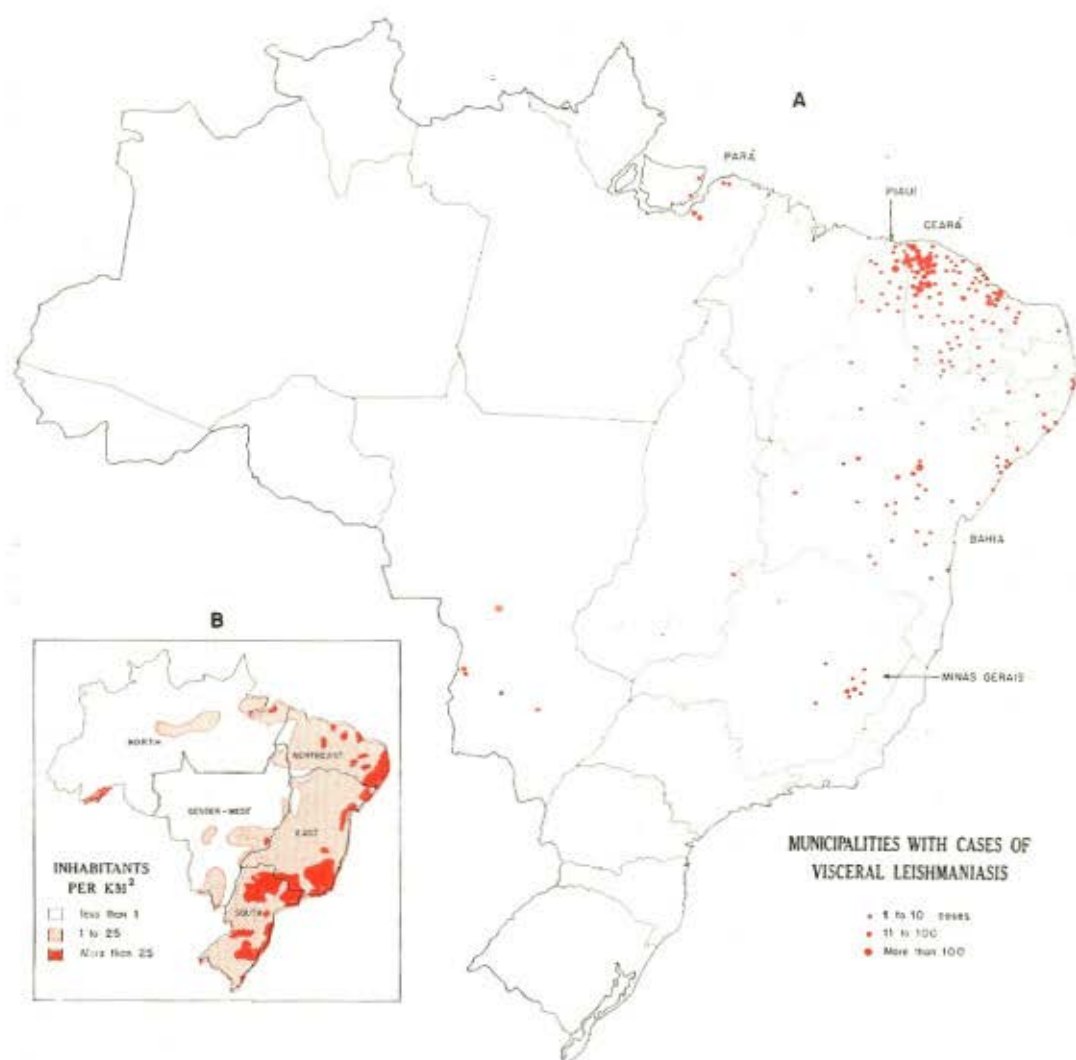


Fig. 1 — Maps of Brazil. A — Administrative division in States and Federal Territories, showing counties where human cases of visceral leishmaniasis have been diagnosed *in vivo* or *post mortem*. B — Regional division and population density.

Central-Western and Southern — and the distribution and density of the human population^{*}.

The maps give an idea about the distribution and prevalence of visceral leishmaniasis in Brazil, as it is presently known. In ap-

preciating these data, one has to bear in mind the markedly unbalanced demographic density: the Northern (i.e., Amazonian) and Central-Western regions have extensive areas practically unexplored and their population of about 0.5 inhabitants per square kilometer, contributes with only 4.2 per cent of the total for the country (1950 Official Census).

Visceral leishmaniasis has been found chiefly in the Northeastern region and the upper part of the Eastern region, with small foci in the Northern and Central-Western

* Based on data from the "Instituto Brasileiro de Geografia e Estatística". Although the "regions" do not exactly fit within geomorphic or climatic zones, they are fairly representative of distinctions in geographical landscapes, prevailing climate, population density economic development and other characteristics.

regions; the lowest part of the Eastern region and all the Southern states seem to be free of the disease. It is worth to emphasize that these are the most populated areas in Brazil and also the most developed in all aspects of human activity. The sharp difference in economical development is responsible for a steady migratory movement southwards and many cases of kala-azar have been diagnosed in southern centers, all of them among immigrant laborers or their families. So, although continuously imported, the disease apparently failed to establish itself in the Southern states.

The whole endemic area has an equatorial or tropical climate, but the main known foci are within the semi-arid zone which occupies a large part of the Northeastern region and which is subject to prolonged droughts. Here, on the dry plains locally called "ser-

In a careful study of the main endemic area in Ceará^{29, 30}, we have seen that about fifty per cent of the rural population inhabit the plains and forty per cent the plateaus. The remaining ten per cent live on the foothills ("pés-de-serra") or in valleys between hills ("boqueirões"), on lands which are much valued because they are considered good for small agriculture and cattle-raising (Figs. 3 and 4). These latter ten per cent have supplied more than 60 per cent of the kala-azar cases diagnosed in the area during a 16-month period, and the occurrence of several cases per family at the same time or in close sequency, was a common fact among them. Informations gathered among the local population led us to the conclusion that in those foothills and valleys kala-azar has been long endemic with periodical epidemic outbreaks. That in the



Fig. 2 — A view of the semi-arid plains of Northeastern Brazil (the "sertões"), where kala-azar is sporadic.

tões" (Fig. 2), stand the remains of the original, much eroded plateau — the "ser-ras" — with altitudes up to 1,000 meters.

More than 95 per cent of the human cases of kala-azar have been found among rural inhabitants or in villages that differ from the rural environment by little more than the close agglomeration of dwellings³⁴. A few patients, however, have contracted the disease in towns or the outskirts of cities.

Brazilian endemic area the foothills and valleys seem, indeed, to provide the best environment for the transmission of visceral leishmaniasis has been confirmed, both by our own and others' observations of several different foci in the States of Ceará, Piauí, Bahia and Minas Gerais^{29, 41}.

The disease is also present in the plains, specially in the more humid areas bordering the larger rivers, as, for instance, the mar-



Fig. 3 — Valleys between hills in Northeastern Brazil ("boqueirões"), where kala-azar is endemic with epidemic outbreaks.



Fig. 4 — The residence of a kala-azar case, on a foothill, State of Ceará.

gins of lower Jaguaribe River (in Ceará), or along the sea coast. On the other hand, it is rare or absent on the plateaus above 300 meters altitude.

All those peculiarities in the distribution and prevalence of visceral leishmaniasis in

Brazil, such as they are presently known, have been discussed in some detail because (as we shall see later) they seem to fit so closely within the peculiarities in the distribution and prevalence of a single species of sandfly — *Phlebotomus longipalpis*.

VERTEBRATE HOSTS

Spontaneous visceral leishmaniasis has been detected in four species of vertebrates in Brazil: man, dog, cat and the wild dog *Lycalopex vetulus*, locally known as "raposa", or fox.

Only once has visceral infection of the cat been reported here: one out of 38 specimens examined in an endemic locality in the State of Pará¹⁶. In two areas in Ceará, where the disease was frequent among the human and dog populations, all the 142 cats examined by the Authors^{27, 20} and 214 by ALENCAR *et al.*⁶ were negative. Since this animal is also difficult to infect in the laboratory²¹ and rarely bitten by the local sandfly vector²⁰, it is thought to play no role in the epidemiology of visceral leishmaniasis in Brazil and thus it shall be discussed no further.

Infection in man

This follows the same generally known pattern. However, a few facts shall be mentioned in some detail, chiefly those which are, by and large, considered as distinctive of the various "types" of kala-azar.

Age distribution. — In the foci studied in Ceará, 67 per cent of the kala-azar patients were in the 0-4 age group and 85 per cent were less than 10 years old². In other areas where the disease is less prevalent or thought to be more recent, the difference of incidence between children and adults is less sharp^{41, 21}.

Severity of infection, response to treatment. — There is almost no information about the occurrence of asymptomatic or atypical cases.

Untreated typical cases of the disease have nearly always a fatal outcome*. On the other hand, response to treatment is usually

* We have followed a case that recovered before starting treatment and after contracting typhoid fever. Both infections were well documented through spleen smears and blood cultures and both evolved to complete cure without any specific treatment. Dwellers in the endemic areas refer to a few cases who recovered after having presented symptoms identical with those of fatal cases in the same household.

very good and there is only one recorded case of possible resistance to both antimony and diamidine compounds⁵².

Parasites in peripheral blood. — Blood cultures are frequently negative and parasites are usually so scanty²⁷ that blood smears are thought to be of little use for diagnostic purposes, although a few cases have been accidentally discovered through the examination of blood smears for other purposes.

Cutaneous lesions and dermal parasitism. — Aside from the peculiar pigmentation that may be seen in some patients, macroscopical skin lesions which might be attributed to the disease seem to be quite rare in Brazilian kala-azar. Personally we made careful searches on many patients and out of 31 found with any type of skin lesion (most probably due to mycotic or staphylococcal infection), scrapings and sections were examined: only once, in a child not yet treated did we find leishmaniae, around an ulcer formed on a traumatic lesion²⁷. Another similar case has been recorded⁵³ and we have also seen the interesting case studied by PRATA & DOMINGUES⁵⁰, of a patient who, during the period of visceral involvement, presented on the limbs numerous nodular lesions richly parasitized. This patient still showed these lesions with parasites months after a prolonged treatment and an otherwise complete clinical recovery⁴⁹.

On the other hand, infection of macroscopically normal skin, during the visceral involvement, has been detected by various workers^{15, 51}. In a small series, we examined sections of one sample of each of 43 patients: in 7 the derma was parasitized, one quite heavily³⁵.

Sequellae. — Except for the above mentioned case with nodular lesions, the patients whose skin had been parasitized during visceral involvement were negative when again examined after treatment²². Typical post-kala-azar dermal leishmaniasis (e.g. cutaneous lesions appearing *after* the cure of the visceral disease) has been recorded only once in this country¹⁰.

The finding of leishmaniae in liver sections of a few patients months after clinical cure

has been reported⁴⁹ but recidives seem to be infrequent.

Diagnostic methods. — Spleen puncture, the chief method used before^{14, 15}, has been largely substituted by sternal puncture as safer for diagnostic purposes. Brazilian workers have a growing and most interesting experience with the complement fixation test using acid fast bacilli as antigen, and NUSSENZWEIG^{42, 43}, has introduced the quantitative technique. Sera of patients with Chagas' disease, tuberculosis or leprosy may give positive reactions but at much lower titers, and the test is considered very useful for early diagnosis (obviously not dispensing with the search for parasites), evaluation of cure and surveys.

Infection in dog

Through repeated examination of 156 dogs found in the small foci studied during 1937-1938 in the State of Pará, 7 infections were detected by CHAGAS and co-workers¹⁵. In the following years one more canine infection was found, in a locality in the State of Pernambuco where one human case had been diagnosed⁴⁸. Notwithstanding these findings, the actual importance of canine leishmaniasis in Brazil remained unrealized until 1953, when our studies of Ceará foci were started.

In a series of surveys²⁰ we found infection in proportions up to 8.6 per cent among dogs examined in areas with human kala-azar, and some facts indicated the possible occurrence of a previous epizootic outbreak. Several surveys were made since, by different workers^{24, 6, 8, 30, 44, 3}, and it has been found that canine leishmaniasis is at least as widely spread as the human disease.

The number of dogs examined in the whole endemic area is now of many thousands and, for the State of Ceará alone, ALENCAR⁴ gives a total of 279,423, between 1953 and 1960. The global proportion of dogs found with parasites (in skin and/or liver smears) was 1.3 per cent, but in different foci higher rates — as high as 27.5 per cent — have been recorded.

The disease among dogs is, therefore, focal as among humans and, by and large, they

are both coincident. It has been observed, however, that in larger towns or their surroundings canine leishmaniasis may be highly prevalent whereas the human disease is rare or absent, as we first pointed out²⁵. In other words, while the incidence of the human disease shows a definite rural predominance, for the canine infection the distinction between rural and urban incidence seems to be less sharp.

Naturally infected dogs may present the whole well known spectrum of clinical aspects, from the apparently healthy to the miserable final stage. Here, as elsewhere, infection in this animal is characterized by a severe attack on the skin, with heavy parasitism and various types of macroscopical lesions, besides the visceral involvement.

Diagnosis of canine leishmaniasis. —

Surveys have been made chiefly through systematic skin biopsy and liver puncture of all dogs found. However, these direct methods fail to detect all infections, specially the early ones, which, on the other hand, may be detected through the complement fixation test with tubercle bacilli antigen.

According to NUSSENZWEIG *et al.*⁴⁴ and others^{8, 4}, the CFT is much more sensitive than one microscopic examination of skin and liver smears. Among animals with positive CFT and negative smears, these were found positive in some, after new slides were made or, months later, when the disease became clinically evident. When performed in non endemic areas the test was always negative, but it is positive in dogs with trypanosomiasis⁹.

One of the chief limitations for the wide use of CFT in surveys of canine leishmaniasis being the difficulty in obtaining good samples of serum under field conditions, PELLEGRINO & BRENER⁴⁶ worked out a simple technique, using blood which is collected and dried on filter paper. The blood is taken from the border of one ear after a skin biopsy has been performed. CFT is made with eluates of the dried blood and when positive is complemented by the examination of skin smears. This method should be extremely useful for large surveys, specially when the elimination of the largest possible number of infected dogs is one of the chief

methods relied upon for the control of human leishmaniasis, as it has been the case in some Brazilian areas.

Infection in the fox "*Lycalopex vetulus*"

Without minimizing the importance of the dog in the epidemiology of visceral leishmaniasis in Brazil, we have always felt that a wild reservoir should be looked for. Indeed, isolated human cases have been found with no apparent connection with any domestic source of infection. So, as soon as our work was started in Ceará in 1953, an effort was made to have wild animals captured for examination, specially the foxes (Fig. 5) which, we had been told, were quite abundant in the area. We were fortunate enough to find infection in the very first specimen of this mammal which we had the opportunity to examine²³. During our stay in the area a total of 33 foxes were examined and 4 (12.1 per cent) were found infected^{27, 20}. They were all of the same species, identified by J. Moojen (zoologist, Museu Nacional) as *Lycalopex vetulus*. A recent paper⁴ reports the natural infection of 7 out of 173 foxes (4.4 per cent), also in Ceará, during 1960.

The distribution of parasites in the fox was as in the dog and infection develops in the same way. One of the infected animals that we studied had an entirely healthy appearance which included aggressiveness. Another specimen, on the contrary, presented all symptoms of the late stages of the disease as seen in dogs, including skin lesions, keratitis and paresis of hind legs (Fig. 6) and died in cachexia²⁰.

Other wild reservoirs of visceral leishmaniasis have been sought for in Brazil. More than one thousand wild animals — carnivores (including foxes of another species), primates, marsupials, rodents, cheiroptera and others — have been examined by various authors^{15, 48, 27, 20} without success*. However, examination of viscera smears is

* Leishman's bodies have been found in viscera of the two-toed sloth *Choloepus didactylus*, of the Amazon, but they are thought to represent a stage in the life-cycle of the endoerythrocytic crithidia *Endotrypanum schaudinni*, found in the same host²⁰.

insufficient to exclude infection, as recently demonstrated by workers in Africa^{37, 38}, and these investigations should be pursued using more sensitive methods.

VECTORS

Since the studies of CHAGAS and co-workers^{14, 15}, *Phlebotomus longipalpis*** has been suspected of acting as a vector of visceral leishmaniasis. It had been captured in most localities where cases of the disease had occurred and was found infected after feeding on infected dogs^{36, 11, 12}.

After extensive observations on the biology of *P. longipalpis*^{26, 20, 28} we have shown that this species is probably the only one with epidemiological significance in Northeastern foci. It seems to be, indeed, the chief vector in the whole Brazilian endemic area.

The following facts led to these conclusions:

1) In this country the known geographical distribution of the disease fits very closely within the limits of the known distribution of *P. longipalpis*. This sandfly seems to be well adapted to the different climatic conditions prevailing in the endemic area — from the Northern foci and their equatorial environment to the Northeastern ones with their semi-arid climate. Here the species shows a definite seasonal variation, its density starting to increase by February and reaching its maximum by May — about two months after the peak of the rainfall. It is, on the other hand, very resistant to dry weather and can be captured, although in small numbers, even after prolonged droughts.

2) *P. longipalpis* made up to 97.1 per cent of more than 134,000 sandflies of fifteen species caught by the Authors in an endemic area of the State of Ceará²⁰, and percentages of 92, 95.7, 99.9 and 99 were obtained in other foci studied in the States of Ceará, Piauí and Bahia, respectively^{20, 39}.

3) Far from being a strictly domestic species, *P. longipalpis* was, nevertheless, the

** For workers who divide the sandflies (*Phlebotominae*) in genera this species belongs to genus *Lutzomyia*.

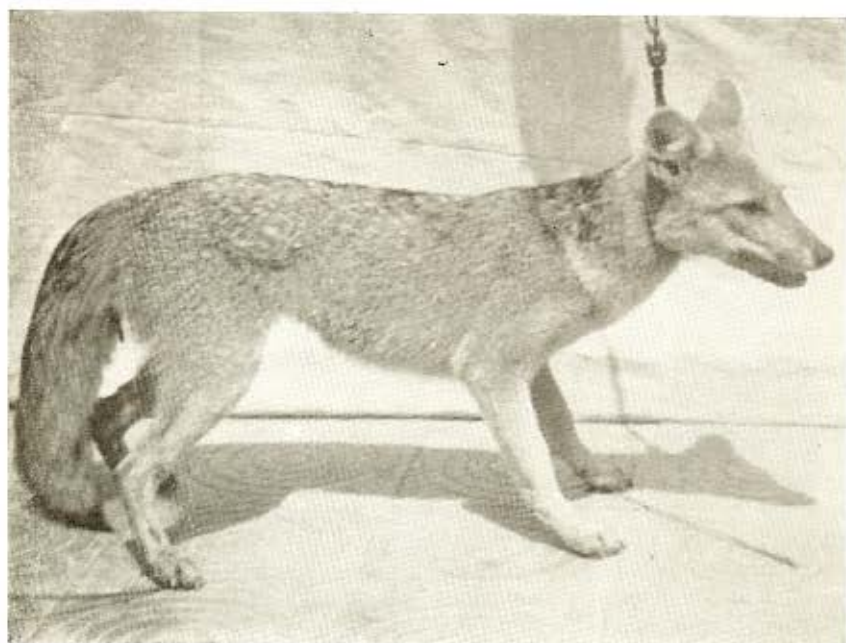


Fig. 5 — The fox *Lycalopex vetulus*.



Fig. 6 — A naturally infected fox *Lycalopex vetulus* in the late stage of visceral leishmaniasis.

only blood-sucking insect captured indoors in many of the studied foci.

In daytime this sandfly has been regularly found outside houses, in several sites such as tree holes, caverns, rock crevices, animal burrows, shrubs, on the ground under leaves, etc. However, captures made in these natural resting places were usually much less productive than those made, within the same time period, in outbuildings serving as animal quarters, or inside houses: the average numbers per hour in animal shelters (corrals, stables, chicken-pens, etc.) and in houses were, respectively, 272.3 and 61.2, against 14.3 in natural resting places; considering only the female specimens, the above averages were 58.3, 33.1 and 6.6.

Although more numerous in animal quarters, *P. longipalpis* was often found in quite large numbers inside human dwellings*. Moreover, the proportion of female over the male specimens was generally much greater in the latter than in the former. During a 24-hour capture, for instance, 3,082 specimens were collected in one house, 2,608 of them being females; in another house, 1,984 specimens, including 1,411 females, were caught in 2 1/3 hours.

4) *P. longipalpis* feeds on several species of warm-blooded animals**, including birds.

Man is readily bitten, both outdoors and indoors, and specially during the night. Among our most productive outdoor captures one, made on a boy, from 6 to 8 PM, yielded 807 specimens including 572 females. In cloudy or rainy weather, however, this sand-

fly could be often seen biting at daytime and, in a particular occasion, of 377 females collected while engorging on persons inside a house, 70 per cent were caught between 6 a.m. and 6 p.m., 18 specimens from 2 to 3 p.m. Opportunities of being bitten by *P. longipalpis* are, therefore, very frequent among the human population — including the most domestic and also the most susceptible (to visceral leishmaniasis) part of it, i.e., young children.

Dog also attracts *P. longipalpis* females in large numbers, specially in outdoor captures, and this sandfly was seen to engorge easily on the fox *L. vetulus*, both in captivity and under natural conditions.

5) *P. longipalpis* has been found with natural leptomonal infection of the anterior portion of the digestive tract in two kala-azar foci^{31, 39}.

6) Its experimental infection by *L. donovani* has been easily and repeatedly obtained by feeding specimens on infected dogs^{36, 12, 27}, humans^{32, 27} and the fox *L. vetulus*³³. In the sandfly, infection of the digestive tract was always anterior and very often it was massive, blocking the pharynx valve and sometimes invading the proboscis.

No other sandfly is known so far in Brazil presenting such a pattern in its behavior which, together with its great susceptibility to infection by *L. donovani*, is responsible for the efficiency of *P. longipalpis* as a vector of this parasite.

There are some interesting facts that better illustrate the coincidence in distribution and prevalence of visceral leishmaniasis and *P. longipalpis* in Brazil.

In the Amazon Region, the only known foci of visceral leishmaniasis are restricted to small areas in the low portion of the river valley, near the Atlantic coast — areas where *P. longipalpis* does occur. On the other hand, during a detailed survey of the sandfly fauna made along the river up to the Peruvian frontier, DAMASCENO *et al.*¹⁹ made abundant collections including many different species among which, however, *P. longipalpis* was absent, except in the lower Amazon.

* In houses, *P. longipalpis* was found to rest on walls and ceiling, mostly near the corners and close to the large earthen water jars which are an essential domestic item in the semi-arid areas of Northeastern Brazil. Many specimens, however, were found deeply located inside narrow cracks of the inner walls of the mud huts, from where we used to dislodge them with cigarette fumes.

** It is interesting to mention that another species of sandfly — *P. oswaldoi* — that we have frequently found inside houses, seems to feed only on cold-blooded animals: we have seen it engorging on lizards that inhabit wall cracks, and many engorged females caught indoors or in caverns and tree holes, when dissected, always contained nucleated red blood cells.

In the Sobral area as already stated, we have observed that visceral leishmaniasis is more prevalent in the foothills and valleys along the slopes of the Serra da Ibiapaba. In a series of comparative captures²⁰ made through an eight-month period, *P. longipalpis* represented 95.8 per cent and 99.6 per cent of the sandflies captured inside houses and outdoors (on animal baits), respectively. The average numbers per hour for the species were 75.8 and 135.9 for each type of capture. In the adjoining dry plains as well as on the plateau, *P. longipalpis* was again the predominant species but it was far less abundant, as shown by the average per hour figures both inside (7.2 and 7.2) and outside houses (20.2 and 1.3)*.

TRANSMISSION

Most probably imported from southern Europe by early settlers, visceral leishmaniasis seems to have acquired in this country the following distinctive epidemiological features:

- 1) although lowly endemic or even sporadic among the human population in most of the large area through which it expanded, it occurs also in epidemic waves that reach a great percentage of the susceptible population in limited foci;
- 2) having found a vector which is attracted by several vertebrate species and feeds both indoors and outdoors, the disease maintains itself through both domestic and wild reservoirs.

Dog is the chief domestic reservoir and this is due primarily to its heavy dermal parasitism. But man certainly can be an important reservoir under some circumstances.

We examined skin sections of 49 dogs with visceral leishmaniasis and found parasites in 77.6 per cent²⁷, while, as stated be-

fore, of 43 human skin samples, only 16.3 per cent were positive³⁵. Also, in the skin of dogs parasites were usually much more abundant.

In infection experiments made with *P. longipalpis* on 16 canine and 14 human cases (both unselected as far as microscopical evidence of dermal parasitism was concerned), 75 per cent of the former and 28.5 per cent of the latter infected the sandflies. Of 238 phlebotomi that fed on dogs 24.8 per cent became infected, against 14.8 per cent of the 81 which fed on the human cases. However, on both hosts infection of 100 per cent of the sandflies was obtained in some trials and blocking of the pharynx and invasion of mouth parts was achieved²⁷.

So, both hosts are capable of infecting the vector. Under conditions such as we have described in some foci²⁰ — where, during epidemic outbreaks, human cases outnumber the canine cases — the importance of man as a reservoir must not be overlooked.

Nevertheless, this is not the typical picture in most of the endemic area. Although the available data are unfit for statistical studies (since infections are not detected by the same means²¹), prevalence among dogs seems to be usually much greater than among humans. In towns along the Jaguaribe River Valley, for instance, 56 human cases were recorded in ten months, in a population of about 150,000, while 11 dogs were positive in a sample of 121 examined⁶. In other areas the discrepancy is still more accentuated and this is specially true in larger towns, as already pointed out.

As far as the incidence of the human disease is concerned, the one factor that seems to be most important is the abundance of the vector. That is, in the presence of other obvious epidemiological factors (such as infected reservoir and susceptible population), human kala-azar is more prevalent where and when the density of *P. longipalpis* is higher.

On the other hand, canine leishmaniasis seems to be able to maintain itself at relatively high levels even where and when the density of *P. longipalpis* is quite low. This

* Mucocutaneous leishmaniasis is endemic in Ceará's plateaus and here we very frequently caught, in outdoor captures, two species of sandflies — *P. whitmani* and *P. migonei* — which are the incriminated vectors of *L. braziliensis* in Southern Brazil. Both species were rare in the plains below and so is mucocutaneous leishmaniasis.

would be understandable had the vector demonstrated a definite predilection for dog instead of man as a source of its bloodmeals. This has not been so, however, in a large series of captures made in different hours and localities, both inside houses and outdoors, using man and dog as baits; *P. longipalpis* females caught while engorging were frequently very numerous on both hosts, sometimes more so on one of them, sometimes on the other²². Also, no evidence has been gathered up to now pointing to another species of sandfly as possible vector of visceral leishmaniasis among dogs, at least in the areas studied by the Authors. The fact awaits an explanation, and we think that transmission among dogs should be further investigated.

The one wild reservoir of visceral leishmaniasis found up to now in Brazil — the fox *L. vetulus* — is as good a source of infection for phlebotomi as the dog, or, maybe, even better. Leishmaniae are as scarce in its blood as in dog's and man's, but dermal parasitism is frequent and can be very intense: it was detected in 3 of 4 specimens which we found infected in Ceará and in 2 of them it was much heavier than in any of the dogs we examined. Samples taken from the muzzle, which was edematous and entirely glabrous, were specially rich^{27, 20}. Of 10 *P. longipalpis* females which fed on a sick fox all became infected, some very intensely so, with leptomonads blocking the pharynx and filling the mouth parts^{33, 27}.

The fox attracts *P. longipalpis*, as already mentioned. In a few crepuscular captures, performing 17¼ hours, in which it was possible to use this animal as bait, the average number of sandflies collected per hour was 11.8, of which 27 per cent were females, most of them engorged.

Thus *P. longipalpis* is capable of carrying the parasite between fox, dog and man, but, here again, we believe that the possibility of other means of transmission among foxes deserves more investigation.

The distribution of the fox *L. vetulus* is not exactly known but, according to Moojen (in DEANE²⁰), it extends to most of Brazilian hinterland, except the Amazon Valley and the Southern States. It is very common

in the whole Northeastern region, where it frequently preys on domestic fowl and thus comes close to human dwellings.

It is likely that epizootics occur among foxes as they seem to occur among dogs living in the same foci where the human population is subject to epidemics. In one of these, in the Northwest of the State of Ceará, 3 foxes were found infected out of 10 examined within a short period. On other hand, among 23 foxes captured on the neighbouring plains, only one had visceral leishmaniasis^{27, 20}.

Adding to those data the ones recently obtained by ALENCAR⁴, a total of 206 *L. vetulus*, all from Ceará, have been examined with 11 positives, or 5.3 per cent, a proportion four times higher than the global proportion for dogs in the same area. It should be emphasized, however, that the rates of infection recorded may not represent a reliable index of the prevalence of parasitism: foxes being wild animals that can only be obtained by trapping or shooting, it is likely that the diseased specimens, which are less agile and sometimes even blind due to keratitis, are easier to catch.

The severity of the disease in the fox suggests that this does not represent an ancient indigenous reservoir such as the one searched for by CHAGAS, but that it is, on the contrary, a rather recent host of *L. donovani*.

Lycalopex vetulus is not essential for the maintenance or spreading of visceral leishmaniasis in Brazil, but its importance cannot be overlooked when control of the disease is envisaged.

The control measures adopted in Brazil are multisided and include: 1) systematic search and treatment of human cases; 2) DDT spraying of human dwellings and animal shelters; 3) systematic search for diseased dogs and elimination of all those found infected or even with only suspicious symptoms.

The search and treatment of cases have several obvious advantages.

DDT spraying has brought encouraging results in the endemic area of Ceará⁴, since

P. longipalpis is very sensitive to the insecticide³⁰.

The systematic elimination of sick dogs has been carried to quite an extent in the State of Ceará, where 78,929 animals were killed up to the end of 1960, from a total of 279,423 examined since 1953⁴.

Destruction of foxes seems to be an unavoidable complement for the above mentioned control measures. It would bring the added advantages of freeing the population from a voracious carnivore which preys on their fowl and of destroying also a recognized and dangerous rabies reservoir. A better knowledge of the distribution and biometrics of *L. vetulus* should be very useful.

RESUMO

Leishmaniose visceral no Brasil: distribuição geográfica e transmissão.

Depois de um sucinto apanhado histórico, os Autores discutem a distribuição geográfica do calazar no Brasil relacionando-a às condições mesológicas que favorecem a proliferação do transmissor, *Phlebotomus longipalpis*. Comparam a importância dos hospedeiros vertebrados — homem, cão e raposa *Lycalopex vetulus* — como fontes de infecção e se referem às características biológicas do vetor ligadas à transmissão da doença. Discutem, finalmente, alguns dos aspectos epidemiológicos peculiares assumidos pelo calazar no país e sua influência nas medidas de profilaxia.

REFERENCES

1. ALBUQUERQUE, A. F. R.; BRITO, S. & MORAES, M. O. — Importante foco do mal de Chagas e de leishmaniose visceral americana no vale do Cariri (Estados do Ceará e Pernambuco). O Hospital 21:61-69, 1942.
2. ALENCAR, J. E. — Leishmaniose visceral no Novo Mundo. Publicações médicas (Rio de Janeiro) 196:71-87, 1956.
3. ALENCAR, J. E. — Calazar canino. Impr. Oficial, Fortaleza, Brasil, 342 pgs., 1959.
4. ALENCAR, J. E. — Profilaxia do calazar no Ceará, Brasil. Rev. Inst. Med. trop. São Paulo 3:175-180, 1961.
5. ALENCAR, J. E.; CANTIDIO, W. M. & CAVALCANTE, D. N. — Calazar em Fortaleza. Presented at XIII Congr. brasil. Hig., Fortaleza, 1956.
6. ALENCAR, J. E.; HOLANDA, D. & CAVALCANTE, J. D. N. — Calazar no vale do Jaguaribe, Ceará, 1955. Rev. brasil. Malariol. & D. trop. 8:33-47, 1956.
7. ARAGAO, T. C. — Surto de leishmaniose visceral na zona Norte do Ceará. Com. 3ª Reun. Saúde públ. Est. Ceará, september, 1953.
8. BRENER, Z. — Calazar canino em Minas Gerais. Thesis, Fac. Med. Univ. Minas Gerais, Brazil, 90 pgs., 1957.
9. BRENER, Z. & PELLEGRINO, J. — Reações imunológicas cruzadas em cães naturalmente infectados com doença de Chagas e leishmaniose visceral. Rev. brasil. Malariol. & D. trop. 10:45-49, 1958.
10. CALDEIRA, O. V. & BOGLIOLO, L. — Leishmânides dérmicos na leishmaniose visceral (kala-azar) no Brasil. O Hospital 51:193-205, 1957.
11. CHAGAS, A. W. — Infecção do *Phlebotomus intermedius* pela *Leishmania chagasi*. Brasil méd. 53:1-2, 1939.
12. CHAGAS, A. W. — Criação de flebotomos e transmissão experimental da leishmaniose visceral americana. Mem. Inst. Oswaldo Cruz 35:328, 1940.
13. CHAGAS, E. — Primeira verificação em indivíduo vivo, da leishmaniose visceral no Brasil. Brasil méd. 50:221-222, 1936.
14. CHAGAS, E.; CUNHA, A. M.; CASTRO, G. O.; FERREIRA, L. C. & ROMANA, C. — Leishmaniose visceral americana (Nova entidade mórbida do homem na América do Sul). Relatório dos trabalhos realizados pela Comissão encarregada do estudo da Leishmaniose Visceral Americana em 1936. Mem. Inst. Oswaldo Cruz 32:321-385, 1937.
15. CHAGAS, E.; CUNHA, A. M.; FERREIRA, L. C.; DEANE, L.; DEANE, G.; GUIMARAES, F. N.; PAUMGARTEN, M. J. & SA, B. — Leishmaniose visceral americana (Relatório dos trabalhos realizados pela Comissão encarregada do estudo da Leishmaniose Visceral Americana em 1937). Mem. Inst. Oswaldo Cruz 33:89-229, 1938.
16. CHAGAS, E.; FERREIRA, L. C.; DEANE, G.; DEANE, L. & GUIMARAES, F. N. — Leishmaniose visceral americana. II. Aspectos epidemiológicos. Mem. Inst. Oswaldo Cruz 33:138-206, 1938.

17. CUNHA, A. M. — A aglutinação e o diagnóstico diferencial das leishmânias. Brasil méd. 52:849-855, 1938.
18. CUNHA, A. M. & CHAGAS, E. — Nova espécie de protozoário do gênero *Leishmania* pathogenico para o homem, *Leishmania chagasi* n. sp. (Nota prévia). O Hospital 11: 3-9, 1937.
19. DAMASCENO, R. G.; AROUCK, R. & CAUSEY, O. R. — Estudos sobre *Phlebotomus* no Vale Amazônico. Parte VI. Contribuição ao conhecimento da distribuição geográfica e da incidência por tipo de captura, de 64 espécies identificadas. Rev. Serv. especial Saúde públ. 2:817-843, 1949.
20. DEANE, L. M. — Leishmaniose visceral no Brasil. Estudos sobre reservatórios e transmissores realizados no Estado do Ceará. Thesis, Fac. Med. Univ. S. Paulo, Brazil, Ed. S.N.E.S., Rio de Janeiro, 162 pgs., 1956.
21. DEANE, L. M. — Epidemiologia e profilaxia do calazar americano. Rev. brasil. Malariol. & D. trop. 10:431-450, 1958, and Proc. VI Intern. Congr. trop. Med. & Malaria 3: 754-778, 1958.
22. DEANE, L. M. — Reservatórios da *Leishmania donovani* no Brasil. Rev. Assoc. méd. brasil. 7:161-169, 1961.
23. DEANE, L. M. & DEANE, M. P. — Encontro de leishmânias nas vísceras e na pele de uma raposa, em zona endêmica de calazar, nos arredores de Sobral, Ceará. O Hospital 45:419-421, 1954.
24. DEANE, L. M. & DEANE, M. P. — Encontro de cães naturalmente infectados por *Leishmania donovani* no Ceará. O Hospital 45:703-707, 1954.
25. DEANE, L. M. & DEANE, M. P. — Leishmaniose visceral urbana (no cão e no homem) em Sobral, Ceará. O Hospital 47: 75-87, 1955.
26. DEANE, L. M. & DEANE, M. P. — Sobre a biologia do *Phlebotomus longipalpis*, transmissor da leishmaniose visceral, em uma zona endêmica do Estado do Ceará. I. Distribuição, predominância e variação estacional. Rev. brasil. Biol. 15:83-95, 1955.
27. DEANE, L. M. & DEANE, M. P. — Observações preliminares sobre a importância comparativa do homem, do cão e da raposa (*Lycalopex vetulus*) como reservatórios da *Leishmania donovani*, em área endêmica de calazar no Ceará. O Hospital 48:61-76, 1955.
28. DEANE, L. M. & DEANE, M. P. — Observações sobre os abrigos e criadouros de flebotomos no Noroeste do Estado do Ceará. Rev. brasil. Malariol. & D. trop. 9:225-246, 1957.
29. DEANE, L. M.; DEANE, M. P. & ALENCAR, J. E. — Tipo de região e prevalência da leishmaniose visceral em uma área endêmica do Ceará. Rev. paulista Med. 46:130, 1955.
30. DEANE, L. M.; DEANE, M. P. & ALENCAR, J. E. — Observações sobre o combate ao *Phlebotomus longipalpis* pela dedetização domiciliária, em focos endêmicos de calazar no Ceará. Rev. brasil. Malariol. & D. trop. 7:131-141, 1955.
31. DEANE, M. P. & DEANE, L. M. — Infecção natural do *Phlebotomus longipalpis* por leptômonas, provavelmente de *Leishmania donovani*, em um foco de calazar no Ceará. O Hospital 45:697-702, 1954.
32. DEANE, M. P. & DEANE, L. M. — Infecção experimental do *Phlebotomus longipalpis* em caso humano de leishmaniose visceral. O Hospital 46:487-489, 1954.
33. DEANE, M. P. & DEANE, L. M. — Infecção experimental do *Phlebotomus longipalpis* em raposa (*Lycalopex vetulus*), naturalmente parasitada pela *Leishmania donovani*. O Hospital 46:651-653, 1954.
34. DEANE, M. P. & DEANE, L. M. — Observações sobre a transmissão da leishmaniose visceral no Ceará. O Hospital 48:347-364, 1955.
35. DEANE, M. P. & DEANE, L. M. — Sobre o encontro de leishmânias na pele de doentes de calazar. Rev. paulista Med. 50:204, 1957.
36. FERREIRA, L. C.; DEANE, L. & MANGA-BEIRA, O. — Infecção do *Phlebotomus longipalpis* pela *Leishmania chagasi*. O Hospital 14:2-3, 1938.
37. HEISCH, R. — The isolation of *Leishmania* from a ground squirrel in Kenya. East African Med. J. 34:183, 1957.
38. HEISCH, R.; GRAINGER, W. E. & HARVEY, A. E. S. — The isolation of a *Leishmania* from gerbils. J. trop. Med. & Hyg. 62:158-159, 1959.
39. LOPES, J. A. S. — *Phlebotomus longipalpis* naturalmente infectados com formas em leptômonas na cidade de Jacobina, Estado da Bahia. Rev. med. Paraná (Brasil) 25: 57-58, 1956.
40. LOPES, J. A. S. & SARNO, P. — Leishmaniose visceral canina em Jacobina, Estado da Bahia, Brasil. Bol. Fundação Gonçalo Moniz (Salvador, Bahia) 11, 1956.

41. MARTINS, A. V.; BRENER, Z.; MOURÃO, O. G.; LIMA, M. M.; SOUZA, M. A. & SILVA, J. E. — Calazar autóctone em Minas Gerais. *Rev. brasil. Malariol. & D. trop.* 8: 555-563, 1956.
42. NUSSENZWEIG, V. — Contribuição para o estudo da reação de fixação do complemento na Leishmaniose Visceral com antígeno extraído de bacilos de tuberculose. Thesis, Fac. Med. Univ. S. Paulo, Ed. S.N.E.S., Rio de Janeiro, 119 pgs., 1958.
43. NUSSENZWEIG, V. — Diagnóstico sorológico da leishmaniose visceral humana e canina. *Proc. VI Intern. Congr. trop. Med. & Malaria* 3:779-790, 1958.
44. NUSSENZWEIG, V.; NUSSENZWEIG, R. & ALENCAR, J. E. — Leishmaniose visceral canina nos arredores de Fortaleza, Estado do Ceará: inquérito sorológico utilizando a reação de fixação do complemento com antígeno extraído do bacilo da tuberculose. Observações sobre o diagnóstico e a epidemiologia da doença. *O Hospital* 52:107-129, 1957.
45. PARÁ, M. — Papel da viscerotomia no diagnóstico do calazar no Brasil. Presented at "Jornada sobre Calazar", Salvador, Bahia, Nov. 12, 1960 (in press, Mem. Inst. Oswaldo Cruz).
46. PELLEGRINO, J. & BRENER, Z. — Reação de fixação do complemento com sangue dessecado no diagnóstico do calazar canino. *Rev. brasil. Malariol. & D. trop.* 10:39-44, 1958.
47. PENNA, H. A. — Leishmaniose visceral no Brasil. *Brasil méd.* 48:949-950, 1934.
48. PONDÉ, R.; MANGABEIRA, O. & JANSEN, G. — Alguns dados sobre a leishmaniose visceral americana e a doença de Chagas no Nordeste Brasileiro (Relatório de uma excursão realizada nos Estados do Ceará, Pernambuco e Bahia). *Mem. Inst. Oswaldo Cruz* 37:333-352, 1942.
49. PRATA, A. — Cura parasitológica do calazar. *O Hospital* 51:571-577, 1957.
50. PRATA, A. & DOMINGUES, A. — Leishmaniose dérmica. *O Hospital* 50:541-558, 1956.
51. PRATA, A. & PIVA, N. — Presença de leishmânias em pele aparentemente normal de pacientes com calazar. *O Hospital* 49: 481-486, 1956.
52. SILVA, J. RODRIGUES DA — Leishmaniose visceral (calazar). Thesis, Fac. Nac. Med. Univ. Brasil, Rio de Janeiro, 498 pgs., 1957.
53. VERONESI, R.; CASTRO, R. M.; MARQUES, J. C.; FIORILLO, A. M.; ZUCOLLOTO, M.; CZAPSKY, J.; SALLES, H. L. B. & AMATO NETO, V. — Leishmaniose visceral (calazar) no Brasil. Estudo do quadro clínico e humoral de 15 novos casos. *Rev. Hosp. Clinicas (S. Paulo)* 10:86-111, 1955.

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