Research on Control Strategies for the Leishmaniases

Proceedings of an International Workshop held in Ottawa, Canada, 1—4 June 1987
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RESEARCH ON CONTROL STRATEGIES FOR THE LEISHMANIASES

Proceedings of an International Workshop held in Ottawa, Canada, 1-4 June 1987

Program and Proceedings Editors:
B.C. Walton, P.M. Wijeyaratne, and F. Modabber

Sponsored by
International Development Research Centre, Ottawa, Canada,
in association with
UNDP/World Bank/WHO Special Programme for Research and Training in Tropical Diseases, Geneva, Switzerland,
and
Instituto de Medicina Tropical "Alexander von Humboldt"
Universidad Peruana Cayetano Heredia, Lima, Peru, and
Centro de Investigación en Salud "Dr Hugo Lumbrreras Cruz"
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ACKNOWLEDGEMENTS

This workshop was originally scheduled to be held in Lima, Peru, hosted by the Instituto de Medicina Tropical, "Alexander von Humboldt" of the Universidad Peruana Cayetano Heredia. For much of the early arrangements in Lima, our appreciation goes to Luis Guevara of the Instituto de Medicina Tropical. The success of the Ottawa workshop was due in large measure to the organizational efficiency of IDRC's Conference Coordinators Lyse Lavictoire and Julie Lalonde, and to Angie Anton of the Travel Section. I am also grateful for the work done by the Tropical and Infectious Disease Sector's secretaries, in particular Sue Davies who kept up the pressure even after the workshop to put the final touches on the "Proceedings" that came from Bryce Walton's dedicated hands.

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FOREWORD

International Workshop on Research on Control Strategies for the Leishmaniases

The scientists who met in 1975 to plan the Special Programme for Research and Training in Tropical Diseases (TDR) included the leishmaniases primarily as an excellent model for the study of the biochemical and immunological aspects of host parasite interactions. At that time, not enough epidemiological data on the leishmaniases existed to enable public health authorities to gauge their impact upon the health and well being of the peoples of the developing world.

However, reports of increasing incidence from many parts of the world, underscored by actual epidemics following the interruption of malaria control programs, caused considerable concern. On this basis, in December 1977 the TDR Scientific Working Group on the Leishmaniases recommended that all research avenues which held some promise of producing new methods for the control of these diseases should be pursued.

The intervening years have substantiated the wisdom of the approach taken by the Scientific Working Group. Extensive epidemiological data, including those presented at this workshop, have shown the profound impact of the leishmaniases and have established them as major public health problems in many regions of the world. The severe social and economic consequences of this disease complex have been recognized and the pressing need for more effective measures to control the leishmaniases has now been accepted by the research community and health authorities.
This workshop was planned by the International Development Research Centre's (IDRC) Health Sciences Division, in association with the UNDP/World Bank/WHO Special Programme for Research and Training in Tropical Diseases (TDR) and the Instituto de Medicina Tropical "Alexander von Humboldt" of the Universidad Peruana Cayetano Heredia (IMT, AvH, UPCH) to bring together leading experts to discuss gaps in knowledge in this field and to formulate research approaches leading towards strategies for control of the leishmaniases. The breadth of the discussions at this workshop illustrate the evolution in the perception of these diseases and highlight the severity of the problem and the need for more research in promising areas recommended by the Scientific Working Group. We have come a long way towards understanding the nature and scope of the leishmaniases and their impact upon populations. However, much research remains to be done before adequate control measures will be available to those who need them. We hope that the report of this workshop will stimulate some of this research.
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LEISHMANIAS: A GLOBAL PROBLEM

Bryce C. Walton

INTRODUCTION

Leishmaniasis is the name applied to an infection with any of the protozoan parasites of the genus *Leishmania*. This insect-transmitted parasitic disease is the least known, most misunderstood, and until very recently, the least studied, of any of the major parasitic diseases.

In the last decade there has been a tremendous increase in appreciation of the importance of the leishmaniasis. It is of interest that a little over ten years ago leishmaniasis was included among the six diseases chosen for attention by the UNDP/WORLD BANK/WHO Special Programme for Research and Training in Tropical Diseases (TDR), not because it was considered to be of major public health importance, but primarily because it represented an immunological model of special interest which might be useful in the study of other tropical diseases. The participants of the First Scientific Working Group on the Leishmaniasis were all persons with special knowledge and expertise on the leishmaniasis, and they were astounded, and some rather indignant, to learn that leishmaniasis had not been considered a priority disease problem by WHO. However, selection of priority problems by WHO is the result of a number of countries reporting the disease as a problem to the World Health Assembly. It was readily apparent that reliable data on leishmaniasis, even rudimentary distribution and prevalence information, were available in exceedingly few countries. In the absence of data regarding the disease, there was an understandable reluctance on the part of most countries to report it to the Assembly as a problem, so leishmaniasis had never come under consideration. When this situation was recognized, gathering of distribution and prevalence data was made a priority goal of the Steering Committee, and the major emphasis of the investigations sponsored by TDR in the first years of the leishmaniasis program was on documenting what the Scientific Working Group considered to be a fact; that the leishmaniasis were indeed a significant problem that needed to be recognized. The advent of a significant level of support for epidemiological studies over much of the world rapidly produced convincing evidence of the extent and seriousness of the problem. An exceptional interest in leishmaniasis has occurred since this initial step, and in the last decade TDR studies, as well as greatly augmented research support outside the program, have generated a much clearer picture of the complex nature of the factors involved in leishmaniasis as a global problem. Knowledge of the many and complex elements involved in transmission of the infection is required as a basis for any control effort and better understanding increases the possibility of success. The purpose of this workshop is to examine the body of knowledge now available, utilize it to devise effective control strategies, and indicate where adequate information is still lacking. The elements which may affect control efforts are so many and so complex that even a brief summary would be beyond the scope of this presentation, and no pretense is made of presenting a complete review. Only some relevant key factors will be touched upon, with an attempt to include
highlights of newer information available, with a view to providing a framework for the discussions and deliberations of this workshop. In addition to the biological and epidemiological factors pertinent to control efforts, some factors related to social organizations and behavior which affect how man deals with the problem are also included. For lack of a more precise term, this category is labeled Political/Social/Economic Implications. Most of these topics in both categories will be the subject of a more thorough and authoritative treatment by other participants.

BIOLOGICAL/EPIDEMIOLOGICAL IMPLICATIONS

Prevalence and Distribution

The global total of leishmaniasis cases is unknown, but undoubtedly is in the millions. A 1979 estimate by a WHO panel of 400,000 new cases per year is now considered to be a gross underestimation; an annual incidence of 1.5 to 2 million cases is likely, based upon extrapolations from data now available. Many of the presentations in this workshop represent excellent examples of new information emerging on the real prevalence of the various forms. A discussion of the global significance of any disease undoubtedly must consider the extent of geographic distribution, and the widespread occurrence of leishmanial infection is well known. It is endemic on five continents, and the shaded areas on distribution maps show as a heavy band covering much of the central portion of the globe, with significant incursions into temperate zones in some areas. Human disease has been reported to occur in over 100 countries. The endemic zones have a surprising degree of climatic and ecological variety; they occur at altitudes from below sea level in the Jordan Valley and up to 3,000 meters in the Andes; they are in humid tropical rainforests of the Americas and in semi-arid areas and even extremely dry desert regions over the world. Distribution of transmission sites within endemic areas is often discontinuous, with separate, widely scattered, foci. Different clinical forms and different species of *Leishmania* often occur in the same area.

Human cases tend to occur in remote areas lacking communications and where medical facilities and diagnostic capabilities are scarce or absent. Surveillance programs and reporting systems are rare and in many areas where the problem is most acute, statistics are often completely lacking or grossly inaccurate. In spite of the scarcity of reliable data due to these conditions, there is no doubt that there is a growing number of cases in most endemic areas, and cases are being diagnosed in many areas where the infection was not known before. Most leishmaniases are zoonotic, and the cycle occurs in nature over vast areas where humans are not affected. However, population pressures worldwide are resulting in man entering new lands in agricultural development projects, colonization schemes, petroleum development, and other activities which bring him in contact with the natural cycle, and outbreaks are often associated with these activities. Such situations present both a special challenge and a special opportunity for control efforts.
The Parasite

The old concept of three or four species of *Leishmania*, with each producing a separate clinical disease, has definitively been laid to rest. The methodology of molecular biology has made possible the identification of the causative parasite from individual cases and revealed that there is no absolute correlation of *Leishmania* taxa and the clinical disease produced; simple cutaneous lesions can be due to *L. donovani* subspecies which normally cause visceral disease<sup>4</sup> and *L. mexicana* can cause mucosal lesions<sup>5</sup> or visceralizing disease<sup>5</sup>. Advances in taxonomic knowledge of the leishmanias have resulted in the recognition of many distinct taxa; at least 15 separate species or subspecies are currently recognized to infect man.<sup>3</sup> A list of these, with their geographic distribution and the disease manifestation produced, is given in Table 1.

Disease Manifestations

An extremely diverse array of disease manifestations is produced by these various *Leishmania* which cause human infections. These vary from simple cutaneous ulcers, to severely debilitating, mutilating mucous lesions, or fatal visceral disease. Some infections are self healing, but others are relentlessly progressive and resistant to all known drugs. Three major clinical forms have long been recognized; Visceral leishmaniasis (VL), Cutaneous leishmaniasis (CL), and Mucocutaneous leishmaniasis (MCL). In addition to the differences in clinical manifestation the pattern of pathogenesis, ease of diagnosis, means of treatment, and probable outcome of these forms, differ so greatly that they must be regarded as separate disease entities. Consequently, the plural "Leishmaniases" is used as the collective term for leishmanial disease, and the singular "leishmaniasis" only for the separate individual entities. In addition to these historically recognized disease types, rare atypical cases, such as ocular infections<sup>7</sup> and even bone involvement<sup>8</sup> have been recognized. Leishmanial parasites are now included among the list of agents affecting AIDS patients and a bizarre infection of the intestinal submucosa has been encountered in San Francisco. A fourth clinical form, Disseminated Cutaneous Leishmaniasis (DCL), has been found to occur with sufficient frequency that it is now also accepted as a distinct entity, along with VL, CL, and MCL. Also called Anergic Cutaneous Leishmaniasis, DCL occurs in Africa and the New World. It is a purely cutaneous infection with nonulcerating nodules and plaques which eventually disseminate over almost the entire body to produce a condition closely resembling lepromatous leprosy. The infection is resistant to all known anti-leishmanial drugs, although some success has been achieved with heat therapy. It occurs only in individuals with a defective cellmediated immune response, and only with certain *Leishmania* species which have an intrinsic ability to produce this condition. It is associated with *L. aethiopica* in Africa, and *L. mexicana* subspecies in the Americas, hence DCL results only in the case of infection in a host with an unusual immune condition, by a parasite with special innate characteristics. It was once so rare that it was regarded only as an oddity of academic interest, but it is now being reported with ever increasing frequency and wider distribution in the Americas. Because of the...
devastating consequences to the patient, it is recognized as a special public health problem.

Vectors/Reservoirs/Transmission

A single universal strategy for control is not possible because of the great diversity of the situations in which the infection is transmitted to man. The structure of foci, i.e., the vector and reservoir involved, vary widely, and control measures must vary to suit each individual situation. For example, elimination of the mammalian reservoir, a strategy which was successfully employed for dogs in China and Brazil against kala azar, and with Rhombomys in the Soviet Union against CL, is not a viable solution in the Americas where many species of wild forest animals are the reservoir. In some areas the reservoir is completely unknown. Similarly, measures against the phlebotomine sandfly vectors must vary according to the very different habits and habitats of the many species involved. Gaining the knowledge which is needed to devise control measures is not simply a matter of supporting a few field studies. More than 500 species of sandflies have been described, but the role in transmission is known for relatively few. There is a natural tendency to study those species which bite man and to neglect those which do not. However, some species which are not anthropophilic could play a key role in the epidemiology of some areas by maintaining a reservoir of infection by transmission from rodent to rodent. If such a species is vulnerable, it could possibly provide a more effective point of intervention in the transmission cycle than measures against a less vulnerable species which transmits the infection from rodent to man.

POLITICAL/SOCIAL/ECONOMIC IMPLICATIONS

Social/Governmental Factors

The astounding degree of neglect of the problem of leishmanial infection for so many years is largely a phenomenon related to the politico-social status of the majority of those infected. Not only are the leishmaniases mainly a problem of the most economically underdeveloped and disadvantaged regions of the world, but they tend to be concentrated in the lowest socio-economic classes who have minimal political power to influence action by the government. Generally the leishmaniases are chronic and debilitating, rather than rapidly fatal diseases, and therefore even large numbers of cases do not capture the attention of the press and public health authorities as do more dramatic outbreaks of "killer" diseases. This is further compounded by the location of the majority of infections in remote areas where the patients are not a constant reminder of the problem.

Official recognition of leishmaniases as a public health problem is sometimes not forthcoming, even though government authorities are well aware of the gravity of the situation. Official recognition of a disease problem is accompanied by the implicit need to solve or alleviate the problem, but those responsible can see no way to do so. Prevention, or even reduction of number of cases, is currently not possible for a variety of reasons; vaccine is non-existent, and means to control vectors
or reservoirs are not known, or not feasible. Consequently, it is easier to ignore the existence of a disease which can neither be prevented nor treated, and which affects the politically uninfluential. This is an understandable, if not forgiveable, course of action for government officials facing many other serious and pressing problems. It is gratifying to note that several governments in Latin America have officially recognized leishmaniasis as a public health problem for the first time within the past two years. It is very commendable that the social responsibility to combat the disease was accepted in face of the tremendous financial, technical, and administrative difficulties involved.

**Economic Factors**

Even governments with a strong social conscience and a desire to alleviate the problem are often without the means to do so. Treatment is expensive; the cost of the WHO-recommended course of pentavalent antimonial for South American CL/MCL is at least US$75.00 for a single patient; the cost of the drug to treat existing cases almost surpasses the total budget for Primary Health Care in some countries. However, even if the drug is available, treatment is not feasible in many cases because of the need for daily injections over a period of weeks. Hospitalization for this period is beyond the resources of the government and the individual. Daily visits to Primary Health Care facilities are not possible for those who cannot leave their crops unattended or be absent from work for such extended periods, and they therefore elect to forego treatment, since the disease is not fatal, but starvation is.

Although the statement made in the opening paragraph is still valid - that leishmaniasis is the least known and most misunderstood of all the major parasitic diseases - it is indeed heartening that we have progressed to a point where serious consideration can be given to planning control activities. It is especially significant, and perhaps symbolic, that vaccination, as opposed to the leishmanization of antiquity, is now discussed as a realistic strategy and not just as an academic possibility. This International Workshop for Control Strategies for the Leishmaniases marks the entrance into a new era in the study of an ages old disease which remains an important cause of human suffering and a barrier to economic development.
Table 1.

Names, geographic distribution, and disease manifestation of *Leishmania* infecting humans.

<table>
<thead>
<tr>
<th>Species/subspecies</th>
<th>Clinical disease</th>
<th>Geographic area</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>L. donovani donovani</em></td>
<td>VL, PKADL</td>
<td>India, Africa, Asia</td>
</tr>
<tr>
<td><em>L. d. infantum</em></td>
<td>VL, CL*</td>
<td>Circum-Mediterranean, Mid-East, South &amp; Eastern Europe, USSR</td>
</tr>
<tr>
<td><em>L. d. chagasi</em></td>
<td>VL, CL*</td>
<td>S. America, Meso-America</td>
</tr>
<tr>
<td><em>L. tropica</em></td>
<td>CL</td>
<td>Mid-East, Europe, N. Africa, India</td>
</tr>
<tr>
<td><em>L. major</em></td>
<td>CL</td>
<td>Mid-East, Africa, India, Asia</td>
</tr>
<tr>
<td><em>L. aethiopica</em></td>
<td>CL, DCL*</td>
<td>Ethiopia, Kenya (Highlands)</td>
</tr>
<tr>
<td><em>L. mexicana mexicana</em></td>
<td>CL, DCL*</td>
<td>Meso-America, N. America?</td>
</tr>
<tr>
<td><em>L. m. amazonensis</em></td>
<td>CL, DCL</td>
<td>Brazil, Panama</td>
</tr>
<tr>
<td><em>L. m. pifanoi</em></td>
<td>DCL</td>
<td>Venezuela</td>
</tr>
<tr>
<td><em>L. m. garnhami</em></td>
<td>CL</td>
<td>Venezuela (High altitude)</td>
</tr>
<tr>
<td><em>L. m. venezuelense</em></td>
<td>CL</td>
<td>Venezuela</td>
</tr>
<tr>
<td><em>L. peruviana</em></td>
<td>CL</td>
<td>Peru (High altitude)</td>
</tr>
<tr>
<td><em>L. braziliensis braziliensis</em></td>
<td>CL &amp; MCL</td>
<td>South &amp; Central America</td>
</tr>
<tr>
<td><em>L. b. panamensis</em></td>
<td>CL &amp; MCL</td>
<td>Central America, W. Colombia</td>
</tr>
<tr>
<td><em>L. b. guyanensis</em></td>
<td>CL</td>
<td>N.E. S. America</td>
</tr>
</tbody>
</table>

VL = visceral leishmaniasis
CL = cutaneous leishmaniasis
MCL = mucocutaneous leish.
DCL = disseminated cutaneous leishmaniasis

* = rare manifestation
# = taxa not recognized by some authorities
REFERENCES

CURRENT SITUATION OF VISCERAL LEISHMANIASIS IN INDIA
WITH SPECIAL REFERENCE TO WEST BENGAL

A. Nandy, M. Addy*, A. Chowdhury**, and A. Ghosh**

INTRODUCTION

Kala azar in India, once relegated to a medical rarity during the late 1940's, reappeared in the 1960's in north Bihar, India after a lull of about two decades, and attained epidemic form in the early 1970's. Although it was reduced below the level of public health importance, the disease was never totally eradicated. Cases of post kala azar dermal leishmaniasis (PKDL), a suspected reservoir of infection for sandflies, and occasional cases of active kala azar continued to be seen in the special clinic of the Calcutta School of Tropical Medicine during this period. The factors responsible for the apparent disappearance of the disease were supposedly:

a. successful chemotherapy of all cases,
b. acquired protective immunity in the population, and
c. decrease in vector density following mass indoor residual insecticidal spray (DDT) under the National Malaria Control Programme followed by the National Malaria Eradication Programme (NMEP).

Following withdrawal of the DDT spray operation as a strategy of the NMEP, there was gradual increase in the vector population. An alarming degree of anthropophilism in *P. argentipes* was demonstrated by Das et al.*2* Further, with the declining trend in transmission, there was a gradual increase in the susceptible human population. Thus, the stage was almost set for a large scale transmission to start. A forecast of such a possibility came from Sen Gupta in 1973*2*. The number of kala azar cases diagnosed at the special clinic of the Calcutta School steadily increased during the 1970's, most of which came from Bihar, in the grip of an epidemic outbreak which reached its peak in the late 1970's. However, a small number of sporadic cases among the indigenous population in West Bengal at that time, raised reasonable suspicion of local transmission there, as well.

CURRENT SITUATION OF VL IN INDIA:

After the phenomenal decline in the VL incidence in India during the early 1950's, kala azar in India remained sporadic in many states, including Bihar, West Bengal, Assam, Tamilnadu, Jammu, Kashmir Gujrat and Himachal Pradesh*3*. (Fig. 1) It was in the early 1970's that the disease was seen to be reappearing in few districts in north Bihar, namely Muzzaffarpur, Baishali, Sitamari and Samastipur*3*. By 1977, the estimated total number of VL cases in Bihar alone was said to be 100,000

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INDIA
STATES AT RISK OF KALA-AZAR

Fig. 1.
with 4,500 deaths. However, in Bihar, the maximum number of cases (41,953) was reported in 1978, declined to approximately 11,000 in 1986 following intervention measures. As more and more cases were reported from Bihar since 1971, the affected area also grew, and the disease started involving more districts of the state, finally making its way across the border to West Bengal in 1980. The current distribution of VL in Bihar and West Bengal is indicated in Figure 2.

Current Situation in West Bengal

It was in early 1980 that information came to us regarding a suspected outbreak of kala azar in Harishchandrapur block of Malda, a district of West Bengal sharing a common border with the District of Katihar of Bihar, and the disease was subsequently confirmed as kala azar by our team. The local transmission possibly started in 1978. (Fig. 3) Almost simultaneously another focus was identified about 15 km north of Calcutta, at the village of Peyarabagan in the district 24-Paraganas. A particular feature of this outbreak at Peyarabagan, which drew immediate attention, was the exclusive involvement of a particular tribal community, the "Oraons", at the outset. This group had migrated from the Sundarbans 25-30 years ago. It was noted that the Oraons at Peyarabagan did not have any social or geographical link with either Bihar or Malda of West Bengal. While the source of infection for the Malda outbreak could be traced to the Katihar district of Bihar, the source in the case of Peyarabagan remained far from clear.

Spread and Distribution:

Since its first detection in 1980 in Malda and 24-Paraganas, kala azar in West Bengal was observed to follow two distinctive patterns of spread. The one originating in Harishchandrapur swept quickly through all the blocks of the district Malda, and through population migration, reached Murshidabad in later part of 1980. From Malda the disease also went north to West Dinajpur where it was first detected in 1982. However, the spread was quick, and quite general, involving the population irrespective of any particular ethnic group. In contrast, the one originating in Peyarabagan, 24-Paraganas, remained by and large, confined within the Oraon community. It spread focally, strictly through migration of the infected population to start with, followed by local transmission within Oraon communities of other parts of 24-Paraganas, as well as neighboring districts, such as, Nadia and Hooghly. That population played a pivotal role in determining the nature and extent of spread of the disease was clearly evident from the outbreaks in Malda, and more so in 24-Paraganas among the Oraon communities. Moreover, the spread in the districts of 24-Paraganas, Nadia and Hooghly was observed to be enormously influenced by the social and cultural behaviour of the particular tribal community involved.

The incidence in West Bengal by year is given in Table 1. The maximum number of cases (85%) was observed to occur within two and half decades of age, 45% within the first and 76% within the second decade. The youngest patient was seven months old and the oldest 60 years. Males suffered twice the rate of females.
FIGURE 2.
Clinico-Pathological Aspect:

The most common clinical presentation was with anaemia and hepatosplenomegaly and long continued fever not responding to conventional therapy. In a series of 450 cases 2% [9/450] presented without fever.

Table 1.
Morbidity and mortality due to kala azar in different districts of West Bengal 1980-1986 (May)

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Malda</td>
<td>295</td>
<td>304</td>
<td>515</td>
<td>367</td>
<td>479</td>
<td>560</td>
<td>191</td>
<td>2,711</td>
</tr>
<tr>
<td>(4)*</td>
<td>(5)</td>
<td>(0)</td>
<td>(0)</td>
<td>(0)</td>
<td>(0)</td>
<td>(0)</td>
<td>(0)</td>
<td>(9)</td>
</tr>
<tr>
<td>Murshidabad</td>
<td>14</td>
<td>564</td>
<td>490</td>
<td>907</td>
<td>667</td>
<td>638</td>
<td>213</td>
<td>3,493</td>
</tr>
<tr>
<td>(0)</td>
<td>(0)</td>
<td>(0)</td>
<td>(0)</td>
<td>(0)</td>
<td>(0)</td>
<td>(0)</td>
<td>(0)</td>
<td></td>
</tr>
<tr>
<td>West Dinajpur</td>
<td>-</td>
<td>-</td>
<td>172</td>
<td>1375</td>
<td>3839</td>
<td>2960</td>
<td>757</td>
<td>8,383</td>
</tr>
<tr>
<td>(1)</td>
<td>(7)</td>
<td>(0)</td>
<td>(0)</td>
<td>(0)</td>
<td>(0)</td>
<td>(0)</td>
<td>(0)</td>
<td>(13)</td>
</tr>
<tr>
<td>24-Paraganas</td>
<td>24</td>
<td>49</td>
<td>57</td>
<td>68</td>
<td>48</td>
<td>88</td>
<td>269</td>
<td>603</td>
</tr>
<tr>
<td>(2)</td>
<td>(0)</td>
<td>(0)</td>
<td>(0)</td>
<td>(0)</td>
<td>(0)</td>
<td>(0)</td>
<td>(0)</td>
<td>(13)</td>
</tr>
<tr>
<td>Nadia</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>26</td>
<td>26</td>
</tr>
<tr>
<td></td>
<td>(0)</td>
<td>(0)</td>
<td>(0)</td>
<td>(0)</td>
<td>(0)</td>
<td>(0)</td>
<td>(0)</td>
<td></td>
</tr>
<tr>
<td>Hooghly</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>4</td>
<td>4</td>
</tr>
<tr>
<td></td>
<td>(0)</td>
<td>(0)</td>
<td>(0)</td>
<td>(0)</td>
<td>(0)</td>
<td>(0)</td>
<td>(0)</td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>333</td>
<td>917</td>
<td>1234</td>
<td>2717</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*(n)=deaths

or an initial febrile phase followed by afebrile one. About 9% of cases had hemorrhagic manifestations in the form of epistaxis and gum bleeding. Pulmonary tuberculosis and leprosy (tuberculoid) were found to be associated in 5 and 2 cases respectively. But, by and large, both the severity of clinical presentation and number of complications was much lower compared to that seen in the earlier epidemics. Generalized superficial lymphadenopathy was observed in 90% of the patients, including cervical, axillary, epitrochlear and inguinal. Amastigotes could be demonstrated in 89% of the biopsied lymph nodes. As stated earlier**, the epitrochlear lymphadenopathy was considered to be more pathognomonic. Subsequently, an unknown clinical entity in Indian kala azar, that of "lymphatic leishmaniasis" was reported in two persons from a kala azar endemic village in the district of 24-Paraganas**. It was suggested that these subjects, without any fever, or hepatosplenomegaly, might have an unsuspected role in the transmission of the disease.
Laboratory Diagnosis:

Although demonstration of parasites in bone marrow, spleen, or lymph nodes, and anti-leishmanial antibodies in patient's serum are the methods used for diagnosis of VL and PKDL in city hospitals, the formol gel test still remains the first line diagnostic procedure at the rural level in West Bengal. However, in a series of 300 cases of parasitologically confirmed cases of kala azar, 40% were observed to be formol gel test negative. Apart from its false positivity, the observed high degree of false negative results emphasizes the danger of using the test as a field diagnostic procedure and the urgency to replace it with a low cost, easy method with higher sensitivity and specificity.

Chemotherapy:

Sodium antimony gluconate remains the drug of choice for the treatment of kala azar in West Bengal. All of 450 cases treated with a regimen of 10mg/kg/day for 15-24 days responded favorably. However, 1.33% cases came back with a second attack of VL after 15-18 months. Without a prospective parasitological study, it is difficult to interpret these cases either as re-infection or relapse.

Post Kala Azar Dermal Leishmaniasis:

In a prospective study of 350 cases of kala azar to study the evolution of PKDL, no significant relationship was observed between the development of PKDL and the total amount of antimony compound received during treatment for VL. Further, it was found that 2-2.5% of cases of PKDL did not have a history of VL. The average time taken to manifest PKDL varied from 6-18 months. These cases of PKDL appeared during the late declining phase of an epidemic at a particular locality. The earliest clinical manifestation was hypo-pigmented lesions over the face, which progressed to nodular type lesions without treatment. Parasites were very difficult to demonstrate in the hypo-pigmented types, but were more abundant in the nodular variety. While the DTH reaction (leishmanin test) was almost absent in the nodular type, it could be elicited more regularly in the hypo-pigmented type. Development of promastigotes in the midgut of laboratory bred P. argentipes following feeding on the nodular type of PKDL emphasized the potential of these cases to serve as a source of parasites in the community.

Leishmanin Test Survey:

About 18% of the otherwise normal population, mostly the household contacts of kala azar cases, were observed to have a positive leishmanin test. This provides a possible indication of the occurrence of subclinical infections during the epidemic outbreak.
REFERENCES:

5. State Health Department of Bihar, Report presented in Inter-State Meeting on Kala-azar, Calcutta, 1986
PRESENT SITUATION OF KALA AZAR IN CHINA

Xu Zhi-biao

INTRODUCTION

Kala azar or visceral leishmaniasis was formerly very prevalent in China, but was brought under control after a nationwide campaign against kala azar which started in 1949, and now only sporadic cases occur in remote areas of Northwest China. Although it is not presently an important public health problem, because of the demonstrated ability of the infection to be re-established in an area from a wild animal reservoir, it is being closely monitored and studied.

HISTORICAL SITUATION:

Kala azar was prevalent in North, East and Northwest China before 1949, but the exact incidence is not clear due to the lack of epidemiological data from that era, since surveys were not done at that time. However, it is known that kala azar was prevalent in 16 municipalities, provinces or autonomous regions. It was rampant in 7 of them: Jiangsu, Anhui, Shandong, Hebei, Henan, Shaanxi and Gansu, with the prevalence rate as high as 35.0-50.4/10,000 and moderately endemic in 6: Beijing, Liaoning, Shanxi, Sichuan and Xinjiang. Sporadic cases were seen in Inner Mongolia, Ningxia and Qinghai. The estimated total number of patients was 0.6 million. Most endemic areas were located in low alluvial plains with an altitude <50 m above sea level, and the annual rainfall around 600-800 mm, whereas in the endemic areas in Northwest China as Gansu and Xinjiang, the altitude is >1,000 m above sea level, even up to 2,000 m, with a drier climate and average rainfall <100 m. Patients seen in the endemic areas were mostly children of 5-10 years in East and North China and were <5 years in Gansu and the other endemic areas in the Northwest. Patients in the desert endemic areas in the Xinjiang autonomous Region were mostly infants <2 years, although sometimes lympho-glandular leishmaniasis occurred in adult immigrants from non-endemic areas.

Mass survey and treatment, along with elimination of the canine reservoir and some vector control measures, have been carried out in endemic areas since the establishment of New China in 1949, and the disease was brought under control in 1958.

SURVEYS OF RESERVOIR HOSTS OF KALA AZAR:

Dogs are the main reservoir host in most endemic areas, especially in the hilly and mountainous areas. According to data reported by different authors (Table 1.) the infection rate of dogs in the urban area of Beijing was 110-140/10,000, and varied from 388/10,000 to less than 1/10,000 to 3/10,000 in rural areas.

A large number of wild animals, including various wild rodents and a small number of large carnivores have been examined in Northwest China, but no reservoir host of human leishmaniasis was found except for
Rhombomys opimus, from which a strain of non-pathogenic Leishmania gerbilli was isolated by our Shanghai colleagues. In 1982, an infected racoon dog \( (Nyctereutes procyonoides\) Gray) found in a suburb of Beijing near the Great Wall. The Leishmania isolated from this animal were characterized as having the isoenzyme pattern of \( L.\) infantum.

Table 1.

Infection rate of dogs in endemic areas

<table>
<thead>
<tr>
<th>Locality</th>
<th>Year of Infection survey</th>
<th>Infection rate (per 10,000)</th>
<th>Infected dogs/ dogs examined</th>
</tr>
</thead>
<tbody>
<tr>
<td>Beijing</td>
<td>1939-40-41,</td>
<td>110-140</td>
<td>27/2,474</td>
</tr>
<tr>
<td>Liaoning</td>
<td>1955-1958</td>
<td>204</td>
<td>11/539</td>
</tr>
<tr>
<td>Hebei</td>
<td>1956</td>
<td>142</td>
<td>19/1,271</td>
</tr>
<tr>
<td>Sichuan</td>
<td>1956-1957</td>
<td>15.2-388</td>
<td>2/1,320</td>
</tr>
<tr>
<td></td>
<td>1973-76-77</td>
<td></td>
<td>31/798</td>
</tr>
<tr>
<td>Gansu</td>
<td>1952-1955</td>
<td>56</td>
<td>90/16,016</td>
</tr>
<tr>
<td>Shannxi</td>
<td>1954</td>
<td>43</td>
<td>133/30,641</td>
</tr>
<tr>
<td>Qinghai</td>
<td>1954-1958</td>
<td>88.1</td>
<td>10/1,135</td>
</tr>
<tr>
<td>Shandong</td>
<td>1951-1958</td>
<td>11.0</td>
<td>34/30,979</td>
</tr>
<tr>
<td>Henan</td>
<td>1957</td>
<td>8-36</td>
<td>1/1,258</td>
</tr>
<tr>
<td></td>
<td>1953-1957</td>
<td></td>
<td>13/3,652</td>
</tr>
<tr>
<td>Shanxi</td>
<td>1959</td>
<td>14.9</td>
<td>12/8,048</td>
</tr>
<tr>
<td>Anhui</td>
<td>1951-1957</td>
<td>0.9</td>
<td>1/10,879</td>
</tr>
<tr>
<td>Jiangsu</td>
<td>1951-1957</td>
<td>0</td>
<td>0/16,403</td>
</tr>
<tr>
<td>Henan</td>
<td>1957</td>
<td>0</td>
<td>0/179</td>
</tr>
<tr>
<td>Hubei</td>
<td>1957</td>
<td>0</td>
<td>0/571</td>
</tr>
<tr>
<td>Xinjiang</td>
<td>1957-1958</td>
<td>0</td>
<td>0/237</td>
</tr>
<tr>
<td></td>
<td>1974</td>
<td>0</td>
<td>0/125</td>
</tr>
</tbody>
</table>

Table 2.

Wild Animals Examined In Suburbs of Beijing (1980-1982)

<table>
<thead>
<tr>
<th>Name</th>
<th>Number Examined</th>
<th>Number with amastigotes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Squirrels</td>
<td>136</td>
<td>0</td>
</tr>
<tr>
<td>Wild rodents</td>
<td>30</td>
<td>0</td>
</tr>
<tr>
<td>Hares</td>
<td>34</td>
<td>0</td>
</tr>
<tr>
<td>Badgers</td>
<td>23</td>
<td>0</td>
</tr>
<tr>
<td>Racoon dogs*</td>
<td>36</td>
<td>1</td>
</tr>
<tr>
<td>Fox</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Weasels</td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td>Roe deer</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Total</td>
<td>263</td>
<td></td>
</tr>
</tbody>
</table>

* \( (Nyctereutes procyonoides)\).
EPIDEMIOLOGICAL TYPES OF KALA AZAR IN CHINA

There are three epidemiological types of kala azar in China, each with different vectors and reservoirs. In addition there is a purely rodent form which is not known to infect humans; these are:

1. The anthroponotic type, which occurs chiefly in the endemic areas in East China. It is mainly a disease of humans, and dogs play a minor role in the transmission. *P. chinensis* and *P. chinensis longiductus* are the main sandfly vectors.

2. The cynonotic type, which is seen mainly in the hilly and mountainous endemic areas where a canine reservoir host plays an important role in its transmission. *P. chinensis* is also the main sandfly vector.

3. The zoonotic type, which is found in the newly reclaimed desert areas. Patients are usually under 2 years, although sometimes adults may be infected in the form of lympho-glandular leishmaniasis. *P. alexandri* is the main sandfly vector.

4. *L. gerbilli* was isolated from *Rhombomys opimus* in Gansu and was named by Wang et al. in 1964. Various kinds of laboratory animals have been inoculated with the parasite, but infection was obtained only in Chinese hamsters by intratesticular inoculation with amastigotes. It is non-pathogenic to man. Sandfly vectors are *P. mongolensis* and *P. major wu*.

Table 3.

<table>
<thead>
<tr>
<th>Age and sex distribution of 80 cases of kala azar seen in Xinjiang</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
</tr>
<tr>
<td>male: 41</td>
</tr>
<tr>
<td>---------------------------------------------------------------</td>
</tr>
<tr>
<td>Age distribution:</td>
</tr>
<tr>
<td>2-6 months: 17 cases (21.25%)</td>
</tr>
<tr>
<td>7-12 months: 39 (48.75%)</td>
</tr>
<tr>
<td>1-2 years: 15 (18.75%)</td>
</tr>
<tr>
<td>2-3 years: 8 (10.00%)</td>
</tr>
<tr>
<td>3-4 years: 1 (1.25%)</td>
</tr>
</tbody>
</table>
Fig. 2 | KALA AZAR in CHINA
(present distribution)

1. Xinjiang
2. Gansu
3. Inner Mongolia
4. Ningxia
5. Qinghai
6. Shaanxi
7. Shanxi
8. Henan
9. Sichuan
10. Hubei
11. Anhui
12. Jiangsu
13. Shandong
14. Hebei
15. Liaoning
Table 4.

Signs and symptoms in 89 cases of infantile kala azar

<table>
<thead>
<tr>
<th>Symptom</th>
<th>Number of Cases</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Irregular fever</td>
<td>68 cases</td>
<td>85.00%</td>
</tr>
<tr>
<td>Nightsweat</td>
<td>44</td>
<td>55.00%</td>
</tr>
<tr>
<td>Coughing</td>
<td>50</td>
<td>62.50%</td>
</tr>
<tr>
<td>Impaired appetite</td>
<td>41</td>
<td>51.25%</td>
</tr>
<tr>
<td>Dyspepsia</td>
<td>35</td>
<td>43.75%</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>26</td>
<td>32.50%</td>
</tr>
<tr>
<td>Abdominal distention</td>
<td>15</td>
<td>18.75%</td>
</tr>
<tr>
<td>Vomiting</td>
<td>13</td>
<td>16.25%</td>
</tr>
<tr>
<td>Splenomegaly</td>
<td>80</td>
<td>100.00%</td>
</tr>
<tr>
<td>Hepatomegaly</td>
<td>50</td>
<td>62.50%</td>
</tr>
<tr>
<td>Enlarged lymph glands</td>
<td>25</td>
<td>31.25%</td>
</tr>
<tr>
<td>Malnutrition</td>
<td>8</td>
<td>10.00%</td>
</tr>
</tbody>
</table>

CHARACTERIZATION OF LEISHMANIA ISOLATES IN CHINA

A total of 14 Leishmania isolates have been studied in China, including two from Shandong (patients), 5 from Xinjiang (4 from patients and one from sandfly), three from Sichuan (two from patients and one from a dog), one from Henan (patient), one from Shaanxi (patient), one from Gansu (patient) and one from a racoon dog in Beijing. All of these, except two from Xinjiang patients and one from a Gansu patient, were identified as L. infantum by isoenzyme electrophoresis. The isolate from Gansu was identified as L. donovani; those from Xinjiang need further identification.

Table 5.

Identifications of Leishmania Isolates from China by Isoenzyme Electrophoresis Patterns

<table>
<thead>
<tr>
<th>No. of strains</th>
<th>Locality</th>
<th>Source</th>
<th>Identification</th>
</tr>
</thead>
<tbody>
<tr>
<td>2</td>
<td>Shandong</td>
<td>patients</td>
<td>L. infantum</td>
</tr>
<tr>
<td>1</td>
<td>Henan</td>
<td>patients</td>
<td>L. infantum</td>
</tr>
<tr>
<td>2</td>
<td>Sichuan</td>
<td>patients</td>
<td>L. infantum</td>
</tr>
<tr>
<td>1</td>
<td>Sichuan</td>
<td>dog</td>
<td>L. infantum</td>
</tr>
<tr>
<td>1</td>
<td>Gansu</td>
<td>patient</td>
<td>L. donovani</td>
</tr>
<tr>
<td>1</td>
<td>Shaanxi</td>
<td>patient</td>
<td>L. infantum</td>
</tr>
<tr>
<td>1</td>
<td>Beijing</td>
<td>racoon dog</td>
<td>L. infantum</td>
</tr>
<tr>
<td>2</td>
<td>Xinjiang</td>
<td>patients</td>
<td>L. infantum</td>
</tr>
<tr>
<td>2</td>
<td>Xinjiang</td>
<td>patients</td>
<td>L. infantum or L. donovani?</td>
</tr>
<tr>
<td>1</td>
<td>Xinjiang</td>
<td>sandfly</td>
<td>L. infantum</td>
</tr>
</tbody>
</table>

14 Total
CONTROL PROGRAMS IN CHINA

The program for leishmaniasis control forms part of the broader disease control program and is comprised of six elements:

1. Control Network for endemic and infectious diseases:

   Since the establishment of New China, a network for controlling epidemic and endemic diseases has been set up in every province in the nation, and in each of those high endemic areas, a Provincial Kala azar Prevention Station or Institute was established. There is a Health and Epidemic Prevention station in each county, and 2-3 physicians in each village hospital are assigned to the task of controlling endemic or infectious diseases, including kala azar. Suspected cases are referred to physicians in provincial stations for diagnosis, and information concerning cases or epidemics is rapidly reported to the Department of Epidemic Prevention in the Ministry of Public Health.

2. Training of local physicians and health workers:

   Various training courses on the diagnosis and control of kala azar at the professional and technical level have been held in different endemic areas, according to necessity, to maintain an adequate level of training of the responsible personnel.

3. Mass survey and mass treatment:

   All patients found to be infected in the surveys were treated free of charge with Stihek, a pentavalent antimonial preparation (stibophen) manufactured in China. Approximately 688,888 persons have been treated with this drug with satisfactory results.

4. Mass killing of dogs in endemic areas:

   Since dogs have been proved to be the main reservoir host in most endemic areas in China, mass killing of dogs was chosen as a control tactic, and carried out with fruitful results in this disease.

5. Elimination of vector sandflies:

   The widespread spraying of insecticides such as DDT or Gammexane once a year during sandfly season has been employed in the endemic areas as a means to eliminate vector sandflies.

6. Surveillance:

   Every year personnel of the Provincial or County Health and Epidemic Prevention Stations go to the localities where kala azar had been prevalent previously, to check the density of sandflies and spray insecticides when it is deemed necessary.
Current control situation in China

Since 1958 kala azar has been under control except in those years of the "Cultural Revolution" when all Health and Epidemic Prevention Stations were closed. The recurrence of kala azar was reported in the suburbs of Beijing and other endemic areas in 1968-1975. At the present time, since the resumption of control measures, there are only a small number of sporadic cases occurring in remote desert areas of Northwest China. Surveillance is maintained to guard against recurrence in former endemic areas.

PROBLEMS REMAINING TO BE SOLVED

Kala azar is not a serious Public Health problem in China at this time, but there are still some problems to be solved. The control of zoonotic type leishmaniasis in the desert areas is very difficult. The wild type sandfly vector is also difficult to eliminate by ordinary measures. The control program must be continued to prevent re-establishment of endemic areas, and must depend upon an active and effective surveillance system. This should be upgraded, so data from endemic areas is accumulated and analyzed by computer for correlation in case of any recurrence of transmission.
LEISHMANIASIS IN KENYA
Mutuku J. Mutinga

VISCERAL LEISHMANIASIS

Although visceral leishmaniasis (VL) had been known for many years in the Mediterranean area and also in Asia, it was only in the beginning of this century that the causative organism was recognized. Forbes was the first to demonstrate parasitologically the presence of visceral leishmaniasis in Kenya in a patient admitted at Eldoret hospital. It was, nevertheless, the description of a kala azar epidemic among the Kenyan soldiers forming the King's African Rifles (K.A.R) by Cole et al. and Anderson that awakened the interest of the health authorities and researchers to the importance of the disease in Kenya. Since the epidemic among the soldiers did not occur until after they had been to Ethiopia, there is a strong belief that the soldiers contracted the disease in Ethiopia and southern Sudan.

Kitui Focus:

In 1952/1953, there was a major epidemic outbreak affecting about 3,000 people in Tseikuru, in Kitui District (see map). Although control measures were taken, the disease did not disappear completely and by 1954 some 68 cases were reported. Between 1957 and 1969, a further upsurge of the disease occurred and 1,487 cases were reported during the four years (367, 160, 279, and 581 cases respectively). In 1963 another disease outbreak was experienced in this focus and again in 1980 reports of increasing numbers of patients was confirmed by surveys. This focus has remained endemic for kala azar, with sporadic epidemics.

Meru Focus:

This focus is adjacent to and continuous with the Kitui focus but separated by the Tana River. The ecological conditions are very similar, as are the occupational and other social practices in the two foci. In 1959 surveys conducted in 9 countries of Meru district, covering 11,188 persons, revealed 0.74% positive cases of kala azar. An epidemic outbreak occurred in 1960-1962, during which 365 cases were diagnosed.

Machakos Focus:

Kala azar was first reported in Machakos district between 1942-1950 by Fendall. That author considered that the disease was introduced in the district, possibly by military activity. The cases were mainly compiled from records in Nairobi and Machakos hospitals. In 1972-1977, however, there were 130 cases reported in the Machakos focus, mainly from the district hospital and clinical centres. The Arthi River valley origin of these cases is well documented. The epidemic outbreak reached its peak in 1988, when approximately 2,000 cases of kala azar were diagnosed during that year. This focus, unlike the other endemic foci of kala azar in Kenya, has a comparatively higher population density and experiences higher rainfall. The population is settled in individual
small farm lands along the Arthi River Valley where each family grow crops like maize, pigeon peas, cowpeas, and an assortment of vegetables and fruit trees for their own domestic consumption. Cotton and castor seeds are also grown as cash crops in the area.

Masinga Focus:

The Masinga focus lies between the Kitui and Machakos, and separated by the Yatta Plateau. The Yatta Plateau was formerly a game reserve and kept the two foci separated. In this focus four series of dams have been constructed since 1968, with the fourth dam completed in 1981. Surveys conducted before the construction of the dam in Masinga revealed the presence of the known vectors of visceral leishmaniasis but there had been no cases prior to the construction of the series of dams. Between 1978 and 1981, over 50 cases were reported (Ministry of Health Records). The majority of these were young children. This focus was therefore a result of introduction of the disease from Kitui, which lies immediately adjacent to the Masinga focus. The influx of people from the two districts, Kitui and Machakos, in search of employment and irrigated land, resulted in the introduction of the disease to Machakos Arthi River Valley by the people from the area returning from Masinga. Hence, the Masinga focus was a bridge between Machakos and Kitui kala azar foci.

Baringo and West Pokot Foci:

These two foci are situated within the Rift Valley. The Baringo focus was established as endemic for kala azar in 1955 and 1956, and it was suggested that probably the introduction of the disease in this area followed cattle trade routes. The population in these two foci is comprised of pastoralists who are very mobile with their flocks, in search of better pastures. Forty cases were diagnosed in 1954-56 in Baringo district and in 1957, 104 cases were detected from Baringo towards the eastern foothills of Kamasia range, Kerio Valley, Lake Bogoria area, and North of Lake Baringo. Investigations in 1981 by Leeuwenberg et al. confirmed the continued local endemicity of the disease in this focus. In West Pokot, the first case was reported in 1956, and thereafter, 38 cases were reported. Epidemiological surveys in 1970's revealed many more cases and the importance of the disease in the area was highlighted.

From the time kala azar was established to be endemic in Kenya, the disease has continued to show a very rapid spread. Cases of the disease have been detected all over the low land arid zone of the country North of the Equator and also South of the Equator, in Kitui, Machakos, Meru district and, to a very small degree, in Embu district. The arid zone which is endemic for leishmaniasis lies below 5000ft above sea level. The disease is potentially dangerous because it is not only very debilitating, but fatal as well; in Kenya, it is known to have a mortality rate of over 90% if untreated. Furthermore, although the disease was previously known to be limited to sparsely populated areas whose inhabitants are nomads who have difficulty in obtaining food and water, (hence suffer from malnutrition) the recent Machakos district disease epidemic outbreak in a comparatively stable population of high density has shown some changes in its trends of spread. Since 1957, only
parasitologically proven cases are reported as kala azar to the Kenyan Ministry of Health. However, because of lack of better diagnostic procedures, splenic and sternal puncture are the only means of diagnosing the disease and there are very few doctors who have the time and facilities to routinely carry out these procedures. Consequently, many more cases of the disease exist than are reported.

Kala azar in Kenya is mainly a disease of children and youths and more boys than girls acquire the disease. There are suggestions, from various epidemiological investigations, that this result from differences in immunity. Other environmental or behavioral factors so far assessed have not been able to explain these differences.

Animal Reservoirs of Visceral Leishmaniasis:

Ever since VL has been considered endemic in Kenya, the disease was deemed, for various reasons, to have an animal reservoir. These include the sporadic nature of the disease, and the occasional unexplainable disease epidemics. Heisch examined various animals in the Kitui district focus, including mongoose, spiny mice, gerbils, lizards, aardwolf, ground squirrels, genet cats, ichneumons, naked rats, monkeys, bush babies, elephant shrews, rock hyraxes and porcupines. These examinations were negative except for a hamster which had been inoculated with emulsified spleens of 3 mongooses (Helogale) which was found to be infected 10 months later. This investigator also found another hamster positive for Leishmania after it was inoculated with pooled spleens from 300 gerbils. However, he cautioned against acceptance of these two isolations because of the possibility of cross infection in the laboratory, since the hamster was in the same room with another group of infected hamsters and the cages were infested with bed bugs.

In the Rift Valley, he later examined 1,780 wild animals by culture in NNN medium and isolated four strains of Leishmania. Of these, 3 were from gerbils (Tatera robusta) and one from a ground squirrel. These strains later were sent to the Liverpool School of Tropical Medicine along with our own isolates from Baringo, and identified as Leishmania major. In studies on animal reservoirs in the Rift Valley in Baringo and West Pokot, 839 wild animals and 80 domestic dogs were examined in search of kala azar reservoirs. (Table) From these came 61 isolates; 55 from lizards, one from a domestic dog, one from an owl, one from a hawk. One of the isolates from a gerbil Tatera sp. proved to be L. major. In the Machakos focus, 288 sickly-looking emaciated dogs were examined by culturing splenic aspirates in NNN medium and Leishmania were isolated from two dogs. The isolates from these dogs and the one from the Rift Valley (West Pokot) were characterized biochemically in Liverpool and identified as L. donovani. Later in Kitui, more work on reservoirs was carried out on suspected vectors of kala azar, mainly canines. These included 76 dogs, 12 mongooses (Helogale sp.) and 12 genet cats (Genetta sp.). Four leishmanial isolates from mongooses and 1 from a genet cat were made. These were typed, but none were identified as L. donovani parasites. Therefore the dog is the only incriminated reservoir of the disease in East Africa, to date. The search, however, has not been exhaustive; many areas of investigation are very inaccessible by road and a difficult environment to work in.
Vectors of Leishmaniases:

The search for vectors and reservoirs of visceral leishmaniasis in Kenya started with the onset of the disease epidemic during and after the second World War (1921-27), although sandflies had successfully been reared in the country much earlier. The phlebotomine sandflies so far described in Kenya fall within the two major Old World genera, i.e. Phlebotomus and Sergentomyia. From both genera, infective human Leishmania parasites have been isolated and identified and, hence, species from both genera are deemed to be vectors of leishmaniases in Kenya.

The following species of Phlebotomus are found in Kenya:

**Phlebotomus duboscqi** Neveu-Lamaire 1906
**Phlebotomus rodhaini** Parrot 1930
**Phlebotomus orientalis** Parrot, 1936
**Phlebotomus saevus** Parrot and Martin, 1939
**Phlebotomus guggisbergi** Kirk and Lewis, 1952
**Phlebotomus martini** Parrot, 1936
**Phlebotomus celiae** Minter, 1962
**Phlebotomus vansomerinae** Heisch, Guggisberg, & Teesdale, 1956
**Phlebotomus elgonensis** Ngoka, Madele and Mutinga, 1975
**Phlebotomus pedifer** Lewis, Mutinga and Ashford, 1972
**Phlebotomus heischi** Kirk and Lewis, 1950

Of the twelve species belonging to the genus Phlebotomus, five have been incriminated or suspected as vectors of leishmaniases in Kenya, these include *P. martini*, *P. celiae*, *P. vansomerinae*, *P. duboscqi* and *P. pedifer*.

The genus Sergentomyia in Kenya includes the following 27 species:

**Sergentomyia squamipleuris** Newstead 1912
*S. africana* Newstead 1912
*S. ingrami* Newstead 1914
*S. teesdalei* Minter 1963
*S. serrata* Parrot and Malbrant, 1945
*S. kitonyi* Minter, 1963
*S. kirki* Parrot 1948
*S. squamipleuris* Newstead 1912
*S. harveyi* Heisch, Guggisberg, and Teesdale 1956

*S. dicipliens* Theodore 1931
*S. yusafi* Sinton 1930
*S. durenii* Parrot 1934
*S. schwetszi* Adler, Theodore, and Parrot 1929
*S. antennata* Newstead 1912
*S. bedfordii* Newstead 1912
*S. gracilis* Kirk and Lewis 1952
*S. blossi* Kirk and Lewis 1952
*S. garnhami* Heisch and Guggisberg 1956
*S. adleri* Theodore 1933
*S. rosanna* Heisch, Guggisberg, and Teesdale 1956
*S. multidens* Heisch, Guggisberg, and Teesdale 1956
Of the above mentioned species of the genus Sergentomyia, some have been shown to harbor infective leishmanias of man and wild animals and some have been experimentally infected. Some of the sandfly species infected with either promastigotes or amastigotes have also been shown to be anthropophilic. These include *S. garnhami*, which has been incriminated as a possible vector of *L. donovani* and *S. ingrami* and *S. garnhami* as vectors of *L. major*.

**CUTANEOUS LEISHMANIASIS**

In Kenya, two forms of cutaneous leishmaniases have been established i.e. *Leishmania aethiopica* and *L. major*. The epidemiology of both diseases has been studied in great detail. *L. aethiopica* is a zoonotic disease; the parasite is harboured by tree and rock hyraxes and the giant rat. The vector of *L. aethiopica* is *Phlebotomus pedifer*, which is a cave sandfly not found in lowlands below 5,000 ft above sea level. The first focus of the disease was described only in 1969 and early 1970s. The caves which harbour the vector of *L. aethiopica* are located in the forest. The movement of people in search for more, or better, agricultural land has brought man in contact with the vector (*P. pedifer*). Some of the caves are large enough to accommodate large animals, including elephants. The consequent modification of the colony by man could drive away the wild animal reservoirs on which the vectors feed, and lead to either disappearance of the disease in the vectors which inhabit the caves, or the vectors could modify their feeding behavior and start to feed mainly on man himself, thus establishing a human-to-human disease cycle. Although the disease is known to occur on the slopes of Mt. Elgon and both the Mau and Aberdares escarpments of the Rift Valley, it is possible that the disease has a much wider spread in high altitude areas of the Eastern Africa Region where the vectors and wild reservoirs exist.

The occurrence of *Leishmania major* has been established much more recently in Kenya. It was accidentally discovered during a search for animal reservoirs of *L. donovani* in lowland Kenya. A focus has now been identified in Baringo district, in the Rift Valley; the disease is considered to be zoonotic. In this area where the disease has been encountered in wild animals, no human cases have been encountered except for an expatriate caucasian family, living in the Rift Valley diagnosed as having *L. major*, and believed to have contracted the disease locally. Also, a case of cutaneous leishmaniasis reported by Southgate and Minter might have been *L. major*. It is possible that a meticulous search for active lesions might reveal more cases, but at the moment the infection seems to be essentially confined to wild rodents.
Prevalence of Kala-azar cases in Kenya, 1975-1984
The main vector of *L. major* is *P. duboscqi* whose resting and breeding sites have been shown to be mainly inside rodent burrows.\(^{29,30,37}\) Secondary zoonotic vectors have been shown to be *P. martini* and *Sergentomyia ingrami.*\(^{29}\) Leishmania parasites have been isolated in nature from these two phlebotomine sandfly species\(^{30}\) and laboratory experiments have confirmed the vector potential of *S. ingrami.*\(^{29}\) Although *P. duboscqi,* is currently an animal burrow dweller, it has been shown to invade human dwellings elsewhere.\(^{44}\) The current animal burrow restriction may be merely opportunistic and due to an abundance of rodents inside the burrows on which *P. duboscqi* and other suspected vectors feed. Since the current focus is within an irrigation scheme, the time may come when rodents' feeding activities might extend to food being produced for human consumption and the destruction of the rodents will be deemed necessary. If this happened, lack of food for the flies inside the burrows could necessitate their movement from burrows to human dwellings and the disease could then spread to man. So far the animal reservoirs encountered in the Baringo focus are several species of rodents, which include Nile rat, gerbil, elephant shrew and ground squirrel.\(^{41,33,42}\) Recent work has shown that the vectors will feed freely on a variety of hosts including avians, reptiles and mammals (Mutinga unpublished). The existing list of reservoirs might well be extended.

The recent discovery of this zoonotic focus of *L. major* raises the question of how widespread the disease might be in East Africa in general, and Kenya in particular. There are no obvious reasons why it should be restricted to this focus. The animal reservoirs are indeed encountered throughout arid Kenya, and it is likewise possible that the vectors have a wide distribution, as well. This, however, remains to be established through investigations. The search for vectors in animal burrows requires special techniques of trapping, including castor oil sticky traps, light traps and animal baited traps which will assist in establishing whether or not other *Leishmania major* foci do exist elsewhere. Several questions are posed by the coexistence of *L. major* in the same focus with *L. donovani.* These include whether or not there exists some degree of protection upon exposure to one from or the other of the two diseases.

**CONTROL OF LEISHMANIASIS IN KENYA**

There is not one set rule on the control of leishmaniases which is applicable throughout the world; mainly because different geographical regions have different sandfly vectors which inhabit different habitats or ecological niches. It is, therefore, imperative that before any control measures are carried out, either on a large or small scale, that a detailed investigation of the disease, vectors and reservoirs be undertaken. The investigations could include the type of disease being transmitted, the role of the vectors and the reservoirs of the disease in the environment. It would be also essential to establish the identity of specific vectors and reservoirs involved, their behavior and relative abundance in the environment, their biology, breeding and resting sites and natural factors that influence their multiplication and dispersal.
In Kenya during the first epidemic outbreak of VL in the early 1950's, several control strategies were applied. These included vector control, screening patients and treatment and immunization. The vector control experiment programme was initiated in 1964 by the Division of Insect-borne Diseases of the Ministry of Health in the Kitui focus. Approximately 16 square miles of endemic area was covered. In this area, approximately 2,670 termite hills and 665 human dwellings were sprayed with 3,285 gallons of 2% DDT made from wettable powder. Hand powered spray equipment was used for this operation over a period of 33 days during the dry months of June-July 1965. The frequency of termite hills per square mile averaged 165. At the end of the operation, a degree of control equivalent to 87.57% was achieved for total species of sandflies in the area and 87.84% and 94.96% for S. garnhami and "Synphlebotomus" complex respectively. It was concluded that the campaign was successful in interruption of kala azar transmission by selective spraying at a cost of £10 sterling (UK) per square mile. The use of DDT has since been highly restricted and records show that VL epidemics have surfaced in these same sprayed areas, indicating reinvasion of vectors in the controlled areas.

In 1960 a large-scale vaccination trial against VL involving over 3,000 persons was carried out in the Kitui focus. Live cultures of a ground squirrel strain of Leishmania were used. The strain produced cutaneous nodules in human beings and appeared to protect completely against infection with L. donovani, but a six year follow up indicated that the protection did not stand up under natural conditions.

During the kala azar epidemic outbreak in Machakos focus located approximately 90 km East of Nairobi, the ICIPE and the Division of Insect-borne Diseases of Ministry of Health, cooperated in strategies aimed at containing the epidemic. Significant information on resting sites and behavior of vectors have been gained elsewhere in the country, the dog had been incriminated as reservoir of Leishmania donovani. The ICIPE "sticky trap" meant for trapping low density sandfly population was developed, with a large clear polythene sheeting set around the entire wall of the human dwellings, either inside or outside the houses. The traps were also set around termite hills, open places in fields and in bushy areas within the zone affected by disease. Large numbers of sandflies were trapped along with other dipterans. Using this technology the vectors of L. donovani in the area were identified and the behavior of the sandflies studied in detail. This trap proved also to have a tremendous potential in the control of vectors, because the population of both P. martini and S. garnhami, the vectors of the disease in the area, dropped to significantly low levels both inside houses and in the fields in the area under investigation. During the campaign, all parasitologically diagnosed kala azar cases were treated. Sickly dogs from affected homes were killed. The population was mobilized for public health education and to destroy all termite hills within a 20m radius of homes. Monitoring of flies caught inside and outside homes was maintained to evaluate species quantity and infection rates. The people were educated on use of sticky trap and how to apply them effectively themselves. The results have been remarkable. In an area with approximately 2,000 cases in 1979, the disease has virtually disappeared.
For high altitude vectors of *L. aethiopica*, i.e. *P. pedifer*, which inhabit caves, the approach to control of the disease has been to advise people to avoid the caves, but young people are not very easily kept away from such adventurous exercises and consequently, a few cases occur from time to time. However, control of the vectors in the caves, is feasible through the application of either insecticides or biological control, because of the restricted breeding and resting sites inside the caves.

The control measures against vectors of *L. major*, i.e., *P. duboscqi*, are more difficult because of their specialized niche, the animal burrows. *P. duboscqi* breeds deep inside animal burrows, unlike *P. martini* and *S. ingrami*, which breed near the entrance. The discovery of the breeding sites is a very important finding and opens possibilities of targeted control strategy planning. However, one has to consider the reservoirs and the environment before any final decision is made. Animal bait in conjunction with sticky traps have given very good results and need to be assessed further. A species of mite has been identified in ICIPE which is predacious on sandfly eggs and larvae and the efficacy of this mite in the control of animal burrow populations is in progress.

REFERENCES

28. Okot-Kotber, et al.,

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Examination of animals for Leishmania Donovani in Kenya  
Heisch 1962

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Wild and domestic animal examination for Leishmania in Baringo and West Pokot Districts 1973-1976
Ngoka & Mutinga, 1978

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<td>Arvicanthis niloticus</td>
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<td>Bdeogale crassicauda</td>
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<td>Canis mesomelas</td>
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<tr>
<td>Canis familiaris</td>
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<td>Tribe caprini</td>
<td>Goats</td>
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<td>Ceropithicus aethiops</td>
<td>Vervet monkey</td>
<td>7</td>
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<td>Erythrocebus patas</td>
<td>Patas monkey</td>
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<td>-</td>
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<tr>
<td>Genetta trigina</td>
<td>Blotched genet)</td>
<td>26</td>
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<tr>
<td></td>
<td>cat</td>
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<td></td>
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<tr>
<td></td>
<td>small spotted genet</td>
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<td>genet cat</td>
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<td>Otomys sp.</td>
<td>Vlei rat</td>
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<td>-</td>
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<td>Papio anubis</td>
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<tr>
<td>Procavia habessinica</td>
<td>Hyrax</td>
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</tr>
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<td>Rhynchotragus sp.</td>
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<td>5</td>
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<tr>
<td>Tatera robusta</td>
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<td>27</td>
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<td>Taterillus</td>
<td>Gerbil</td>
<td>21</td>
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<td>Xerus erythropus</td>
<td>Striped ground</td>
<td>18</td>
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<tr>
<td></td>
<td>Squirrel</td>
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Total 700 4
Lizard and bird flagellate recoveries in Baringo and West Pokot Districts 1973-1976, Ngoka and Mutinga

<table>
<thead>
<tr>
<th>Species</th>
<th>Common name</th>
<th>No. examined</th>
<th>No. with flagellates</th>
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<td>Agama agama</td>
<td>Rock/agama</td>
<td>80</td>
<td>16</td>
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<tr>
<td>Latastia longicaudata</td>
<td>Lizard</td>
<td>10</td>
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<td>Mabuya sp.</td>
<td>Lizard</td>
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<td>33</td>
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<tr>
<td>Hemidactylus sp.</td>
<td>Gecko</td>
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<td>1</td>
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<tr>
<td>Varanus sp.</td>
<td>Monitor lizard</td>
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<tr>
<td>Testudo pardelis</td>
<td>Leopard tortoise</td>
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<td>0</td>
</tr>
<tr>
<td>Bubo Africa</td>
<td>Spotted eagle owl</td>
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<td>1</td>
</tr>
<tr>
<td>Therathopius ecaudatus</td>
<td>Bateleur</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Gerrhosaurus m. Bottegois</td>
<td>Plated lizard</td>
<td>5</td>
<td>0</td>
</tr>
<tr>
<td>(Hawks)</td>
<td>Hawks</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>Total</td>
<td></td>
<td>219</td>
<td>59</td>
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Sandfly emergents from Marigat Baringo District soil samples obtained from eight different habitats

<table>
<thead>
<tr>
<th>Habitat</th>
<th>Termite hill</th>
<th>Animal burrows</th>
<th>Tree holes</th>
<th>Human dwellings</th>
<th>Animal enclosures</th>
<th>Shade trees</th>
<th>Open ground</th>
<th>Rock cleft</th>
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<tbody>
<tr>
<td>No of productive samples</td>
<td>2</td>
<td>12</td>
<td>4</td>
<td>2</td>
<td>5</td>
<td></td>
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</tr>
<tr>
<td>Approx. weight of samples</td>
<td>51kg</td>
<td>167.5kg</td>
<td>55kg</td>
<td>15kg</td>
<td>165kg</td>
<td></td>
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<tr>
<td>P. Martini</td>
<td>8</td>
<td>45</td>
<td>2</td>
<td>2</td>
<td>1</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>P. Duboscqi</td>
<td>-</td>
<td>45</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>S. Ingrams c</td>
<td>57</td>
<td>1820</td>
<td>255</td>
<td>461</td>
<td>137</td>
<td>1</td>
<td>-</td>
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<tr>
<td>S. Schretzi</td>
<td>19</td>
<td>75</td>
<td>8</td>
<td>23</td>
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<td>S. Antennatus</td>
<td>277</td>
<td>1846</td>
<td>12</td>
<td>235</td>
<td>49</td>
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<td>-</td>
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<tr>
<td>S. Bedfordi</td>
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<td>446</td>
<td>8</td>
<td>4</td>
<td>4</td>
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<td>S. Africanus</td>
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<td>6</td>
<td>4</td>
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<tr>
<td>S. Graingeri</td>
<td>-</td>
<td>5</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>S. Clydei</td>
<td>15</td>
<td>84</td>
<td>4</td>
<td>8</td>
<td>1</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>S. Adleri</td>
<td>4</td>
<td>9</td>
<td>-</td>
<td>-</td>
<td>1</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>S. Affinis</td>
<td>3</td>
<td>12</td>
<td>2</td>
<td>-</td>
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</tbody>
</table>
CURRENT SITUATION IN REGARD TO CUTANEOUS LEISHMANIASIS IN KENYA

John I. Githure

RESEARCH TRENDS

Cutaneous leishmaniasis (CL) causes disfiguring lesions and life-long scarring. Loss of worktime due to this disease, especially in new development projects or in military training, has an important economic consequence. Cutaneous leishmaniasis of the Old World is normally caused by three species of Leishmania: *L. major*, *L. tropica*, and *L. aethiopica*. Cutaneous lesions caused by *L. donovani* are also reported in East Africa, Asia, and the Mediterranean region. All four of these species of *Leishmania* have been reported in Kenya.

Cutaneous leishmaniasis caused by *L. aethiopica* was first reported in the Mt. Elgon region of Kenya by Kungu *et al.* The vector was identified as *Phlebotomus longipes* while the hyraxes were incriminated as the reservoirs of this disease. Recently, several cases of diffuse cutaneous leishmaniasis caused by *L. aethiopica* acquired in the Aberdare range in Nyandarua District have been treated at the leishmaniasis clinic of the Kenya Medical Research Institute (KEMRI) (P.A. Kager and R. Muigai, personal communication). The Aberdare range represents another focus of *L. aethiopica* in addition to the Mt. Elgon focus.

*Leishmania major* was first isolated from a ground squirrel and gerbils by Heisch and Heisch *et al.* in Baringo and West Pokot Districts in Kenya. They thought they had isolated *L. donovani*, however, these strains were later characterized as *L. major*. Recently, workers at KEMRI and the International Centre for Insect Physiology and Ecology conducted an epidemiological survey of leishmaniasis in Baringo District, Kenya. Search for vectors of *Leishmania* resulted in the discovery of *P. duboscqi*, the vector of *L. major* in West Africa. A few months later Beach *et al.* isolated *L. major* from *P. duboscqi* and also from lesions on the hand caused by the bite of the same fly. The parasites from the lesions and those isolated from the fly were indistinguishable from a *L. major* reference strain on isoenzyme analysis and Balb/c mice inoculated with these isolates developed lesions on the nose. Other isolations of *L. major* were also made from *P. duboscqi*.

Search for animal reservoirs of leishmaniasis resulted in the isolation of *L. major* from five different species of rodents: *Tatera robusta*, *Arvicanthis niloticus*, *Taterillus emini*, *Mastomys natalensis*, and *Aethomys kaiserl.* The latter three species represented newly recorded hosts of *L. major*. In addition, *L. major* was isolated from a naturally infected vervet monkey (*Cercopithecus aethiops*) trapped in Thika, Kiambu District of Kenya (Binhazim, A.A. personal communication). Their findings represent the first recorded case of a naturally infected non-human primate with *L. major*. Experimental infections in several species have been carried out to determine the suitability of East African primates as animal models of cutaneous leishmaniasis caused by *L. major* (Githure *et al.* unpublished). The vervets, sykes and baboons demonstrated a self-cure phenomenon after about three months post...
infection which suggests that these species may afford promising models for immunological investigations.

After the discovery of the rodent/fly/rodent cycle of L. major in Baringo District, a case finding survey was done by KEMRI investigators, and during this study L. major was isolated from three patients who had lesions on the face and arms (Muigai et al. in press). This is the first record of an indigenous case of cutaneous leishmaniasis due to L. major.

Cutaneous leishmaniasis caused by L. tropica was discovered through 3 isolates from three Americans aged 9, 12 and 34 in 1985 and 1986. These isolates were indistinguishable from a L. tropica reference strain by isoenzyme analysis and were not infective to Balb/c mice. The boy age 9, and his sister age 12, were born and brought up in Kenya. The boy had never left the country but the girl had visited the USA at the age of 5 years. These children reside in Laikipia District and had visited Samburu, Narok, or Nakuru Districts. A 34 year old American who is also a resident in Kenya visited these same Districts six months preceding the onset of leishmanial skin lesions in 1986. He had also not travelled outside Kenya during the 8 years previous to onset of the disease except for a 10 day trip to Zaire in 1984. Although these patients were of American origin, their only potential exposure to sandfly bites was in Kenya. The authors report that this is the first record of L. tropica in Kenya, or any locality in the Sub-saharan region of Africa.

Leishmania donovani, the causative agent of visceral leishmaniasis (VL) can also cause cutaneous leishmaniasis. This disease is referred to as post kala azar dermal leishmaniasis (PKDL), a papular or nodular rash on the face and upper extremities which occurs during the treatment of VL or within several months or years after completion of therapy.\(^{(2,19)}\) This disease occurs infrequently in Kenya with an incidence of 2% among patients treated for VL.\(^{(1,2)}\) Simple cutaneous lesions without evidence of visceral involvement due to this parasite, as reported from North Africa,\(^{(5)}\) have not been reported from Kenya.

In an attempt to understand the epidemiology of leishmaniasis in Kenya, a Leishmania cryobank was established in KEMRI to cryopreserve isolates from patients, sandflies and animals. Between January 1981 and April 1987, leishmanial isolates from patients [295], sandflies [196], rodents [75], lizards [13] and a monkey [1], (excluding isolates from other countries) were cryopreserved in the Nairobi Leishmania Bank in KEMRI. These isolates are routinely characterized by isoenzyme electrophoresis and some of them inoculated into laboratory animals. The use of \(k\)DNA probes has been established as an additional technique for differentiating these isolates.

**RECOMMENDATIONS**

Treatment of cutaneous leishmaniasis is the most effective way of controlling the spread of this disease. The Clinical Research Centre of KEMRI has been conducting case finding surveys and systematic treatment of leishmaniasis patients mainly from Baringo, Machakos and Kitui endemic foci since 1980. Patients positive for either visceral or cutaneous
leishmaniasis are treated at KEMRI and a policy of follow-up of patients at 3, 6 and 12 months post-treatment is strictly applied.

The existence of **L. major** in Kenya is well documented in Baringo District. Search for this parasite in animals, sandflies and man should also be carried out in other regions of Kenya to determine the prevalence of this disease. **L. aethiopica** has been recorded from two mountainous regions of Kenya, Mt. Elgon and Aberdare range. The prevalence of this parasite in other highland regions should also be investigated, especially on the slopes of Mt. Kenya which is above 1500m. Investigations should also be intensified to establish the transmission pattern of **L. tropica** in Laikipia, Narok, Samburu and Nakuru Districts of Kenya. However, the reports to date suggest that there is a potential risk of an epidemic of cutaneous leishmaniasis if an ecological shift takes place, for example, settlement or commercial schemes or controlling the rodent population. There is therefore a need to make cutaneous leishmaniasis a notifiable disease in Kenya.

**REFERENCES**

CURRENT STATUS OF VISERAL LEISHMANIASIS IN ETHIOPIA

Teklemariam Ayele

INTRODUCTION

Ethiopia has a surface area of 900,000 km², and a population of about 42 million (1984 census). Its topography consists of northern and central plateau separated by the Ethiopian Rift Valley from the southeastern plateau. The Ethiopian plateaus abruptly fall to the lowlands in the east but the fall is more gradual in the west. The northern and central plateau is tilted towards the west and water drains in that direction through the Blue Nile, Takeze, Baro and Akobo rivers. The southeastern plateau drains toward the Indian Ocean through the Juba river of Somalia with all its tributaries from Ethiopia and the Wabi Shebele river. The Awash and Omo rivers drain to the east and south, respectively.

The climate of Ethiopia ranges from 'Kur' (very cold) at altitudes of 3,300m and above with mean annual temperature of 10°C or less to 'Dega' (highland at 2,300-3,300m with mean temperatures of 10-15°C, 'Weina Dega' at 1,500-2,300m and mean temperatures of 15-20°C, 'Kola' (hot) at 500-1,500m with mean temperatures of 20-30°C, and 'Bereha' (very hot) less than 500m with mean temperatures of 30-40°C. The amount of rainfall decreases from southwest to northeast and east because of the long distance that has to be traversed. Finally the descent of the air stream at the eastern escarpment of the plateau warms the air and the areas below are in the rainfall shadow. The higher regions of the southwest (Illubabor, Kefa) where rainfall is abundant in summer are wet most of the year. In general, the highlands experience adequate rainfall with more moderate and cooler temperatures while the lowlands have higher temperatures with low, unreliable, rainfall that sometimes results in long periods of drought.

Most of the Ethiopian people live in the highlands, but recently large number of people from the highlands have resettled in fertile lowland areas. The highlanders are settled agriculturalists and the native lowlanders are nomadic or semi-nomadic and largely herdsmen by occupation.

These topographical, climatic, and population characteristics are some of the important determinants of visceral leishmaniasis (VL) and cutaneous leishmaniasis (CL) transmission in Ethiopia. The occurrence of VL in Ethiopia has been described by several authors. Fevro-Luzzi described nine cases from the lowlands of Eritrea, although the exact residence of these patients was not indicated. Anderson reported 136 cases and, of these, 87 were infected in southwestern corner of Ethiopia, at the mouth of the Omo River north of Lake Turkana. Tekle et al. described 13 cases of VL from Humera and Memgesha and Abuhay reported 27 cases from the Metema-Humera lowlands. Maru also reported 14 cases from Metema-Humera and 4 cases from other parts of Gondar. Fuller et al. examined 2,723 people and found 2 cases of VL in Southwestern Ethiopia. Lindtjorn and Lindtjorn and Olafsson
have demonstrated the presence of VL in southern Ethiopia along the Segen and Woito Valleys. Ayele and Ali recently reported the findings of a three year country wide survey. 

The current situation of VL in Ethiopia is known from on-going studies.

PEOPLE AND METHODS

Active and passive surveillance were conducted from January 1981 to April 1987; during the latter half of the period, active case finding was restricted to members of the Aba Roba Farmer's Association. In active surveillance the team went to suspected endemic localities where patients were examined, particularly for hepatosplenomegaly. However, each case was also examined for fever, emaciation and pallor. All suspected of having VL were seen for further clinical and laboratory examinations. Definitive diagnosis was made by demonstration of amastigotes, either by smear, or NNN culture of spleen or bone marrow aspirates.

During passive surveillance, suspected VL patients were referred to our team from hospitals, health centres and clinics. Most of the referred patients came from the Armed Forces and Police Hospitals in Addis Ababa. All military personnel were found to be free of VL before going to endemic areas.

Suspected cases were examined and interviewed using a standard questionnaire. Laboratory examinations include, Hb, CBC, ESR, blood film for malaria and relapsing fever, formol gel test, and spleen or bone marrow aspirate (smear or culture examination).

Sandflies were caught by light traps, resting catches using mouth aspirator, sticky traps, knock-down spray catches with pyrethrum solution, and human bait captures.

RESULTS

Geographical Distribution of Cases

Of 1,837 persons initially screened for VL during the study period, 300 were subjected to complete examination and 173 were confirmed as having VL (Figure 1, Table 1). The majority of cases [108] were contracted in the Segen Valley; in 52 cases the infection was acquired along the Red Sea coast, 4 in Gelana River Basin, 3 from northwestern lowlands (Teseney), one in the Ganale River Basin, 2 in northwestern lowlands and one in West Moyale. There were two cases from the Danakil Depression, one was from Ghibdo (Asset) and the other from Raya and Kobo.

Distribution by Age and Sex

The military personnel contracted the infection while on temporary duty in the endemic area. All but one were adult males. On the other
Fig. 1. Map showing distribution of visceral leishmaniasis cases in Ethiopia (1981-87)
the Segen Valley. Age and sex distribution of cases is presented in Table 2. The male to female sex ratio 3.5:1. About 40% were under 20 years of age and 41% were children below 15 years of age. All but two military patients were over 20 years of age.

Table 1.

Distribution of Visceral Leishmaniasis by Administrative/Geographic, Region and Locality 1981-87

<table>
<thead>
<tr>
<th>Administrative/Geographic</th>
<th>Locality</th>
<th>Number Diagnosed</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gemu Gofa</td>
<td>Aba Roba</td>
<td>48</td>
</tr>
<tr>
<td></td>
<td>Galga</td>
<td>16</td>
</tr>
<tr>
<td></td>
<td>Goynada</td>
<td>10</td>
</tr>
<tr>
<td></td>
<td>Kormale</td>
<td>8</td>
</tr>
<tr>
<td></td>
<td>Gera</td>
<td>7</td>
</tr>
<tr>
<td></td>
<td>Sogem</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>Kolme</td>
<td>4</td>
</tr>
<tr>
<td></td>
<td>Gabo</td>
<td>4</td>
</tr>
<tr>
<td></td>
<td>Neyela Segam</td>
<td>3</td>
</tr>
<tr>
<td></td>
<td>Tobelana Kuchale</td>
<td>3</td>
</tr>
<tr>
<td></td>
<td>Kashule</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>Saba</td>
<td>2</td>
</tr>
<tr>
<td>Eritrea</td>
<td>Red Sea Coast</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Algena, Nakfa, Afabet</td>
<td>52</td>
</tr>
<tr>
<td></td>
<td>Asmat, Haltal, Melebo</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Teseney</td>
<td>3</td>
</tr>
<tr>
<td>Welo</td>
<td>Danakil Depression</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Ghibdo</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>Raya and Kobo</td>
<td>1</td>
</tr>
<tr>
<td>Sidamo</td>
<td>Gelana River Basin</td>
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</tr>
<tr>
<td></td>
<td>Gelana</td>
<td>4</td>
</tr>
<tr>
<td></td>
<td>Southern lowlands</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Moyale</td>
<td>1</td>
</tr>
<tr>
<td>Bale</td>
<td>Genale River Basin</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Wadera</td>
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</tr>
<tr>
<td>Gondar</td>
<td>Northwestern lowland</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Metema</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>Wolkait</td>
<td>1</td>
</tr>
<tr>
<td>Total</td>
<td></td>
<td>173</td>
</tr>
</tbody>
</table>

Clinical Findings

The most frequent symptoms were fever, abdominal enlargement and weakness and the most frequent signs were splenomegaly, pallor, wasting and hepatomegaly (Table 3 and 4).
Table 2.

Age and Sex distribution of visceral leishmaniasis in Ethiopia (1981-87)

<table>
<thead>
<tr>
<th>No. in age group</th>
<th>Sex</th>
<th>Ratio</th>
<th>Total</th>
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<tr>
<td>1-10</td>
<td>M</td>
<td>F</td>
<td></td>
</tr>
<tr>
<td>31</td>
<td>40</td>
<td>93</td>
<td></td>
</tr>
<tr>
<td>11-20</td>
<td>131</td>
<td>37</td>
<td>3.5:1</td>
</tr>
<tr>
<td>&gt;20</td>
<td>93</td>
<td></td>
<td>164*</td>
</tr>
</tbody>
</table>

* In 9 cases age and sex were not specified.

Table 3.

Frequency of symptoms of visceral leishmaniasis in Ethiopia (1981-87)

<table>
<thead>
<tr>
<th>Symptoms</th>
<th>No. of pos/ No. exam.</th>
<th>%</th>
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</thead>
<tbody>
<tr>
<td>Fever</td>
<td>169/173</td>
<td>97.7</td>
</tr>
<tr>
<td>Enlarged abdomen</td>
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<td>86.1</td>
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<tr>
<td>General complaints (Weakness, headache, dizziness)</td>
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<td>Weight loss</td>
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<tr>
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<td>19/173</td>
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Table 4.

Frequency of Signs of Visceral Leishmaniasis in Ethiopia (1981-87)

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<th>Signs</th>
<th>No pos/ No exam.</th>
<th>% pos</th>
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<tr>
<td>Splenomegaly</td>
<td>171/173</td>
<td>98.8</td>
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<td>Pallor</td>
<td>148/173</td>
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<td>Wasting</td>
<td>146/173</td>
<td>84.4</td>
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<td>Hepatomegaly</td>
<td>121/173</td>
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<td>Fever</td>
<td>103/173</td>
<td>59.5</td>
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<td>Edema</td>
<td>14/173</td>
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<tr>
<td>Lymph node enlargement</td>
<td>11/173</td>
<td>6.4</td>
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<tr>
<td>Jaundice</td>
<td>8/173</td>
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<tr>
<td>Darkening of the skin</td>
<td>5/173</td>
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<td>Ascites</td>
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</table>
The spleen was palpable in almost every patient and the liver was palpable in more than two thirds of our cases. A grading of splenic and liver enlargement is presented (Table 5). Liver enlargement exceeded 10 cms only in 4 cases while spleen enlargement was more frequently observed. Patients with longer duration of illness were severely emaciated.

Table 5.
Grading of liver and spleen enlargement in visceral leishmaniasis in Ethiopia (1981-87)

<table>
<thead>
<tr>
<th>Enlargement (Cms)</th>
<th>Liver No. Patients</th>
<th>%</th>
<th>Spleen No. Patients</th>
<th>%</th>
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<td>30</td>
<td>17.3</td>
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<td>6-10</td>
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<td>11-15</td>
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<td>39</td>
<td>22.5</td>
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<td>16-20</td>
<td>1</td>
<td>0.6</td>
<td>23</td>
<td>13.3</td>
</tr>
<tr>
<td>&gt; 20</td>
<td>--</td>
<td>--</td>
<td>4</td>
<td>2.3</td>
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<tr>
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<tr>
<td>Total</td>
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<td>100.0</td>
<td>163</td>
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Table 6.
Frequency distribution of hemoglobin levels and white blood cell counts in visceral leishmaniasis in Ethiopia (1981-87)

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<th>Hb in gm %</th>
<th>No. (and %) among 100 patients</th>
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<td>&lt; 5</td>
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<tr>
<td>9-10</td>
<td>48</td>
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<tr>
<td>&gt; 10</td>
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</table>

<table>
<thead>
<tr>
<th>WBC/mm³</th>
<th>No. (and %) among 158 patients</th>
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<td>1000-2000</td>
<td>32</td>
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<tr>
<td>2001-3000</td>
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<td>3001-4000</td>
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<td>4000-5000</td>
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<td>Over 5000</td>
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</table>
Laboratory Results

Over 80% of VL cases had a Hb of 20 gm % or less (Table 6); about 50% of the cases fell into the range of 5-8 gm %. Over 80% had a WBC count of 4000/mm³ or less. Severe leucopenia of 2000/mm³ or less was seen in 60% of the cases.

Entomological Findings

Twenty species of sandflies were identified from a collection of 6,115 specimens in southwestern Ethiopia. These included 4 Phlebotomus and 16 species of Sergentomyia (Tables 7, 8).

DISCUSSION

The finding of new foci of VL in Gelana, along the Red Sea Shore, Danakil depression, Moyale, Segen Valley and near Gambella demonstrated a wider spacial distribution of the disease than had been known in Ethiopia. The possibility of anthroponotic transmission at Aba Roba is suggested. The fact that three infected children aged 5, 6 and 10 years from Goynada denied a history of travel to the valley floor, the known endemic area, further raises our suspicion of transmission of VL also occurring at Goynada above the escarpment in Aba Roba Farmer's Association. These observations need confirmation by detailed studies on autochthonous infection, vector, and reservoir host.

The preponderance of the disease in males (3.5:1) may be due to risks of their occupation. Male farmers and male children herding cattle and military personnel travelling through endemic areas had a higher risk of infection than women, who tend to stay in the villages.

The leading signs and symptoms of VL were fever, enlarged abdomen, weakness, splenomegaly, pallor and wasting. Complaints of diarrhea, sweating and anorexia were relatively common, while cough and epistaxis were rare. Edema, jaundice, darkening of skin and ascites were infrequent findings. No marked generalized lymphodenopathy was seen in Ethiopia. Post-kala azar dermal leishmaniasis was not encountered in our patients, either during or 1-2 years after treatment.

From our subjective evaluation, Ethiopian VL patients were seen in both acute and chronic stages of the disease. The former occurred mostly in military personnel and the latter in the indigenous population in endemic areas. In the acute stage the majority presented with high fever, palpitation, profuse sweating, moist skin, and were too ill to walk. Three presented in a typhoid-like state (toxemic). In patients presenting a typhoid-like state, VL must be considered in the differential diagnosis.

The patients with the chronic stage of the disease showed dry, scaly skin, hair changes, wasting, but were ambulatory. One of our patients was well nourished and clinically asymptomatic, presenting only splenomegaly and L. donovani in spleen aspirate. Such protean manifestations of VL call for awareness on the part of clinicians of the
diverse presentations of the disease, to achieve early diagnosis and treatment.

Leucopenia with lymphocytosis was the most frequent laboratory finding. About 61% had WBC counts of 3000/mm³ or less, and 82% had anemia.

The sensitivity and specificity of the formol gel test was about 82% and 55%, respectively, based on 186 VL suspects. The false negatives (36%) and false positives (23%) in our series are too large to encourage the use of this method as a screening test. In our opinion, examination of smears from spleen aspirate is the cheapest, fastest, and most reliable technique for diagnosis.

The entomological findings at Aba Roba Farmer's Association were interesting, in that two members of the subgenus Synphlebotomus (P. martini and P. celiae) have been added to the sandfly fauna of southwest Ethiopia (M. Mutinga and T. Ayele). To date no P. orientalis, the presumed vector of VL in Ethiopia, has been found in this VL endemic locality. The association of human cases of VL and P. martini and P. celiae in the Segen Valley suggests that these vectors play a role in the transmission of the disease.

REFERENCES

Table 7.
Species and number of sandflies collected from the Segen valley, southwest Ethiopia between March 1982 and March 1985

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Table 8.
Species, sex, and number, of sandflies collected with various methods from the Segen valley, southwest Ethiopia between March 1982 and March 1985

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CURRENT SITUATION REGARDING L. AETHIOPICA IN THE HIGHLANDS OF ETHIOPIA

Teferi Gemetchu

INTRODUCTION

Before embarking into the current situation of L. aethiopica in the highlands of Ethiopia, it may help to briefly review the historical development of research and other activities on cutaneous leishmaniasis (CL) in the highlands of Ethiopia.

Cutaneous leishmaniasis has been known to exist in Ethiopia since it was reported by Martoglio in 1913. Other Italian investigators also reported CL from highland regions of Ethiopia. Balzer et al. first reported diffuse cutaneous leishmaniasis (DCL) from Ethiopia. Later, Poirier, Price and FitzHerbert, Bryceson and Nichol and Bryceson and Leithead expanded knowledge of the geographic distribution, clinical features and treatment of CL in the Ethiopian highlands.

The first detailed epidemiological study on CL is that of Lemma et al. They studied the epidemiology of CL in Aleku (Wollega Administrative Region), Wurgessa (Wollo Adm. Region) and Sebeta-Meta Abo (Shoa Adm. Region), and showed that the sandfly Phlebotomus longipes was the vector in these areas. Later, Foster and Foster et al. carried out a longitudinal study on the ecology of P. longipes in Sebeta and gathered important information on the feeding, breeding and resting habits, flight range and infection rates of this species of sandfly.

Later Ashford et al. carried out further work on the epidemiology of CL in the highlands of Ethiopia. They discovered Ochollo and proved P. pedifer to be the sandfly vector here. Their most important finding was the discovery of hyraxes (Procavia capensis and Heterohyrax brucei) as the reservoir hosts of CL in the highlands of Ethiopia. Bray et al. described L. aethiopica as the causative agent of CL in the highlands of Ethiopia and Kenya.

CURRENT SITUATION OF L. AETHIOPICA

Clinical and Epidemiological Observations

Since the early 1970s no sound epidemiological study has been carried out on CL in Ethiopia. However, this was not because CL was not important in Ethiopia; but rather because priority was given to visceral leishmaniasis (VL) by TDR/WHO and other funding agencies and research on CL was neglected in favor of the funded VL programs. Nevertheless, observations have been made by scientists and clinicians working at the All Africa Leprosy and Rehabilitation Training Centre (ALERT) and the Armauer Hansen Research Institute (AHRI) on cases that came from different administrative regions of Ethiopia to seek treatment.
Most DCL patients came to these centres (hospitals) thinking that they had contracted leprosy because of the similarity to that disease.

In Ethiopia CL manifests itself as localized cutaneous leishmaniasis (LCL), oro-nasal (mucosal) leishmaniasis (ONL), and diffuse cutaneous leishmaniasis (DCL). It has been proved that the parasite responsible for all three forms is *L. aethiopica*. Ethiopian oro-nasal leishmaniasis involves the naso-pharyngeal region but does not metastasize nor result in extensive tissue destruction when compared to the typical American mucocutaneous leishmaniasis (Dr. David Humber, personal communication). The diffuse form is said to be uncommon in Ethiopia and this form occurs as a result of failure of cell mediated immunity to develop in some individuals.

Cutaneous leishmaniasis is reported to exist in almost all the 14 administrative regions (Dr. David Humber and Ato Ahmed Ali, personal communication). Most of the foci lie at an altitude of between 150m and 2,700m. The disease is primarily zoonotic with the parasite being maintained between hyraxes and sandflies (*P. longipes* and *P. pedifer*). In some situations (e.g. Kutaber-Wollo) inhabitants of villages found near hyrax habitats tend to suffer from CL. Children who tended domestic animals were infected in villages located some distance from the hyrax habitat. However, villages such as Ochollo are actually built on the rock hills that are the natural habitats of hyraxes and *P. pedifer*. Here, infected sandflies readily bite all ages and both sexes, indoors and outdoors. Although systematic surveys have not been done in all the administrative regions, it appears that the above situation (proximity of hyrax-sandfly and human habitation) may hold true for all the endemic CL foci in highland Ethiopia.

Recent observation carried out at ALERT reported a total of 104 CL cases coming to the hospital for treatment between 1981 and 1983. Of these, 98 were patients with LCL while 6 were DCL patients. The age range was from 10 to 29 years, and included more males (64) than females (40); 74.5% (73 of 98) had single lesions, 20.4% (20 of 98) had two lesions and 5.1% (5 of 98) had three or more lesions. The nose was the commonest site of involvement followed by cheek, forehead, lips, ear, chin, limbs and neck. Six DCL and 63 LCL cases were admitted to the hospital and/or treated. The majority of the patients were from Shoa Administrative region and 19 were from Addis Ababa. The duration of the disease ranged from one month to 10 years; the majority of the patients (83.7%) had the disease for less than one year. Patients with DCL had a mean duration of the disease of over 5 years.

A more recent study on the situation of CL in Ochollo is that of Drs. David Humber and Genene Mengistu of the Addis Ababa University (personal communication). They made a survey of the entire peasant association living in the four villages of Ochollo. The total population was around 3,000. They noted scars on 22-40% and active lesions on 3-5% of the population of the four villages. Two DCL cases were found in Ochollo. One is an old woman who may have had the disease for over 20 years, and the other is a 9-year old girl who had the disease for about 5 years. The two DCL cases were from different villages which are not physically far from each other. Although this is as yet unpublished, and
the data may require further refinement, we can say that about the same number of persons with scars and active lesions were seen by Drs. Humber and Genene (up to 45%) as those reported by Ashford et al. (41.1%) from a population sample of 895 persons.\(^{14}\) The work of Drs. Humber and Genene shows that transmission of \textit{L. aethiopica} is still going on in Ochollo at approximately the same, or slightly higher, rate.

**Control Activities**

There is no well planned control activity for \textit{L. aethiopica} in the highlands of Ethiopia. Only people who manage to reach ALERT, AHRI and the Institute of Pathobiology in Addis Ababa get treated. In the early 1980's a suggestion was put forward to undertake a pilot control project for CL at Ochollo. The baseline data collected up to 1980 indicate a prevalence level considered sufficient to warrant control of this disfiguring disease. A multidisciplinary approach involving treatment of cases, destruction of sandflies, elimination of hyraxes by trapping or killing, and a programme of health education and participation of the Peasant Association was proposed. However, for unknown reasons the proposal was not implemented.

Traditionally, people have tried to treat CL lesions by applying heat, leaves and leaf extracts, and tattooing the area surrounding the lesions. Almost all of these resulted in disfiguring the face or the part treated. I was informed by Dr. Humber that Dr. Franklin Neva of NIH, Bethesda tried controlled heat treatment on DCL cases at ALERT, but the results were not encouraging.

\textit{Leishmania aethiopica} is known to be resistant to antimonial compounds (e.g. Pentostam) and that the main treatment in use today is pentamidine methylate (Lomodine: Specia, Paris, France). Lomodine has a number of adverse side effects, such as severe nausea, vomiting and diabetes and is contraindicated in LCL infections\(^{17,19}\). Treatment of DCL patients with pentamidine resulted in some clinical improvement, however, it has been suggested that the drug should be used with caution. Three of the 6 DCL patients were smear negative on discharge from hospital while the other 3 remained smear positive. One of the three smear negative patients became positive 1-2 years after discharge. It appears, therefore, that pentamidine is not an effective drug for the treatment of \textit{L. aethiopica}. Treatment of CL patients with Ketoconazole is currently under investigation at ALERT.

**REFERENCES**

CURRENT SITUATION IN REGARD TO LEISHMANIASIS IN ALGERIA

S. Belazzoug

INTRODUCTION

Three forms of leishmaniasis are known to occur in Algeria: visceral leishmaniasis (VL) and two forms of cutaneous leishmaniasis (CL). All constitute a Public Health problem of considerable importance.

EPIDEMIOLOGICAL SITUATION

Visceral leishmaniasis is endemic in northern Algeria in the mountainous sub-humid bioclimatic zone. The disease affects mainly children under 5 years of age. There are around 200 diagnosed cases per year.

Zoonotic cutaneous leishmaniasis (ZCL) occurs in the steppe region of northern Sahara. In addition to the "historical" focus of Biskra, where a serious resurgence is occurring, there is a geographical spread as well. Epidemics frequently occur which involve several thousand cases per year. In the case of M'sila, the outbreak occurring in this previously uninfected area is probably due to agricultural development. An effort to control this new focus using DDT has failed.

A National Committee for the elaboration of a control programme was established in 1986.

The second form of cutaneous leishmaniasis is located in the northern part of Algeria along the mediterranean coast, i.e. the endemic zone of visceral leishmaniasis. Its parasitological, epidemiological, and clinical characteristics distinguish it from the ZCL endemic in the steppe regions (Table 1).

ISOENZYME CHARACTERIZATION OF LEISHMANIA

Isoenzyme identification of Leishmania isolates from patients and animals, using 12 enzymes [MDH, ME, IDH, 6-PGDH, G-6-PDH, DIA, MP, ASAT, PGM, FH, MPI, GPI] has proven to be a powerful epidemiological tool and have resulted in:

- the identification of L. infantum as the causative agent of human VL in both northern and southern Algeria.

- the identification of L. infantum from canine leishmaniasis, thus confirming the dog as the reservoir of human infection.

- the identification of L. major from patients originating from the arid zone of northern Sahara, establishing the zoonotic nature of the foci of this area.
the discovery of the same zymodeme of *L. major* in humans and *Psammomys obesus* (Rodentia:Gerbillidae), establishing the role of this animal as a reservoir.

- the discovery of a new enzymic variant of *L. infantum* for the Nucleoside Phosphorylase as the causative agent of CL in northern Algeria. (Differing by one electromorph from the agent of VL).

Table 1.

Differences between cutaneous leishmaniasis caused by *L. major* and *L. infantum* in Algeria

<table>
<thead>
<tr>
<th>Parameter</th>
<th><em>L. major</em></th>
<th>NP variant</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Clinical picture</strong></td>
<td>&quot;moist&quot; lesions</td>
<td>&quot;inflammatory&quot;</td>
</tr>
<tr>
<td></td>
<td>rural type CL</td>
<td>lesions</td>
</tr>
<tr>
<td><strong>Number of lesions</strong></td>
<td>Often numerous</td>
<td>Usually single</td>
</tr>
<tr>
<td><strong>Location</strong></td>
<td>Face and limbs</td>
<td>Face</td>
</tr>
<tr>
<td><strong>Incubation</strong></td>
<td>Short</td>
<td>Longer</td>
</tr>
<tr>
<td><strong>Duration</strong></td>
<td>3-5 months</td>
<td>More than year</td>
</tr>
<tr>
<td><strong>Amastigotes</strong></td>
<td>Large (3.2µ)</td>
<td>Small (2.1µ)</td>
</tr>
<tr>
<td><strong>Parasites in lesions</strong></td>
<td>Scarce</td>
<td>Numerous</td>
</tr>
<tr>
<td><strong>Culture in NNN medium</strong></td>
<td>Easy</td>
<td>Difficult</td>
</tr>
<tr>
<td><strong>Seasonal occurrence</strong></td>
<td>Aestivo-autumnal</td>
<td>Perennial</td>
</tr>
<tr>
<td><strong>Epidemic outbreaks</strong></td>
<td>Common</td>
<td>None</td>
</tr>
<tr>
<td><strong>Vector</strong></td>
<td><em>Phlebotomus papatasi</em></td>
<td><em>P. perniciosus?</em></td>
</tr>
<tr>
<td></td>
<td></td>
<td><em>P. longicuspis?</em></td>
</tr>
<tr>
<td></td>
<td></td>
<td><em>P. perfiliei?</em></td>
</tr>
<tr>
<td><strong>Reservoir</strong></td>
<td>Rodent</td>
<td><em>Psammomys obesus</em></td>
</tr>
<tr>
<td></td>
<td></td>
<td><em>Meriones shawi</em></td>
</tr>
</tbody>
</table>

REFERENCES

CURRENT SITUATION IN REGARD TO LEISHMANIASIS IN TUNISIA

M.S. Ben Rachid and R. Ben-Ismail

INTRODUCTION

Both visceral leishmaniasis (VL) and cutaneous leishmaniasis (CL) occur in Tunisia. Both forms constitute a public health problem; VL is not highly prevalent, but the mortality rate in untreated cases dictates that attention must be given to diagnosis and treatment, and periodic outbreaks of CL involve thousands of people and are a major problem.

VISCERAL LEISHMANIASIS

Visceral Leishmaniasis (VL) has been known in Tunisia since 1903, where the first case of infantile mediterannean kala azar was reported by Laveran and Cathoire. The foci are stable and almost all cases come from the sub-humid and semi-arid zones of the north; 77% of cases are less than 5 years old and of 699 cases reported since the discovery of the disease in Tunisia, only 20 (2.8%) were in patients over 14 years of age. Splenomegaly (99.2%), hepatomegaly (64%), fever (93.2%), weight-loss (62.4%) and anemia (98.2%) are the most frequent clinical signs. Current annual incidence is about 40 reported cases. Patients are generally of modest and rural origin. Mortality is 5 - 8%.

The causative parasite is L. infantum s.str. (zymodeme LON. 49, London = MON. 1, Montpellier; 6 typed human isolates). Amastigotes are small: 2 to 3.5µ.

Dogs are a proven reservoir host (20 typed strains). It is notable that canine VL is more widely distributed than the disease in man, especially in urban areas. Foxes and jackals are suspected of playing a role as reservoirs.

Phlebotomus perniciosus, P. perfiliewi and P. longicuspis are the suspected vectors.

CUTANEOUS LEISHMANIASIS

There are three clinical forms of cutaneous leishmaniasis in Tunisia, that affect both sexes and all age groups.

Sporadic cutaneous leishmaniasis

This form is observed in the North in the VL foci. Over 96% of cases have a single lesion on the face. Typically the lesions are distinguishable clinically from zoonotic CL or anthroponotic CL and consist of small crusty ulcers surrounded by a notable erythematous reaction. Presentation of cases reveals no particular transmission season. About 20 cases are observed each year. The parasite is difficult to maintain in culture and has not yet been typed. The amastigotes are always less
than 3\(\mu\) in diameter. This form of CL is probably the same as that found in similar biotopes in neighbouring Algeria where it is known to be caused by \(L.\) \textit{infantum}. The vector and the reservoir host are unknown.

**Zoonotic cutaneous leishmaniasis:** (ZCL)

ZCL is widespread in the centre and the south of the country. (semi-arid and arid zones). A new outbreak arose in 1982 in the central area where the disease was previously unknown. Since 1982, the epidemic has rapidly spread from the governorate of Kairouan to cover parts of 8 other governorates (Sidi Bouzid, Gafsa, Sfax, Mahdia, Tozeur, Kebili, Gabes and Kasserine). More than 20,000 cases were reported (active and passive case detection) since the beginning of the epidemic.

This form produces multiple lesions that heal in less than six months, leaving disfiguring scars. Secondary infection is frequent. There is a seasonal occurrence of the outbreaks (Aestivo-autumnal). The causative agent is \(L.\) \textit{major} (zymodeme MON 25, Montpellier; 30 human isolates typed). Amastigotes are large (4 to 6.5\(\mu\)) and it is easy to obtain parasites in culture. Leishmania were isolated from 3 rodent species: \textit{Psammomys obesus} (9 stocks), \textit{Meriones shawi} (1 stock) and \textit{Meriones lybicus} (1 stock). Typing is currently being undertaken in the Istituto Superiore di Sanita, Rome - (L. Gradoni - M. Gramiccia and S. Bettini). \(L.\) \textit{major} was confirmed in \textit{M. shawi} by other workers. Other rodent species may be involved as reservoir hosts in some foci.

\textit{Phlebotomus papatasi} is a proven vector of ZCL in Tunisia (Grade 3; 2 typed stocks).

**Anthroponotic cutaneous leishmaniasis** (ACL)

ACL is endemic at a lower level than ZCL and occurs principally in the South-East (pre-saharan zone) of the country. About 78% of cases have only one lesion, and over half the lesions are on the face. Unlike ZCL, healing is delayed and exceptional cases have been seen of six years duration. The current prevalence of ACL is unknown, but it is clearly less than that of ZCL.

The causative agent is \(L.\) \textit{tropica} (Zymodeme MON. 8, Montpellier). \textit{Phlebotomus sergenti} is the suspected vector but \(P.\) \textit{papatasi} and \(P.\) \textit{chabaudi} are also present in the affected area.

**Control Activities and Programs**

Leishmaniasis are notifiable diseases in Tunisia. Presently, only ZCL is considered as a major public health problem. No direct control of leishmaniasis is in progress, as the situation (causal agents, vectors or reservoirs hosts) is still unclear for some leishmaniasis forms (SCL, ACL). Concerning ZCL, further work on the vector and the reservoirs hosts is needed before implementing pilot control trials. Limited actions have been tried using brodifacoum (Klerat\textsuperscript{R}); and anticoagulant rodenticide) against \(P.\) \textit{obesus} and zinc phosphide against \textit{Meriones sp.}
CURRENT SITUATION WITH REGARD TO LEISHMANIASIS IN SUDAN,
WITH PARTICULAR REFERENCE TO THE RECENT OUTBREAK
OF CUTANEOUS LEISHMANIASIS IN KHARTOUM.

Sayda Hassan El Safi, W. Peters* and D. Evans*

INTRODUCTION

The Sudan is recognized as one of the most endemic areas of leishmaniasis in the world and three clinical forms of leishmaniasis, visceral, mucosal (oro-nasal) and cutaneous are all found. There have been numerous outbreaks of visceral leishmaniasis (VL) in Sudan and sporadic cases of both cutaneous leishmaniasis (CL) and mucosal forms have occurred since the first report of leishmaniasis in 1904. In 1976/77, however, for the first time, there was a large epidemic of cutaneous leishmaniasis to the North of Khartoum along the banks of the Nile, and then in early 1985 there was a second but smaller epidemic in a new area on the banks of the White Nile. During 1985 and 1986 a very large epidemic of CL flared up in the densely populated area of Khartoum province and many thousands of people suffered lesions.

This paper traces the history of leishmaniasis in the Sudan and considers the recent epidemic of cutaneous leishmaniasis in detail.

VISCERAL LEISHMANIASIS

Neave'1 described the first case of VL in Sudan; since then several workers have described various aspects of the disease. A kala azar Commission was set up in 1989 which investigated the disease over a four year period2. They found that the endemic area stretched along the Blue Nile and its tributaries and included the upper reaches of the Atbara River. A few cases resulted from patrols in remote areas of the country or from military camps3-4. Some years later a severe outbreak was reported from Melut and Kaka in the Upper Nile Province in Southern Sudan by Stephenson5. In 1956 a violent epidemic took place between the Blue and White Niles in areas previously thought to be free of the disease6. Between 1960 and 1964 a team from NAMRU-3 (The United States Naval Medical Research Unit based in Cairo) studied all aspects of the disease in Paloich Area in Upper Nile7.

Other reports of VL have been made by Shamseddin8 who found a case in Khartoum Province, Hamza et al.9 who reported it in 22 schoolchildren in the village of El-Khogalab in Khartoum Province, and by Satti (personal communication) in Ed Elish village in the White Nile province in 1982. The most recent outbreak was in El Dinder in Blue Nile province in 1985. Thus, the main endemic area for kala azar is in east and central Sudan stretching from Malakal in the south to Kassala in the northeast. Other foci have been found in the west in both El Fasher and El Nahud; Kapoeta in the far South and the recent outbreak in the Khartoum Area. (Figure 1.)

*London School of Hygiene and Tropical Medicine.
Fig. (1)

Distribution of Leishmaniasis in the Sudan

Endemic area of kala azar
Cutaneous leishmaniasis
Mucosal leishmaniasis
The clinical features of VL in Sudan have commonly been prolonged fever, hepatosplenomegaly, loss of weight, anaemia, generalised lymphadenopathy and epistaxis. Most of the patients have been in their teens, and the ratio of males to females has been three to one. Diagnosis was usually confirmed by the demonstration of amastigotes in bone-marrow, lymph nodes, and/or splenic aspirate. Most cases of VL in Sudan have responded satisfactorily to intravenous treatment with Pentostam for one month.

The vector of VL in Sudan was determined by the NAMRU-3 group to be Phlebotomus orientalis and the same study showed that two rodents and two carnivores were reservoir hosts. The rodents were the Nile rat Arvicanthis niloticus and the spiny mouse Acomys albigena while the carnivores were the genet and serval cats (Genetta gennetta and Felis serval).

MUCOSAL AND MUCOCUTANEOUS LEISHMANIASIS

The first report of ML in Sudan was by Christopherson in 1914 and several other reports have been published since. Milosev et al. described 16 cases seen in Khartoum between 1963 and 1966, of which 4 cases were not from a kala azar endemic area. These authors believed that L. donovani was the causative agent. Abdalla et al. reported a further 19 cases, bringing the total reported from Sudan by 1975 to 51, all adult males.

Clinically the patients fell into 4 groups, depending on the location of the lesions viz., Oral; Nasal; Oro-nasal; and Laryngeal.

Two types of lesions were encountered:

a) fungating tumours in which the mucosa was irregularly nodular, fissured, firm, and red.

b) diffuse ulcerative lesions in which the mucosa was pale, uniformly swollen, and covered with scabs.

None of the 51 patients had a history of cutaneous leishmaniasis and in this respect ML in the Sudan differs from that caused by L. braziliensis of South America, where metastatic lesions in the mucosa usually follow primary skin lesions.

The Sudan ML responded to two 10 day courses of intravenous treatments with Pentostam, (600 mg daily) with a break of one week between courses.

CUTANEOUS LEISHMANIASIS

Cutaneous Leishmaniasis (CL) was first reported in the Sudan in 1910 in two Egyptians who had contracted the disease in their own country. Archibald then reported a nodular form of CL in a Sudanese adult male from the Nuba mountains of Kordofan Province in 1914. Two
cases of Oriental sore were reported by Christopherson\(^{18}\), one from Khartoum province and one from Blue Nile Province. Kirk and Drew\(^{17}\) reported 5 patients, one from Blue Nile and 4 from Darfur. Cahill\(^{18}\) described skin lesions in 4 Americans who had apparently contracted the disease in the Blue Nile and Upper Nile Provinces. Abdalla et al.\(^{19}\) described 21 cases, of which most were from Darfur and Kordofan with a few from Kassala and Blue Nile, plus one from Khartoum.

Since these very sporadic reports there have been three recent outbreaks. The first, which was the first reported epidemic of CL in Sudan, started in 1976/77 in the Shendi-Atbara area about 170 km to the North of Khartoum and this outbreak spread along the banks of the Nile, both northward to the Northern Province and southward to reach Khartoum. The second outbreak was in early 1985, involving at least 80 cases in El Garrasa and neighbouring villages in the White Nile Area, which was previously believed to be non-endemic for leishmaniasis.

**The Recent Outbreak of CL in Khartoum Province.**

Suddenly in October 1985 cases of CL started to appear from Tuti Island, an island of about 10,000 inhabitants at the junction of the Blue and White Niles in the centre of the three towns of Khartoum, Khartoum North, and Omdurman. Subsequently there was a gradual increase in the number of cases reaching the dermatology clinics in Khartoum, indicating the commencement of an epidemic. In 1986 there was a dramatic increase in the number of cases and the infection was being transmitted throughout the three towns, and the Khartoum Province. From September 1986 through March 1987, almost 10,000 cases were reported from the various health centres in the Khartoum Province.

**Epidemiology of the outbreak.**

In this study the records of the disease in the Commission of Health Affairs were examined retrospectively. When the commission became aware of the outbreak, weekly reports from all the health centres in Khartoum Province were requested, but these date only from September 1986 when the epidemic was already at its peak. A picture of the population breakdown and geographical distribution as indicated by these reports was built up. A total of 9,657 cases were reported during the 7 months in which case reports were sent in to the Commission.

Figure 2 shows the total number of cases reporting to the health facilities in the Khartoum area by month, and it indicates that by September 1986 the disease was already at, or past, peak incidence. Nevertheless, new cases continued to appear for a further 6 months before dropping dramatically in March 1987.

Figure 3 shows separately the distribution of cases between the clinics in Khartoum, Omdurman, Khartoum North and East Nile. The results suggest that in Khartoum and East Nile the pattern was very similar and past its peak by October, while in Omdurman the peak was later, in November 1986. In Khartoum North there was a much lower prevalence of disease during the reporting period. It has been suggested that the reporting system was not strictly adhered to in Khartoum North, but it
also is possible that the disease had peaked in this area much earlier, and spread from Khartoum North to the other towns.

At the time of this study the infections were widespread in the province, but the areas of greatest density were along the banks of the river Nile, as shown in Figures 4 and 5.

Figures 6 and 7 show the age distribution of the infection in September and October, respectively, and the curves are very different. The peak age group in September is 20-24 years, but in all age groups the number infected is high. By October the age-prevalence curve is much steeper, with a peak prevalence at age 15-19.

In addition, the data suggest that more males (61%) were infected than females (39%). People from all ethnic groups and socio-economic classes were equally affected.

The vectors.

A survey of the sandfly population in the area revealed 4 species, viz.,

- *Phlebotomus papatasi*
- *Sergentomyia clydei*
- *S. antennata*
- *S. squamipleuris*

*P. papatasi* was the dominant species, forming about 52% of the total catch. However, dissection of several thousand sandflies by different workers did not reveal a single infected individual to confirm the vector species. (O. Abdel Nur, personal communication).

The highest density of sandflies was found in villages surrounded by cultivation and also from villages with open spaces with refuse, debris and dilapidated buildings. Sandflies were found both indoors and out of doors in equal numbers.

Reservoir hosts.

In addition to the probable vector, there was a considerable population of potential reservoirs of infection in *Arvicanthis niloticus* and *Genetta gennetta* and individuals of both species were found infected.

Clinical features.

Between 6th October and 1st December 1986 a total of 736 patients presented at the Leishmaniasis Clinic at the Omdurman Tropical Diseases Hospital and all were investigated by the author. All patients were clinically examined and interviewed. Skin smears were taken from the edge of one lesion from each patient to be stained and examined for the presence of amastigotes. Where lymphadenopathy was present, lymph nodes were aspirated and the aspirate was stained and examined for amastigotes. To identify the parasite, skin scrapings were cultured and isolates were sent to the London School of Hygiene and Tropical Medicine.
The patients usually presented at the clinic with lesions of one to three months duration (Table 1), and 26.6% of the patients had received some previous treatment for CL before appearing at the hospital. The types of lesions encountered are shown in Table 2. The most common lesions were deep ulcer (44%) but 23% were superficial ulcers and 23% were papules and/or nodules. Small numbers of infiltrative lesions and fungating masses were also seen. Sometimes small satellite papules appeared around the original lesion, which themselves could ulcerate and coalesce with the original lesion. The deep ulcers involved the full thickness of the skin, with thick, raised, hyperaemic edges and indurated base. The lesions varied in size from a few millimeters to 7 cm in diameter. Multiple lesions were very common among these cases, with over 80% of patients having more than one lesion. The maximum encountered was in a patient with 50 lesions, though 2 to 8 was most common. The mean number was 4.

Table 3 shows the distribution of the lesions over the body. Thus, 65.6% of the patients had at least one lesion on the lower limbs and 49.5% had a lesion on the upper limbs. Facial lesions occurred in 6.3% of patients.

Lymphatic involvement was noticed in 18.6% of cases in the form of lymphadenitis and lymphangitis, sometimes with beaded lymphatic cord extending from the lesion. However, Leishmania were not found in smears or in cultures of aspirate taken from the lymphatics and lymph nodes.

Diabetes was a concurrent ailment in 23 of the patients and their lesions were apparently more severe. Itching proved to be a common symptom, being experienced by 61.5% of the patients (Table 4). Other complaints included pain (37.5%) and fever (17.1%), while secondary infection which delayed the healing of the lesions was found in 18.3% of the cases.

The diagnosis was confirmed in 88% of the cases by demonstration of amastigotes in the skin smears taken, and parasites were usually abundant and easy to find.

Identification of the parasite.

A number of isolates were obtained from the same series of patients by cultures of skin scrapings in Evan's medium, NNN medium and in RPMI + 20% foetal calf serum. Identification of a number of these isolates after mass cultivation was carried out by isoenzyme electrophoresis and by monoclonal antibodies. Typing by these two methods proved that the species responsible for this epidemic was Leishmania major. (El-Safi, Evans and Peters, in preparation)

Control Activities.

a) chemotherapy.

The patients investigated at the Tropical Diseases Hospital were divided into three categories:
i) those with very minor lesions who were reassured and released with no chemotherapy.

ii) those with moderate lesions who were treated as outpatients with Rifampicin and Metronidazole.

iii) those with severe lesions, especially those with concurrent diabetes. These were admitted to hospital and treated with a course of Pentostam intravenously for 3-4 weeks.

All except 2 patients were successfully treated with one course of Pentostam but the two needed a second course to effect a cure. The drug was well tolerated by all the patients with no apparent cardiotoxic effects. Some patients complained of muscular pain and fatiguability. Intralesional chloroquin was used for a short time, but this regimen was stopped after complications were encountered, including cellulitis and sloughing of the whole limb from three patients.

In February 1987, at the 23rd Pan Arab Medical Congress held in Khartoum, some experiences and results from the epidemic were reported during a session on leishmaniasis:

Of those outpatients who could be followed, some 91.7% were cured or showed marked lesion regression with intramuscular Pentostam and 70.4% cases responded to Septrin®.

Intralesional pentostam was very effective in limited cases and oral Metronidazole gave poor results®.

Other treatments used were monomycin, topical application of liquid nitrogen, and topical application of a mixture of chloramphenicol, chloroquin and Metronidazole, the latter with variable results. Tinidazole was reported to have given satisfactory results in 43 out of 50 cases treated®.

b) vector control.

Indoor spraying with residual insecticides was carried out from September through November 1986 using Malathion 50% and Fenrithion 40%. In January 1987 a massive campaign of indoor, outdoor and aerial spraying was instigated, aimed at complete coverage of the province. Indoors, Malathion 50% was used and by March 1987 the coverage achieved was:

- Khartoum Area 36%
- East Nile 84% - 100% in different villages.
- Khartoum North 78%
- Omdurman 60%

The greatest restraint was financial and unavailability of chemicals. Outdoor spraying was with DDT 25% and this is still continuing. Aerial spraying was successfully utilized in 4 inaccessible areas, namely the green belt of eucalyptus trees to the South of Khartoum, the Sunt Forest near the junction of the two Niles, and two sewage farms in Khartoum and Khartoum North.
c) Rat control.

In May 1987 the Plant Protection Department will embark on a national rat control campaign using zinc phosphide. By March 1987 the epidemic had declined dramatically, but whether this was due to seasonal factors or to the effectiveness of the vector control operations, cannot be determined.

DISCUSSION

This is the third epidemic of CL in Sudan and the first one ever reported from Khartoum province. It was a most severe outbreak in terms of number of persons infected and the severity of the lesions. Prior to the outbreak in 1976/77 there had only been sporadic cases reported.

In this outbreak, reporting was not mandatory until the epidemic was at, or past, its peak and yet almost 18,000 cases were recorded. In addition to this number, many unreported cases must have occurred; people with only minor lesions, or others who went to private doctors, obtained their drug directly from a pharmacy, or even from infected friends.

The fact that the most affected areas in Khartoum Province were those along the River Nile's banks pointed to the optimum geographical and ecological conditions for the breeding of sandflies and Nile rats. The lower infection rate in Khartoum North may have been due to the epidemic having started in this town when the sewage system broke down in 1985 and rats increased dramatically. If this was the case, then the epidemic in Khartoum North would have been over by the time the reporting commenced. Evidence to support this hypothesis is circumstantial.

The age prevalence curve from September 1986 showed that all age groups were affected, which suggests that this epidemic was a new phenomenon hitting a non-immune population. The duration of the disease, multiplicity of lesions, and lymphatic involvement, were indicative of the causative agent being L. major, and this was confirmed in London by biochemical identification. (El-Safi, Evans and Peters, in press.)

Possible cause of the epidemic.

a) Human behavioral factors.

During the last five years the population of Khartoum, Omdurman and Khartoum North have all increased due to the immigration of many people from the drought stricken areas in the West of Sudan. Most of these immigrants have settled in squatter or shanty towns on the fringes of the main city and have found casual labouring jobs or worked as domestic servants. The infection may have been introduced by these immigrants from areas known to be endemic for CL.

A second possible human source of the infection is a reservoir from the 1977 outbreak in Shendi, although this seems to be unlikely.
A third possible source of the infection is from the 1985 outbreak in the White Nile village of El Garrassa, which seems to be more likely because of the shorter time period between the outbreaks. It is possible that visitors from El Garrassa and nearby villages to Tuti Island could have been the source of this new outbreak.

Finally, it is possible that the source could be Saudi Arabia, which is known to be endemic for \textit{L. major}. There is considerable travel between Sudan and Saudi Arabia, and therefore it is possible that the infection was actually imported.

b) Vector factors.

In Khartoum Province there was very low rainfall for more than five years followed by heavy rains in 1985 and 1986. Thus, the cracked and dry soils became waterlogged, creating ideal breeding situations for the sandfly.

In addition it had always previously been the practice to spray the three towns with insecticide twice a year, before and after the rainy season, but this practice was stopped 6 years ago, probably due to shortage of funds.

c) Reservoir host factors.

The pattern of drought followed by rainfall may also have led to the rodent population coming into the city and increasing. Reports that Nile rats were on the increase started in 1985, and this coincided with the breakdown of the sewage system in Khartoum North. By 1986 the rat population was estimated to be in the region of 150 per mile, which is well above the epidemic rate of 4 per mile. Because of the large numbers of rats in the fields many spilled over and were to be found in houses, factories, and offices. (fide Ministry of Agriculture.)

As natural infection has been demonstrated in the Nile rats, this increase in their population density may have played a major role in the causation of this epidemic of cutaneous leishmaniasis. A further possibility is that infection of dogs or other domestic animals from the rats may have taken place and a new reservoir established.
HISTOGRAM SHOWING THE CASES OF CUTANEOUS LEISHMANIASIS IN KHARTOUM AREA DURING SEPTEMBER 1986 TO MARCH 1987

Fig. (2)
Fig. (3)

HISTOGRAM SHOWING CASES OF CUTANEOUS LEISHMANIASIS BY MONTH AND LOCATION IN KHARTOUM AREA DURING 1988
Table 1.
Duration of lesions in 736 patients reporting to the leishmaniasis clinic at the Hospital for Tropical Diseases, Omdurman

<table>
<thead>
<tr>
<th>Duration</th>
<th>Number of patients</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 1 week</td>
<td>29</td>
<td>3.9</td>
</tr>
<tr>
<td>1 week - 1 month</td>
<td>32</td>
<td>17.9</td>
</tr>
<tr>
<td>1 month - 2 months</td>
<td>260</td>
<td>35.3</td>
</tr>
<tr>
<td>2 months - 3 months</td>
<td>150</td>
<td>20.4</td>
</tr>
<tr>
<td>&gt; 3 months</td>
<td>143</td>
<td>19.4</td>
</tr>
<tr>
<td>Unknown</td>
<td>22</td>
<td>3.1</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>736</strong></td>
<td></td>
</tr>
</tbody>
</table>

Table 2.
Types of lesions in 736 patients reporting to the leishmaniasis clinic at the Hospital for Tropical Diseases, Omdurman

<table>
<thead>
<tr>
<th>Types of lesion</th>
<th>Number of patients</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Deep ulcers</td>
<td>327</td>
<td>44.4</td>
</tr>
<tr>
<td>Superficial ulcers</td>
<td>169</td>
<td>23.0</td>
</tr>
<tr>
<td>Papules/nodules</td>
<td>170</td>
<td>23.1</td>
</tr>
<tr>
<td>Other (infiltrated lesions and fungating masses)</td>
<td>12</td>
<td>1.6</td>
</tr>
<tr>
<td>More than one type of lesion</td>
<td>58</td>
<td>7.9</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>736</strong></td>
<td></td>
</tr>
</tbody>
</table>
Table 3.
Distribution of lesions on the body in 736 patients at the leishmaniasis clinic at the Hospital for Tropical Diseases, Omdurman

<table>
<thead>
<tr>
<th>Site of lesion</th>
<th>Number of patients</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lower limbs</td>
<td>483</td>
<td>65.6</td>
</tr>
<tr>
<td>Upper limbs</td>
<td>364</td>
<td>49.5</td>
</tr>
<tr>
<td>Face</td>
<td>46</td>
<td>6.3</td>
</tr>
<tr>
<td>Back</td>
<td>29</td>
<td>3.9</td>
</tr>
<tr>
<td>Chest</td>
<td>12</td>
<td>1.6</td>
</tr>
<tr>
<td>Abdomen</td>
<td>7</td>
<td>1.0</td>
</tr>
<tr>
<td>Buttock</td>
<td>1</td>
<td>0.1</td>
</tr>
</tbody>
</table>

Table 4.
Clinical features in 736 patients at the leishmaniasis clinic at the Hospital for Tropical Diseases, Omdurman

<table>
<thead>
<tr>
<th>Symptoms</th>
<th>Number of patients</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Itching</td>
<td>449</td>
<td>61.0</td>
</tr>
<tr>
<td>Pain</td>
<td>276</td>
<td>37.5</td>
</tr>
<tr>
<td>Fever</td>
<td>125</td>
<td>17.0</td>
</tr>
<tr>
<td>Lymphatic involvement</td>
<td>78</td>
<td>10.6</td>
</tr>
<tr>
<td>Diabetes</td>
<td>23</td>
<td>3.1</td>
</tr>
<tr>
<td>Secondary infection</td>
<td>135</td>
<td>18.3</td>
</tr>
<tr>
<td>Previous treatment</td>
<td>196</td>
<td>26.6</td>
</tr>
</tbody>
</table>
Fig (4)

THE DISTRIBUTION OF CUTANEOUS LEISHMANIASIS IN GREATER KHARTOUM AREA DURING
The distribution of cutaneous leishmaniasis in Khartoum area. During September/October 1986.
Fig. (6)

HISTOGRAM SHOWING NUMBER OF CASES OF CUTANEOUS LEISHMANIASIS BY AGE GROUP IN KHARTOUM AREA DURING SEPTEMBER 1986.
Fig (7)

HISTOGRAM SHOWING NUMBER OF CASES OF CUTANEOUS LEISHMANIASIS
BY AGE GROUP IN KHARTOUM AREA DURING OCTOBER 1986
ACKNOWLEDGEMENTS

The work reported in this paper was supported by a grant from the WHO/World Bank/UNDP Special Programme for Research and Training in Tropical Diseases.

This study would not have been possible without the cooperation received from many people, particularly Dr. Abdel Jalil Mohamad Awad El Karim, Director of the Omdurman Tropical Diseases Hospital, Dr. Bushra El Tom and Dr. Abdel Gadir El Kadaro at Omdurman. To those who have assisted in many ways, I would like to express my gratitude: In Khartoum, Dr. Ahmed M. Arabi, Director General of the Commission of Health Affairs and Mr. Osman Ali Abu Bakr, Deputy Director, Environmental Health Department. From the Ministry of Agriculture I received information from Dr. Mohamad A/Aziz Mohamad, Plant Protection specialist, and Dr. Abdel Gawi Mahir, Chief Entomologist. From the National Council for Research I thank Professor El Sheikh Mohgoub, Dr. Mohamad Hamad Satti, Dr. Asim A. Daffalla for their advice and Dr. Alan Fenwick for his assistance during the preparation of the final manuscript.

For technical assistance I thank Omer Mohamad Ahmed and Mohamad Mahgoub.

REFERENCES

LEISHMANIASIS IN BOLIVIA: CURRENT SITUATION

Bermudez H., Recacoechea M., Urjel R., Villarroel G., Dujardin J. C.*
and Le Ray D.*

BACKGROUND

Although leishmaniasis has been reported from all tropical areas of Bolivia, two zones have deserved special attention. One of these is "Los Yungas" near La Paz (provinces of South Yungas, North Yungas, Larecaja and Tamayo) situated in the northeast part of Bolivia in the foothills of the eastern range of the Andes. It is a rough area, with altitudes from 1,888 to 6,888 ft. (Fig 1). The climate is very humid and the area has been inhabited since the Columbian period by different ethnic groups (Negro, Aymara, Quechua and Spanish). The Instituto Boliviano de Biologia de la Altura (IBBA) in La Paz is carrying out studies in this zone.

The second zone is that of Yapacani (provinces of Ichilo and Sara) northeast of Santa Cruz, at the edge of the eastern lowlands (llanos orientales) at an altitude of 600 to 1,200 ft. This area has numerous rivers, streams, and swamps prone to flooding, and is covered by humid tropical virgin forest. This is the study area of the Centro Nacional de Enfermedades Tropicales (CENETROP) in Santa Cruz. The human population has been increasing since the 1950's. Today the inhabitants engage in agriculture, as well as construction of roads and railways, logging operations, hunting, and fishing. The majority of the population is composed of Quechuas, originally from the Andean plateau (altiplano) and valleys, and a smaller proportion is Aymara of eastern Bolivian origin.

VISCERAL LEISHMANIASIS

Visceral leishmaniasis (VL) was first encountered in dogs by Angles et al. in the Yungas. Desjeux et al. described the first case of human leishmaniasis in a child from the same region and characterized the isolates from dog, vector and man, including that from the above mentioned child, as L. chagasi.

Velazco, who first studied the vectors in Los Yungas, reported the presence of Lutzomyia longipalpis in and around houses. Subsequently, Le Pont and Desjeux incriminated L. longipalpis as the usual vector of L. chagasi at three localities in Los Yungas with infection rates of 0.8% to 4.2%. No vector control studies have been reported.

CUTANEOUS/MUCOCUTANEOUS LEISHMANIASIS

Human cases of mucocutaneous leishmaniasis have been known in the Andes (Yungas) since the precolonial period. In colonial times, the disease was known as the "Mal de los Andes" or "Anti Oncocoy". During the

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republican period, mucocutaneous leishmaniasis was reported by various professionals, but there was confusion with respect to the etiology. The disease was frequently observed among soldiers during the war of Acre (1903-1904) in the Pando Department.

Desjeux et al.\(^6\) in Los Yungas reported 113 clinical cases of cutaneous leishmaniasis. Prevalence was highest between 3,000 and 4,200 ft, especially among males of 10 to 30 years, with a predominance (81%) of mucosal forms.

De Muynck et al.\(^7\) conducted a clinical and epidemiological study (including clinical diagnosis, Montenegro skin test, direct parasitological examination and histopathology) in the colony of Yapacani. A prevalence of 1.6% was found in 7,577 inhabitants examined (121 proven cases and 384 suspected cases) with a predominance in males between the age of 15 to 49 yrs. Incidence among the new colonists was 8% in the first year after arrival. Hunters were the most vulnerable group. Cutaneous ulcers were chiefly on the lower limbs. Mucosal involvement was found in 46% of the patients with a predominance of nasal lesions.

Among outpatients seen at CENETROP over a 3-year period, 29% of the ulcerative cutaneous lesions were caused by \textit{Leishmania} and prevalence was highest among males involved in agriculture.\(^8\).

In the Yungas, Walton et al.\(^9\) studied the reactivation of the disease after years of inapparent infection following healing of the primary cutaneous lesion. Extreme facial mutilation was found almost exclusively among negroes.

For diagnosis, direct parasitological examination and histopathology have similar efficacy (33.6% and 37.9%, respectively) until the third month of cutaneous lesion, while the Montenegro skin test was positive in 88.4%.\(^\text{11}\) In patients with mucosal lesions, direct parasitological examination had a sensitivity of 8.5% as compared to 25.9% for histopathology, and the Montenegro test was positive in 97.2% of cases. A simple, efficient method using a match stick for collecting material from cutaneous and mucosal lesions for direct parasitologic examination has been described.\(^\text{12}\) La Fuente et al.\(^\text{13}\) succeeded in cultivating human \textit{Leishmania} in a modified Difco Agar Base medium. Azoque\(^\text{14}\) reported that in histopathological sections of cutaneous and mucocutaneous lesions, i) in presence of the parasite, a plasmocytic infiltrate is frequently present, and ii) when the parasite cannot be found, the infiltrate is of a lymphocytic and/or granulomatous type.

De Muynck et al.\(^\text{15}\) indicated that by using Glucantime (pentavalent antimonial), 100% of cutaneous cases who finished their treatment underwent clinical cure (out of 100 patients diagnosed, 59 initiated treatment and 47 finished it) while only 50% of patients with the mucocutaneous form achieved clinical cure. Recacoechea et al. (data not published) attempted to shorten the duration of therapy and to lower drug dosage. For cutaneous lesions a total of 0.5 g/kg was injected over a period of 5 or 10 days. For mucosal infections, 1.0 g/kg was injected either over 20 consecutive days or over 2 periods of 10 days separated by a 15-day interval. Results were inferior to those of the standard.
LEISHMANIASIS IN BOLIVIA
STUDY AREAS

- LOS YUNGAS DE LA PAZ, IBBA
- YAPACANI, CENETROP. 1975-1983
- YAPACANI, CENETROP. 1984 ONWARD

Fig. 1 - Location of the study areas of leishmaniasis in Bolivia.
Fig. 2 - Geographic distribution of 241 cases of leishmaniasis in Bolivia, according to Recacoechea (1983).
therapy with a total of 1.2 g/kg injected over 20 consecutive days for CL, and 2.4 g/kg over 2 series of 12 days separated by 15 days for MCL.

The areas endemic for leishmaniasis within the Department of Santa Cruz were outlined by Balcazar in 1946. Recently, Recacoechea located the geographical origin of out patients, according to the probable site of infection. The majority of the patients came from various provinces of the Department of Santa Cruz (provinces Ichilo, Sara, Ibanez, Velasco, Nuflo de Chavez, Chiguitero, Santiesteban and Cordillera), the others were from Departments Beni, Pando, Cochabamba (Chapare) and La Paz (Los Yungas), most of them residing in colonized areas of Yapacani, Chapare and Yungas (Figs. 2 and 3).

Biochemical identification of the causative Leishmania was first reported by Desjeux et al. By isoenzyme analysis they ascribed 10 human isolates from Los Yungas (North and South), Alto Beni and Beni to L. b. braziliensis.

Attempts to identify the phlebotomine fauna in Bolivia were initially made by Velazco. This author in a systematic study carried out in Los Yungas demonstrated the presence of 13 species of phlebotomines: Lutzomyia longipalpis, Lu. sallesi, Lu. nevesi, Lu. serrano, Lu. dendrophila, Lu. punigeniculata, Lu. shannoni, Lu. campbelli, Lu. boliviana, Lu. trinidadensis, Brumptomyia brumpti and Warilea yungasi, including 2 new species (Lu. boliviana and Warilea yungasi). Other authors studied the sandflies sporadically. LePont et al. discovered L. yucumensis, a cryptic sibling species of Lu. carrerai and the putative vector of leishmaniasis in Bolivia. Later the same authors isolated a strain of L. b. braziliensis from the gut of Lu. yucumensis. LePont and Desjeux described a new anthropophilic subspecies, Lu. nunestovari anglesi.

THE YAPACANI LEISHBOL FIELD PROJECT, 1984-1987

Our knowledge of the ecology and epidemiology of leishmaniasis in Bolivia is fragmentary. Parasite transmission takes place in a sylvatic cycle of difficult accessibility. Populations at risk are moving from the Andean valleys and altiplano to colonize the primary forest. A multi-disciplinary approach, integrating primary health care, epidemiology, clinical surveillance, entomology, parasitology, immunology and cell biology, and molecular biology, is a necessity. Such an approach must provide the populations at risk with immediate health benefits by relying on the local community resources. Given those considerations, in 1984 CENETROP initiated a long-term longitudinal, integrated project aiming at the "Characterization, surveillance and control of leishmaniasis in Bolivia" (LEISHBOL Project).

This project was initiated in the pilot area of Yapacani, a recently colonized region of lowland primary forest (Amazonian "llanura"), along the railway under construction to the Beni, from Ayacucho Station to Punta Rieles (Fig. 3).
LEISHMANIASIS IN THE DEPARTMENT OF SANTA CRUZ, BOLIVIA

- PRESENT PILOT AREA (FROM 1984)
- PREVIOUS AREA (1975-1983)

Fig. 3 - Location of the CENETROP study areas of leishmaniasis in the department of Santa Cruz, Bolivia.
Fig. 4 - Map of the Yapacani pilot area surveyed for leishmaniasis since 1984 by CENETROP.
The area covers 240 km² and includes a population of 1,800 inhabitants along both sides of the railway, of which 30% are settled in small villages (Estación Yapacani, Estación Ayacucho, Chapaco, Estación Molina, María Auxiliadora, Paraiso, Yesquero, Sirari, Ocuarena, Marabol, Estación Menacho, Km 191, Km 195, and Punta Rieles), and 70% are dispersed.

As the area had no health resources, Villarroel et al. organized a Primary Health Care project aiming at a system of service delivery to the population by using traditional, local health resources identified by the communities and technically adapted to the region. Human local resources called Community Health Representatives (CHR) were trained generally for diseases prevalent in the area, and specifically for tuberculosis, malaria, and leishmaniasis. They are also trained for vaccination and intestinal deparasitization campaigns, for management of oral rehydration units, and acute respiratory infection units, and for other activities corresponding to the national health programme, including local community pharmacies. The CHRs received minimal necessary technical material, with logistic back-up from the National Health Ministry and from CENETROP.

Recacoecha et al. ('23) initiated a specific clinical and immunological (Montenegro skin test, serology) survey of two populations: (i) those grouped in villages (Punta Rieles and Yapacani) in which an initial survey of 236 people showed 2 ulcers, 6 scars (locally acquired infection) and 12% Montenegro positive; after 2 years no new cases were recorded; (ii) dispersed population (between Chapaco and Villa Nueva, 47 km) in which 946 persons were shown to have 8 active ulcers and 10 scars, acquired in the adjacent primary forest. The survey was carried out with the assistance of a rural physician and with the participation of the communities (CHR, alcalde, corregidor, teacher, et cet.).

For the characterization of the etiological agent, Urjel et al. have isolated 17 stocks from patients coming from Yapacani and other areas, of which 7 were typed in collaboration with IBBA. Using 10 enzymes, 6 isolates corresponded to L. b. braziliensis and 1 from a patient in Yapacani to L. m. amazonensis. The same isolates were also characterized using pulsed field gradient gel electrophoresis (PFG) for separation of chromosome-sized DNA molecules, and their identity, as established by enzyme analysis, was confirmed (Dujardin et al., in preparation).

With respect to the animal reservoir, 76 rodents and marsupials were processed by Urjel and examined parasitologically and serologically for leishmanial infection. None was parasitologically positive by direct examination. One rodent (identification in progress) serum was strongly positive by precipitation-in-gel test for L. m. amazonensis. (Le Ray, personal communication)

Vector trapping (Bermudez et al.) led to the identification of 23 species of phlebotomines in Yapacani at Puerto Grether, Luna Nueva, and trapping sites 1 and 2 in Punta Rieles and Marabol. (Fig. 3) Three species belonged to the genus Brumptomyia (B. pentacantha, B. galindoi and B. avellari) and 18 to the genus Lutzomyia (Lu. vucumensis, Lu. davisi, Lu. carrerai carrerai, Lu. amazonensis, Lu. dendrophila, Lu. shannoni, Lu. punctigeniculata, Lu. antunesi, Lu. shawi, Lu. nordestina,
Lu. nevesi, Lu. serrana, Lu. auraensis, Lu. calcarata, Lu. gomezi, Lu. saulensis, Lu. walkeri and Lu. evangelistai).

Monthly density of sandflies was monitored with Shannon traps at 2 sites in Punta Rieles. The first site was located in marshy primary forest which flooded during the rainy season (Fig. 3). Between April 1983 and March 1984, density was low with an average of 0.16 to 7 Lu. yucumensis/trap/hr between the hours 19:00 to 24:00 (Fig. 4a). Ten other species were sporadic: Lu. dendrohyla, Lu. shannoni, Lu. auraensis, Lu. antunesi, Lu. calcarata, Lu. saulensis, Lu. amazonensis, B. pentacantha and B. avellari) and no Lu. carrerai carrerai were encountered. The second site, which was not prone to flooding, was located in a primary forest, 10 km North of the first site (Fig. 3). Between October 1984 and September 1985 density in Shannon traps, during the hours of 19:00 and 20:00, was quite variable (Fig. 4b). The highest density of Lu. yucumensi was observed in February 1985 with 75.71 sandfly/trap/hr. In November, January and May, the density was 19.75, 15.42 and 18.83 respectively, and below 6.5 in the following months. At this site Lu. carrerai carrerai was captured continuously with an average monthly density between 0.83 and 0.43. This comparative study indicates that dry forest (frequented by hunters, loggers, etc.) bears a higher risk for infection by Leishmania than lower places prone to flooding (frequented by fishermen on their way to streams and ponds).

The present classification of phlebotomines rests on the morphology of genitalia. Considering the need for a rapid identification of the species before dissection, special attention was paid to external morphology, in particular the number, color, shape and localization of sclerites of the mesonotum and pleura. A pictorial key was developed which proved to be accurate for daily use by field technicians (Bermudez et al., in preparation).

Natural infection of phlebotomines with promastigotes of Leishmania was studied by dissection and microscopic examination of 4,539 Lu. yucumensis, 636 Lu. davisi, 22 Lu. carrerai carrerai, 26 Lu. calcarata, 38 Lu. dendrohyla, 8 Lu. shannoni, 10 Lu. auraensis, 7 Lu. antunesi, 4 Lu. gomezi and 2 Lu. nevesi. Four Lu. yucumensis and one L. c. carrerai were found positive for promastigotes of Leishmania. These positive sandflies were all trapped during the dry season (March, April and May 1985, May and September 1986). They were subinoculated into hamsters, but so far only one hamster has developed an incipient nodule.

Between May and September 1986, density of phlebotomines was monitored by CDC traps at 40 cm, 5 m, 10 m, and 15 m above ground (Fig. 5) at the dry lowland capture station. Lu. yucumensis density increased with height above ground with an average of 0.5 phlebotomine/day/trap at 40 cm, 2.6 at 5 m, 3.2 at 10 m and 4.9 at 15 m. Lu. davisi had a similar behaviour: 0.3 at 40 cm, 2.5 at 5 cm, 3.0 at 10 m and 2.9 at 15 m. Other species were found sporadically.
Fig. 5 - Monthly mean number of the main sand fly species (Shannon trap) at two sites in Yapacani, Bolivia.

MARSHY LOWLAND

DRY LOWLAND

L. yucumensis

Rainy season

L. carrerai carrerai
Fig. 6 - Monthly mean number of L.yucumensis (CDC trap) at four levels above ground in the dry lowland (Yapacani, Bolivia, March-September 1986).
CONCLUSIONS AND RECOMMENDATIONS

Visceral leishmaniasis exists in Bolivia, at least in "Los Yungas" of La Paz, where transmission to man occurs in and around houses. Lu. longipalpis is responsible for the transmission of L. chagasi, the dog is a domestic reservoir, nothing is known about sylvatic reservoirs. It would be important (i) to consider peridomestic vector control in the Yungas, and (ii) to investigate other areas of the country, especially along the borders with Brazil.

Cutaneous/mucocutaneous leishmaniasis is endemic and enzootic in almost all the tropical regions of Bolivia. Prevalence is highest in recently settled populations; 1.6% in Yapacani where incidence was 8% during the first year of residence. Groups at highest risk are males of working age: 10-30 years of age in Los Yungas, 15-49 years in Yapacani.

Mucosal involvement is frequent: 46% in Yapacani, 81% in Los Yungas where racial predisposition has been reported. Social impact is considerable. Chemotherapy with pentavalent antimonials (Glucantime) appears to be very efficacious at the cutaneous stage (100% clinical cure at CENETROP). Standardized protocols, alternative drugs, and follow-up evaluation should be further developed.

Cutaneous leishmaniases in Bolivia are due to both L. b. braziliensis and L. mexicana amazonensis. Both species coexist in Yapacani, a fact relevant to treatment decision.

Lu. yucumensis, a proven vector of L. b. braziliensis in the Yungas, is also a putative vector in Yapacani where Lu. carrerai could be responsible for the transmission of L. m. amazonensis, a point to be investigated soon. In Yapacani, studies suggest that transmission to man occurs mainly in dry lowlands during the dry season, from May to September. Enzootic transmission takes place not at ground level, but at >15 m above ground as suggested by density of Lu. yucumensis increasing with height. Studies based upon trapping sandflies and mammals higher in the canopy, mating and feeding rates, and bloodmeal identification, should be developed.

So far nothing is known about animal reservoirs of mucocutaneous leishmaniasis in Bolivia, a point which deserves further attention.

The only first line control measure for cutaneous leishmaniasis which is feasible at this stage in Bolivia is early diagnosis and treatment of the patients, since infection is acquired exclusively in forest and colonization environments. In the absence of medical attention in such environments, the implementation of community health schemes and the training of local community health representatives must be considered as the first essential step towards active search, timely diagnosis, and referral for treatment of leishmaniasis patients.
ACKNOWLEDGEMENTS

Research reported here was supported by the EEC Programme "Science and Technology for Development" [grant STD-M-022-B to DLR and HB] and by the UNDP/WORLD BANK/WHO Special Programme for Research and Training in Tropical Diseases (grant 780.555 to CENETROP). We wish to express our warm gratitude to the field workers of the Yapacani pilot area, to Ron Gooding for revising the English version of this paper and to, Sabine Desager for typing it with care and endless patience.

REFERENCES

CURRENT SITUATION IN REGARD TO LEISHMANIASIS IN BRAZIL

Roberto Badaró

INTRODUCTION

The leishmaniasis extend from the extreme North to the South of Brazil, with highly endemic areas in the North and Northeast regions of this continental country. In the last ten years over 60,000 cases were reported. Obviously, we have to understand that the system for collection of data by the Superintendancy of Campaigns Against Diseases of the Ministry of Health (SUCAM) has been much improved in recent years.

CUTANEOUS/MUCOCUTANEOUS LEISHMANIASIS

The majority of those cases (75%) were diagnosed as cutaneous (CL) or mucocutaneous leishmaniasis (MCL). Figure 1. shows that the distribution of the number of MCL cases reported has increased dramatically compared to earlier years. The distribution of those cases by year, for each state in Brazil is shown in Table 1. It is clear that in 1985 and 1986, the number of cases doubled as compared to 1984. Two states, Amazonas and Ceará, are the leaders in the prevalence of this disease in Brazil, but in some states in the Northeast, e.g. Maranhão and Bahia, MCL is highly endemic and some times overlaps the distribution of visceral leishmaniasis (VL). In the past decades the occurrence of MCL was essentially restricted to those persons penetrating the humid riverine forest or to devasted forest regions cleared for development of urban areas. However, in some areas already colonized, the infection and the disease are still endemic, with some epidemic outbreaks.

The disease predominantly occurs in young adults males, although several cases have been reported in women and children, especially in areas where the disease is highly endemic and populations of the vector are found in or near the houses.

The clinical presentation of the cutaneous disease varies from single self-healing lesion to serious disseminated cutaneous disease. Also, diffuse cutaneous leishmaniasis (DCL) has also been reported in Brazil and is related to L. mexicana amazonensis. The mucosal disease is classified into single or multiple types, according to whether one or more mucosal surfaces are involved. The majority of the patients with mucosal involvement have a single nasal lesion. Septal perforation with collapse of the anterior nares, polyps, and disfigurement cases with complete loss of the cartilaginous septum, lips and nose have been reported. The mucosal involvement is related to L. braziliensis braziliensis infection, usually as a result of the metastasis from a skin lesion. Grimaldi 12 has characterized several strains isolated in the endemic areas in Brazil: L. braziliensis braziliensis is still the most prevalent species in the country. However, L. mexicana amazonensis has been isolated in patients with mucosal involvement. It is curious that in Brazil, L. mexicana amazonensis has been isolated from patients over all the spectrum of clinical leishmaniasis; that is to say, single or multiple lesions,
disseminated, and mucosal disease. Last year *L. amazonensis* was also associated with the aetiology of VL for the first time.

The epidemiology of *L. b. braziliensis* infection is still undefined. Older studies and a recent one by Lainson¹² suggest that there is a strong correlation between clearing of forests and leishmaniasis. In a five year prospective study of CL in an endemic area, conducted in the village of Três Braços located 200 km Southwest of Salvador, the capital of the State of Bahia, there was evidence for peridomiciliary and forest transmission of *L. b. braziliensis*.

Based on 7,538 person-years of observation from 1980 to 1984, the five year incidence of CL in the village was 8.4/1,000, while that for MCL was 10/100,000. The annual incidence of new cases of leishmaniasis was 8.1/1,000 persons ranging from 2.7 to 15.5 during the 1980 to 1984 period. The considerable variation in incidence of disease observed during the prospective study was also noted in other endemic areas in Brazil. The clinical characteristics of cutaneous and mucosal leishmaniasis in this study showed that the site of primary lesions was the leg in 73.2% of 358 persons with active leishmaniasis. Others primary sites were the arms in 38 persons (10.6%), trunk in 37 persons (10.3%), head and neck in 19 persons (5.3%), and nose in two persons (0.6%). Two or more active lesions were simultaneously present in 93/358 patients (26%). The occurrence of mucosal leishmaniasis in the population was 10/2,494 (4/1,000) and 2.7 in the 369 patients presenting with CL.

The mucosal disease occurred in a median of 6 years after the primary skin lesion and was more common in males, in those with either large or multiple antecedent skin lesions, and in those who had not received complete antimony therapy of the primary lesions.

The overall prevalence of the disease was 14.9%. Most disease occurred between 10-30 years of age. Disease rates were lowest in the very young with only 21 cases (4%) in children less than 5 years of age and 35 cases (11%) in children 6-9 years. There were 50% more males than females with leishmaniasis (220 males/151 females = 1.46/1).

ELISA testing was positive in 85% of those tested during the first two years after the primary lesions and remained positive for 5 to 40 years in 27% of patients. The *Leishmania* antigen skin testing (Montenegro's reaction) was positive in 96% of patients with recent lesions and remained positive in 70% of patients. Patients with mucosal disease are hypersensitive and all had positive serologic and skin tests.

The vector and reservoir of *L. braziliensis braziliensis* is not identified, but *Lutzomyia whitmani* occurs in high density around the homes in the village of Três Braços and would be a likely vector for the peridomiciliary transmission. The dog has been a suspected reservoir for *L. b. braziliensis*, although it has not been proved. Recently the donkey *Equus asinus* was found infected with *L. braziliensis* in those areas where peridomiciliary transmission occurs.

The echimyid rodent, *Proechimys sp.*, is the major reservoir host of *Leishmania mexicana amazonensis*. *Proechimys* is a very common animal in
the Amazon forest and the infection rate with *L. m. amazonensis* is frequently in the region of 25% or more. The vector is *Lutzomyia flaviscutellata*, a low flying and nocturnal sandfly which is not greatly attracted to man, who is an accidental host.

**VISCERAL LEISHMANIASIS**

Visceral leishmaniasis is predominantly endemic in the Northeast of Brazil. Of the 9,075 cases reported, half of them come from four highly endemic states, Ceará, Bahia, Piauí, and Maranhão. Figure 2 shows the distribution of those cases by year from 1979 to 1986. The peak incidence of kala azar cases was seen in 1985; this is in accordance with an epidemic spurt starting in 1984 in the states of Bahia, Ceará, Maranhão and Piauí. Also, in Marajó island, in the state of Pará, where no cases had been previously reported, 161 cases were reported in SUCAM from 1984-1986. This fact, associated with the occurrence of cases in the capital of Maranhão and Piauí, confirmed the outbreak of VL in this period in Brazil. Table 2 shows the distribution of the cases reported to SUCAM from 1979-1986, per state according to the regional directory.

Visceral leishmaniasis in Brazil is associated with *Leishmania donovani chagasi*. Sporadic cases have been recently reported related to *L. mexicana amazonensis* infection. There is no question about the vector being *Lutzomyia longipalpis* for the *L. donovani chagasi* infection. The dog plays an important role as a source of infection for man. The existence of a wild mammal reservoir of *L. d. chagasi* is possible in Brazil. Lainson (2) has isolated *L. d. chagasi* from the skin and viscera of a fox, *Cerdocyon thous* more than once. In the most highly endemic area in Brazil, the maintenance of the sandfly infection is correlated with the high rate of infection of the dogs. Undoubtedly, the dog is the principal reservoir host of *L. donovani chagasi* in this country, although wild animals, such as *C. thous*, can be implicated as the primitive host.

In the Old World VL, e.g. India, post kala azar dermal leishmaniasis (PKDL) makes it possible for man to serve as the major reservoir. In Brazil it has not so far been proved that man has a real role as a source of infection for the sandfly. On the other hand, the presence of *Leishmania* in normal skin or in a non-characteristic depigmented skin lesion has been demonstrated in post kala azar patients in Bahia. The role of such patients as a reservoir is not clear at the present time.

A prospective study conducted in Jacobina, Bahia, Brazil from 1980 to 1986 has demonstrated some epidemiological features of American VL in Brazil. Annual surveys were done in a mean of 636 families and 2,246 children during 1980-1984. The prevalence of the disease was 3.1% for children up to 15 years of age, and the annual incidence was 4.3 cases per 1,000 children. The number of children with disease fluctuated yearly and seasonally. The peak month for onset of symptoms was September, and 74% of cases occurred between July and November. The 48 patients with leishmaniasis identified from 1980 to 1984 included 22 girls and 26 boys. The median age was 3.2 years and the mean age was 3.4 years; 78% of cases occurred in children less than five years old. Serological testing using ELISA to detect anti-leishmania antibody
indicated that 7.5% of children were infected with Leishmania each year and that the ratio of disease to infection was 1:8.5 for the whole area and 1:4.5 for the section in the study area with the highest prevalence of the disease. Eighty-six children identified by positive ELISA, with spectrophotometer reading (≥ 0.050) were available for follow up. The children were segregated into four groups based on their clinical evaluation at the time of their first positive ELISA and on their subsequent clinical course. Seventy children in Group 1 were completely asymptomatic and had normal physical examinations. Thirty-eight children in Group 2 (subclinical) had mild constitutional symptoms (malaise, diarrhea, low work-play tolerance), as well as intermittent hepatomegaly for one to three years. These patients with subclinical manifestations of L. donovani chagasi infection were self-healing and did not require therapy. Thirteen children in Group 3 (sub-clinical, progressing to full-blown visceral leishmaniasis) were initially indistinguishable from children in Group 2, but progressed to develop classic acute visceral leishmaniasis during the ensuing two to 15 months. Fifteen children in group 4 developed acute VL within eight weeks of the documentation of seropositivity, and did not have the prolonged mild illness that characterized Groups 2 and 3.

The existence of asymptomatic infection and subclinical VL was reported by Leishman in 1906. In this prospective study done in Bahia, we demonstrated strong evidence that the subclinical forms of the disease and the asymptomatic infection are much more frequent than the classic form of visceral leishmaniasis, known by the secular name kala azar. This severe form of the disease, characterized by prolonged fever, hepatosplenomegaly, anemia, leukopenia, hyperglobulinemia and occurrence of bleeding phenomena may represent the tip of the iceberg in the VL problem in Brazil.

CONTROL PROGRAM

The leishmaniasis control program in Brazil is the responsibility of the SUCAM. Since 1979, the Health Ministry of Brazil has emphasized the necessity of a continuous program to control leishmaniasis in the endemic areas. However, the budget available to support this program is not sufficient to cover the total extension of this very large country. Also, several other difficulties in the management of the program have impeded success in most areas where it has been applied.

Basically the program consisted of:

1) Identification and treatment of active cases;
2) reduction of sandfly populations;
3) reduction of the reservoir.

The majority of the patients with cutaneous leishmaniasis are diagnosed within a month of disease onset. Sometimes where the disease is highly endemic, the patients initiate treatment by themselves, following the recommendations of any neighbor who claims experience. The result is that the annual prevalence of the disease in the endemic areas sometimes is higher than the incidence.
Visceral leishmaniasis is much more difficult to diagnose than the cutaneous disease in the field. Usually the patients are sick for a long periods (months, over a year) before being diagnosed.

Pentavalent antimonials remain the front-line drug for treatment of leishmaniasis in Brazil. Several different schedules have been tried. The most popular is the administration of daily doses of 20–30 mg/Kg/Sb (intravenous or intramuscular) during fourteen to 30 days. Patients with mucosal involvement usually require long-term therapy, otherwise relapse is frequent. Amphotericin B is the drug recommended as second line therapy for patients unresponsive to antimony therapy. Except for the requirement of long period of hospitalization, it is very effective in our patients.

Table 3 shows the results of attempts to identify the most important vector in the highly endemic areas by sandfly surveys. This program is strictly related to the VL areas. Also, dog serological surveys were initiated in the states of Ceará, Maranhão and Piauí. As shown in Table 4, the positivity rates of the indirect immunofluorescence test (IFA) in 1981 and 1983 were significantly higher than in other years. If we compare Table 2 and Table 4, the incidence of human VL cases is increased in the years subsequent to those with higher dog seropositives!

Spraying campaigns were done at the same time, and follow the pattern of the Chagas' Disease Control program. Spraying was not done as a follow-up to sandfly surveys; insecticides were sprayed mostly at the house where the reduviidae were found and it was much more efficient for Chagas' disease than for leishmaniasis. Table 5 shows some results of this program.

The dogs that were positive in Leishmania IFA were caught and eliminated by intravenous injection of potassium chloride. Table 6 shows specific data concerning this program.

ACKNOWLEDGEMENTS

I am grateful to Dr. João Batista Furtado Vieira for providing the information concerning the SUCAM program.

REFERENCES

Table 1.
Number of cutaneous and mucosutaneous Leishmaniasis cases reported to the SUCAM by states (Regional Directory in Brazil) 1979 - 1986

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Table 2.

Number of visceral leishmaniasis cases reported to the SUCAM by states (Regional Directory in Brazil)
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</table>

Total 91 165 359 1,120 1,124 1,911 2,511 1,794 9,075
Table 3.
Leishmaniasis control program in Brazil
SUCAM activities: 1979 - 1986

<table>
<thead>
<tr>
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Table 4.
Leishmaniasis control program in Brazil
SUCAM activities: 1979 - 1986

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<td>749,449</td>
<td>611,148</td>
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</table>

Total 28.00%
Table 5.
Leishmaniasis control program in Brazil
SUCAM activities: 1979 - 1986

<table>
<thead>
<tr>
<th>Year</th>
<th>No. Municipalities done</th>
<th>No. Places done</th>
<th>Houses Treated</th>
<th>Residual DDT</th>
<th>Other insecticide</th>
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<tbody>
<tr>
<td>1979</td>
<td>12</td>
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<td>-</td>
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<td>14</td>
<td>97</td>
<td></td>
<td>-</td>
<td>11,196</td>
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<td>-</td>
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<td>27,393</td>
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<td>1986</td>
<td>32</td>
<td>761</td>
<td></td>
<td>71,701</td>
<td>26,074</td>
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<tr>
<td>Total</td>
<td>-</td>
<td>-</td>
<td>196,615</td>
<td>226,201</td>
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</table>

Table 6.
Leishmaniasis control program in Brazil
SUCAM activities: 1979 - 1986

<table>
<thead>
<tr>
<th>Year</th>
<th>No. Municipalities done</th>
<th>No. Places done</th>
<th>No. Houses done</th>
<th>No. Eliminated</th>
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<tr>
<td>1979</td>
<td>15</td>
<td>120</td>
<td>225</td>
<td>260</td>
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<tr>
<td>1980</td>
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<td>1982</td>
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<td>13,072</td>
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<td>91</td>
<td>1,781</td>
<td>6,985</td>
<td>11,939</td>
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<tr>
<td>Total/Brazil</td>
<td>-</td>
<td>-</td>
<td>42,688</td>
<td>52,357</td>
</tr>
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</table>
Figure 1.
Number of cutaneous or mucocutaneous leishmaniasis cases reported to SUCAM by year from 1979 to 1986 in Brazil

No. cases

15,000-

10,000-

5,000-

0-


Figure 2.
Number of visceral leishmaniasis cases reported to SUCAM by year from 1979 to 1986 in Brazil

No. cases

2,500-

2,000-

1,500-

1,000-

500-

0-

LEISHMANIASIS IN COLOMBIA: HIGHLIGHTS OF A PUBLIC HEALTH PROBLEM
Bruno L. Travi

INTRODUCTION

According to Werner and Barreto leishmaniasis has been present since pre-Columbian times, although the first parasitologically confirmed case in Colombia was reported in 1929. Other reports were based on clinical descriptions and, thus, possible confusion with mycotic and bacterial diseases invalidate them as reliable data. Between 1929 and 1979 only a total of 624 cases of leishmaniasis were reported to the National Institute of Health (INAS), whereas between 1981 and 1986 this figure increased to 9,366, undoubtedly reflecting better case detection and diagnosis.

CURRENT SITUATION

Approximately 1,500 to 2,000 new cases per year are reported to INAS and it is likely that this number is below the actual incidence of the disease. Human cutaneous and/or visceral leishmaniasis cases have been detected in every administrative section of the country with the exception of the Departamento Atlántico and San Andrés and Providencia Islands. Several species and subspecies of Leishmania are present in Colombia. The etiological agent of visceral leishmaniasis (VL) was identified as L. donovani chagasi while the L. braziliensis complex with its three subspecies have been recognized in the country and are responsible for the majority of tegumentary lesions. However, L. m. mexicana and L. m. amazonensis were infrequently associated with human disease.

From the clinical standpoint, INAS has recently reported four patients with diffuse cutaneous leishmaniasis and a 6.5 overall percentage of mucocutaneous cases. The highest prevalence of the latter clinical form are found in the Departments of Huila, Cundinamarca, Boyacá, and Caquetá.

In general terms, the geographic distribution of the L. braziliensis complex could be described as widely disseminated throughout the different regions of the country, with a clear preponderance of L. b. panamensis on the Pacific coast. On the other hand, L. b. braziliensis is predominant in the central and easter regions of Colombia. L. b. guyanensis is mainly present in the eastern part of the country, but isolation from patients has been less frequently accomplished as compared with the other subspecies of L. braziliensis.

Visceral leishmaniasis seems to be not as frequent as in other South American countries, such as Brazil, despite its presence in several administrative sections of Colombia, i.e., Santander, Cundinamarca, Tolima, Sucre, Huila, Córdoba, and Bolívar as shown in Figure 1. Ecologically L. b. chagasi is mainly distributed in the tropical rainforest, 400 to 800 m above sea level, with an average temperature of 25.5°C and an annual rainfall of 100-200 mm. Wild reservoirs are unknown...
FIGURE 1. VISCERAL LEISHMANIASIS IN COLOMBIA.
FIGURE 2. VECTORS OF \textit{L. braziliensis} IN COLOMBIA.
but, as has been observed in other endemic foci of VL the New and the Old World, the Colombian foci are characterized by the presence of infected dogs. *Lutzomyia longipalpis*, a zoophilic/anthropophilic sandfly with peri- and intradomiciliary activity, has been associated with the transmission cycle of this parasite.

Recently information has emerged concerning reservoirs and vectors of leishmaniasis in Colombia. In the Pacific coast region *L. b. panamensis* was isolated from the viscera of the sloth *Choloepus hoffmanni*<sup>11</sup>. No other published observation on *Leishmania* reservoirs are available, and it seems that the sympatric transmission of *L. b. braziliensis* and *L. b. panamensis* is taking place through mammalian hosts which are difficult to detect, as are those involved in the *L. b. braziliensis* foci in Brazil<sup>12</sup>. Accordingly, both in Colombia and in Brazil dogs were the only mammalian hosts other than man from which *L. braziliensis* could be isolated.

On the other hand, vector studies have been more rewarding; members of the *L. braziliensis* complex were isolated and taxonomically identified at least from three species of sandflies (Figure 2). Natural infections have been detected in *Lu. umbratilis* with *L. b. quyanensis* in the Intendencia of Amazonas and *Lu. spincrassa* with *L. b. braziliensis* in Norte de Santander.<sup>14</sup> *Lu. trapidoi* was found infected with *L. b. panamensis* in the Departamentos of Nariño and Tolima.<sup>15</sup> National control measures against visceral leishmaniasis have been recently implemented, and campaigns at community level to attract the affected population's attention to this health problem were carried out in the Departamentos of Huila and Tolima. Indirect control of sandfly populations resulted from antimalarial spraying campaigns, but no quantitative data are available to evaluate the effectiveness of these control measures in diminishing the incidence of visceral leishmaniasis.

Case detection and treatment are the only public health measures implemented for tegumentary leishmaniasis and no other approaches will probably be considered until more effective and affordable prophylaxis and control are available. Colombia, as most of the countries in Latin America is still in the process of understanding the epidemiological situations in which transmission is occurring and estimating what proportion of the population is at risk of acquiring the disease. Surely, basic and applied research on leishmaniasis at the regional level will yield information in the development of appropriate control strategies.

REFERENCES

10. Corredor, A. et al., 1981. op. cit. 7:3
CURRENT SITUATION IN REGARD TO LEISHMANIASIS IN COSTA RICA

H. Hidalgo and A. Víquez

INTRODUCTION

Leishmaniasis in Costa Rica has a high incidence and wide geographic distribution over most of the nation. Although the presence of the disease was suspected by Dr. Clodomiro Picado as early as 1914, the first cases were reported by Dr. Antonio Peña-Chavarria in 1924. Since that time various authors have published articles on the epidemiological, clinical, and therapeutic aspects of the disease.

Visceral leishmaniasis has not yet been reported, but the presence of the New World vector, Lutzomyia longipalpis, in great numbers in the Province of Guanacaste suggests that human cases of this clinical form could occur at any time.

CLINICAL FORMS

The principal clinical form encountered is cutaneous leishmaniasis, (CL) although there are also some mucocutaneous cases. This form often produces horrible facial mutilations which create a social stigma as does the disfigurement of leprosy. The simple cutaneous lesions can be large, and multiple lesions are common. They cause great suffering, are debilitating, and self-healing usually occurs only after many months. Some cases never self-cure. The specific drug is very expensive, and the treatment is long and makes heavy demands on the health care services of the nation. Because of the great suffering of large numbers of persons and the economic drain caused, leishmaniasis is a serious public health problem in Costa Rica. It currently occupies 7th place on the list of reportable diseases (Table 1).

EPIDEMIOLOGICAL SITUATION

In the following tables, information is presented regarding:

- Annual distribution and rates per 100,000 inhabitants for the years 1973 to 1985
- New cases according to month of notification 1982-1985
- New cases by age group and rates per 100,000 1985
- New cases by Province and rates per 100,000 1985
- Distribution by Province according to sex 1985

Geographic distribution of cases is shown on Map 1.

*Department of Sanitary Dermatology, Ministry of Health
As in other areas of the Americas, the infection is a zoonosis, with sylvatic mammals as the natural host, and man is only an accidental host. Two species of sloth and a rodent have been found naturally infected\(^1\). Domestics dogs are occasionally infected and could serve as a secondary peridomiciary reservoir. There are 17 species of anthropophilic sandflies, of which 5 species (Lutzomyia yleophilator, Lu. sanguinaria, Lu. geniculata, Lu. evansi, Lu. panamensis) constitute 82% of all phlebotomines captured biting man.\(^2\)

An area of special interest is the Canton of Acosta, in the Province of San José, with a high incidence rate (329.89 per 100,000 inhabitants in 1984) where agricultural development has essentially eliminated the native forest which is usually necessary to maintain the life cycle, and the predominant sandfly is a man-biting species which had heretofore been known only from Venezuela. This distribution could be that of an introduced species. It has recently been described as a new species, Lutzomyia youngi\(^4\) and studies are in progress to confirm its role as the vector of leishmaniasis in the area.

REFERENCES

DISTRIBUCION GEOGRAFICA DE LA LEISHMANIASIS EN COSTA RICA (1986)

Fuente: Depto. Dermatología
Ministerio de Salud

Tasas por 100.000 Habitantes.
## Table 1.

Obligatory reportable diseases of greatest incidence
Costa Rica, First Semester of 1986

<table>
<thead>
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<th>Disease</th>
<th>No. cases per 10,000 inhabitants</th>
<th>Rate</th>
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<tr>
<td>1. Influenza</td>
<td>11,201</td>
<td>420.30</td>
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<tr>
<td>2. Venereal diseases</td>
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<td></td>
</tr>
<tr>
<td>a) Blenorrhagia</td>
<td>3,796</td>
<td></td>
</tr>
<tr>
<td>b) Syphilis</td>
<td>733</td>
<td></td>
</tr>
<tr>
<td>c) Soft chancre</td>
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</tr>
<tr>
<td>d) Chancre w/o specified aetiology</td>
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<td></td>
</tr>
<tr>
<td>Total:</td>
<td>5,079</td>
<td>190.58</td>
</tr>
<tr>
<td>3. Chicken pox</td>
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<td>86.27</td>
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<td>4. Haemhorragic conjunctivitis</td>
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<td>73.62</td>
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<td>5. Hepatitis</td>
<td>1,537</td>
<td>57.67</td>
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<td>6. Parotiditis</td>
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<td>33.88</td>
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<tr>
<td>7. Leishmaniasis</td>
<td>767</td>
<td>28.78</td>
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<tr>
<td>8. Measles</td>
<td>456</td>
<td>17.11</td>
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<td>9. Malaria</td>
<td>310</td>
<td>11.63</td>
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<td>10. Bacterial meningitis</td>
<td>186</td>
<td>6.82</td>
</tr>
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</table>

Source: Dept. of Epidemiological Surveillance
Ministry of Health August 1986
Table 2.
Leishmaniasis in Costa Rica
Annual distribution of number of new cases and rate per 100,000 inhabitants

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<th>Year</th>
<th>No. cases</th>
<th>Rate</th>
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<td>996</td>
<td>54.18</td>
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<tr>
<td>1974</td>
<td>708</td>
<td>36.84</td>
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<td>1975</td>
<td>633</td>
<td>32.16</td>
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<tr>
<td>1976</td>
<td>648</td>
<td>32.11</td>
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<tr>
<td>1977</td>
<td>1,271</td>
<td>60.56</td>
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<tr>
<td>1978</td>
<td>1,821</td>
<td>85.66</td>
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<td>116.84</td>
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<td>56.12</td>
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Table 3.
New cases according to month of notification

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<td>105</td>
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<td>March</td>
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<td>157</td>
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<tr>
<td>April</td>
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<td>175</td>
<td>123</td>
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<td>June</td>
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<td>July</td>
<td>186</td>
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<td>225</td>
<td>136</td>
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<td>196</td>
<td>124</td>
</tr>
<tr>
<td>October</td>
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<td>December</td>
<td>111</td>
<td>250</td>
<td>84</td>
<td>62</td>
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</table>

Source: Dept. of Sanitary Dermatology
Table 4.
Distribution of new cases according to age group and rate per 100,000 inhabitants 1985

<table>
<thead>
<tr>
<th>Age group</th>
<th>No. cases</th>
<th>Rate</th>
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<tr>
<td>0 - 9</td>
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<td>10 - 19</td>
<td>388</td>
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<td>20 - 29</td>
<td>226</td>
<td>44.02</td>
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<td>67</td>
<td>32.58</td>
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<td>41</td>
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<tr>
<td>60 or more</td>
<td>44</td>
<td>29.33</td>
</tr>
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</table>

Total 1,459 56.12

Source: Dept. of Sanitary Dermatology

Table 5.
Distribution of new cases by province and rate per 100,000 inhabitants 1985

<table>
<thead>
<tr>
<th>Province</th>
<th>No. cases</th>
<th>Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>San Jose</td>
<td>139</td>
<td>14.53</td>
</tr>
<tr>
<td>Alajuela</td>
<td>249</td>
<td>54.11</td>
</tr>
<tr>
<td>Cartago</td>
<td>78</td>
<td>26.79</td>
</tr>
<tr>
<td>Heredia</td>
<td>38</td>
<td>17.82</td>
</tr>
<tr>
<td>Guanacaste</td>
<td>13</td>
<td>6.17</td>
</tr>
<tr>
<td>Puntarenas</td>
<td>312</td>
<td>109.11</td>
</tr>
<tr>
<td>Limon</td>
<td>630</td>
<td>346.22</td>
</tr>
</tbody>
</table>

Total 1,459 56.12

Source: Dept. of Sanitary Dermatology
Table 6.

Distribution of new cases by province according to sex, and rate per 100,000 inhabitants 1985

<table>
<thead>
<tr>
<th>Province</th>
<th>Male Cases</th>
<th>Male Rate</th>
<th>Female Cases</th>
<th>Female Rate</th>
<th>Total Cases</th>
<th>Total Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>San José</td>
<td>72</td>
<td>15.70</td>
<td>67</td>
<td>13.80</td>
<td>139</td>
<td>14.53</td>
</tr>
<tr>
<td>Alajuela</td>
<td>117</td>
<td>50.74</td>
<td>132</td>
<td>58.85</td>
<td>249</td>
<td>54.11</td>
</tr>
<tr>
<td>Cartago</td>
<td>37</td>
<td>25.72</td>
<td>41</td>
<td>29.07</td>
<td>78</td>
<td>26.79</td>
</tr>
<tr>
<td>Heredia</td>
<td>14</td>
<td>13.66</td>
<td>24</td>
<td>23.12</td>
<td>38</td>
<td>17.82</td>
</tr>
<tr>
<td>Guanacaste</td>
<td>8</td>
<td>7.73</td>
<td>5</td>
<td>4.98</td>
<td>13</td>
<td>6.17</td>
</tr>
<tr>
<td>Puntarenas</td>
<td>147</td>
<td>92.87</td>
<td>165</td>
<td>110.66</td>
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<td>109.11</td>
</tr>
<tr>
<td>Limon</td>
<td>341</td>
<td>330.64</td>
<td>289</td>
<td>306.51</td>
<td>630</td>
<td>346.22</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>736</strong></td>
<td><strong>56.61</strong></td>
<td><strong>723</strong></td>
<td><strong>55.69</strong></td>
<td><strong>1,459</strong></td>
<td><strong>56.12</strong></td>
</tr>
</tbody>
</table>

Source: Dept. of Sanitary Dermatology
CURRENT SITUATION IN REGARD TO LEISHMANIASIS IN ECUADOR

Eduardo A. Gómez L.

INTRODUCTION

Leishmaniasis is a prevalent infection in Ecuador which affects areas under development and has an undoubted adverse effect on agricultural development and colonization of new territories. Although both cutaneous and mucocutaneous forms occur, the identity of the causative parasites and the true prevalence, distribution, and importance of the disease are incompletely known. There is one report of a case of visceral leishmaniasis, but the evidence for its existence is doubtful.

GEOGRAPHIC DISTRIBUTION

The principal endemic area of leishmaniasis exists in a long fringe along the west side of the Andes, running from north to south, roughly paralleling the coast. There are also other smaller endemic areas in the country, especially on the Amazonic side of the Andes and a small portion of the jungle (Fig. 1). There is a small focus in the high Andean valleys in the province of Azuay. The affected Departments (Provinces) are: Esmeraldas, Manabi, Pichincha, Guayas, Los Ríos, Azuay, El Oro, Loja, Napo, Pastaza, Morona and Zamora.

CURRENT PREVALENCE AND INCIDENCE

As a zoonosis, leishmaniasis is present in every humid forest of our country; that is, everywhere with the exception of most of the high Andes region. However, there are areas where the human disease has occurred frequently because of human activities over many years, with little variation. Unfortunately data does not exist concerning prevalence and incidence in most areas. The only information is from data from field medical centers in these areas, which is very deficient and is far from showing the true incidence in those areas. Many patients do not seek medical attention, their lesions eventually heal spontaneously, and there is no record. The available information on cases is shown in Table 1.

SURVEILLANCE METHODS

Although the first case of human leishmaniasis was described 67 years ago, in 1920, there has been little additional information gathered. The reporting of leishmanial infection has only recently been made obligatory and few data available. However, data is now collected and analyzed by the Ministry of Health. Surveillance is limited to case finding and their have been no epidemiological surveys. Recently, starting in 1982, some studies on the vector and reservoirs have been accomplished. This year parasites have been isolated from man and animals for identification, but the results have not as yet been received.
DIAGNOSIS

**Direct methods:** Detection of parasites in smears from ulcers is the principal and most frequently used means of diagnosis. Isolation of parasites by culture has just been instituted as a routine method in the National Institute of Hygiene and Tropical Medicine (INHMT).

**Indirect methods:** Antigen for skin testing (Montenegro) is now produced at INHMT, but has not yet been utilized for epidemiological studies. Serological diagnosis is essentially not used in Ecuador.

CONTROL PROGRAMS

There is not a Leishmaniasis Control Program in Ecuador, and none is planned for the near future. However, leishmaniasis has now been made a reportable disease, and information on the occurrence of cases is being gathered by the Ministry of Health.

SANDFLY VECTOR RESEARCH

Research on vectors of leishmaniasis started only five years ago, not as part of any control plan, but purely as an academic research activity. A pilot area was chosen and studied during a period of two years, and some collections were made in a few other strategic locations (Fig 2).

Six man-biting species of *Lutzomyia* were detected, and two of them were found naturally infected with promastigotes.

These parasites were inoculated into the nose and at the base of the tail in hamsters, and a number of animals developed nodules and ulcers containing amastigotes. Cultures were not possible at that time, and the stocks were not isolated for identification.

The man-biting species of *Lutzomyia* which have been found to date in Ecuador are: *Lu. gomezi*, *Lu. serrana*, *Lu. trapidoi*, *Lu. hartmanni*, *Lu. panamensis*, and *Lu. shannoni*. The two species found naturally infected to date are *Lu. trapidoi* and *Lu. hartmanni* or (*peruensis*? - these species can be differentiated only in the males).

During this research the habits of the insects, such as biting activity, flight habits, and hourly density were studied, and weather and geographical conditions very carefully observed.

Experimentally, one generation of *Lu. trapidoi* has been raised in the laboratory. However, in our institution, facilities do not exist for the colonization of sandflies at this time and this was not pursued further.

RESERVOIR HOST RESEARCH

Although the number of mammals investigated to date is not large enough to yield definitive knowledge of the relative importance of
different species as reservoirs, naturally infected animals of four species have been found: 1) *Choloepus hoffmani*, 2) *Potos flavus*, 3) *Sciurus granatensis*, and 4) *Tamandua tetradactyla*. Only one specimen of each species was found infected.

No lesions were visible on these animals; promastigotes were isolated from liver in blood agar media (DFS), cultures from spleen and blood were negative. Amastigotes were seen in inoculated hamsters in each case. We are awaiting results from the Reference Centers where these parasites were sent for identification.

**HUMAN HOST RESEARCH**

This year, as the result of a PAHO consultant visit, it has become a routine procedure at the National Institute of Hygiene and Tropical Medicine to attempt to isolate parasites from patients for identification and investigation, and three stocks have now been established in culture. An epidemiological survey to identify *Leishmania* from human hosts in various parts of the country is planned. Leishmanin antigen is being distributed to medical facilities, and Montenegro tests are being done in other parts of the country, as well as in Guayaquil.

Much still needs to be done to understand the true importance of leishmaniasis in Ecuador. Although the present effort is modest, research has begun and information is being gathered toward that goal.

**Table 1.**

Incidence of Leishmaniasis by Province in Ecuador During the years 1983-1986. (Approximations)

<table>
<thead>
<tr>
<th>Provinces</th>
<th>1983</th>
<th>1984</th>
<th>1985</th>
<th>1986</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Esmeraldas</td>
<td>220</td>
<td>270</td>
<td>295</td>
<td>307</td>
<td>1,092</td>
</tr>
<tr>
<td>Pichincha</td>
<td>150</td>
<td>110</td>
<td>210</td>
<td>215</td>
<td>685</td>
</tr>
<tr>
<td>Manabi</td>
<td>210</td>
<td>272</td>
<td>253</td>
<td>-</td>
<td>735</td>
</tr>
<tr>
<td>Los Rios</td>
<td>12</td>
<td>8</td>
<td>391</td>
<td>73</td>
<td>484</td>
</tr>
<tr>
<td>Guayas</td>
<td>142</td>
<td>156</td>
<td>240</td>
<td>140</td>
<td>678</td>
</tr>
<tr>
<td>Azuay</td>
<td>12</td>
<td>29</td>
<td>70</td>
<td>52</td>
<td>163</td>
</tr>
<tr>
<td>El Oro</td>
<td>1</td>
<td>4</td>
<td>-</td>
<td>-</td>
<td>5</td>
</tr>
<tr>
<td>Loja</td>
<td>5</td>
<td>22</td>
<td>-</td>
<td>1</td>
<td>28</td>
</tr>
<tr>
<td>Napo</td>
<td>7</td>
<td>5</td>
<td>12</td>
<td>17</td>
<td>41</td>
</tr>
<tr>
<td>Pastaza</td>
<td>7</td>
<td>11</td>
<td>9</td>
<td>6</td>
<td>33</td>
</tr>
<tr>
<td>Morona Santiago</td>
<td>11</td>
<td>-</td>
<td>-</td>
<td>1</td>
<td>12</td>
</tr>
<tr>
<td>Zamora Santiago</td>
<td>2</td>
<td>-</td>
<td>4</td>
<td>17</td>
<td>23</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>779</td>
<td>887</td>
<td>1,484</td>
<td>829</td>
<td>3,978</td>
</tr>
</tbody>
</table>
Figure 1.
Geographical distribution of leishmaniasis in Ecuador

Provinces
1. Esmeraldas
2. Pinchincha
3. Manabi
4. Los Rios
5. Guayas
6. Azuay
7. El Oro
8. Loja
9. Napo
10. Pastaza
11. Morona Santiago
12. Zamora Chinchipe

Figure 2.
Endemic area study sites for research on transmission
CURRENT SITUATION IN REGARD TO LEISHMANIASIS IN GUATEMALA

Miguel F. Torres

INTRODUCTION

Guatemala is a small country, located in the northern part of Central America. It presents multiple ecological habitats; dense tropical humid forests, highlands with many volcanoes, desert zones, etc. The majority of the indigenous population (at least 22 ethnic groups, descendants from the Maya) live in the highlands and do not suffer from leishmaniasis. Both visceral and cutaneous leishmaniasis have been diagnosed in Guatemala and sporadic mucocutaneous cases appear.

VISCERAL LEISHMANIASIS

The endemic area of visceral leishmaniasis is restricted to the area around Guastatoya, El Progreso, which is located in the arid Motagua River Valley, which is also an endemic area for coccidioidomycosis. A total of only six cases of visceral leishmaniasis have been diagnosed in children less than one year of age, all of whom died. It is assumed that this clinical presentation of leishmaniasis is caused by Leishmania donovani chagasi, transmitted by Lutzomyia longipalpis, but this has never been demonstrated.

CUTANEOUS LEISHMANIASIS

Epidemiologically, more importance is placed in the northern endemic zone of cutaneous leishmaniasis that includes all the Department of El Petén, and the northern parts of the Departments of Huehuetenango, El Quiché, Alta Verapaz and Izabal. The lowlands of El Petén are of great archaeological significance to Guatemala. There, a magnificent civilization flourished; the Maya. The highest point of art refinement and scientific progress was achieved during the classical period at El Petén and surroundings (300 A.D. to 900 A.D.), with Tikal as the main ceremonial center with many temple-pyramids that still exist. For reasons unknown to contemporary science, the Maya disappeared from El Petén around 900 A.D., while only a few groups, like the Lacandones, wandered through the jungles. Contemporary socio-political situations have forced the Lacandones to migrate across the Usumacinta River, to the west shore in Chiapas, Mexico. The population at high risk to acquire leishmaniasis in El Petén are the non-indian "ladino" population, and the military personnel who enter the jungle to control the "guerrillas".

Paleopathological studies have shown that the Maya suffered at least the mucocutaneous forms of leishmaniasis. This is clearly seen in clay figurines from Nayarit in northern Mexico as well as the "huacos" of ancient cultures of Peru, Ecuador, and Bolivia.

There are many dermatologic presentations of cutaneous leishmaniasis acquired at El Petén: the classic dermal ulcer, acneiform, mycetomatoid,
etc. The typical form is the destruction of the ear, called "chicleros ear", because it is acquired by the people who go into the jungle to collect "chicle" sap from the chicozapote trees. Hence, the highest incidence has been observed in males from 20 to 29 years, for occupational reasons. Accidental auto-inoculation in laboratory personnel resulting in infection has been documented.

Very recently, during collaborative preliminary studies by the (U.S.) Center for Disease Control/Universidad del Valle/Military Hospital, it has been possible to isolate the following parasites from cutaneous leishmaniasis acquired at El Petén which were identified by DNA probes and isoenzyme patterns by collaborating scientists:

1. Five strains of Leishmania mexicana mexicana
2. Six strains of Leishmania braziliensis braziliensis

These findings are in press in the American Journal of Tropical Medicine and Hygiene. The presence of \textit{L. b. braziliensis} could explain the sporadic appearance of mucocutaneous cases in the country. The presence in Guatemala of \textit{Leishmania braziliensis panamensis} is also suspected, because it has been isolated by Honduran investigators near the Guatemalan border. Until the present time, the only demonstrated sandflies from El Petén infected with \textit{Leishmania mexicana mexicana} are:

1. Lutzomyia (Nyssomyia) olmeca olmeca
2. Lutzomyia (Nyssomyia) ylephiletor

Many other species of sandflies occur in the country that are still unidentified and their role in the inter-reservoir and human transmission of the leishmaniases remains to be established. The reservoirs in the jungle have just begun to be studied. These are mainly small rodents of the genera \textit{Heteromys}, \textit{Ototylomys} and \textit{Sigmodon hispidus}, as well as small marsupials of the genus \textit{Didelphis}. Research in this field should be strengthened in the future.

Guatemala, in general, is very rich in traditional medicine. For many years the people of Petén have been utilizing the sap of the Chechén tree (\textit{Metopium browei}) and at least two other wild trees to treat cutaneous leishmaniasis. This point deserves profound study, because it has been observed that persons have apparently been cured with this treatment. Currently, the drug of choice for treatment of cutaneous leishmaniasis is pentavalent antimony (Glucantime), but some resistant cases are encountered. This drug is scarce and expensive. For this reason, cryosurgery with liquid nitrogen spray and heat treatments are under study in military personnel. There is an urgent need to develop multidisciplinary research on the leishmaniasis of Guatemala.
CURRENT SITUATION IN REGARD TO CUTANEOUS LEISHMANIASIS (CHICLERO - ULCER) IN MEXICO


HISTORICAL BACKGROUND

There remains little doubt regarding the indigenous nature of the different forms of American cutaneous leishmaniasis. With reference to Mexican cutaneous leishmaniasis, Fray Diego Lopez de Cogolludo in his History of Yucatan related his contact with "Itzaez from the Peten" (indigenous Mayans) with "rotted ears". This disease was accurately described and classified as a form of leishmaniasis by Seidelin in 1912, who also observed that the parasites had morphological characters similar to Leishmania tropica. Biagi in 1953 isolated and cultured the parasite in NNN medium and gave it the name of L. tropica mexicana. In 1965 Biagi and Disney found naturally infected Lutzomia olmeca olmeca and confirmed the role of this insect as the vector of Mexican cutaneous leishmaniasis, well known as Chiclero's Ulcer, in neighboring Yucatan. Farfan in 1922 recommended antimonial preparations for treatment of chiclero ulcer.

GEOGRAPHICAL DISTRIBUTION

It was pointed out by Shattuck in 1933, that, "The only known endemic focus of cutaneous leishmaniasis (CL) in Mexico is in the Peninsula of Yucatan". We now know that CL is endemic in the forest regions of the states of Campeche, Quintana Roo, Tabasco, Oaxaca and Chiapas, as it has been reported by Farfan-Lopez, Beltran and Bustamante, Martinez-Pompeyo, Lepviaka, Biagi, and Andrade et al.

THE PARASITE

Biagi in 1953 isolated the parasite and named it L. tropica mexicana, due to the fact that the clinical aspects of chiclero ulcer were more closely related to Old World cutaneous leishmaniasis. Garnham in 1962 emended the classification to L. mexicana and later Lainson and Shaw changed it to L. mexicana mexicana. Andrade et al. in 1985 in collaboration with Dr. Grimaldi (Instituto Oswaldo Cruz, Rio de Janeiro) characterized three strains isolated from human beings by isoenzymes and identified all of them as Leishmania mexicana mexicana. Grimaldi et al. in 1987 characterized these strains by monoclonal antibodies and also identified them as L. mexicana mexicana.
THE VECTOR

In 1953 Biagi started his study of the insects suspected to be responsible for transmission to human beings. He reported Phlebotomus cruciatus, P. shannoni, P. panamensis and P. flaviscutellatus to be the most common anthropophilic species. In 1965 he reported P. flaviscutellatus naturally infected by L. mexicana mexicana. Between 1964 and 1966 Disney, working in Belize, showed that the most common species was Lutzomyia olmeca olmeca and found naturally infected specimens. It is well known and accepted that the subfamily Phlebotominae comprehends several genera. In the Old World the genus Phlebotomus is found, and in the New World, Lutzomyia. It is clear than Disney accurately modified Theodor's classification and both referred to the same vector.

Our knowledge with reference to the vector is very limited. It is necessary to study faunistics, seasonal variation in density of sandfly populations, diurnal activity, effects of humidity, migration, flight range, age composition of populations, feeding preferences, the relationships between sandflies and Leishmania and epidemiological significance of sandflies. Furthermore, it is interesting to point out that the views expressed by our patients are similar to the information gathered by Farfan in 1922. They say that the flies which cause the disease are parasitic on the wild turkey (Agriocharis ocellata), the curassow (Krax) and the guan (Penelope). The fly is called "mosca chata" or "mosca chiclera". Indeed, it would be interesting to study the role of this insect as a possible vector of the disease.

NATURAL HOSTS

There is a complete absence of knowledge with reference to the natural host of Leishmania mexicana mexicana in Mexico. Lainson and Strangways-Dixon studied chiclero's ulcer in the forest of Belize. They found the following reservoirs among forest rodents: the tree rat Ototylyomys phyliotis, the spiny pocket-mouse Heteromys desmarestianus and the vesper-rat Nyctomys sumichrasti, with infection rates of 40%, 10.3% and 12.5% respectively. The parasite was found to be restricted to the skin and associated with small, inconspicuous lesions located principally on the base of the tail. About 350 wild-caught animals representing 18 different mammalian species were also examined with negative results. Furthermore, they inoculated foxes, squirrels, armadillos, agoutis, pacas, porcupines, and spider-monkeys, which all appeared to be resistant to infection, although one of four common opossums, Didelphis marsupialis which were inoculated, did develop a visceral infection. They concluded that the disease in Belize is a zoonosis with the rodent population acting as a reservoir of infection for man and that the epidemiology is likely to prove the same in the neighbouring countries of Mexico, Guatemala and Honduras.

CLINICAL SITUATION

A total of 63 patients have been treated in the IMSS (Social Security) Hospital in Campeche, Camp. and/or our Research Center from 1982
through 30 April 1987. Patients were enrolled when they demonstrated at least one ulcerated, papular, or nodular skin lesion of more than 2 weeks duration, which was not attributable to trauma or other etiology. At time of enrollment, a clinical history (age, sex, race, occupation, all places of residence, and travel, place and time of disease onset, family history, cause and treatment of lesions, lesion number, localization, size, dermatological description, lymphatic involvement) was recorded.

Diagnostic methods.

The diagnosis of cutaneous leishmaniasis was suggested by an appropriate history of exposure in an endemic area and the presence of the characteristic skin lesions. Diagnosis was based on: (1) direct demonstration of the parasite, (2) intradermal (Montenegro) test, and (3) histopathological examination. Parasitologic diagnosis of leishmaniasis was defined as the visualization of amastigotes in tissue sample material and/or the isolation of replicating promastigotes. For smears the skin surface was cleansed with 70% alcohol, the outer border of skin lesions was held between finger and thumb to prevent bleeding. Then a superficial slit with a scalpel blade was made and dermal tissue scraped with a spatula onto a glass slide, air dried, fixed in methanol, and stained with Giemsa. The slide was examined at 1000x under oil immersion for amastigotes. One 4 mm diameter punch biopsy was taken from the lesion border in 20 patients, fixed in 10% formalin, imbedded in paraffin and sectioned. Samples from the lesion border were obtained by aspiration through a 26-gauge needle into a tuberculin syringe containing 0.1 ml PBS. Aspirates were inoculated into Senekje's medium. Once inoculated, the Senekje's culture tubes were maintained at 27°C and viewed thrice weekly at 100x through an inverted microscope for the presence of promastigote forms.

The leishmanin (Montenegro) test was performed as follows: Leishmanin was a suspension of 1x10⁶ washed promastigotes of Leishmania mexicana mexicana (strain M/HOM/MEX/83/UAHYCV) characterized by zymodemes and monoclonal antibodies, in 0.5% phenol-saline. This leishmanin has been tested in Mexico and Guatemala. An intradermal injection of 0.1 ml on the volar surface of the forearm was examined after 24-48 hours and induration was measured by the "ball-point-pen" technique.

Clinical aspects

From our 63 patients 46 (73%) had a duration of lesion <12 months and were classified as acute. The other 17 (27%) had an evolution which ranged from 1 to 38 years and were classified as chronic. Parasite demonstration was possible by biopsy in 44%, by smears in 53%, and isolation/culture of promastigotes in 61.5%. The intradermal (Montenegro) leishmanin test was positive in 96%. The age, sex, duration, location, and number of lesions are indicated in tables 1, 2, 3 and 4. Clinical presentation commonly observed in 96% of the cases was ulcerous. Lymphatic involvement was found only in 2/63 (3.17%). Histologic characteristics are presented in Table 5.

Mexican CL, well known as Chiclero's ulcer, starts as a nodule at the site of inoculation. A crust develops centrally, and when it falls away
exposes an ulcer. When located on the ears, which is the most common presentation, it tends to become chronic and edema and thickening of the ear occurs. The secretion of the ulcer is usually sero-fibrinous, sticky and contains blood which gives the crust a black appearance. In later stages the secretion can become purulent, and when the process advances, the edges of the ulcer become undermined, and considerable destruction of the ear, and deformation due to cicatricial retraction, can be observed. In these cases it is not possible to demonstrate parasites by the methodology described.

In conclusion, Mexican cutaneous leishmaniasis is commonly a single, painless, ulcer which, when located on the extremities or trunk, tends to heal within a few months, but when located on the ear, tends to become chronic, causing disfigurement and a lifelong psychological impact.

**Treatment**

A trial to treat patients with Mexican CL with meglumine antimoniate started in 1986. Patients considered suitable for inclusion in the trial had parasitologically confirmed active lesions or chronic lesions with a history of exposure in an endemic area, presence of the characteristic skin lesion, and suggestive biopsy. Systemic administration of 10-20 mg/kg/day until cicatrization and negative smears and culture, were given to patients with risk of disfigurement (lesions located on ears and/or face), persistent active lesions, and multiple lesions. Local administration has been given to patients with limited single lesions and no risk of disfigurement. We have treated 15 patients to date, and observed response to treatment in all of them. Duration of treatment ranged from 10 to 33 days. With reference to toxic effects, it was necessary to remove one patient who presented an allergic (urticarial) reaction on the 9th day of treatment.

**EPIDEMIOLOGICAL SITUATION.**

Leishmaniasis control is usually hampered by ignorance of the true prevalence and underestimation of the human suffering and disability caused by the disease. It is clear that, due to a wide diversity of clinical forms and epidemiological situations, each focus requires separate and specific control principles and methods.

Our knowledge of Mexican CL is still in a developing state. The main reason is that this disease has only recently been declared a notifiable disease, and incidence and prevalence studies are still going on. However, it is well known and accepted that there is an endemic problem in the Yucatan Peninsula, as has been proven by excellent earlier research. In 1942 Beltran and Bustamante performed an epidemiologic study in 58 chiclero settlements with a total population of 1,506, and found a cutaneous lesion index of 11%. A few years later Biagi in 1953, studying a total population of 83, found a cutaneous lesion index of 41%, an active lesion index of 3.5% and an allergic index of 43%. In 1986 Andrade et al. initiated a study, supported by the IDRC, to determine incidence and prevalence of Mexican cutaneous leishmaniasis.
Study area

The state of Campeche consists of 56,858 km² of lowland tropical terrain, situated in the south west of Yucatan Peninsula. It is bordered on the north by the state of Yucatan, on the south by Tabasco and Guatemala, on the east by the state Quintana Roo and on the west by the Gulf of Mexico. The climate is tropical, humid and warm. The average annual rainfall ranges from 1,300-1699 mm. The major ecological zone is very humid tropical forest which comprehends 59.73% of the total area.

Study population

In Campeche there is a total population of 533,793 inhabitants. Of these, approximately 45% work in the very humid tropical forest. The IMSS-COPLAMAR (health services for rural areas) consists of 26 rural health posts and one hospital, which serve 57,475 inhabitants. We have selected 7 rural health posts located in the very humid tropical forest with a total population of 11,022, and obtained a random sample of 515 individuals from men ranging between 15-44 years old.

Methodology

In all subjects an inquiry (age, sex, race, occupation, all place of residence and travel, family history of CL, suggestive scars) was recorded. Furthermore, an intradermal (Montenegro) test was injected on the volar surface of the forearm, examined after 48 hours and measured by the "ball-point-pen technique". In patients with active lesions, a complete clinical history was recorded, and a parasitological diagnosis confirmed.

Preliminary results.

In Table 6, intradermal (Montenegro) test positivity for each rural health post is presented. A wide variety of response was observed, however a positivity rate ranging from 24-99% with a ~43% supports our suspicion of high endemicity, based on previous studies.

Table 7 shows age distribution of intradermal positivity. There is a direct correlation between age and positivity consistent with a longer exposure time and cumulative higher risk of infection in older people.

Relation to occupation is shown in Table 8. Although, Mexican CL remains known as Chiclero's Ulcer, the data indicate that chicle gathering is no longer the major occupation of people living in Campeche.

Control activities.

The objective of surveillance is to define the public health importance of leishmaniasis, both quantitatively and geographically. Prevalence studies permit the determination of an immediate problem, and case detection results in early treatment, which is important for control. Incidence studies can determine the potential size of the problem. Finally, long-term studies may be carried out to determine the incidence of transmission as well as disease. To date, area control of vectors and reservoirs (unknown) remains impracticable.
REFERENCES

1. Lopez de Cogolludo D., 1688. Historia de Yucatan, 1st edit, Madrid
Table 1.

Age and sex of 63 cases (percent) of Mexican cutaneous leishmaniasis

<table>
<thead>
<tr>
<th>Age</th>
<th>Female</th>
<th>Male</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>0-9</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>10-19</td>
<td>1</td>
<td>10</td>
<td>11</td>
</tr>
<tr>
<td>20-24</td>
<td>0</td>
<td>14</td>
<td>14</td>
</tr>
<tr>
<td>30-39</td>
<td>1</td>
<td>13</td>
<td>14</td>
</tr>
<tr>
<td>40-49</td>
<td>0</td>
<td>10</td>
<td>10</td>
</tr>
<tr>
<td>50-59</td>
<td>0</td>
<td>7</td>
<td>7</td>
</tr>
<tr>
<td>&gt;60</td>
<td>0</td>
<td>7</td>
<td>7</td>
</tr>
<tr>
<td>Total</td>
<td>2(3)</td>
<td>61(97)</td>
<td>63(100)</td>
</tr>
</tbody>
</table>

Table 2.

Duration of lesions of 63 cases of Mexican cutaneous leishmaniasis

<table>
<thead>
<tr>
<th>Evolution</th>
<th>Number</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 year</td>
<td>46</td>
<td>73</td>
</tr>
<tr>
<td>1-10</td>
<td>8</td>
<td>13</td>
</tr>
<tr>
<td>10-20</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>&gt;20</td>
<td>7</td>
<td>11</td>
</tr>
<tr>
<td>Total</td>
<td>63</td>
<td>100</td>
</tr>
</tbody>
</table>

Note: 15/17 (88%) of chronic lesions located on the ears.
### Table 3.

Location of lesions in 63 cases of Mexican cutaneous leishmaniasis

<table>
<thead>
<tr>
<th>Site on body</th>
<th>Number</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ear</td>
<td>37</td>
<td>39</td>
</tr>
<tr>
<td>Face</td>
<td>21</td>
<td>22</td>
</tr>
<tr>
<td>Neck</td>
<td>3</td>
<td>3</td>
</tr>
<tr>
<td>Trunk</td>
<td>5</td>
<td>5</td>
</tr>
<tr>
<td>Upper extremity</td>
<td>17</td>
<td>19</td>
</tr>
<tr>
<td>Lower extremity</td>
<td>11</td>
<td>12</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>94</strong></td>
<td><strong>100.00</strong></td>
</tr>
</tbody>
</table>

### Table 4.

Number of active lesions in 63 cases of Mexican cutaneous leishmaniasis

<table>
<thead>
<tr>
<th>Number active Lesions</th>
<th>Number Patients</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>49</td>
<td>78</td>
</tr>
<tr>
<td>2</td>
<td>5</td>
<td>8</td>
</tr>
<tr>
<td>3</td>
<td>5</td>
<td>8</td>
</tr>
<tr>
<td>4</td>
<td>1</td>
<td>1.5</td>
</tr>
<tr>
<td>5</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>6</td>
<td>1</td>
<td>1.5</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>63</strong></td>
<td><strong>100.00</strong></td>
</tr>
</tbody>
</table>
### Table 7.

**Intradermal (Montenegro) test positivity related to age in Campeche (Mexico)**

<table>
<thead>
<tr>
<th>Age</th>
<th>Number subjects</th>
<th>IDR positive</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>15-19</td>
<td>122</td>
<td>35</td>
<td>28</td>
</tr>
<tr>
<td>20-24</td>
<td>99</td>
<td>39</td>
<td>39</td>
</tr>
<tr>
<td>25-29</td>
<td>71</td>
<td>33</td>
<td>36</td>
</tr>
<tr>
<td>30-34</td>
<td>51</td>
<td>26</td>
<td>51</td>
</tr>
<tr>
<td>35-39</td>
<td>53</td>
<td>34</td>
<td>65</td>
</tr>
<tr>
<td>40-44</td>
<td>54</td>
<td>29</td>
<td>53</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>449</strong></td>
<td><strong>196</strong></td>
<td><strong>43</strong></td>
</tr>
</tbody>
</table>

### Table 8.

**Intradermal (Montenegro) test positivity related to occupation in Campeche (Mexico)**

<table>
<thead>
<tr>
<th>Occupation</th>
<th>Number</th>
<th>IDR positive</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Farmer</td>
<td>268</td>
<td>127</td>
<td>66</td>
</tr>
<tr>
<td>Sawyer</td>
<td>77</td>
<td>25</td>
<td>13</td>
</tr>
<tr>
<td>Lumber</td>
<td>41</td>
<td>25</td>
<td>13</td>
</tr>
<tr>
<td>Others</td>
<td>34</td>
<td>16</td>
<td>8</td>
</tr>
</tbody>
</table>
INTRODUCTION

Cutaneous leishmaniasis (CL) is the most common form of the disease found in Panama, although a smaller number of mucocutaneous leishmaniasis (MCL) case occur. Visceral leishmaniasis (VL) is not known to occur.

IDENTITY OF PARASITES

Presently there are different reports as to the number of Leishmania parasites that occur in Panama. A recent publication\(^1\) has recorded six different parasites for this country, but the origin of the isolates is unclear. Another source\(^2\) indicates that there are four well-characterized and defined parasites in this Central American country. These are: Leishmania braziliensis panamensis Lainson and Shaw, 1972, Leishmania mexicana aristedesi (sic) Lainson and Shaw, 1979, Leishmania hertigi Herrer, 1971 and Leishmania mexicana ssp. Of the four parasites, only two, L. b. panamensis and L. m. ssp. have been isolated from man, the other two having only been found in wild animal reservoirs.

Leishmania braziliensis panamensis.

L. b. panamensis is responsible for all but a few of the cases of leishmaniasis in the Republic of Panama in patients who have actively sought treatment, and 5% of the recorded cases are mucocutaneous.\(^3\) Up to the present date, all the mucocutaneous isolates that have been characterized have been identified as belonging to this taxon.

This parasite is endemic in all the forested areas, primarily in the Central and Eastern regions, with "hot spots" in the areas of Cerro Azul and Cerro Trinidad and throughout the Darien Area (Fig. 1). The principal reason for the increased number of cases reported over the last few years has been the establishment of new settlements in endemic areas. Colonists from the Central Provinces, where there is little or no transmission, are relocated to regions of high transmission, and consequently there is an increase in the number of cases.

The principal mammalian reservoir host is Choloepus hoffmannii, the two-toed sloth\(^4-5\), although other animals have been found harboring this parasite.\(^3\) The sandfly vector is Lutzomyia trapidoi (Fairchild and Hertig)\(^6\), and other natural infections have been found in Lu. ylephiletor (Fairchild and Hertig), Lu. gomezi (Nitzulescu), and Psychodopygus panamensis (Shannon).\(^6-7\)

Most CL patients respond well to conventional treatment with pentavalent antimony preparations, and at the present time there are trials underway that show promising results for alternative treatments\(^8\).
Leishmania mexicana ssp.

Recently a second parasite has been isolated from man in Panamá. This parasite is in the mexicana complex and is in the process of being characterized by enzyme electrophoresis and monoclonal antibodies at Gorgas Memorial Laboratory. This parasite has been found in ten individuals with CL: eight soldiers that were bivouacked in a swampy region of North-Central Panamá, one scientist that contracted it in the Darien region, and a native that was referred to Gorgas Memorial Laboratory. This last individual contracted the infection in the area of Alcalde Diaz, on the outskirts of Panama City, bordering the old Canal Zone.

Even though little else is known of the transmission cycle of this parasite in Panamá, we can say that the reservoir host is probably a rodent and the sandfly vector may be a member of the Lutzomyia flaviscutellata complex. Here the only known member of this complex is Lu. olmeca bicolor Fairchild and Theodor.({}^{3})

Leishmania hertigi hertigi

Leishmania h. hertigi has never been isolated from man. This parasite has only been reported from the natural reservoir host, the tropical porcupine, Coendou rothschildi Thomas, of which up to 89% of the animals examined have been found infected.({}^{3}) No sandfly has yet been incriminated as the vector.

Leishmania mexicana aristidesi

This parasite has only been found to occur in sylvatic animals, and has not yet been isolated from man. The isolates that have been made to date include those from the rodents Oryzomys capito, Proechimys semi-spinosus, Agouti paca and one of the murine opossums, Marmosa robinsoni.({}^{3}) The sandfly vector species of this parasite is unknown, but the affinity of Lutzomyia olmeca bicolor to rodent-baited traps in the area, and the relationship of other closely related sandflies with other L. mexicana complex parasites({}^{10}) makes it a suspect.

Epidemiology

Leishmaniasis in Panamá is reported throughout the year (Table 1). There is a decrease in the number of cases reported during the dry season months of January through April, and with the onset of rains there is a rise in transmission which usually peaks during the earlier part of this season from May to August, when more cases are reported.

During the years 1965 to 1976, Leishmania transmission was moderate in the Republic of Panamá, with approximately 100 cases reported every year, with the exception of the 1969-1970 biennium when there was an increase, and in 1968 and 1971 when very few cases were reported (Table 2). Since 1977, however, a constant increase in cases has occurred.

The principal regions of Leishmania transmission in the Republic of Panamá have been in the provinces of Colón, and Panamá, as well as in the
Comarca of San Blas (Table 3). These are endemic areas where land development and colonization programs are under way, and therefore there is more man-parasite contact. The majority of cases reported from the metropolitan region could probably be attributed to this source. In the past few years, transmission in Bocas del Toro and Cocle provinces has increased. The Bocas del Toro region lies on the North Coast of Panamá, while the province of Cocle lies in the South-Central region, East of the Azuero Peninsula. The regions of Chiriquí, where there has always been agricultural development due to its rich volcanic soils, as well as the Central Province of Veraguas and the Azuero Peninsula (comprising the Provinces of Los Santos and Herrera), have always been areas of low leishmania transmission. This latter region is not rich in humid forests. The Darien region, which is humid tropical forest throughout, has few cases of reported human leishmaniasis due to the isolation of the region and the low population of the area (1.9% of the country).

Leishmaniasis incidence in men is slightly higher than it is in women; throughout the years, men have accounted for 55% to 65% of the infections, while women for 35% to 45%. (Table 4)

The pattern of CL infections of adults versus those in children has changed little over the last 9-10 years (Tables 5 and 6). The increase in cases that does occur corresponds to the higher overall number reported in all age groups, which in turn, reflects the colonization and agricultural activity in the country. The migration of entire families to new residential sites in endemic areas puts more children at risk, who previously were free from infection in non-endemic areas.

The percentage of infected infants of 1 year or less of age, shows that there is little transmission (2 to 6%) in this age group. The percentage of infections in pre-school children from 1 to 4 years of age increases the second year for which we have data (1978) and has slowly continued to increase, accounting for approximately 28% of the cases reported, for the past four years. The infection rate in school age children (ages 5 to 15) has changed little over the past years, and this age group accounts for about 30% of the cases reported throughout the years. The incidence in adults has decreased from 54% in 1978 to 46% in 1985.

CONTROL

Control studies for New World leishmanias are very few. In Panamá there is a report of one control attempt carried out by Chaniotis et al. (11), but in which the results were limited. In a pilot study to control sandflies, these authors applied Ultra-Low Volume malathion bimonthly, and were only able to obtain a 30% reduction in the anthropophilic sandfly population in a nine month period. These authors recognized the fact that they had only used one insecticide and one frequency of application, and were confident that a better system could be developed to reduce the risk of infection in special groups of people, such as miliary troops and road construction crews.
ACKNOWLEDGEMENTS

I would like to thank the Ministry of Health, in particular Mr. Tejada, for providing the statistical records that were available. I am also grateful to colleagues from MEDDAC, Dr. Byron Chaniotis, and Gorgas Memorial Laboratory, Dr. John Petersen, Dr. Rolando Saenz, Dr. Howard Christensen, and Ms. Anita Vasquez for the information they generously provided.

REFERENCES

2. Petersen, J.L. (Personal Communication)
8. Saenz, R., (Personal communication)

Table 1.
Cases of leishmaniasis reported in the Republic of Panama by month 1977-1982

<table>
<thead>
<tr>
<th>Year</th>
<th>Jan</th>
<th>Feb</th>
<th>Mar</th>
<th>Apr</th>
<th>May</th>
<th>Jun</th>
<th>Jul</th>
<th>Aug</th>
<th>Sep</th>
<th>Oct</th>
<th>Nov</th>
<th>Dec</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>1977</td>
<td>9</td>
<td>7</td>
<td>16</td>
<td>20</td>
<td>32</td>
<td>25</td>
<td>38</td>
<td>35</td>
<td>18</td>
<td>81</td>
<td>48</td>
<td>8</td>
<td>222</td>
</tr>
<tr>
<td>1978</td>
<td>20</td>
<td>7</td>
<td>25</td>
<td>28</td>
<td>56</td>
<td>17</td>
<td>34</td>
<td>39</td>
<td>23</td>
<td>47</td>
<td>18</td>
<td>18</td>
<td>342</td>
</tr>
<tr>
<td>1979</td>
<td>53</td>
<td>16</td>
<td>33</td>
<td>39</td>
<td>60</td>
<td>17</td>
<td>20</td>
<td>17</td>
<td>14</td>
<td>23</td>
<td>14</td>
<td>22</td>
<td>287</td>
</tr>
<tr>
<td>1980</td>
<td>25</td>
<td>35</td>
<td>45</td>
<td>68</td>
<td>76</td>
<td>80</td>
<td>160</td>
<td>45</td>
<td>39</td>
<td>29</td>
<td>26</td>
<td>29</td>
<td>657</td>
</tr>
<tr>
<td>1981</td>
<td>71</td>
<td>65</td>
<td>57</td>
<td>90</td>
<td>97</td>
<td>92</td>
<td>95</td>
<td>62</td>
<td>74</td>
<td>31</td>
<td>40</td>
<td>30</td>
<td>884</td>
</tr>
<tr>
<td>1982</td>
<td>56</td>
<td>52</td>
<td>46</td>
<td>42</td>
<td>57</td>
<td>67</td>
<td>65</td>
<td>92</td>
<td>51</td>
<td>54</td>
<td>62</td>
<td>91</td>
<td>735</td>
</tr>
</tbody>
</table>

Mean 39 30 37 46 58 56 66 48 38 24 34 32 500
### Table 2.

**Cases of leishmaniasis reported in the Republic of Panamá by year 1965-1986**

<table>
<thead>
<tr>
<th>Year</th>
<th>Number of cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>1965</td>
<td>93</td>
</tr>
<tr>
<td>1966</td>
<td>92</td>
</tr>
<tr>
<td>1967</td>
<td>73</td>
</tr>
<tr>
<td>1968</td>
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<td>1970</td>
<td>326</td>
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<tr>
<td>1971</td>
<td>29</td>
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<tr>
<td>1972</td>
<td>119</td>
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<tr>
<td>1973</td>
<td>118</td>
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<tr>
<td>1974</td>
<td>81</td>
</tr>
<tr>
<td>1975</td>
<td>132</td>
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<td>111</td>
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<td>1977</td>
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<td>1979</td>
<td>288</td>
</tr>
<tr>
<td>1980</td>
<td>667</td>
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<tr>
<td>1981</td>
<td>804</td>
</tr>
<tr>
<td>1982</td>
<td>735</td>
</tr>
<tr>
<td>1983</td>
<td>1239</td>
</tr>
<tr>
<td>1984</td>
<td>968</td>
</tr>
<tr>
<td>1985</td>
<td>983</td>
</tr>
<tr>
<td>1986*</td>
<td>1500</td>
</tr>
</tbody>
</table>

*Projected number of cases

### Table 3.

**Cases of leishmaniasis reported in the Republic of Panamá by geographical region 1977-1985**

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Metropolitan</td>
<td>35</td>
<td>39</td>
<td>46</td>
<td>86</td>
<td>86</td>
<td>31</td>
<td>51</td>
<td>25</td>
<td>35</td>
</tr>
<tr>
<td>Azuero</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>4</td>
<td>1</td>
<td>2</td>
<td>2</td>
<td>19</td>
</tr>
<tr>
<td>Bocas del Toro</td>
<td>7</td>
<td>33</td>
<td>47</td>
<td>132</td>
<td>132</td>
<td>234</td>
<td>170</td>
<td>198</td>
<td>227</td>
</tr>
<tr>
<td>Cocle</td>
<td>30</td>
<td>17</td>
<td>47</td>
<td>84</td>
<td>62</td>
<td>67</td>
<td>178</td>
<td>187</td>
<td>159</td>
</tr>
<tr>
<td>Colón</td>
<td>59</td>
<td>37</td>
<td>22</td>
<td>179</td>
<td>239</td>
<td>198</td>
<td>353</td>
<td>206</td>
<td>365</td>
</tr>
<tr>
<td>Panamá &amp; San Blas</td>
<td>75</td>
<td>141</td>
<td>84</td>
<td>136</td>
<td>228</td>
<td>176</td>
<td>260</td>
<td>225</td>
<td>187</td>
</tr>
<tr>
<td>Chiriquí</td>
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<td>9</td>
<td>12</td>
<td>14</td>
<td>22</td>
<td>12</td>
<td>142</td>
<td>70</td>
<td>38</td>
</tr>
<tr>
<td>Darien</td>
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<td>0</td>
<td>5</td>
<td>14</td>
<td>4</td>
<td>6</td>
<td>12</td>
<td>19</td>
</tr>
<tr>
<td>Veraguas</td>
<td>16</td>
<td>63</td>
<td>30</td>
<td>31</td>
<td>17</td>
<td>12</td>
<td>77</td>
<td>43</td>
<td>14</td>
</tr>
<tr>
<td>Total</td>
<td>222</td>
<td>342</td>
<td>288</td>
<td>667</td>
<td>804</td>
<td>735</td>
<td>1239</td>
<td>968</td>
<td>983</td>
</tr>
</tbody>
</table>
Table 4.
Cases of leishmaniasis reported in the Republic of Panamá distributed by sex
1977-1985

<table>
<thead>
<tr>
<th>Year</th>
<th>Male</th>
<th>Female</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>1977</td>
<td>146</td>
<td>76</td>
<td>222</td>
</tr>
<tr>
<td>1978</td>
<td>208</td>
<td>134</td>
<td>342</td>
</tr>
<tr>
<td>1979</td>
<td>163</td>
<td>125</td>
<td>288</td>
</tr>
<tr>
<td>1980</td>
<td>375</td>
<td>292</td>
<td>667</td>
</tr>
<tr>
<td>1981</td>
<td>459</td>
<td>345</td>
<td>804</td>
</tr>
<tr>
<td>1982</td>
<td>406</td>
<td>329</td>
<td>735</td>
</tr>
<tr>
<td>1983</td>
<td>688</td>
<td>551</td>
<td>1239</td>
</tr>
<tr>
<td>1984</td>
<td>533</td>
<td>435</td>
<td>968</td>
</tr>
<tr>
<td>1985</td>
<td>600</td>
<td>383</td>
<td>983</td>
</tr>
</tbody>
</table>

Table 5.
Cases of leishmaniasis reported in Republic of Panamá by age group
1977-1985

<table>
<thead>
<tr>
<th>Year</th>
<th>0 to 1</th>
<th>1 to 4</th>
<th>5 to 14</th>
<th>over 15</th>
<th>Total*</th>
</tr>
</thead>
<tbody>
<tr>
<td>1977</td>
<td>6</td>
<td>18</td>
<td>88</td>
<td>143</td>
<td>222</td>
</tr>
<tr>
<td>1978</td>
<td>11</td>
<td>49</td>
<td>96</td>
<td>186</td>
<td>342</td>
</tr>
<tr>
<td>1979</td>
<td>9</td>
<td>47</td>
<td>68</td>
<td>164</td>
<td>288</td>
</tr>
<tr>
<td>1980</td>
<td>32</td>
<td>97</td>
<td>234</td>
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<tr>
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<td>25</td>
<td>100</td>
<td>265</td>
<td>414</td>
<td>804</td>
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<tr>
<td>1982</td>
<td>46</td>
<td>153</td>
<td>203</td>
<td>333</td>
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<tr>
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<td>62</td>
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<td>513</td>
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<td>53</td>
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<td>270</td>
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<tr>
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<td>287</td>
<td>462</td>
<td>983</td>
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</table>

*Includes cases of unspecified ages
Table 6.
Cases of leishmaniasis reported in the Republic of Panamá by age group
1977-1985*

<table>
<thead>
<tr>
<th>Year</th>
<th>0 to 1</th>
<th>1 to 4</th>
<th>5 to 14</th>
<th>over 15</th>
<th>Total</th>
</tr>
</thead>
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<td>24</td>
<td>64</td>
<td>98</td>
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<td>23</td>
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</tr>
<tr>
<td>1985</td>
<td>4</td>
<td>18</td>
<td>29</td>
<td>46</td>
<td>97</td>
</tr>
</tbody>
</table>

*In percentage of total cases
DISTRIBUTION OF LEISHMANIASIS IN PERU

H. Guerra

INTRODUCTION

As is well known, and has been indicated repeatedly since Tamayo in 1908 published his observations[1], there are two clinically and geographically distinct forms of human tegumentary leishmaniasis which are amply distributed in Peru: the cutaneous Andean form, called "Uta" and the cutaneous and mucocutaneous Amazonian Jungle form, called "espundia".[2,3,4,5] The differences are such, that the diseases must be considered separately, although at present we accept that the agents of both are closely, associated members of the Leishmania braziliensis complex.[6] Unpublished work by our group (Arevalo et al., personal communication) has succeeded, through electrophoretic analysis of more than 12 enzymes tested, in differentiating the agent of Uta, L. braziliensis peruviana from that of Espundia, L. braziliensis braziliensis. Malate dehydrogenase (MDH) was the only enzyme showing the difference.

GEOGRAPHICAL CONSIDERATIONS

Peru is a country with a very accidented topography. The Andes, which run longitudinally as several mountain ranges, provide a variety of environments, where altitude dominates ecology, physiology and even sociology. The Peruvian territory is didactically divided into 8 "natural regions," defined by altitude above sea level (in meters). Listing from west to east, these are:

**Chala or Coastal Region** - 0 to 500 m
The coastal sandy desert, with a high humidity, mist and fog but no precipitation. It is cooled by the cold Humboldt Oceanic Current, and has dunes and bare hills, with vegetation only in the valleys.

**Yunga or Creek Region** - 500 to 2,300 m
Western slopes of the Andean valleys and interAndean valleys. Warm weather, with seasonal changes, pronounced rainy season, scarce, mostly xerophytic flora, low bushes. Agriculture is accomplished through terraces called "andenes". This region has been traditionally held as "unhealthy" because of Uta and human bartonellosis, malaria, etc..

**Quechua or Temperate Region** - 2,300 to 3,500 m
Hilly, with many valleys, large climatological variations according to the seasons. Concentration in agricultural and cattle raising activities, densely populated.

**Suni or Cold Region** - 3,500 to 4,100 m
Accidented terrain, many cliffs and peaks; upper limit of agricultural activity. Cold, thin air. Population less dense, cattle raising and mining are important.
Puna or High Andean Region - 4,100 to 4,800 m
Irregular terrain, including many lakes and mesas, and a portion of the large South-Peruvian mesa. Very cold, thin air. Cattle raising, including South American camelids, is important.

Janca or White (Snowy) Region - 4,800 m and above.
Highest peaks, rocky reliefs, permanent snows, practically no vegetation and animal life. Mining is the most important human activity.

Rupa-Rupa or High Jungle Region - 400 to 1,000 m
The Eastern slopes of the Andes, irregular terrain, with hills, valleys, creeks and many smaller rivers. Warm, humid, abundant rains, much vegetation and tropical fauna. Population is on the increase through migration from the Andean regions; agriculture and cattle raising are important, but mismanagement of the environment is common. Native populations exist and compete with the colonists.

Omagua or Low Jungle Region - 0 to 1,000 m
The great Amazonian plains, tropical rain forest. The rivers are the dominant feature of the environment. Rich fauna and flora. Agriculture and cattle raising activities are not well established. Slash and burn techniques are common in native populations. Some industries, which take people into the forest exist, such as lumber, panning for gold, and oil exploration and extraction.

Those in which the leishmaniases occur are the Yunga, the Rupa-rupa and the Omagua regions.

UTA OR ANDEAN LEISHMANIASIS.

Uta occurs in the Yunga and low Quechua regions, which are well differentiated through the several systematic medico-geographical studies performed by Weiss. Yunga is recognized as the region where leishmaniasis and human bartonellosis (Carrion's disease) are prevalent. Malaria is largely absent from this region at present, due to the efforts of the eradication program.

The main activity of the populations, mostly rural, is agriculture; this has become quite specialized in some areas, providing for example flowers and fruits for the cities, as well producing certain other vegetables mainly for their own use. The small villages which dot the hilly countryside are populated only part time, as most of the inhabitants work in their fields, which may be quite distant, and often considerably higher, forcing the people to have at least resting facilities there. In addition, many homes have planted areas, where women with small children, or old people take care of vegetable gardens. Schools and commerce are concentrated in the largest towns, which hold a Sunday market, while the rest are only simple groups of houses. The traditional organization of the Inca Empire, based on community ownership of the land, solidarity, and many communal activities, including a system of popular consultation through general assemblies (town meetings) is preserved in some areas. In others, organization is less strong, while in still others cooperatives are responsible for economic activities. Civil authorities,
such as mayors, councilors, etc., are elected in accordance with the general practice in Peru. These authorities, and also teachers, policemen, parish priests, sanitarians, nurses or physicians, where they exist, constitute the notables of each township, down to the village level, and all activities of the communities are organized and coordinated through them.

As the region which is closest to the Coast is where the largest cities exist, strong migration, specially of the young, continually occurs. Migration has been a way out for the problem of insufficient land, which has been subdivided among the members of a community into smaller and smaller plots. This migration is even greater when there are unusual circumstances, such as droughts, major natural disasters such as earthquakes and large landslides, or simply bad harvests. Due to the characteristics of the mountains, which are bare, with very sparse, and superficially rooted vegetation, landslides are not uncommon, and usually they block the roads several times during the rainy season.

The migratory pattern to the cities is similar to that in other developing countries, and occurs also with people from the other Andean regions: Quechua, Suni, Puna, etc. Young men, and sometimes also women, decide to leave for the cities to improve their future, lured by job opportunities and other attractions of urban life; in some cases the young people are sent by their parents or other relatives to seek a better education or employment, in the understanding that they would later contribute part of their incomes to them. Those who do get established, mostly as members of the "informal economy", street vendors, unskilled laborers offering their services as gardeners, construction workers, or in small shops, etc., may later bring their families to live with them, causing overcrowding in the "Callejones" (low-rent, rundown lodgements) of the cities. Once this situation becomes intolerable, people become organized, selecting Government lands to begin a barriada or "invasion". Overnight, the selected plot is filled with the dwellings of the squatters, made with sticks and straw, all sporting the Peruvian flag, and a sign bears the name of the settlement, usually that of a prominent political figure of the party in power, of a Saint, or a motto. Quite often the barriadas or "Young Towns" develop from people coming from the same area in the Andes, and many of their habits are preserved. Peruvian law protects these efforts at self-development, and squatters who remain in their plots for two years are often granted their piece of land. Through their solid organization, these Young Towns may over a period of years develop into well-built urbanized sections of the city, with the basic utilities of running water, electricity and sewage.

Butrón, aided by Arzubiaga, studied Andean leishmaniasis and human bartonellosis through a period of 10 months of continuous community work in a typical group of small villages near Lima, between 2,000 and 3,200 m a.s.l., and with access to the road and railroad. The people cultivate flowers, fruits, and other agricultural produce in plots where terraces are in use for several generations. The urban focus of the district in San Jerónimo de Surco (over 1,000 inhabitants), and 18 other villages exist, out of which 3 were studied: Ayas (~150), Huaquicha (~65) and Linday (~60). The conclusions of their study were:
- there had been an increase in the incidence of both diseases, leishmaniasis and bartonellosis, after several years of quiescence, attributed by Herrer to insecticide spraying activities by the malaria eradication program and by the inhabitants for their agricultural products.

- the peak months for appearance of Uta lesions were March, April, June and July. Bartonellosis lesions appeared from April to August.

- many of the newly infected people were children, perhaps attesting to the lasting nature of immunity in adults who had had these diseases in their youth.

- there was an association of leishmaniasis with rural activities, while bartonellosis was more uniformly distributed, with a slight prevalence in urban areas and with rural activities near the villages.

- the higher places, between 2,300 and 2,600 m had more Uta cases, and the opposite was true of new bartonellosis cases (where eruptive lesions were seen by the researchers), which occurred more in lower localities, between 2,000 and 2,300 m above sea level.

- Uta lesions appeared mostly on the face and upper limbs, which are bared during agricultural work.

- Leishmanin is useful: specificity is 94.2%, with a sensitivity of 93.1% in chronic (cicatricial) leishmaniasis, and 88.2% in active cases.

These observations are in general accordance with previous studies. There seem to be distinct vectors for each of the two diseases studied, with that transmitting Uta being more rural and preferring a higher altitude. The sensitivity of both diseases to insecticides seems to be shared, but other factors such as prolonged droughts, heavy rains, extensive land movement, such as landslides and road building, both of which occurred just prior to the period of the study, may have a large influence.

The correlation of altitudes, vectors, and the diseases is particularly interesting. Herrer and Hertig place the limits of Uta between 1,200 and 3,000 m, and those of bartonellosis between 940 and 3,000 m. Lutzomyia peruensis, a main candidate vector for Uta, (especially since Herrer), infected hamsters with homogenates of this species) lives between 1,800 and 3,300 m. Other vectors living at lower altitudes are therefore likely. Lu. verrucarum, long incriminated as the main vector for bartonellosis lives between 940 and 3,000 m.

Herrer attributed the success of insecticide spraying to the fact that not only homes, but also the rough rock fences ("pircas"), used by the inhabitants for penning their animals and for plot delimitation, were sprayed. The hypothesis is that the environment of the mostly arid Yunga region is such that much of the wildlife is concentrated in and near the human dwellings and their cultivated plots, which provide shelter, food, and breeding grounds to the vectors, mostly in the "pircas" and "andenes". The latter may have the most appropriate conditions for breeding of the soil-dwelling sandfly larvae, in the gradations of humidity and
Simplified Physical Map of Peru

Note: A dotted line separates the 3 traditional regions from each other.
Endemic Areas for Uta and Espundia in Peru

Note: Espundia is endemic in the whole Amazonian jungle but cases concentrate near certain rivers.
warmth they contain. The original, still unidentified, wild reservoir of Uta (and its, as-yet hypothetical, wild reservoir of human bartonellosis) would also have come, centuries ago, to the 'new' and richer man-made environment, producing a nearby cycle for each disease, in which man was accidentally involved. Domestic animals such as dogs and commensals such as the rat (Cruzado and Miranda, 1982, personal communication) have been found infected, but their significance as reservoirs is open to question. The greater domesticity of Lutzomyia verrucarum may be due to its better adaptation to this human environment. This vector is now probably sustaining bartonellosis without a wild reservoir, as up to 12-15% of the population have been shown to harbor Bartonella bacilliformis in endemic areas. The remarkable situation of equilibrium in this host-pathogen relationship deserves more attention.

Recent work by our group (Llanos et al., unpublished observations) places significance on the transmission patterns as related to the characteristics of the valleys in the Yunga and low Quechua regions, as exemplified by the valley of Huayllacayán. According to particularly detailed analyses, transmission is very likely to occur in the higher and more narrow part of the valleys, where people may have some of their plots, but which are also an obligatory part of their daily travel to their main agricultural work. As these portions of the valley are close to the rivers, there is vegetation, and with it, wildlife, which may be essential for the maintenance of the disease. At the same time, these areas are adequate for grazing for both cattle and goats, and the shepherds (in many instances small children and women who carry their babies strapped to their backs) become exposed to transmission.

The issue of leishmanin intradermal tests is interesting. The antigen has been shown by many to be useful, but it still hasn't been properly standardized, and therefore cannot be fully exploited. In addition, there always are some positive reactors with no history of disease or of suggestive scars. This situation also occurs in the Peruvian Jungle, where the usual interpretation is that it is the result of infection with other, nonpathogenic Leishmania species, or cross reactions with other Trypanosomatidae.

ESPUNDIA OR AMAZONIAN JUNGLE LEISHMANIASIS

Espundia or Amazonian Jungle leishmaniasis occurs in two of the natural regions, Rupa-Rupa or High Jungle and Omagua or Low Jungle, each a distinctive environment, as described above. Clinical characteristics of the disease in these two regions have not been clearly distinguished, and the agent has been identified, in practically all cases, as Leishmania braziliensis braziliensis.

Small Rupa-Rupa communities are of two main types, native and settlers or "colonos". Native communities were originally nomadic, deriving their food from hunting and fishing, and usually establishing themselves temporarily in a particular locality to begin their slash and burn type of agriculture, selecting small plots which require little maintenance for their crops. After a few years (2 to 4), when the soil no longer could support yield yucca and bananas, they moved on to other
areas to repeat the cycle, leaving the forest to recover by itself in 8 to 10 years. The present situation of the native communities is of a more limited migration, and the adoption of the ways of life of the settlers is becoming more obvious.

The "colonos" come primarily from the Andean highlands, and bring their own technology with them. Those that settle permanently are only a fraction of the migrant workers who come for the harvest season for coca, coffee, or other crops, or to work in the logging industry. Some governments have stimulated colonization of this Jungle region, representing it as a very rich area in need of development through modern means. Unfortunately, the settlers are not adequately prepared for the conditions they encounter, and are not ready to change their traditional habits. They usually work for long periods to clear and burn larger tracts of land and during the sowing and reaping seasons. Disregarding environmental concerns, they often work on the hillsides and hilltops, which may lose topsoil and fertility very rapidly because of the heavy rains. The extraction of valuable woods by the logging industry, without replacement by reforestation, has further damaged the future development of the region.

The towns and cities concentrate commerce and a few industrial enterprises. They are connected through roads with the rest of the country, but during the rainy season (December to March) mud and often landslides make such communication difficult. Many towns have become important centers of trade, and have reasonably well organized schools, hospitals, industries, services, etc.

In the Omagua, or Low Jungle region, the activities of agriculture and industry share some of the tendencies described for the High Jungle. Much less densely populated, the Low Jungle has vast areas which haven't been penetrated except for explorations, for future exploitation (oil, gold, valuable woods, etc.) scientific study, or missionary activities. Native populations differ, and many are now in the acculturation process as are those of the High Jungle region, but others remain more distant, relying on hunting and fishing, a little agriculture, and with only a few contacts with "civilization": a bilingual teacher of their own tribe, nearby settlements or towns where they go for trade, supplies, repair of tools or weapons, or similar reasons. The towns concentrate much of the contact with the rest of the country, through airstrips and roads. Very often the contact between Jungle towns is through the navigable rivers, which establish natural communication links. These rivers are the most important feature of the region for practically all purposes, and the riverine village is probably the "typical" human environment.

Espundia is characteristically a zoonotic disease, transmitted to man only when he enters the Jungle environment. In this regard, the patients are usually males who participate in the explorations mentioned, and particularly large outbreaks have occurred during seismic exploration for oil and the "gold rush" situation in Madre de Dios. In agricultural communities, a situation studied by Calmet and Bartolini (1986, personal communication) in the Central Jungle, the treatment of the forest by the individual may be very important in the transmission of disease. As has been mentioned, settlers remain in the forest for long periods and work in large plots, thus coming in closer contact with large trees and
disturbing more of the forest. Natives avoid this degree of contact, produce much less disturbance of the forest, and are less often infected. Certainly other factors are at play in other areas of the country, such as the Northern Jungle, where natives also frequently suffer from Espundia. In this case, their villages are more likely to be well inside the forest, bringing the total population into a risk zone. The families are probably more protected in their homes, through the fire in the hearth and the smoke that are traditionally always present, but as they constantly enter the forest for agriculture (females) and hunting (males) some transmission is possible.

Reservoirs and vectors of Peruvian Espundia have not yet been defined. Many phlebotomines have been found in the Amazonian Jungle, several of which have been incriminated as vectors of leishmaniasis elsewhere: Lutzomyia olmeca, Lu. anduzei, Lu. gomezi, Lu. umbratilis, Lu. longipalpis, Lu. panamensis, etc. Llanos and Young et al. have published lists of phlebotomines found in Peru. The whole issue of reservoirs has received little attention so far. The fauna present in the Amazonian Jungle is extremely abundant, and efforts in this aspect should begin with species already known to harbor the parasites important for man from work performed in neighboring countries.

It has been surmised that the leishmaniasis cases that North of the Amazon river are caused by L. braziliensis guyanensis and those to the South by L. braziliensis braziliensis. This clinico-geographical hypothesis has yet to be confirmed, since too few isolates from the northern region have been fully characterized for identification.

Areas where intermixing of Andean and Amazonian Jungle leishmaniasis may occur also exist. These are near the "pongos", or in valleys where rivers cut through the Andean mountain range from one region to another. The most important such valleys are those of the upper Marañon river, in the Northern part of the country, of the upper Huallaga near the center, and of the Mantaro and Apurimac in the South. In each of these areas, there is a chance for patients to appear with either Andean or Amazonian forms of leishmaniasis, since the environmental conditions have characteristics of both, there are relatively open geographical conditions, and the intense migration currents which have been already mentioned.

STATISTICAL INFORMATION ON THE LEISHMANIASIS IN PERU

Leishmaniasis is reported routinely by the Health Posts, Health Centers and Hospitals of the Ministry of Health. The central information Office of the Ministry of Health has produced documents which provide an idea of what the magnitude of the diseases were up to the year 1985. Leishmaniasis is listed in these reports, and in spite of the incompleteness of reporting, since many patients never go to see a physician or sanitarian, some tendencies may be observed.

The general trend has been an increase in the number of reported cases from 1976 to 1985: 1,538 to 2,733 per year.
The distribution of the cases reported in 1984 follows the traditional division between the Coast, the Sierra or Highlands, and the Jungle, comprising both Low and High Amazonian Jungle, and therefore the data can be roughly interpreted as to which of the clinical forms is represented. There were 87 cases for the Coast (Yunga), 1,757 for the Sierra (Yunga and Quechua), and 889 for the Jungle (Rupa-Rupa and Omagua). The Andean population being much larger, more leishmaniasis is, not surprisingly, reported from the Sierra, although there is a low reporting rate. People in the endemic Andean areas "pass" the disease as they do other childhood diseases, with between 80 and 90 percent of the population showing leishmanial scars. The Jungle patients (except those who are self employed in agricultural labors) would be expected to report more regularly on their disease, since in 1975 leishmaniasis was declared an occupational disease in Peru, and patients receive free treatment, sick leave, and other benefits. 22

The distribution of the cases in 1985 by month of presentation shows greater numbers around the second quarter of the year, following the more intense rains of the first quarter. The larger sandfly population may allow more efficient transmission, which is more likely to occur during the later months, February and March. People becoming infected in those months would report their disease one or two months later. Chronic cases may report at any time.

The age distribution of the patients, which would be very interesting to analyze by region, is unfortunately given only as national figures. There is an appreciable number of cases in the earlier years, 0-4, 5-9 and 10-14 groups, with over 200 cases in each group, followed by the peak in the 15-19 and 20-24 age groups, with about 400 cases each. The number of cases at later ages then decreasing gradually. The cases of children under 4 are most likely due to early transmission of leishmaniasis in the Andean regions.

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Peru - 1985

Reported Cases of Leishmaniasis by Age - 0 to 75+ Years
Peru - 1985
ANDEAN CUTANEOUS LEISHMANIASIS IN THE
HIGHLANDS OF THE DEPARTMENT OF LA LIBERTAD IN PERU

Hernán Miranda

INTRODUCTION

Human cutaneous leishmaniasis is common in the Andean highlands in the Department of La Libertad, where high prevalence rates are found among the population of newly established agricultural developments. Based upon the clinical features of human disease, and the ecological aspects of the focus at altitudes between 1,500 and 3,000 m above sea level, the infection has been presumed to be "Uta", due to *L. peruviana*, one of the least studied of human leishmanial parasites. Epidemiological investigations under the auspices of the UNDP/World Bank/WHO Special Programme for Research and Training in Tropical Diseases have been ongoing for several years in Pagash, Padai, and La Cresta. Professor L. Cruzado-Razco is the principal investigator and Dr. Aristides Herrer of Lima is advisor to the project. This research was centered upon rodents, since these are believed to be the reservoir of infection.

CLINICAL CHARACTERISTICS

The clinical characteristics of the infection in general conform to those reported for "Uta" in other localities in Peru. The majority of active lesions are found in children from 3 months to 15 years of age, although some occur in adults up to 80 years. Lymphatic involvement is present in 25%, and mucous lesions occur in 3%. The latter findings are unusual in that mucous lesions are not usually attributed to *L. peruviana* infection. However, the mucous lesions are not like the metastatic lesions of *L. b. braziliensis*, but occur only by extension from cutaneous lesions and the upper lip is the only area affected.

One case of Diffuse Cutaneous Leishmaniasis was studied; the patient had a negative Montenegro reaction and nonulcerating disseminated lesions resembling lepromatous leprosy over large areas of the body. He was infected in Pagash and observations cover a period of 22 years. The parasite was isolated and found to be the same as other Uta isolates from the Pagash focus.

IDENTIFICATION OF PARASITES

Isolates from human and rodents were identified by Dr. G. Romero of the Instituto de Medicina Tropical "Alexander von Humboldt" in Lima, using monoclonal antibodies, six isoenzymes, and DNA hybridization. (Also by Dr. Evans of the London School of Tropical Medicine and Hygiene with a battery of six isoenzymes.) The isolates were not distinguishable from *L. b. braziliensis*. This confirms Lainson's belief that *L. peruviana* belongs to the braziliensis complex. However, in hamsters inoculated with strains from both humans and rodents, lesions developed quickly, with nodules developing in one month, and ulcers in three months. Parasites
were very abundant in the lesions and over a 12-15 month evolution, they
developed metastatic histiocytomas which gave the paws the "boxing glove"
appearance characteristic of L. mexicana group infections in this host.

RODENT HOSTS

Isolates of Leishmania from naturally infected rodents were made in
the study areas in Pagash and Padai. Of more than 100 stocks isolated
from man and rodents, 42 were identified: eight were from Phyllotis and-
inum, four from Akodon mollis, four from Rattus rattus, and two from
Thomomys sp. Identification of the rodents was made by Dr. O. Pearson
of the University of California at Berkeley.

VECTORS

The most prevalent sandfly in the endemic area is Lutzomyia peruvensis
(over 97% of forms captured). Lu. mycetayaca and Lu. noguchii also occur
in small numbers. Cruzado has isolated Leishmania from Lu. peruvensis,
which Herrer considers to be the vector of Uta.

TREATMENT

Treatment was desired by almost all patients, and it was considered
ethically obligatory to treat those seen in the study. However, a full
course of pentavalent antimony is neither feasible nor appropriate for
the simple cutaneous ulcers of Uta. A short course of treatment admin-
istered close to where the patients live, and without cost to them, was
the goal. Good results were obtained with 16 injections of Glucantime in
eight days (two per day) at a dosage of 150 mg drug/kg/day. If lesions
were small, 5-10 ml of Glucantime were given daily for 5-6 days with
successful results. Secondary bacterial infections are common, but easily
controlled with penicillin.

DISCUSSION

The name Leishmania peruviana was proposed in 1913 by Vélez-Lopez,
who lived in Trujillo for a long time. The name was proposed two years
after Gaspar Vianna named Leishmania braziliensis in Brazil as a new
species, based upon the grave mucous lesions produced by this parasite,
in contrast to the more benign simple cutaneous lesions of the Old World
caused by L. tropica. Vélez-Lopez assumed that the parasite of the And-
ean highlands was different from L. braziliensis because it did not prod-
uce mucous lesions, and proposed the name on these considerations. It
has remained an accepted name in the literature, but the validity of
regarding it as a separate entity remains to be proved.

The inability to separate L. peruviana and L. braziliensis by iso-
enzymes raises the question that the clinical differences may be due to
temperature differences between the high Andes and the low jungle, which
affect the growth rate, rather than being due to two separate parasites.
INTRODUCTION

The leishmaniases are a prevalent infection and constitute a serious Public Health problem in Venezuela. Clinically the leishmaniases found in the country can be divided into three large groups: cutaneous, mucocutaneous and visceral.

CUTANEOUS AND MUCOCUTANEOUS LEISHMANIASIS

Cutaneous leishmaniasis (CL) and mucocutaneous leishmaniasis (MCL) are endemic in all of the states and federal territories of Venezuela, with the exception of Delta Amacuro. A total of 29,317 cases have been registered by the Division of Sanitary Dermatology since 1955, with an average of 814 yearly.

Clinical aspects

Cutaneous and mucocutaneous leishmaniases start as an erythematous papule that may become papulo-vesicular. This initial lesion enlarges slowly giving rise to the polymorphic clinical aspects of the disease, ulcerous, nodular, lymphangitic, diffuse and others. The evolution, the dissemination of the lesions, and the different clinical forms depend on both the pathogenicity of the Leishmania and the immunological state of the host.

In the ulcerating type, a crust develops centrally which may fall away exposing a crateriform lesion, having raised and infiltrated borders and a granular or vegetant bottom with abundant serous, serohematic or seropurulent secretion. This is the most frequent clinical form and can be easily diagnosed. It is produced by L. b. braziliensis and L. m. venezuelensis. The ulcerous lesion produced by the latter, is usually somewhat smaller.

In the nodular type, nodules are shiny, slightly or non-ulcerated, and are located on the face, ears or chest. These are usually due to L. m. venezuelensis.

The lymphangitic form is relatively frequent, besides the ulcers which may be single or multiple, there are metastases along the lymphatic system. This is also due to L. b. braziliensis.

Diffuse cutaneous leishmaniasis (DCL) is characterized by widely disseminated thickening of the skin in papules, infiltrated plaques or multiple nodules. There is no ulceration or mucosal involvement. The disease does not heal spontaneously and is very resistant to treatment. DCL is due to an immunological defect of the host,15 and can be produced by parasites of the L. mexicana complex.
Cutaneous leishmaniasis is a disease that heals spontaneously in a high rate of cases, leaving a scar with altered pigment. Relapses occur in some of them, producing severe mutilation of the naso-oro-pharyngeal cavity and sometimes death. The mucous complication may occur during the presence of the primary lesion or up to 24 years later.\(^{(1,8)}\)

**Epidemiological Aspects**

The endemic zones are most often found in small villages and settlements near wooded areas. These diseases are more predominantly found in heights ranging from 0 to 1,800 m above sea level, in areas with an average temperature of 25.5°C, relative humidity from 65 to 100% and average rainfall from 700 to 1,249.3 mm or more. They occur indiscriminately in any age, sex or race, but they are more frequent in men than in women, and in adults than in children. In general, they tend to be occupational diseases which are more commonly found in peasants working in deforestation activities for agricultural settlements and extraction of wood and other natural products from the forest, farmers, hunters, tourists, military personnel, and those working in new road construction through the forest.\(^{(1)}\) In this ecological environment *Leishmania braziliensis* braziliensis is most frequently found.

In areas of the Central Western Portion of Venezuela the predominant landscape is xerophytic. On the periphery of Barquisimeto, located with the Turbio River to the south and the Ruezga Creek to the north, with an average rainfall of 700 millimeters, there is dense vegetation found along the Turbio River, while the prevailing vegetation elsewhere (including that along the Ruezga Creek, a Turbio River tributary), tends to be xerophytic. Barquisimeto's relative humidity is 65.4%, with a maximum of 100% in the months of June, July, October, November and December and a minimum of 22% in April. The average temperature is 25.20°C. with a maximum of 34.10°C. in March and a minimum of 15.90°C. in December.\(^{(2)}\)

Since 1974 a significant number of CL cases have turned up in or around Barquisimeto, Venezuela's third-largest city and capital of the state of Lara. One case was found in 1974, three more in 1989, and 89 more during the course of surveys conducted from 1982 to 1984. The disease afflicted people of all ages, and both sexes, but was most common in males and in subjects less than 15 years old; 94.6% of the cases were due to *L. mexicana* venezuelensis.\(^{(3)}\)

**Reservoirs**

*Leishmania* have been found in a variety of wild animals (Table 1).

*Zygodontomys microtinus* at the Ticoporo forest, state of Barinas\(^{(4)}\). Parasites were abundant in smears of the skin and they were easily cultured in N.N.N. medium.

*Proechimys guayanensis* in the same area.\(^{(5)}\) Parasites found in the skin were not isolated.

*Heteromys anomalus*. In the state of Carabobo.\(^{(6)}\) The production of large nodules rich in amastigotes in the skin of hamsters suggests that
the isolate was not *L. b. braziliensis*, as was reported, but a parasite of the *L. mexicana* complex.

*Didelphis marsupialis*. In the periurban area of Trujillo city. The parasite isolated from skin and viscera was *L. b. braziliensis*.

Infections with *L. b. braziliensis* have been found in the skin of dogs and donkeys. Although we believe that these animals, like man, are only circumstantial victims of this disease, more studies are in progress to determine their importance as a reservoir.

A bat, *Phyllostomus astatus*, in the rural settlement of Zipayare, state of Zulia, was found to be infected with *Leishmania* sp.

**Vectors**

More than 40 species of sandflies have been identified in Venezuela of which only fourteen feed on man, and a few of them have been incriminated as possible vectors.

*Lutzomyia panamensis* was found to be infected with unidentified promastigotes and it is the most probable vector of *L. b. braziliensis*.

*L. flaviscutellata*. *L. m. amazonensis* was isolated from this sandfly in the Sierra Parima, Federal Territory of Amazonas.

*L. olmeca bicolor* is the most likely vector of *L. m. venezuelensis*. The frequent location of the lesions on the face and upper extremities is probably related to the habits of the vector.

**Parasites**

The following parasites have been identified as causal agents of leishmaniasis:

*L. b. braziliensis* (Vianna, 1911) has been isolated from humans, dogs and donkeys.

*L. m. venezuelensis* (Bonfante-Carrido, 1980) has been isolated from humans in Barquisimeto and other cities of the states of Lara and Yaracuy.

*L. b. guayanensis* (Floch, 1954) has been isolated from humans in the state of Trujillo.

A parasite similar to *L. m. amazonensis* (Lainson and Shaw, 1972) has been isolated in the Federal Territory of Amazonas in southern Venezuela. It is possible that another isolate from Guarico is the same species.

Controversy exists whether *L. m. pifanoi* (Medina and Romero, 1959), isolated from a few cases of diffuse cutaneous leishmaniasis, and *L. m. garnhami* (Scorza et al., 1979) are distinct taxa.
VISCERAL LEISHMANIASIS

Clinical Aspects

The incubation period of visceral leishmaniasis is from two to five months. The most frequent symptoms are anorexia, malaise, anemia, fever, marked splenomegaly, moderate hepatomegaly, progressive weight-loss, malnutrition, oedema, diarrhoea, lymphadenopathy, ascites, cachexia and death, if untreated. Death generally is produced by an intercurrent infection.

Epidemilogic Aspects

Visceral leishmaniasis (VL) is endemic in all of the states of Venezuela, with the exception of Tachira and Merida states, and the Federal Territories of Amazonas and Delta Amacuro.

The endemic areas are near macrotermic forests at the foot of hills, contiguous with plains of tropical climatology with herbaceous formation and bushes. During the dry season these regions become arid.

VL afflicts principally children from 0 to 4 years of age, but it occurs also in teenagers.

Only man and dog have been found as sources of infection, in spite of research on many other domestic and woodland animals. The dog seems to be the most important reservoir.  

*Lutzomyia longipalpis* is the only species incriminated as the vector of *L. donovani chagasi*.  

CONTROL ACTIVITIES

No programs for control exist at the present time, except for active case-finding and systematic treatment of those infected. All patients are treated with injections of pentavalent n-methyl glucamine antimonate (50 mg/kg) for twenty consecutive days, and after a week of rest, a second series of injections is administered.

Synergistic clinical activity between Paromomycin and methylglucamine is observed in CL patients in Venezuela treated with daily injections for ten days. Also ketoconazole at daily oral doses of 400 mg has been found effective, after 90 days of administration (Scorza et al., personal communication).

An experimental vaccine against leishmaniasis was prepared in 1986 by O'Daly and Cabrera with amastigotes of *L. braziliensis* and *L. donovani*. Parasites were grown in a protein-free medium. This vaccine has been improved (O'Daly, Bonfante-Garrido and Barroeta) by adding other isolates to the original antigen to make it polyvalent. We hope to carry out field trials of this vaccine in humans, during the present year.
Table 1.
Natural infection of Venezuelan sandflies
and mammals with *Leishmania*

<table>
<thead>
<tr>
<th>Host species</th>
<th>Localization</th>
<th>Parasite</th>
<th>State or Federal</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>Lu. migonei</em></td>
<td>intestine</td>
<td>?</td>
<td>Yaracuy</td>
<td>Pifano (1943)</td>
</tr>
<tr>
<td><em>Lu. longipalpis</em></td>
<td>intestine</td>
<td>?</td>
<td>Yaracuy</td>
<td>Pifano (1943)</td>
</tr>
<tr>
<td><em>Lu. panamensis</em></td>
<td>intestine</td>
<td><em>L. braziliensis</em></td>
<td>Yaracuy</td>
<td>Pifano (1959)</td>
</tr>
<tr>
<td><em>Lu. longipalpis</em></td>
<td>intestine</td>
<td><em>L. donovani chagasi</em></td>
<td>Carabobo</td>
<td>Amaral (1961)</td>
</tr>
<tr>
<td><em>Lu. flaviscutellata</em></td>
<td>intestine</td>
<td><em>L. mexicana amazonensis</em></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Proechimys guayanensis</td>
<td>skin</td>
<td><em>L. mexicana s. sp.</em></td>
<td>Barinas</td>
<td>Convit 1968 (cited in Pons, 1968)</td>
</tr>
<tr>
<td>Heteronyx microtus</td>
<td>blood</td>
<td><em>L. mexicana s. sp.</em></td>
<td>Carabobo</td>
<td>Torrealba <em>et al.</em></td>
</tr>
<tr>
<td>Eurydontomys microtus</td>
<td>skin</td>
<td><em>L. mexicana s. sp.</em></td>
<td>Barinas</td>
<td>Kerdel-Vegas and Essenfeld 1966</td>
</tr>
<tr>
<td>Didelphis marsupialis</td>
<td>skin and visceras</td>
<td><em>L. b. braziliensis</em></td>
<td>Trujillo</td>
<td>Scorza <em>et al.</em></td>
</tr>
<tr>
<td>Canis familiaris</td>
<td>skin lesions</td>
<td><em>L. b. braziliensis</em></td>
<td>Zulia</td>
<td>Pons (1968)</td>
</tr>
<tr>
<td>Canis familiaris</td>
<td>skin lesions</td>
<td><em>L. b. braziliensis</em></td>
<td>Lara</td>
<td>Bonfante-Garrido <em>et al.</em> (1981 b)</td>
</tr>
<tr>
<td>Canis familiaris</td>
<td>skin lesions</td>
<td><em>L. b. braziliensis</em></td>
<td>Cojedes</td>
<td>Aguilar <em>et al.</em> (1982)</td>
</tr>
<tr>
<td>Equus asinus</td>
<td>skin lesions</td>
<td><em>L. b. braziliensis</em></td>
<td>Zulia</td>
<td>Pons (1968)</td>
</tr>
<tr>
<td>Equus asinus</td>
<td>skin lesions</td>
<td><em>L. b. braziliensis</em></td>
<td>Lara</td>
<td>Bonfante-Garrido <em>et al.</em> (1981 c)</td>
</tr>
<tr>
<td>Equus asinus</td>
<td>skin lesions</td>
<td><em>L. b. braziliensis</em></td>
<td>Cojedes</td>
<td>Aguilar <em>et al.</em> (1982)</td>
</tr>
<tr>
<td>Phyllostomus hastatus</td>
<td>skin lesions</td>
<td><em>Leishmania</em> sp.</td>
<td>Zulia</td>
<td>Pons (1968)</td>
</tr>
</tbody>
</table>
REFERENCES

20. Pifano, C.F., 1940. Rev Policlin (Caracas) 9:3639
LEISHMANIASIS: SPECIAL SITUATIONS IN OTHER AREAS OF THE AMERICAS

Rafael A. Cedillos and B. C. Walton

UNITED STATES - MEXICO BORDER FOCUS OF CL

Although the information is fragmentary, there is apparently a single focus of leishmaniasis encompassed in the south-central Texas, Coahuila, Nuevo Leon and Tamaulipas area. The northern localities where cases have occurred in Nuevo Leon and Tamaulipas are essentially contiguous with the area of the localities in Texas, and the Rio Grande is no natural barrier for either sandflies or a wild mammal reservoir.

This focus should be considered as quite separate and distinct from the classical Leishmania mexicana mexicana focus on the Yucatan peninsula for several reasons: 1) geographical separation, with no evidence of transmission in the intervening area; 2) differing ecologic conditions (scrub forest vs. tropical forest); 3) different vector (Lutzomyia diabolica, Hall, known anthropophilic species vs. L. olmeca in Yucatan); 4) the proportion of cases which evolve in Disseminated Cutaneous Leishmaniasis (DCL) is relatively high in the northern focus, while this condition is extremely rare in the sylvatic Yucatan area, suggesting that a different parasite is involved.

Parasite and clinical aspects.

Infection in this focus is manifested principally by simple cutaneous ulcers, which are usually self-healing in a period of 8-12 months. The lesion can take many forms and may mimic a great many other dermatologic conditions. In Mexico, some cases have been described as having the "classical" circular lesion of Boton d'Oriente with raised discolored borders and a central excavated ulcer of over 1 cm in diameter. However, in Texas the diagnosis was usually quite early and in most cases the lesion was characterized as a papule.1,2,4,5

Probably the first reported case from this focus was that of Stewart and Pilcher in 1945, of cutaneous Leishmaniasis (CL) in a 6 year old boy from Alice, Texas.5 The second case was reported in 1968 in a 64 year-old Mexican-American woman from San Benito with DCL4 who had lived her entire life near San Benito, except for occasional visits to Tamaulipas and Nuevo Leon. At approximately the same time, the first case in Coahuila was diagnosed by Portales, and reported by Ramos-Aguirre.6

Only one of the 11 cases (9.0%) from Texas was DCL, but of the 16 confirmed or suspect cases in this focus from Mexico from which information is available, 7 (43.8%) were disseminated, hence, probably DCL, although information on the criteria is not available to ascertain if they meet the definition. In 1976 two additional cases of apparent autogenous CL were reported.2,3 A parasite was isolated in hamster and culture, which corresponded biochemically and biologically to L. mexicana mexicana, except that it did not grow quickly and abundantly in culture media.2,7
Vectors. An anthropophilic sandfly, Lutzomyia diabolica, has been found in Texas and Mexico.\(^1\) Its distribution correlates well with the distribution of cases in both areas.

Reservoirs. At present, there is no information available on natural mammalian-hosts in this focus. The domestic feline infection in Uvalde, Texas is of great interest, and it is probably the first report from the New World.

DIFFUSE CUTANEOUS LEISHMANIASIS IN THE DOMINICAN REPUBLIC

Since 1975 when Bogaert-Diaz et al. published the first three cases,\(^1\) a total of 23 cases of DCL have been recorded in the Dominican Republic. No simple cutaneous leishmaniasis has yet been reported. Nodules and infiltrative lesions in different parts of the body were the most common clinical manifestations; in some patients, one or more firm erythematous plaques or hypochromic patches were present.

The nature of the parasite causing DCL in Dominican Republic is speculative but it most likely is a new species. Lainson stated that it may be another subspecies of \(L.\) mexicana or a related parasite because its development in experimentally infected sandfly, \(L.\) longipalpis, was of the \(L.\) mexicana type ("suprapylarian").\(^9\) Schnur et al. arrived at the same conclusion.\(^10\) In 1987, Kreutzer et al.\(^11\) identified 6 isolates from the Dominican Republic as \(L.\) mexicana according to a biochemical characterization using the enzymes glucose phosphate isomerase (GPI), mannose phosphate isomerase (MPI) and phosphogluconate dehydrogenase (GPDH), although other workers consider it to differ from this subspecies.

Vectors.

Two species of sandfly have been reported to occur. \(L.\) cayennensis hispaniola, which feeds on reptiles, and \(L.\) christophei which is known to feed on man.\(^12\) Experimental transmission to hamsters was achieved with the latter species by R. Johnson at the University of Florida (D. E. Young - Personal communication).

Reservoirs.

No information is available, but \(Rattus\) rattus is a suspect.

LEISHMANIASIS IN BELIZE, HONDURAS, NICARAGUA AND EL SALVADOR

Belize

The recent identification of \(Leishmania braziliensis\) braziliensis in cases of CL in British soldiers trained in Southern Belize\(^13\) is a very important epidemiological finding. Both the vector and reservoir of \(L.\) b. braziliensis in Belize are still unknown. Lainson\(^9\) comments that \(L.\) cruciata could be associated to the transmission of this parasite in view of its highly anthropophilic nature.
Honduras

The epidemiological situation of leishmaniasis is still unknown. Both CL and MCL occur in the country. Cases of CL have been reported from the following departments: Copán, Santa Barbara, Comayagua, Francisco Morazán, Yoro, Atlántida, Olancho and El Paraíso. Cases of MCL have only been reported from Yoro and El Paraíso where the infection is superimposed on CL. Only one case of DCL has been reported. Both L. mexicana and L. braziliensis panamensis have been identified in the country. An important focus of visceral leishmaniasis exists, with over 50 confirmed cases. Most are from the southern tip of the country, apparently associated with two river basins. The parasite is indistinguishable from L. donovani chagasi from South America.

Lu. olmeca is the vector associated with the transmission of L. mexicana, and Lu. panamensis is the species most likely associated with L. b. panamensis, although Lu. yiephiletor and Lu. trapidoi also occur in Honduras, as does Lu. cruciata. Lu. longipalpis occurs seasonally in great numbers in the VL endemic area, and is the likely vector, although no naturally infected sandflies have been reported.

No information is available on reservoirs.

Nicaragua

Cutaneous leishmaniasis is distributed in the departments of Jinotega, Nueva Segovia, Madriz and Estelí in the north part of the country; Matagalpa and Boaco in the central area and Chontales, Río San Juan and Zelaya in the southeast. In the region of Matagalpa (Health Region VI) the following numbers of cases were reported in the 1980-83 period:

Table 1 - Cutaneous Leishmaniasis Reported from Matagalpa, Nicaragua

<table>
<thead>
<tr>
<th>Year</th>
<th>Incidence rate 100,000 persons</th>
<th>Cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>1980</td>
<td>143</td>
<td>44</td>
</tr>
<tr>
<td>1981</td>
<td>620</td>
<td>177</td>
</tr>
<tr>
<td>1982</td>
<td>2,107</td>
<td>593</td>
</tr>
<tr>
<td>1983</td>
<td>1,154</td>
<td>230</td>
</tr>
</tbody>
</table>

Of 259 infected people recently reported from this region (Matagalpa) by Missoni and Morelli 236 cases (91.0%) had an exclusively cutaneous localization, 22 (8.5%) presented mucous involvement, mostly with lesions of the nasal septum, and one had nodular cutaneous lesions, probably DCL. On the basis of clinical observations it is suspected that both L. mexicana and L. braziliensis complexes are present.
Lu. olmeca has been identified in the southern part of the country. Lu. ylephiletor and Lu. panamensis have been also reported.

El Salvador

According to available information, 35 cases of visceral leishmaniasis and 7 cases of cutaneous leishmaniasis has been reported in the country up to 1984. Of 31 cases of VL reported, 27 were autochthonous cases and 4 imported cases from Honduras. The majority of cases occurred in children <5 years of age, with 63.6% occurring in children between 1 and 2 years of age. (17)

No information exists on the vectors and reservoirs. However, the following species of sandfly have been reported in the country: Lu. longipalpis (60% of the total captured), Lu. cruciata, Lu. barretoi, Lu. evansi, Lu. deleoni, Lu. cayennensis, Lu. gomezi and Lu. chiapanensis. (17)

Argentina

Cases of leishmaniasis have been constantly reported from the northern provinces of the country: Salta, Jujuy, Tucumán, Santiago del Estero Formosa, Chaco, Corrientes and Santa Fe. From 1954 to 1973, a mean number of 55 cases per year was reported for the country. However, the number of cases increased in 1981 (76 cases), 1982 (138 cases), 1983 (78 cases) and in 1984 (328 cases). In 1985, an outbreak of the disease was reported in Pichanal, Salta with 263 cases reported in the marginal peri-urban area of this small city of 6,000 inhabitants. About 28% and 42% of the cases occurred in children under 15 years of age and in the feminine population, respectively. Are few cases of VL are known from the area.

As preventive measures, active case detection was increased for treatment with pentavalent antimony, the surrounding forest was cleared, and the houses in the affected blocks were sprayed with DDT and BHC. No evaluation is available as to the effectiveness of these measures.

No information is yet available concerning the vector and reservoir in the area.

Note: Dr. Evans, of the London School of Hygiene and Tropical Medicine, reported during this meeting that one isolate received from this area was identified by isoenzyme electrophoresis as L. braziliensis braziliensis.

Paraguay

The number of cases of leishmaniasis has increased in Paraguay in the last 10 years, as shown in Table 2.

The notable increase of cases in 1982 was probably related to an increase of the colonization projects for agriculture. Both CL and MCL have been reported but no identification of the parasite is available. The vector and reservoirs are unknown. There is no national control program at the present time, but plans are being made.
Table 2.

Cases of leishmaniasis reported in Paraguay

<table>
<thead>
<tr>
<th>Year</th>
<th>Number of Cases</th>
<th>Rate/100,000 Persons</th>
</tr>
</thead>
<tbody>
<tr>
<td>1976</td>
<td>16</td>
<td>0.44</td>
</tr>
<tr>
<td>1977</td>
<td>8</td>
<td>0.22</td>
</tr>
<tr>
<td>1978</td>
<td>95</td>
<td>2.66</td>
</tr>
<tr>
<td>1979</td>
<td>79</td>
<td>2.21</td>
</tr>
<tr>
<td>1980</td>
<td>177</td>
<td>4.96</td>
</tr>
<tr>
<td>1981</td>
<td>195</td>
<td>5.46</td>
</tr>
<tr>
<td>1982</td>
<td>1,344</td>
<td>37.67</td>
</tr>
<tr>
<td>1983</td>
<td>103</td>
<td>2.88</td>
</tr>
<tr>
<td>1984</td>
<td>113</td>
<td>3.16</td>
</tr>
<tr>
<td>1985</td>
<td>1,083</td>
<td>30.36</td>
</tr>
<tr>
<td>1986</td>
<td>354</td>
<td>9.92</td>
</tr>
</tbody>
</table>

Source: Department of Rural Health, Ministry of Health

Guyana

An outbreak of CL among military personnel occurred during the period from November, 1977 to March, 1980. One hundred and seven (89%) of 120 military and paramilitary patients were infected in the Barbice Savannahs. The other 18 patients came from seven different hinterland areas. No identification of the parasites was reported.

French Guiana

The number of CL cases has increased notably in the period of 1980-1982 (454 cases in all) in French Guiana (17). The disease locally known as "pian-bois" (forest yaws) is caused by Leishmania braziliensis guyanensis. Lu. umbratilis is the identified vector.

Between 1981-1986, Dr. J-P. Dedet isolated 169 stocks of Leishmania; 87 were identified by Dr. P. Desjeux (IBBA - La Paz, Bolivia) by isoenzyme electrophoresis as L. braziliensis guyanensis (79) and L. mexicana amazonensis (6). The origins of the L. mexicana amazonensis isolates were: Proechimys (3), Lutzomyia flaviscutellata (1) and human cases (2). Two stocks from Lutzomyia umbratilis have a non-certain identification.

CONCLUSIONS

More basic biological and epidemiological information is needed in the majority of these countries to define: a) Geographic limits of the affected areas, b) Distribution and prevalence and incidence of the infection, c) Identification and characterization of parasites isolated from human cases, vectors and reservoirs. d) Major vector and its bionomics. e) Major reservoir and their bionomics.
REFERENCES

CURRENT SITUATION WITH REGARD TO LEISHMANIASIS IN THE COUNTRIES OF THE EASTERN MEDITERRANEAN REGION - AN OVERVIEW

A. Nadim

INTRODUCTION

The Eastern Mediterranean Region of the World Health Organization (WHO) includes 23 countries, from Pakistan on the east to Morocco on the west. What is to be considered here will consist of the following countries: Pakistan, Afghanistan, Iraq, Syria, Lebanon, Cyprus, Jordan, Saudi Arabia, Kuwait, Bahrain, Qatar, United Arab Emirates, Sultanate of Oman, Democratic Yemen (Southern), Yemen Arab Republic (Northern), Egypt and Libya. Also, the situation of leishmaniasis in Turkey will be discussed, although it is part of the European Region of WHO.

The Eastern Mediterranean Region includes some other countries, namely, Iran, Sudan, Somalia, Tunisia, Djibouti and Morocco, but the situation of leishmaniasis in these countries will be presented by other participants. In this presentation, the leishmaniasis situation and control activities (if any) are briefly described for each country, except for Iran and Jordan, which will be presented by other participants.

PAKISTAN

Zoonotic cutaneous leishmaniasis (ZCL) is found in many parts of Pakistan; the endemcity is high in Baluchistan. The true prevalence is not known, but epidemics of the disease are sometimes reported, mostly involving non-immune newcomers to the infected areas. The causative agent is supposedly L. major. In a survey in October 1985 in Uthal, southeastern Baluchistan, 5 of 418 school children had active lesions (1.1%) and 111 had scars (26.5%). The vectors and reservoir animals have not been incriminated. On the basis of the similarity of conditions with those of Rajistan in India, and Southern Baluchistan in Iran, the probable animal reservoir is Meriones hurrianae, because it is a common species, and the probable vectors P. papatasi and P. salehi. During the survey mentioned above, 227 Phlebotomus were collected which consisted of P. papatasi (93.3%) and P. salehi (6.7%).

There is no report of anthroponotic cutaneous leishmaniasis (ACL) from Pakistan.

Visceral leishmaniasis (VL) has been reported from valleys in the north (Balistan) and recently from Azad Kashmir. The total number of cases reported in the country is a little more than one hundred, most of them (60) were found in a survey in 1960 in Balistan. However, in a serological survey in 1979, more than 40% of the sera examined in a population sample had detectable antibodies, suggesting a high rate of asymptomatic cases. There is no information available on the probable vectors or reservoirs. Probably in sporadic cases, transmission is from wild canidae, and in the case of focal outbreaks, possibly also from man
to man. Several species capable of transmitting kala azar are reported from Pakistan (P. major, P. longiductus, P. kandelakii and P. alexandri) but the major vector is not known.

AFGHANISTAN

ZCL is found in the plain areas in the northern part of the country, and possibly also in the southwestern plain, low-land areas. In the northern steppes, in the valley of Amu Darya, it is primarily an infection of the great gerbil Rhombomys opimus, which is most probably transmitted to man by P. papatasi. The disease has a stable endemicity in the infected areas but sometimes with outbreaks in newcomers. ACL is a major health problem in Afghanistan. Its main foci are Kabul, Kandahar and Herat. The disease is also very frequent in provinces neighboring Kabul, like Parwan (city of Charikar and valleys of Panjshir and Ghorband), etc. Also, it is found in other western provinces. Although infected dogs are found on many occasions, it seems that in most cases, transmission is from man-to-man. The suspected vector is P. sergenti which is very abundant in some of the infected areas, especially in the hilly and foot-hill areas. Large scale surveys carried out in 1978-79 showed that some 13-14% of the population studied had had active lesions or scars. In recent years, most of the work on this disease has been limited to Kabul and other larger cities in which treatment centres for the disease exist. The total number of cases reported from these centres in the year 1985 is as follows: Kabul 2,870, Mirbachakot 398, Parwan 435, Kandahar 1,763, Herat 474, Mazar-Sharif 718, Jowzjan 356 and also a few cases from Pariab and Kunduz. Except for Mazar-Sharif and Jowzjan which are located in the northern steppe in which ZCL is prevalent, all other cities are foci of ACL. Because of political problems, determination of the true prevalence is difficult; still, the above figures indicate how important and widespread cutaneous leishmaniasis is in Afghanistan.

A few cases of VL have been reported from various parts of the country in the last 6-7 years. Nothing is known about the animal reservoir or the vector. Many potential vectors exist in the areas in which cases have been found.

IRAQ

ZCL is found all over the country except, for the mountainous areas in the northeast. Most of the cases of CL reported recently in this country are of this type. Population movements due to economic activities or war, expose many people to infection. ZCL has come to attention only in the last 5 or 6 years, but little has been done to clarify its epidemiology. However, it can be said that the epidemiology of the disease is similar to that in the Khuzistan province of Iran (in the southeast) and to that of Jordan and West Bank (in the west and northwest). In all these foci, the vector is P. papatasi and the animal reservoir is the gerbil.

ACL has been known in Baghdad since ancient times (Baghdad boil) and even until two or three decades ago the disease was a universal infection.
of the inhabitants. Apparently in the last two decades, the incidence has fallen considerably, but the disease still exists, causing occasional outbreaks. Like other foci of the disease, it seems that man himself is the main reservoir and *P. sergenti*, the probable vector.

VL is a major health problem in Iraq. The annual number of cases reported range from 600 to 1,500 but the true prevalence is undoubtedly much higher. A number of studies have been undertaken to clarify its epidemiology. The geographical distribution of reported cases indicates that the principal endemic area is Central Iraq and the Greater Baghdad area. Most cases are in children < five years of age, and many of them in children under two. The average annual incidence calculated on the basis of the reported cases is 70/100 000 for children less than five years of age; males and females are almost equally affected. The peak of the presentation of cases is in January and February.

The animal reservoirs are possibly jackals and dogs, since serum surveys of these animals (IPAT) have shown high rates of positivity. The vector is not known. *P. papatasi* is very common in the area and many Iraqi investigators believe that this species is the probable vector, although there is no proof. *P. alexandri* is also found in the infected area, but with a much lower density. This might be a more probable vector since it is known that it can transmit kala azar in Western China.

**SYRIA**

CL has been endemic in Syria since ancient times, but anti-malarial spraying caused a considerable fall in its incidence, and until 1980, only a few sporadic cases were reported each year, so few studies were undertaken to clarify its epidemiology. In recent years, the number of reported cases is increasing and in 1984-85, more than 800 cases were reported from Damascus, Hama, Lattakia, Tartous, Idleb, Aleppo, Ragga and Deir-Ez-Zor provinces. Little is known about the epidemiology of the disease in this country, but undoubtedly both ZCL and ACL occur, the latter in old towns and cities (like Aleppo), and the former in rural areas.

There have been reports of a few cases of VL in Syria (Aleppo, Damascus, Lattakia and Tartous) but no studies have been done to clarify its epidemiological characteristics.

**LEBANON**

There have been known foci of CL in the past; also sporadic cases of VL had been reported but, due to socio-political unrest prevailing in the country, no recent information is available.

**CYPRUS**

Sporadic cases of VL and CL have been recorded in the past, but there seem to be no cases in recent years, because, despite the good medical coverage and reporting system, there are no reports of the disease.
SAUDI ARABIA

ZCL is found in many parts of the country, including Al Hassa in the north east, Al Kharij and Riyad areas in the centre of the country, and provinces of Asir, Jizan and Gassim. The number of recorded cases reached a total of 18,318 in 1983. Apparently the gerbil Psammomys obesus is the main animal reservoir, at least in Al Hassa, because many specimens collected in this area have leishmanial lesions of the ear. Infection has been also found in Meriones crassus, Meriones libycus syrius, Rattus rattus and dogs, in the same area. However, probably their infection, like that of man, is secondary to the disease in Psammomys obesus. The vector of the disease is certainly P. papatasii throughout all infected areas in the country.

ACL is endemic in the southwestern part of the country, mainly in Abha. Some cases of leishmaniasis recidivans are also seen in this area and isoenzyme characterization of some isolates has shown that the parasite is L. tropica. However, epidemiological characteristics of the disease in this area have not been thoroughly investigated.

The overall incidence of CL in the Kingdom in the Hijri Lunar Year of 1403 (1982-83) has been calculated to be 2.1 per thousand of the total population (18,318 cases), more than 50% of which have been seen in foreigners. Seventy eight percent of the cases were males and only 22% females, apparently because most foreigners are male workers, and in Saudis many of the cases occur in the labor force (usually males) who stay at night in areas with infected gerbils and sandflies.

VL is endemic in the southwestern mountainous areas (38 cases reported in 1983). Sporadic cases are also seen in the centre of the country, but the area of contagion of the disease has not clearly been identified. The causative agent has been shown to be similar to the Ethiopian strain of L. donovani. There is no report of studies on the reservoir hosts and vectors, but it is known that P. orientalis, a known vector of VL in the Sudan, occurs also in Gizan, in south-western Saudi Arabia.

KUWAIT, BAHRAIN, QATAR, UNITED ARAB EMIRATES

Some cases of ZCL are reported in Kuwait and Bahrain but most of them are imported. It seems that the number of indigenous cases in Kuwait is increasing. Cases of ACL are also reported from Kuwait.

A few cases of VL have been recorded in Kuwait (mostly imported) and in the Fojairah in the Eastern part of the United Arab Emirates (which is between Oman and Muscat in the Sultanate of Oman).

SULTANATE OF OMAN

CL is very rare. Only a few imported cases have been diagnosed in Sudanis and also a few indigenous cases. The latter have been seen from various areas, possibly being cutaneous manifestations of L. donovani infection.
VL is endemic, and in the period 1972-1977 sixty one cases were recorded, and from 1978 to the end of 1985, 127 cases were seen in Al Nahda Hospital in Muscat. Most of these have been in children. Male cases were a little more prevalent than female cases. The disease is almost confined to the mountainous areas of the north. No study has been carried out to clarify the epidemiological aspects of the disease. Like Iraq, the only suspected vector caught so far is P. alexandri but this is with only a few collection attempts. Possibly further investigations and sandfly collection during the entire active season will show other potential vectors. Nothing is known about the animal reservoir in this country.

YEMEN ARAB REPUBLIC AND DEMOCRATIC YEMEN

CL occurs in both countries. In Yemen Arab Republic the number of cases diagnosed at the Central Health Laboratory during 1980 was 39, increasing to more than 200 per year in 1984 and in 1985. Apparently both ZCL and ACL are endemic in some areas with high prevalence. The former in the low-lands, and the latter in the cities. Cases are seen from Sana'a, Tahima, Ibb, Taiz and Hodeida.

In Democratic Yemen, some mountainous villages in Lahaj Governorate, neighboring YAR, are infected, but there is no information on the prevalence or other epidemiological characteristics of the disease.

VL occurs sporadically in both YAR and Democratic Yemen but its epidemiological features are not known.

EGYPT

Zoonotic cutaneous leishmaniasis occurs in the Sinai and also in some Governorates east and north east of the Delta (Sharkiya, Ismailiya, Beheira, Menoufia, Dakahlia). Also, because of the movements of the temporary laborers going to other endemic countries (Iraq, Saudi Arabia) the number of reported introduced cases is increasing. These are mainly Egyptian male workers returning to Egypt.

The vector is apparently P. papatasi. The animal reservoir is not known but there is a report of finding of amastigotes in the spleen of a few Rattus norvegicus in Ismailiya Governorate. The true prevalence of the disease is not known.

A focus of VL was discovered in 1982 at El Agamy, some 25 kms west of Alexandria. Through epidemiological investigations more than 20 cases have been diagnosed in children. Four human isolates and one isolate from a dog have been typed as L. donovani. Although L. major has also been isolated from a dog in the same area, the focus seems to be the Mediterranean type of kala azar. P. papatasi and P. langeroni have been the only two species of Phlebotomus collected in this area during a two year longitudinal entomological survey. Indoors, 98% of these have been P. papatasi while in outdoor collections 65.5% are P. langeroni and only
34.5% P. papatasii. It seems that P. langeroni is the probable vector because:

(a) it is more abundant in outdoor collections,
(b) it is more attracted to dog bait, and
(c) in experimental L. donovani infection, it shows infection of the head while P. papatasii does not.

LIBYA

ZCL was noticed for the first time in 1971, when 241 cases were reported from Zawia and Garian. The disease appears in the form of outbreaks. The infected areas are Nalut, Jadoo, Yefran, Garian. The vector seems to be P. papatasii and the animal reservoirs Psammomys and Meriones.

A few cases of visceral leishmaniasis have also been reported in the Benghazi area. There is no information on the epidemiological features of the disease.

Jordan

Zoonotic cutaneous leishmaniasis is endemic in the country mostly in Jordan Valley and town and villages in the south east and east of Amman. It seems that the epidemiology of the disease is similar to what has been reported in the West Bank, with P. papatasii as the vector and Psammomys obesus as the main animal reservoir.

The average annual number of cases had been around 80 up to 1982, but since then, the incidence has been increasing to several hundred per year. Visceral leishmaniasis is rare and so far only less than 20 cases have been reported mostly from Karak, Aqaba and Irbid. No study on the epidemiological characteristics of infection has been undertaken.

Turkey

Cutaneous leishmaniasis is endemic in south eastern parts of Turkey in areas neighbouring Iraq and Syria. Also sporadic cases have been reported from the central parts of the country. Most probably these are anthroponotic cutaneous leishmaniasis but L. major infection is known to occur. In the infected areas,
most abundant species of sandflies are *P. sergenti* and *P. alexandri*. The epidemiology of cutaneous leishmaniasis has not yet been carefully studied in Turkey. Kala-azar is seen in Marmara, Aegean, Eastern Black Sea, and the Mediterranean coastal areas. Up to 1982, more than 500 cases had been reported almost exclusively in children, very few cases in adults. Dominant sandfly species in Kala-azar endemic areas are *P. major*, *P. tobbi*, *P. chinensis* and other sandflies belonging to the subgenus Adlerius. It is not known which one is the vector. As for reservoir, it seems that dogs are the main animal reservoirs because in many occasions dogs have been found parasitologically or serologically positive (IFAT). Possibly wild canidae are also playing an important role as the animal reservoir of Kala-azar in Turkey.

**Islamic Republic of Iran**

Zoonotic cutaneous leishmaniasis is found in some foci in the plain areas along the frontier with the USSR in the north-east (Turkeman Sahara, Lotfabad, Sarakhs). In the provinces of Khorassan and Semnan there are other foci situated in the plain areas at the periphery of the central salt desert of Dash-e-Kavir (Esfarayen, Bakran, Bardeskan, Tabas). On the south-western border of the central salt desert in the province of Isfahan, there is also a very extended focus which is the most important of this type of the disease in the country. In all these foci, the main animal reservoir is *Rhombomys opimus* and the vector to man is *P. papatasi*. The agent has been identified as *L. major*.

Other important foci exist in the south-west beyond the geographical distribution of *Rhombomys*. Thousands of cases have been annually reported from these foci in the last 5-6 years. The agent has been identified as *L. major*, and recently Iranian investigators have found several specimens of *Tatera indica* naturally infected in these areas, therefore, it seems that this gerbil is the main animal reservoir.

ZCL is also endemic in the southern part of Iranian Baluchistan, neighbouring Pakistan. In this focus, the animal reservoir has been identified as *Meriones hurrianae* and the vector responsible for the transmission of the disease to man seems to be *P. papatasi*. 
The disease is hyperendemic in the Isfahan area so that 4000-8000 cases are officially reported each year from this part of the country. In Khuzistan, the disease normally has a low endemicity but during the last 5-6 years thousands of cases have been reported among soldiers and war refugees. The situation in Isfahan and Khuzistan was so threatening that the Government launched a programme of mass "leishmanization" of both areas since the beginning of 1982. The foci of the disease in Isfahan and Khuzistan are important probably because both areas are centres of developing new industries to which labourers migrate from all over the country, most of them nonimmune. In addition, there are other types of new-comers to the infected areas in Khuzistan such as soldiers, war refugees, etc. Other foci though very active, were not so important, because except for the great numbers of soldiers sent to the north east frontiers, the disease was confined to the sparsely scattered local population and most cases are in children who are not yet immune. In 1984 and 1985 the disease took the form of epidemics in Turkeman Sahara and Bakran so that thousands of cases appeared in places where the disease was previously present with low endemicity and also, the disease was extended to neighbouring areas. It seems that the previous local strains of L._major with lower virulence has been replaced by strains with much higher virulence imported from war-stricken areas in the South-West.

Anthroponotic cutaneous leishmaniasis is found in the capital city of Teheran as well as in some other large or medium-sized cities (Mashad, Neishabur, and Sabzevar in the north east. Shiraz in the south, Kerman in the south east and Yazd and possibly the city of Isfahan in the central part).

In infected cities, the disease is not evenly distributed, so that in some city quarters it is more prevalent than in others. This is because the species and population density of the sandflies are different in various parts of the same city.

In addition to the affected parts of a city, the disease is usually extended to the neighbouring villages in one or more directions possibly due to the movements of stray dogs or infected people.
The vector of this type of the disease is supposed to be *Phlebotomus sergenti*, since on several occasions this species has been found naturally infected with promastigotes in Mashad in 1967.

In some cities, like Teheran, the disease is found only in those parts of the city which have a high *P. sergenti* population. It occurs in the form of local outbreaks, lasting for two to three years, then dies out to appear again in another part of the city not far from the previous one. Thus, outbreaks move from one part of the city, or nearby village to another. In some other cities like Mashad, the outbreaks have been occurring in the same city quarters since 15 years. This is because of high population turnover in the infected part of the city. In yet other cities, it is seen with a very low endemicity but sometimes heavy epidemics appear due to population increase and unplanned urban development which prepare the ground for an increase of both the sandfly population and the stray dogs (Neishabur in 1974 and Kerman since 1978).

The agent of the disease in Teheran has been identified as belonging to *Leishmania tropica* complex. The agents from other foci have not yet been precisely identified though according to their behaviour in laboratory animals, they seem to be similar (Shiraz) or only slightly different (Mashad).

In almost all these foci, the infection of dogs has been reported along with the infection of man. This may have a high epidemiological importance since it seems that dogs are a better source for infecting sandflies because the sore is usually situated on a part of the body surface available for biting (tip of the nose). Yet there are certain places where dogs apparently do not play a role and where the disease is spread from man to man by the bites of sandflies.

There are no accurate data on the incidence and prevalence of the disease in these foci. Only those cases who have been referred to governmental laboratories are reported to the Health Departments, and most of the cases do not even seek treatment.
The total number of cases seen in health centres in northern parts of the city of Teheran (infected area) is about 1000 cases per year. In Kerman, this figure has been estimated as 600-900 per year and in Shiraz, more than 2000 cases per year. Reports of Health departments in Shiraz and Mashad show a considerable increase in the number of reported cases in the last 7-8 years.

Visceral leishmaniasis is not very prevalent in Iran. The disease has been seen in sporadic form from all over the country except the southern parts of Baluchistan. It seems that the number of diagnosed cases are increasing in several parts of the country. At the present time, the province of Fars in the south and the districts of Meshkin-Shahr and Moghan in the north-west (neighbouring Soviet Azerbaijan) show higher endemicity. In the last 3-4 years on the average 20 cases per year have been diagnosed from the latter area. The number of cases seen in Fars is more than 50 per year. Also in Khuzistan and Teheran area, the number of reported cases are increasing.

The animal reservoir of the disease seems to be wild and domestic canidae: jackals, foxes and dogs have been found infected in various parts of the country. The vector is not known but on the basis of epidemiological evidence, it seems that P. major is the probable vector in most of the infected areas although other phlebotomes belonging to Adlerius or Largassius group may also play a role. In Khuzistan, possibly P. alexandri has a role as vector.
INTRODUCTION

Cutaneous leishmaniasis (CL) is endemic in Israel, occurring mainly in the southern regions of the country. It is scattered in small zoonotic foci in the Negev and Arava but prevalent in the lower and middle Jordan Valley.

The hyper-endemic area in the Jordan Valley comprises about 480 km². It is bordered by the River Jordan in the east, the rocky hills of the Judean Dessert in the west and the southern border is where the Dead Sea touches the mountains. In the north, the distribution of leishmaniasis stops where heavier soil begins. The plain is dissected by three large wadies that drain down from the hills. A few small springs support the growth of tropical vegetation. Otherwise the area is semi-arid, with an annual rainfall of 100mm, reaching 300mm in the northern part.

The human population is sparse, living mainly on irrigated agriculture and most of the area is uncultivated and bushy. The summer is long and average maximum temperatures are 25°C at night and 40°C during the day.

BACKGROUND

CL has been known in the Jordan Valley for many years. The first record was by Huntemuller in 1914. Later, in the 1920s and thereafter Adler's and Theodor's classical studies of leishmaniasis, in which the causative agent and vector were identified, were carried out with material from the region. An early study of the control of the vector, Phlebotomus papatasi, was also carried out there. The zoonotic nature of cutaneous leishmaniasis was first indicated by isolation of Leishmania major (formerly L. tropica major) from the sand-rat Psammomys obesus. A human infection rate of 50% was found by Naggan et al. among soldiers who spent one month in the outskirts of Jericho. These investigators also recognized the major role of the reservoir P. obesus in the epidemiology of the disease. The many cases that have been seen since that time were mostly among incidental visitors and newcomers, as most of the local inhabitants have acquired immunity, hence, it is difficult to evaluate the distribution of the disease and infection potential of the focus on the basis of recorded human cases. The infection potential can really only be evaluated on the basis of rates of infection in animal host species and sandfly vector species, even though transmission from man to man also occurs.

EPIDEMIOLOGICAL ASPECTS

Between the years 1983 and 1987, there has been a gradual decrease in the incidence of leishmaniasis in the Jordan Valley, judging by the
number of cases diagnosed at the Department of Parasitology of the Hadassah Medical School, which was 80, 67, 42 and 28 over the four years respectively (Schnur, unpublished data). These numbers do not represent a uniform sampling, but they do indicate the tendency. A very likely explanation for this phenomenon is that the years 1984 to 1987 were years of drought in Israel and the absence of sufficient rainwater has reduced the zoonotic foci and resulted in a low incidence in man. This assumption is supported by the sporadic data that have been collected in the years 1985 and 1986 during the course of other studies on leishmaniasis.

Observations in the field indicated that there was a drastic decline in the numbers of Psammomys, which were nearly eliminated from most of the endemic region. No burrows were found anywhere except in the northern area. There, only about 8 colonies were counted in the margins of cultivated fields and more were observed along the roads between fields. In the years before the drought, there were numerous burrows everywhere, located at the margins of dirt roads, in uncultivated fields and in wild vegetation. P. papatasi was caught only in the northern area, after unsuccessful attempts in the south. In this area, catches with CDC light traps near Psammomys colonies in the uncultivated margins of fields that were sprayed with insecticides, the average per trap was only 14 flies. On examination of P. papatasi for the presence of Leishmania, the proportion found in females from Psammomys burrows was 9%, while that in flies from nearby fields was 2.7% (Yuval, unpublished data). Since Psammomys is the sole reservoir of the disease, it is not surprising that the reduction of their numbers was expressed in the rate of sandfly infection, which was less than a half that of the previous record.

Zoonotic transmission of the disease was studied in 1980 and 1981 by Schlein et al., who found that Phlebotomus papatasi, the most prevalent species of Phlebotomus, was the only vector and the sand-rat, P. obesus, the most abundant rodent, was practically the only reservoir. Infections of leishmaniasis were also found in the rare Indian rat Nesokia indica. P. obesus digs burrows with several openings in soft soil near concentrations of vegetation, mainly the salt bush Atriplex halimus. The burrows provide shelter and breeding places for the sandflies in the extreme temperatures that prevail above ground and rodents are a source for blood feeding. This proximity of vector and reservoir, in a close association, permits a very efficient cycle of disease transmission and the recorded rate of P. obesus infection was 93%, while that of P. papatasi caught away from P. obesus colonies had a much lower incidence of infection. Scarcity of water was found the main factor limiting the biotope of sandflies and the incidence of leishmaniasis. Average catches near Psammomys burrows were relatively high in the north of the endemic region and the margins of cultivated fields and low in the dry southern area.

CONTROL

Control measures could also have contributed to the decrease in the prevalence of the disease. The results of spraying with methoxychlor had been unsatisfactory and it was replaced by DDT, following laboratory susceptibility tests demonstrating the higher efficacy of the DDT.
The procedure adopted by the Ministry of Health for the last 3 years includes: spraying of 4% DDT on the outer walls and 0.1 to 0.2% permethrin on the inner walls of houses. Further recommendations include the introduction of rags soaked with the low vapour-pressure organophosphorous insecticides bromex or dichlorvos into rodent burrows, within the perimeter of human habitation (H. Pener, personal communication). Rodent burrows in villages and settlements are usually in the vicinity of irrigation and are, therefore, humid enough to support the breeding of sandflies regardless of the surrounding dryness. Treatment of such burrows might be very effective, in the absence of an influx of infected flies from elsewhere. Since the climatic conditions fluctuate and so do the rodent populations, it is very likely that the natural foci will recover. It will then be possible to evaluate the usefulness of the control measures taken.

The conventional use of insecticides against sandflies is indiscriminate and there is, therefore, a reluctance to apply such methods in natural biotopes. We have recently begun to investigate selective approaches in the Jordan Valley. The relative simplicity of this focus, where both the exclusive vector and the reservoir occur in great numbers, offers opportunities for experimental field studies.

Sandflies and the Leishmania they harbour are vulnerable to infections with other micro-organisms in the laboratory and it follows that they are also susceptible in the field. Furthermore, Schlein et al. found a high rate of infection with fungi and bacteria in sandflies collected in the field. It appears that various bacteria, which are otherwise harmless, might be candidate agents for the control of leishmaniasis.

Following the observation that P. papatasi feeds on honeydew from the surface of plants, we sprayed sugar solution containing food dye on groups of bushes in the vicinity of Psammomys colonies. Three days after spraying, 50% of the flies caught at the site were marked by the dye. This marking method could be used to assess the effect a given micro-organism has on the survival of the sandflies and the Leishmania. The test agent can be added to the sprayed dye solution and its influence on caught flies observed back in the laboratory, using caught, unmarked sandflies as controls.

ACKNOWLEDGEMENTS

Studies by the author reported here received support from the leishmaniasis component of the UNDP/World Bank/WHO Special Programme for Research and Training in Tropical Diseases, the Project on Epidemiology and Control of Vector Borne Diseases in Israel (REP-NIH-NIAID-AI 126688) and USAID grant CDR C5-136.
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LEISHMANIASIS IN EUROPE

R. W. Ashford

INTRODUCTION

The comprehensive studies of leishmaniasis in Europe by Adler and Theodor in the 1930s combined with the dramatic reduction in cases following the introduction of DDT and penicillin in the 1940s led to greatly reduced activities until the resurgence of interest led by Professor Rioux and his team from Montpellier. The monograph by Rioux et al. and the subsequent International Colloquium on the Ecology of the Leishmaniases at Montpellier in 1974 led to renewed interest at a time when DDT and other persistent insecticides were being discouraged for domestic use and there was some evidence of a resurgence of cases. Ecological and epidemiological studies were started elsewhere in France, as well as in Italy, Greece, Yugoslavia and Spain. The number of cases remains small, however, with the exception of rare outbreaks such as occurred in Emilia Romagna (N. Italy) in 1971-72. Unfortunately there is no comprehensive system for accurately recording cases internationally so the total number remains unknown. Table 1 summarises the information on the endemic countries of Europe from Zahar and WHO. A brief resume is given by Bray.

PARASITES AND DISEASES

The predominant form of leishmaniasis in Europe is infantile visceral leishmaniasis (VL) caused by *L. donovani infantum*. The decreasing number of cases following the introduction of DDT has frequently been stated but rarely documented. Hertig and Hadjinicolau showed that sandfly populations were greatly reduced in Greece in areas sprayed and Pampiglioni et al. showed a marked reduction of skin test positivity in people aged less than 30 years at Teramo in the Abruzzi region which was endemic for CL. Russo et al. showed a mean incidence of VL in Sicily of 143 cases per annum prior to 1948 and nine cases per annum subsequently. However, the reduction in human cases is by no means fully explained by reduced sandfly populations; transmission among domestic dogs may remain high, as in Tuscany, while human cases are almost unknown.

There has never been a satisfactory explanation of the age distribution of VL in the Mediterranean area. Early workers considered adults to be insusceptible, but Professor Rioux has questioned this, suggesting that a large proportion of individuals were immunised by a cryptic infection at an early age. The relative abundance of infected dogs and of skin test positivity in humans [e.g. Bettini et al.] support the view that transmission is far more frequent than is indicated by the number of human cases. Further, the finding of variation among strains isolated from animals provides candidates for the immunising parasites. However, reduced transmission would, in this case, remove the concentration among infants. While this may have happened in France, where Quilici et al. found 55% of 40 cases were adults, Russo et al. found no change in the age distribution in Sicily following the reduction in
incidence. Further, the small number of cases in adults from Northern Europe, considering the millions who visit the Mediterranean during the transmission season, supports the theory of differential age-susceptibility, rather than immunity acquired by early cryptic infection. Table 2. shows the age distribution of the small number of case of Mediterranean origin reported in England. Improved methods for relating disease rates to transmission rates and for the detection of past or present cryptic infection are required to solve this question.

Cutaneous leishmaniasis has always been less common than visceral in Europe. It has occurred sporadically within the areas endemic for the visceral disease, but also in peripheral areas where the visceral disease is unknown. Unfortunately, many of the cutaneous parasites have proved difficult to isolate and not many have been identified biochemically. Garifallou et al.\textsuperscript{12} have recently identified strains from Greece as \textit{L. tropica}, raising the interesting question of how an anthroponotic parasite persists at such a low rate. Is it, in fact, zoonotic? Or is it more common than is recognised? All other autochthonous cutaneous strains which have been identified are closely related to \textit{L. d. infantum} and are, therefore, likely to be zoonotic with dogs and foxes as reservoir hosts. The geographical isolation of some of these dermotropic strains in Abruzzo and the Pyrenean foothills remains to be explained.

Vectors

Extensive studies, mainly in the Cevennes region of France and in Tuscany (Italy) have greatly increased our knowledge of the biology of sandflies in general. These studies are covered by other papers in the present publication.

Reservoir Hosts

There is no new evidence that man is a reservoir host; it still seems apparent that infected humans are not infective. The only doubt on this is the apparent rapid spread of VL and skin test positivity in the human population of Emilia Romagna in 1971-1972, without apparent evidence of a similar spread in animals.

Dogs continue to be infected at a much higher rate than humans and provide the main reservoir of infection. Recent studies by Bettini's team in Italy have shown canine infection to be widespread in areas where human infection is rare or absent. This may be explained in part by the presence of a 4-enzyme variant of \textit{L. d. infantum} isolated from dogs (and a fox).\textsuperscript{13} In addition to the earlier findings of infected foxes in France, foxes have been found infected in Spain\textsuperscript{14}, Portugal\textsuperscript{15}, and Italy.\textsuperscript{16} The prevalence of infection in foxes has never exceeded 5%, which is usually well below that of the local dogs. As yet there are no studies showing an ecological link between foxes and sandflies so it seems probable that foxes are usually infected by sandflies which have bitten dogs. It is significant that foxes are becoming more familiar and commonly use rubbish tips as food sources\textsuperscript{9} while packs of feral dogs are increasing the potential spread of the parasite to wild areas.\textsuperscript{18}
Bettini's team have also demonstrated a possible role for the black rat *Rattus rattus* in Italy, following the discovery of infected rats in Yugoslavia. Although the proportion of rats infected is usually low, their short life span indicates a higher transmission rate than in foxes. Experimental studies have shown that, at least under certain circumstances, rats can be infective for sandflies.

Professor Bettini has given an admirable account of the up to date details of reservoir hosts for VL in Europe in Ashford and Bettini.

**IMPORTED LEISHMANIASIS**

The growing number of international travellers, especially those working in rural areas outside Europe, has resulted in the frequent importation of a wide variety of leishmaniases into non-endemic parts of Europe. Some 50% of Yugoslav workers on an irrigation project in Libya became infected with *L. major* and the infection of 50 workers on a sewage project in Saudi Arabia was said to have had a cost of $6 million for the company. Unfortunately, these cases are usually unreported or are only reported if they present unusual clinical features.

The figures in Table 3., indicating the importation of about eight cases annually into England, is certainly a gross underestimate of the real number.

The most conspicuous feature of these cases is, perhaps, the extraordinary variety of mis-diagnoses in which they result. It would be invidious to quote examples of this, but there are many in the literature and more which have been quietly forgotten. The education of practitioners in non-endemic areas and the provision of diagnostic facilities for exotic diseases remains an important priority.

**CONCLUSION**

The following pattern seems to fit most of the available facts on European leishmaniases:

1) *L. tropica* circulates in Greece, apparently at an astonishingly low rate which requires explanation;

2) All other leishmaniases transmitted in Europe is caused by parasites which are identical, or closely similar to, *L. d. infantum*. These are transmitted at varying rates among dogs, foxes and probably rats (*Rattus rattus*). Some of the strains may be defined geographically but others circulate sympatrically. Transmission to man is one-way, and occurs at a rate considerably less than in dogs. Most transmission to man results in acquired immunity without apparent infection. Some strains occasionally cause patent infection, especially in immuno-compromised people of all ages.

3) Many questions remain, such as which strains do what, whether there is strain specificity among the vectors, and what is the
difference between a susceptible individual and one who develops a cryptic, immunising infection.

4) Imported leishmaniasis is a growing and underrated problem throughout Europe.

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17. Petrovic, Z., 1975. 2nd Europ Multicolloq Parasitol Trogir pp 97-98
Table 1.

Human cases of leishmaniasis in endemic areas of Europe
Extracted from Zahar (1979) and WHO (1984)

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*References other than WHO (1984) are quoted Fide Zahar (1979); most have not been consulted personally.

Table 2.

Age distribution of VL of Mediterranean origin in England 1975-1982

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PHLS data courtesy of Dr. S. E. J. Young, Editor, Communicable Diseases Report

Table 3.

Cases of leishmaniasis reported to PHLS, England 1975-82

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PHLS data courtesy of Dr. S. E. J. Young, Editor Communicable Diseases Report
THE LEISHMANIASIS AND DEVELOPMENT: RESEARCH ISSUES

P. M. Wijeyaratne

INTRODUCTION TO THE LEISHMANIASIS

The leishmaniases constitute a group of diseases that have been relatively neglected in terms of research in the past; although they are of worldwide distribution. As such, the socio-cultural and economic relationships of the disease remain virtually undocumented, and perhaps also little appreciated. This paper for discussion is attempted with that underlying thought in mind; it is aimed at generating key issues that need to be investigated, and to examine some approaches towards achieving them. This disease is also thought of as an example where research would also have ramifications in the control of other tropical diseases existing in the same area.

The International Development Research Centre has, and continues to, support various research projects on the leishmaniases in different parts of the world and it is considered one of its priority areas of support.

Forms of leishmaniases affecting man and their transmission

The leishmaniases are caused by the protozoan parasites of the genus *Leishmania* and known to occur in man in at least three major clinical forms; visceral leishmaniases (VL), cutaneous leishmaniases (CL) and mucocutaneous leishmaniases (MCL). These three entities were based on clinical distinctions and thought to be due to different parasitic species, respectively, *Leishmania donovani*, *L. tropica* and *L. braziliensis* which are now each known to have several closely related subspecies. The diseases are transmitted by the bite of sandflies, mainly *Phlebotomus* (in the Old World) and *Lutzomyia* (in the New World). The sandflies become infected either from domestic or sylvatic rodents, dogs and other mammals, or less frequently, from man. Human to human transmission (or anthroponosis) of these infections has only been shown to occur in a few areas, such as India and Bangladesh, while transmission from animal reservoirs (or zoonosis) appears to be the widespread mechanism in endemic regions.

Geographic distribution

The geographic distribution of the leishmaniases is quite wide, but scattered. Asia, the Middle East, Africa and Latin America are all affected by one or more of the forms. For instance, VL is endemic in several parts of Africa, the Indian subcontinent and Latin America, and occurs sporadically in China, the Mediterranean Basin, southwest Asia and southern parts of the Soviet Union. CL also has a very similar distribution in the world. MCL, on the other hand, is found in Latin America, although cases of clinically similar oro-nasal disease have also been reported in Ethiopia and the Sudan.
Diagnosis and clinical manifestations

Reliable laboratory diagnosis of the leishmaniases is still dependent on costly and time consuming methods. The techniques generally available in PHC facilities are often deficient in terms of sensitivity and specificity. Intradermal (Montenegro) skin tests, parasite visualization in biopsy material from lesions, bone marrow and liver, and serological tests, are all being used with varying degrees of success.

The clinical manifestations of the leishmaniases show a great variety in the different forms and in different areas. However, in general CL may manifest as simple self-healing lesions of the skin or as widespread diffuse lesions of a painful and chronic nature leading to disfiguring scars. It is known that the time elapsing between infective sandfly bites and the appearance of signs may vary from three weeks to as much as three years.

MCL usually is first manifested as a papular skin lesion which transforms into a crateriform ulcer that could later spontaneously disappear. Commonly, however, parasite invasion of the mucous membrane of the upper respiratory tract occurs, causing extensive destruction of surrounding tissue. Naso-pharyngeal cartilages, including the palate, become eroded, with frequent involvement of the trachea and larynx, resulting in gross mutilation, disfiguration and, commonly, to death due to secondary lung infection due to mouth breathing. Both CL and MCL forms are handled by the affected people in various ways. Traditional treatment methods for cutaneous lesions use drastic local preparations of various types, including battery acid, tar, and toxic herbal concoctions, none of which cure the disease, and often cause severe injury.

The currently available drugs are toxic and may require the patients to be hospitalized for treatment, often for prolonged periods.

VL (or kala azar), involves leishmanial parasites infecting the reticulo-endothelial cells of various organ systems of the body, mainly the spleen, bone marrow, liver, lymph nodes and skin. Anaemia, recurrent fever, loss of weight and increasing enlargement of the liver and spleen are characteristic of VL, and progressive wasting is common. Treatment is often very difficult. Recovery is rare in non-treated cases, which have a high morality rate. After recovery from the acute phase, VL patients may develop cutaneous lesions that persist (post-kala azar dermal leishmaniasis - PKDL). These lesions contain abundant parasites which could constitute a reservoir of infection with relevance to transmission.

Control measures

In principle, the leishmaniases can be controlled by intervention focused on vulnerable pathways in the cycles of transmission, whether it be an anthroponosis or zoonosis. The following are some examples of control measures.

a) Parasite control by treating infected individuals. These measures have been largely unsuccessful due to the lack of effective and feasible
drugs of choice, and due to the presence of animal reservoirs maintaining
the natural cycle.

b) Vector sandfly control measures, either by larvicidal or adulticidal
approaches. In the past, some measure of success was accidentally
achieved during malaria vector control programs using residual insect-
icides. However, the highly varied breeding ecology of sandfly larvae,
as well as the complex and mostly unknown biting habits of adult sand-
flies, does not make this approach feasible in most situations.

c) Preventive measures aimed at protecting the groups at risk in the
community. These approaches have rarely been attempted due to:

i) the risk factors of acquiring the infections not being
identified;

ii) the non-feasibility of using chemicals such as repellents to
impede man-vector contact;

iii) the lack of antileishmanial prophylactic drugs for community-
wide use; and

iv) unpopularity of bed nets to prevent sandfly attack because
they decrease ventilation and make conditions hotter.

d) Animal reservoir control. Although such measures have been
attempted on a very limited scale, impediments to their
success in controlling the disease have been:

i) the lack of complete knowledge of all the reservoir hosts
involved;

ii) some reservoirs are domestic animals and hence the reluctance
for their destruction; and

iii) the lack of economically feasible methods of their control.

It is becoming increasingly apparent that significant cultural asp-
cts and lack of community education on the disease need to be addres-
sed, if the above listed control measures are to be practiced as viable
approaches.

Factors associated with development

a) The affected populations

The Leishmaniases predominantly affect poor rural communities.

Most sufferers belong to the economically viable age groups of
populations.

Often males are more affected and a strong association with occupat-
ional exposure is evident. For instance, in Ethiopia, children
herding livestock show the highest prevalence of CL, acquiring the infection from sandflies infected mainly from the hyrax. In the Ethiopian southwest, the same animal reservoir is associated as the source of infection of VL for coffee-growing adult men.\(^{(4)}\)

In Kenya, livestock herding nomadic populations are mainly affected with VL where sandflies breeding in termite hills and gerbil reservoirs are involved in the transmission of infection.\(^{(5)}\)

In Belize and in the Yucatan peninsula of Mexico, a form of CL, Chiclero ulcer, is acquired mostly from the forest by chicle gatherers, other agricultural workers and children.

In the Andean and Amazonian regions of South America where CL and MCL are common, colonization schemes and resettlement, deforestation and cultivation of new land are known to be associated with widespread human infection, which is acquired from various animal reservoirs. People involved in hunting, fishing and gathering activities are the most affected.

In Bihar and the Bengal regions of India where serious and large outbreaks of VL have occurred, farming populations were predominantly affected in apparently man-vector-man transmission occurring mainly in human habitations.

In Tunisia, as well as in the Middle East, it appears that large scale construction programs for water resources have increased the prevalence of CL and dogs and rodents are incriminated as reservoirs.

b) **Overview of leishmaniasis infection and disease pathways.**

See Figure 1.

c) **Socio-cultural aspects**

The following factors need to be considered in examining socio-cultural aspects relevant to the leishmaniases:

1) General demography and educational status in the community, including occupational surveys.

2) General health status of the community (community diagnosis).

3) Perception on sources and modes of acquisition of leishmanial infection and attitudes towards such modes.

4) Beliefs and practices about leishmaniases.

5) Social and community infrastructural aspects of the population including occupations and services. Patterns of behavior of:
Fig. I. OVERVIEW OF LEISHMANIASIS INFECTION AND DISEASE PATHWAYS

HEALTHY INDIVIDUALS

Leishmanial parasite

Exposure

Anthropophilic Sandfly

Ecological factors

Animal reservoir

Other risk factors

Incubation time

INFECTION/SUB-CLINICAL DISEASE

Spontaneous recovery

Time

Parasite density

Pathogenicity of strain

Immunological factors

Ecological factors

Other risk factors

Other risk factors

Parasite density

Nutritional factors

Intercurrent infections

Immunological factors

DISEASE

CL. DCL. MCL. VL. PKDL

Treatment/no treatment

Acute/Chronic

Death

Treatment/no treatment

Immunological factors

DEBILITY

IMPAIRMENT

SOCIAL/ECONOMIC HANDICAPS

DEATH

Treatment

Recovery
(1) sub-clinical infection carriers,
(2) acute cases, and
(3) chronic cases.

vi) General comprehension level about health and disease and prevention and control, and the use of any health facilities. The idea of risk factors in leishmaniasis. Social interactions in the community.

vii) If resettlement schemes, migrant workers or nomadic populations are involved, examine three basic levels, e.g., at point of origin, en route, and at final destination; and duration of movements, frequency, etc.. Recreational and leisure patterns in the community as may be related to leishmanial transmission and its impact and effects.

viii) Possible influence of leishmaniasis on educational attainment, development and motivation of the community.

ix) Influence of leishmaniasis on household activities, e.g., child care, cooking, backyard farming productivity, etc..

d) Economic factors

The following economy-related issues need to be examined in relation to the leishmaniases:

1) Sources of income in the community and employment patterns.

ii) Ownership of land and other assets.

iii) Nomadic populations and sources of income/survival and productivity.

iv) Access to resources, e.g., hunting, fishing, gathering.

v) Agricultural patterns in the community including schemes for mechanization, commercial enterprises, etc.

vi) Colonization schemes, forestation and forest clearance activities, irrigation schemes and other development projects in the area.

vii) Local political and economic structure.

viii) Location and distribution of houses and their design.

ix) Domestic animals, livestock and other animals - distribution.

x) Existence of temporary and permanent labor pools.

xi) Individual treatment costs for leishmaniasis.
xii) Loss of time at school/work/home at different levels of disability/morbidity associated with the leishmaniases.

xiii) Associated losses in income/revenue and savings and investment opportunities.

xiv) Hospitalization costs.

xv) Costs of preventive care.

xvi) Costs associated with animal reservoirs and their control or elimination.

xvii) Costs of efforts at disease control in the community.

xviii) Priority given to leishmaniases by:
   i) local physicians
   ii) Health Department
   iii) Ministry of Health

Developmental considerations and discussion

For developing countries, which constitute about 75% of the global population (or 'Less-developed countries', or the 'Third World') "development" is the key objective and is usually thought of in terms of planned intervention. Major obstacles in the path of development include widespread and wide varieties of parasitic diseases frequently exacerbated by malnutrition and other health conditions. The leishmaniases are a typical and important example.

Disease control with the intention of producing decreased morbidity, decreased mortality, and general economic development, is considered necessary to improve the "quality of life." The links between disease and poverty, including the idea that people are sick because they are poor and become poorer because they are sick, also appear logical.

If endemic diseases such as the leishmaniases debilitate the population and eventually deplete the labor force of its vitality, they constitute barriers to progress. Therefore, it is widely held that public health interventions are prerequisites for economic development, implying that poverty can be prevented by disease control. However, careful thought should also be given to possible negative aspects of such interventions. For instance, as learned from the example of successful malaria control in Sri Lanka, the implications of decreased mortality, increased life expectancy, and the resultant lowering of per capita income should all be considerations. In fact, despite exceptional decline in fertility and improvement in family planning and health, Sri Lanka's GNP has not had a significant boost. The arguments, in this case, have been that population density and other economic factors have added to the inadequacies of simplistic considerations.

On the other hand, the consideration of development, developmental projects and macrodevelopmental schemes and their impact on the leishmaniases are of increasing urgency. Massive internationally funded
schemes of various types are now rampant in various parts of the tropical world. Water resource development schemes or large dam construction projects, or others associated with deforestation or reforestation; migration; resettlement; or road building, usually cause widespread ecological disturbances and communities are subjected to significant changes in their biological, physical or socio-cultural environment. Whatever are the specific attributable factors, exacerbation of the leishmaniases has been considered as a by-product.

We have, today, very little knowledge of the precise impact of developmental projects on parasitic diseases including the leishmaniases. We have even a lesser understanding of the possible mechanisms involved in the effect of leishmaniasis on behaviour or effect on learning capacity, development and work efficiency. More reliable data on prevalence and incidence is needed in relation to infection and disease, with precise and usable information on vectors and reservoirs in relation to their habitats, as well as a better understanding of traditions, customs and practices in relation to the disease in the community.

Information to be provided to the ministries and planners in the country, should be shown in the context of the communities' needs and demands, along with the essentials for intervention, and the impact on development, short term and long term. Every macrodevelopment project must have a component which considers all factors in relation to leishmaniasis if prevalent in the community. Practical, feasible, sustainable approaches to prevention and control need to be identified through reliable research findings. There is a great need for input from the affected communities, with their active involvement and their in depth enlightenment towards a more effective role in the overall process of intervention.

Available technology, whether for more sensitive diagnosis, community surveillance or epidemiological methodology, needs to be exploited and applied; costs and benefits are of prime importance. Useful information from various disciplines attacking the problem of leishmaniasis could be the key contribution toward the elimination of this infection as an obstacle in the path of development.

REFERENCES
INTRODUCTION

Of the three factors which can be said to have a bearing on the transmission process of tropical diseases, the parasite, the vector and man, quite a lot is known about the first two. However, we know very little about the third, about the social aspects which are involved in the transmission and control of tropical diseases.\(^1\)

This is due, in part, to the fact that sustained willingness to incorporate the social sciences into the area of health has not existed, although well known figures in the scientific field have talked about its importance for some time. On the other hand, limitations existing in the state-of-the-art of the social sciences have made difficult an incorporation of this discipline which could make a scientific contribution and effect practical conclusions.

It is important that social aspects be taken into consideration among the factors involved in the transmission of tropical diseases, in order to formulate suitable control policies.\(^2\)

THE SOCIO-ECONOMIC DIMENSION OF LEISHMANIASIS

There is little information about the social and cultural factors relating to leishmaniasis, although some data does exist on the social groups most affected by the disease and some of their attributes which appear to be relevant to its transmission.

Principal among these we find the age and sex of the population. The disease seems to be more predominant among men than women according to data in Khartoum;\(^3\) in Egypt;\(^4\) in Ethiopia;\(^5,6\) in Brazil;\(^7\) in Bolivia;\(^8\) and in Venezuela.\(^9\) This fact would seem to be related to the occupation and type of habits of the male population.

The age data is divergent: in Costa Rica cases have been reported in children under 9 years of age;\(^10\) in a study in Brazil it was observed that the majority of the patients with leishmaniasis were less than five years old;\(^7\) in Peru it was noted that the main incidence of the disease was among those between the ages of 15 and 39, which is the working age group;\(^11\) however in the Sudan no difference with respect to age was found.\(^3\)

These two variables should be interpreted according to the territorial area in which the group of individuals studied is found, in order to study the disease both on the rural and urban levels.

Traditionally the transmission of the disease had been considered as a strictly rural problem. However, cases on the urban level are known
in large cities such as Teheran, Mashad, Neishabur and Sabzevar. However, the disease is not evenly distributed within these cities, "so that in some city quarters it is more prevalent than in others". In one community in NE Brazil, it was found that of ten children studied nine had lived in the city from their birth. In Venezuela urban cases have been reported in two large cities, Barquisimeto and Trujillo.

On the rural level I consider that there are two types of large population groups which should be considered separately: those who live in endemic areas and those who travel to endemic areas.

In the first group, population movement is considered as the key element in understanding the risk of contracting the disease. In this case the type of movement and the reasons for moving should be studied. It has been established that movement is due to: occupational reasons, military reasons, and to the habits of the population. Occupational reasons in this instance are related to large scale projects such as dams or forest clearing activities as reported from Peru, or road construction activities as in the case of Panama and Venezuela. The nature of this type of movement is transitory. People travel with the intention of returning, but not immediately. The same is so for the military groups which have been among the most reported and which have served not only in contracting the disease by travelling to endemic areas but also as an element in its diffusion and introduction into new areas on their return to their place of origin. The risk of contracting the disease as a result of military activities is reported from Panama from Venezuela; from Ethiopia; from Kenya; from Israel; from the Iran-Irak war; from action against guerrillas. The possibility of diffusion has also been reported. In Machakos in Kenya it was considered that "the disease was introduced in the district, possibly by military activity". In Khuzistan, Iran, where the disease had had low endemicity, due to the war thousands of cases have been reported among soldiers and war refugees.

A distinct case is movement to endemic areas by people who go for short periods for recreational or pleasure activities. This group is exposed to the risk for less time but is also harder to identify and evaluate. In the case of the Jordan Valley, the disease is found among visitors or newcomers, as most of the local inhabitants have acquired immunity. In Venezuela cases among tourists have been reported and in Kenya among people who go caving.

People who return from endemic areas become spreaders of the disease in areas of low endemicity as in Khartoum, Omdurman and North Khartoum, where an epidemic broke out which was believed to have had its origin in the migrants from the "drought stricken areas of the West of Sudan", from Shedin, El Garrasa or Saudi Arabia.

In the case of people who live in endemic areas the situation is somewhat different, since although population movement may take place, such movements are more routine in which case people would have greater exposure, but one cannot discount the possibility that they could have also developed an immunity. In this group the risk is related to three different circumstances: the type of occupation which might mean staying
in places in which there is a risk of contracting the disease, the existence of conditions in the home which may encourage or prevent its transmission and the establishment of new settlements.

Those occupations which have been considered as bearing greater risk are the following: shepherding activities in Peru; pastoralists searching for better pastures in Baringo, Kenya; male children herding cattle in Ethiopia; hunters and fishermen in Bolivia and Venezuela. One particular "collecting" activity which has been reported in Guatemala and Mexico as showing high incidence of the disease is that of the people who go into the jungle to collect the chicle sap from the Chicozapote trees.

In some cases, differences of incidence have been noted between various ethnic groups, as in the case of the blacks of the Yungas and of the "ladinos", non-indigenous people who go into the Peten jungle in Guatemala or of the non-indians in the case of Peru, where investigators attribute the incidence to a method of cultivation which differs from that traditionally used by the indigenous population. However, in the Sudan it has been reported that "people from all ethnic groups and socioeconomic classes were equally affected".

Another factor which has been repeatedly reported has been the setting up of new settlements in endemic areas. This is the case in Panama where "colonists from central provinces are relocated to regions with high transmission".

Finally, the house has been considered as an important variable in transmission, both because of the nature and condition of the house: poor illumination, on stilts, presence of flat ceiling, as well as its location in relation to the forest and breeding grounds. In a study in Brazil it was found that proximity to breeding grounds was not significant; in Costa Rica it was thought that the proximity of the house to the road was a protective factor and in French Guyana it was found that "the more removed the houses were from the forest edge, the less was the incidence of leishmaniasis in the people who lived in them".

A general overview would suggest that the disease affects the underdeveloped and disadvantaged regions and the lowest socioeconomic classes and that little action has been taken because the disease does not capture the attention of the press and there is no official recognition of leishmaniasis as a public health problem or because there exists "an underestimation of the humans suffering it".

CONCLUSIONS

If we compare the social aspects referred to here, with those reported by other research into the social aspects of malaria and Chagas' disease, we will find certain similarities and differences. Variables such as occupation, migration and habits are repeated for the different diseases. With respect to malaria it is clear that migratory movements and the nature of work of certain occupational groups constitute a fundamental factor in the transmission of both diseases. In the
case of Chagas' disease, the home constitutes a common factor, although it would seem that the importance of the house is not the same in both diseases. I believe there are other factors not yet studied, such as the type of belief with respect to the disease, which could be of great importance in understanding the behavior of the population towards the leishmaniases, as has been the case with other diseases.

In-depth studies are needed on the social and cultural factors relating to the transmission of the leishmaniases which may be useful in orientating control policies, especially if the participation of the population in this process is desired. One factor which could orientate considerably such studies would be to establish a common data base on the social, cultural and economic aspects which should be taken into consideration in any research carried out on the leishmaniases, or which can be collected for the health services. If we manage to make comparable information available on the social aspects in various countries, we would be able to significantly advance our understanding of the disease, but above all, it would be of great help in establishing control policies.

REFERENCES

INTEGRAL STRATEGIES FOR SOCIO-SANITARY CONTROL:  
THE CASE OF LEISHMANIASIS IN THE CENTRAL JUNGLE OF PERU

Jaime Calmet B.

INTRODUCTION

Consequent to the natural concerns of our team in relation to the serious problems encountered in our study (see preceding paper) we were pleased to learn of the possibility to present in this Workshop a report intended to outline some guidelines of an alternative policy of colonization, in order to promote a more rational use of human and natural resources. We think such policy would limit the impact that this process is having on health of the population, and especially, on the prevalence of leishmaniasis.

Essentially, this paper tries to answer two questions considered fundamental: Should a policy of control of leishmaniasis in the central jungle of Peru be propitiated? And, by what means can we achieve its control? Assuming that we understand leishmaniasis as part of the social problem that fashions it, we make an integral proposal of social sanitary control.

In order to more clearly present such a complex problem we have divided the paper into three sections: The first one, tries to justify the economic considerations that necessitate support of those control measures at this time. In the second part, we state some patterns of alternative planning policy for the colonizations of the Peruvian Amazon, which will permit the control of leishmaniasis in the central jungle of our country. Finally, a concrete proposal is presented as a model of action to fashion the alternative colonization planning under the policy.

ECOLOGICAL-SOCIAL COSTS OF COLONIZATION AND CONTROL POLICY FOR LEISHMANIASIS IN THE CENTRAL TROPICAL FOREST OF PERU

Great emphasis has been placed in recent years on the attempt to justify the initiation of activities for the control of diseases, especially tropical diseases, in terms of criteria derived from an analysis of the relative costs of the disease and cost of probable control measures. On the one hand, we have the repercussions of the disease on the productive apparatus, and man-hours lost, and on the other, the costs of implementing the proposed control programme were measured. By comparing these it is possible to arrive at a "cost-benefit" analysis of relative alternatives, a model which has played an important role in rationalizing health expenditure, which especially in countries like ours, is severely limited as a result of generalized poverty. Nonetheless, we believe this model also has important limitations which we attempt to consider in our example of leishmaniasis in the Central Tropical Forest of Peru.
We consider this type of analysis to be incomplete. Especially since, within a society masked by conflicts of interest, where benefits for some always imply losses for others, to speak of "benefits" is necessarily to transmit this concept according to a specific sector likely to benefit, and within whose perspective the analysis is embedded. Concretely, most known studies of this kind have taken advantage of the attempt to estimate the impact of the health phenomenon in terms of the interests of capital, the principal promoter and financial supporter of these studies. Paradoxically, this has led them even at times to accept the "natural" conclusion of sickness or death, where these have little impact on the productive apparatus, or where their control represents high costs for capital. We share a concern that these studies have always been considered as a health control problem in the sphere of national social-economic policy. We propose the need for an analysis of the process which is both broader and more integral, in order to permit the design of correct control proposals. In common with the preceding paper, we attempt to "discover the general rationality or logic of the socio-sanitary process", and to understand the social interests of the disease involved, at the same time putting forward an alternative which is beneficial to the sectors which constitute the majority of our society.

In the specific case of the colonization of the Peruvian Amazon, the highest profit rates for capital and its greatest possibilities for effective gain, its "logic" or "rationality", would seem to be based on a significant reduction in production costs at the expense of the rational use of human and natural resources. The accelerated destruction of the ecosystem and the over-exploitation of manpower are the factors currently permitting relative profits, and thus, regional and extra-regional capital accumulation.

Capital is not concerned by the destruction of the ecosystem because it does not represent a cost to capital. The primary forest is a "freely available" resource and in order to possess it, it is only necessary to occupy it (the only investment being in transport to the location). Its exploitation is only limited by its exhaustion or total destruction. At present, 270,000 hectares per year are felled, and around seven million hectares of primary tropical forest have been irrevocably lost. If this trend is not reversed, it is estimated that by the year 2000 more than 350,000 new hectares per year will be opened up, and a total of ten million hectares will have been destroyed*. Of these, around 80% are "abandoned", without active agricultural use, in the so-called "purma" or fallow periods. Furthermore, and as a product of the extreme fragility of the environment and the inadequate use of technology, a high percentage of these abandoned areas have also irreversibly lost their original aptitude for agricultural use.

The impact which this process is having on the migrant population itself, and on their conditions of life and health, as well as their

*Four times the size of Holland and more than half that of West Germany.
culture, that is to say, the "social" costs of the process of colonization, have only recently begun to be evaluated during the past few years. In spite of the notable contributions in this field, progress has been limited due to the methodological difficulties involved in measuring these costs and the complexity of the analysis of results.

Within this same "logic" of capitalism, with the objective of reducing costs, and thus maximizing profit rates (in this case at the expense of human resources) capital has attempted to conserve to a considerable extent the relations of production characteristic of the stage prior to the presence of a mercantile economy, wherein family labor power, is not remunerated in cash. This is even more important in the case that concerns us here since, given the rudimentary technology employed, labor is the main investment in the productive process.

Two parallel processes result from this. One is the generalization of rapid capitalization of those sectors which have greater access to family human resources (extended families: consanguine kin, brothers, cousins, nephews, fictive kin, ritual kin). This has made possible a process of regional accumulation and internal differentiation, creating a sector of "rich" peasants acting as intermediaries for major capital interests. An important part of this accumulated capital is directed in a permanent fashion to trade, especially as a basis for usury, as in the credit-patronage systems of "habilitación" and "enganche", which, as well as allowing high rates of profit, establish the dependence of labor on capital and thus guarantee the continued availability of labor.

On the other hand, these characteristics of the social relations of production and non-remunerated labor have also resulted in a parallel process of impoverishment of the rest of the population, the majority who were already poor before migrating, and only tell upon nuclear family labor (wife and children) for the productive process. This labor must both ensure the reproduction of the family and maintain ties with richer "kinsmen", the intermediaries who articulate them with the market. Furthermore, it is through these peasant intermediaries that relations are maintained with Andean communities of origin, relations which are always vital to success in the colonization process.

Associated with this gradual process of impoverishment, the changes in the social relations of production have also caused important ruptures in the ideological sphere, and in the cultural sphere, with were of fundamental importance for the reproduction of life. Migration, by breaking the chain of oral transmission, would seem definitively to have accentuated this process.

The final consequence of the introduction of the mercantile economy and the generalized poverty it has caused, as well as the rupture of cultural values which accompanies this, has seriously affected the quality of life of the inhabitants of the central tropical forest of Peru. Their real living conditions have been affected, including of course levels of health. A good example of this is leishmaniasis, just one example in a universe dominated by malnutrition, alcoholism and psychosomatic disorders, with infant mortality over 200% and life expectancy well below 50 years.
It is these extremely high "ecological and social costs", of which leishmaniasis is a part, which make it necessary to intervene urgently in order to correct the present dynamics of the process of Amazonian colonization. In spite of the fact that these do not represent real costs to capital, we propose that society should of necessity act to control the irrationality of this process. The Amazon, with its ecological diversity, its rich variety of genomes, and its vast cultural perspective, are the patrimony, not only of Peruvian society, but of all humanity. The responsibility is thus a shared one.

GUIDELINES FOR AN ALTERNATIVE PLANNING POLICY FOR THE COLONIZATION OF THE PERUVIAN AMAZON

Faced with the complexity of the problem, it is difficult to state a solution. It has thus been necessary to consult various Peruvian specialists in order to make a serious attempt to respond to this enquiry. Nonetheless, their opinions did not entirely coincide, and most viewed the problem exclusively, on preferentially, from the viewpoint of their own discipline. The ideas presented below are not so much personal opinions as an attempted synthesis of progressive thinking in our country regarding the complex problem of the prevailing irrational colonization policy. Naturally, this is an individual, and thus incomplete, effort especially due to the limitations of my own monodisciplinary training. Nevertheless, I venture to offer it as a theoretical exercise and with the principal aim of making the biomedical specialists present aware of the need for an inter-sector, inter-disciplinary control strategy.

As is clear, the main objective of the following proposal is to diminish excessive ecological-social costs. This involves the conservation of the ecosystem, since the Amazon is the common patrimony of society as a whole, and since its destruction would have a generalized impact on the health of the population, both within and outside the region. It is also sought to recuperate what we believe should be the main objective of the productive process: the satisfaction of the needs of the producer. In order to reverse the trend towards external centralization, it is proposed that the productive process be oriented preferentially towards the satisfaction of consumer needs of the family and the region.

In the following two sub-sections it is sought to cover the diverse levels of the social process. In the first, the guidelines for a policy relating to the general conditioning factors in the productive process are considered: the availability of natural resources, capital and human resources (labor). In the second, we present guidelines for policy relating this process itself: the characteristics of the "ideal" system of resource use, of commercialization and also the social sector which should support and develop this proposed.

In this part of the paper, in the interest of clarity and comprehensibility, we employ a schematic presentation of the general guidelines for an alternative colonization policy. This might be helpful, given the large number of variables involved and the difficulty in comprehending them when they are unfamiliar.
Resource use and its General Conditioning Factors

Broadly, we attempt to specify what should be the general policy guidelines in the field of the structural conditioning factors of agricultural systems: human, capital and natural resources.

Cultural-ideological aspects (knowledge)

- large-scale education of the population. Diffusion of knowledge.
- the search for appropriate technology, applied scientific research and the revaluation of traditional techniques.
- The need to change the concept which is generally held in society in the Amazon, the famous myth of "El Dorado", of infinite and easily accessible riches. In the specific case of agriculture, awareness of the limited agricultural potential of the ecosystem. Rather than continuing to expand the agricultural frontier at the expense of the Amazon, better use of soil should be encouraged in regions more apt for agriculture, especially the highlands.
- the need for a new concept of the colonist: not as a transitory occupant, but as part of society in general, the land being a resource belonging to him and his descendants as well as to that society.

Human Resources (Labor Power)

- in a global fashion, more rational resource use should reduce the demand for labor. Diversified use of the ecosystem will permit important savings in the effort necessarily expended by families or the reproduction of their life process.
- Nonetheless, the need to increase wealth in order to improve real living conditions makes indispensable a gradual process of restructuring of social relations of production, whose essential objective should be to maximize the efficiency of available human energy:
  * encourage, in agricultural work, the most symmetrical forms of reciprocity and mutual aid (day for day and task for task).
  * create incentives for collective, communal agricultural activities (communal "faena" as practiced by the native groups).
  * promote a collective forum -communal assembly- for the regulation of wages (daily and contract rates).

Natural Resources

- Modify the conception of the exclusively agricultural utility of the tropical forest, seeking to identify other usable resources apart from the soil.
- propitiate the classification of soils according to their principal use capacity, identifying zones for agricultural and forestry use and for conservation.
- the principal objective would be to encourage a more accurate view of the real availability of natural resources, such as to encourage the best possible use of these. The construction of roads and highways, which is the principal stimulus for the expansion of colonization should be rationalized, avoiding the construction of major routes through zones of low agricultural potential, and orienting investment
towards the improvement of existing road networks, especially secondary ones.

Capital

- propitiate the greater availability of capital by identifying probable sources of finance: the State (Agrarian Bank, Development Corporations Special Projects, etc.), private capital, non-governmental development organisms (both national and overseas).
- Recognize the need for capital investment, not only in the productive process, but also in the promotion of collective commercialization circuits, which would avoid the indirect appropriation of benefits by regional commercial interests (rich peasants, intermediaries).
- Propitiate a more appropriate distribution of existing State credits, attempting to give priority attention to the poorest sectors of the peasantry. In a parallel fashion it is necessary to restructure the respective legislation currently in force.
- stimulate the reinvestment of regional surpluses in the productive process, avoiding their diversion towards private trade, and the consequent speculative use of capital in the systems of credit-patronage ("habilitación" and "enganche") which consist in the advancing of goods on credit for later payment in kind.

The Use of Natural Resources - Ideal Characteristics

In this case it is sought to specify the characteristics of an alternative system of resource use. The most important production aspects are taken into account, as well as the system of commercialization which is the main motive force of the proposal.

Productive Aspects

- In global terms, the tendency sought is towards the gradual intensification of the different natural resources which are available.
- promote diversified resource use, by creating incentives for the association of agricultural, forestry and livestock uses (agroforestry) such as to seek the maximum efficiency of the ecosystem. In the area of forestry, propitiate the use of primary and secondary forest not only for the selective exploitation of high value species such as mahogany and cedar, but rather the integral use of resources. This includes the use of other timber species for, energy generation (firewood), the use of medium size trees for posts for electricity or telephone cables or for construction, the industrialization of residual products, pulp for paper, handles for tools, etc.. In addition, other forest products apart from timber: plant raw material for industry, gums, resins, plant extracts, medicinal plants, ornamental plants, etc.. In the field of livestock, especially important is the creation of incentives for small stock breeding (poultry, rodents, pigs, etc.) and pisciculture, as well as other more efficient forms of transformation of vegetable into animal energy.
- In the specifically agricultural field:
  * promote the association of different annual crops in the same plot, intercropping of annual crops, seeking to encourage species
which are fully adapted to the environment. In imitation of the natural forest, the use of the sub-soil under root crops is associated with the planting of creepers on the surface, and small medium and large bushes with different productive cycles. Areas devoted to the monocrop production of maize and rice (non-irrigated) should be progressively reduced since they cause erosion and exhaust the soil.

* stimulate the gradual replacement of commercial annual crops by permanent ones, especially those with lesser labor requirements for harvesting (cacao, achiote - Bixa Orellana).

* encourage a balance between fallow periods and the use of supplies, such as to conserve soil fertility:
  ** improved seed, fertilizer-manure: especially the "informal" kind, pesticides.

* improve the techniques of human agricultural labor
  ** preparation of the soil and sowing: appropriate use of furrows and "canellones".
  ** weeding-pruning: use of spades rather than machetes, use of protective intercrops.
  ** harvesting: conservative, avoiding plant damage in the case of permanent crops.

- although not strictly speaking, the intensification of resource use, semi-industrial transformation of a simple kind at local level will be encouraged within the region, thus making it possible to give surplus value to production and improve terms of exchange with the extra-regional sphere.

Commercialization

In general, the aim is to combine actions in the internal and external sectors, on the one hand encouraging efforts to negotiate better international values for our export products, while at the same time seeking to diminish the participation of intermediaries between the producer and the consumer, to the benefit of both.

- **On the international plane**: the Central problem, shared by other non-manufactured products exported from different regions of the country, is the unequal exchange between rich buying nations and poor producing ones. Our proposal, which fortunately now seems to be part of Latin America's commercial policy, is to pro-pitiate subregional trade agreements or associations of producing nations, in order to change the terms of exchange.

- **On the national plane**: promote collective commercialization through producer's organizations, from the communal and microregional to the regional and rational levels; articulation with existing commercialization cooperatives; the need to identify (as mentioned earlier) probable sources of finance for these activities: state, private, etc.; seek to weaken gradually the "usury" systems of capital deployment constituted by the "habilitation" and "enganche" credit patronage systems.
Community Organization

- In order to make this proposal viable, it is necessary to attempt to incorporate the largest possible number of social sectors, especially all those with whom the proposal does not involve conflicts of interest. This is the population most affected by the irrationality of the current process, affected by disease, and which is the logical candidate to support and promote the project since it stands to benefit by the social and sanitary control programmes. In addition, since this sector is directly linked to the productive process, it possesses greater capacity to exert pressure and thus greater negotiating potential with other interest groups which exist in society.

- The choice of a specific control policy, as an essential social fact, is the result of that specific moment of a permanent process of negotiation between the diverse interest groups which exist in that specific society. By departing from an individual towards a collective instance of negotiation, the organization of the community or its diverse levels constitutes the most viable alternative in order to attain significant improvements in the real negotiating capacity of this social sector upon which the proposal is based.

- Community organization, in addition, seems to be an important instance for the regulation of the innovatory social relations of production which are introduced. The impact of the market economy, as mentioned in the previous paper, has not only resulted in a reorientation of the productive process towards the exterior (external centralization) but also accelerated very significantly the process of internal differentiation between migrant peasants. Communal organization in this context should represent an effective instance of control of the differences of interests which have arisen internally from the changes in the social relations of production.

ACTION MODEL FOR SOCIO-SANITARY CONTROL IN THE CENTRAL TROPICAL FOREST

Having specified the guidelines for an alternative colonization policy in the previous section, we here propose an action model which will make its practical implementation viable. In general, given the complexity of the problem, the action model also contemplates the progressive coverage of different levels.

It is proposed to initially act simultaneously on two different, but complementary, levels:

(1) the gradual creation of a national consciousness of this topic, especially amongst those sectors most directly involved which at the first stage would be academic, political and labor organizational spheres.

(2) a parallel action promotion of community organization, among the affected population of migrant peasants in the central forest of Peru.

To summarize, it is proposed to combine action on these two levels with the principal aim of encouraging the formation of a critical awareness of the problem, in order to stimulate by means of collection work,
the development of an integral action programme. By resolving the problems of external centralization and internal differentiation characteristic of the introduction of the mercantile economy in the central forest of Peru, it is sought to promote a more rational use of human and natural resources, with the ultimate aim of limiting the impact of the process on the health of the population.

Academic-political Level

Objectives

The central aim of action at this level is to create within the national society a greater consciousness of the situation faced by the central jungle region of our country, at the same time aiming to create receptiveness towards an alternative proposal for Amazonian colonization.

In immediate terms, the constitution of a group of professional persons, State authorities, political and labor organization leaders with an interest in this problem, who would seek to gradually broaden their shared knowledge of the theme, in order to then commit themselves to a common project for the modification of existing conditions.

The ultimate objective is to gradually bring this academic/political level into contact with the community level of action, (see next subsection), making the two parties mutually aware of the need for their complementary contributions in order to attain the reversal of the current orientation of the productive process, and especially in order to escape from the tendency towards the external centralization of the agricultural product and its benefits; and, as an alternative, to re-orient it towards the satisfaction of internal needs (national, regional, microregional and communal).

Themes for Discussion

Here we attempt to present an initial proposal for discussion topics. Detailed specification of the topics to be considered should only be undertaken when the specific human group involved has been decided upon. There follow certain specifications of discussion topics which result from the consideration of the principal factors relating to the problem of leishmaniasis and the colonization of the central jungle region of Peru.

The central point of the discussion is the proposal for the content of an alternative colonization policy, as expressed in the previous section. Complementing this, some additional themes are proposed, especially those relating to the disciplines directly linked to the problem: bio-medical sciences, agro-forestry, and social sciences. We do not attempt (nor consider it desirable to do so) to locate the themes within the ambit of a specific discipline. As postulated in the section on methodological considerations in the previous paper, we consider that the attempt to clarify or resolve complex social problems should necessarily and by virtue of the nature of such problems be essentially interdisciplinary.
The following are specific areas for thematic review:

**The Social Epidemiology of leishmaniasis**
- brief introduction to the biological bases of the disease, transmission mechanisms, clinical presentations, control models employed.
- social, economic, cultural and ecological aspects related to leishmaniasis among the peasant migrant population.
- other social and economic activities related to leishmaniasis in the Peruvian Amazon: gold, oil, timber.

**Resource Use and the Tropical Forest**
- diversity in the use of resources, and conservation of the tropical forest.
- forestry and livestock uses - general aspects.
- agricultural uses of the soil - general aspects.
- agricultural soil use and the fragility of the tropical Amazonian ecosystem.
- structural factors which conditions soil use:
  * availability of resources and intensification of soil use
  * crop patterns and social relations of production (commercialization).

**The Colonization Process in the Peruvian Amazon**
- socio-historical context of the colonization of the Peruvian Amazon:
  * forms of penetration of capital: commercial agriculture, extractive activities and zones of "refuge" for natives.
  * the extension of the agricultural frontier: factors of expulsion and attraction affecting migrants.
- the impact of the market economy in the Amazon region, subsistence strategies and processes of internal differentiation.
- Role of the regional (Amazonian) economy in the national and international economy.

**Sectors Involved**

**Academic**

In the first stage it would be sought to incorporate sectors linked to universities, or to research and promotion organizations which specialize in this specific problem area. In order to form the nucleus of this component, at least three institutions would be called upon, one specializing in each of the branches which have been identified as bearing on the problem: biomedical sciences, agro-forestry and social sciences.

Secondly, the coverage should then be broadened, attempting to incorporate especially those universities and institutions which centre their activities in the Peruvian Amazon.
Political-Governmental

We would attempt to obtain the participation of representatives of diverse state organisms, both at the parliamentary level and at that of the executive branches (ministries, official organisms, social promotion organisms).

Labor-organizational

We would attempt to call upon the organized popular sectors, especially those linked to peasant problems (peasant federations, native federations).

Working Methodology

The central interest here is to encourage the creation of a common space for discussion and reflection, which would permit the gradual creation of a consciousness of the problem which is confronted, of its probable origins, and possible alternative solutions.

The initial strategy considered is that of holding forums in order to capture the interest of small groups of concerned persons who would form working groups. These would involve 8-12 meetings per year, in which the review of bibliographic topics would be combined with the presentation of work carried out in Peru, round tables, and special guests; in order to cover the most important aspects of knowledge regarding the theme.

The ultimate aim would be to hold a seminar-workshop, which in 2 or 3 days would be able to define a common proposal for an alternative solution to the problem of colonization in the Peruvian Amazon and its impact on the health of the population involved.

The level of Community Action

Objectives

To convince the population with which we have been working of the need for an integral and collective development programme as the only option enabling them to improve their real living conditions and thus their levels of health (including especially susceptibility to leishmaniasis). In the short term, the most important aim is to consolidate the fieldwork already initiated, maintaining the community health programme and seeking to extend it by the incorporation of a stable, formal technico-productive component and community commercialization component.

The intention here is twofold: as a model-experiment it will permit us to demonstrate the feasibility of such a project, and secondly, by the demonstration effect it will encourage the imitation and diffusion of the knowledge generated.

At the same time, the populace will be encouraged to become aware of the need to articulate the project, and especially the community organization, with other populations sharing the same problems. At the first
stage, this process should involve the incorporation of the other communities within the district (region). In the medium term, other regions within the Peruvian Amazon which share the same colonization problems should be identified. In addition, priority should be given to relations with the more organized sectors of the peasantry, as well as with other similar promotion projects, both governmental and non-governmental.

The ultimate objective is to consolidate a community organization capable both of linkage to the action component and to the academic-political level, in order to exert pressure on society in general towards a more rational colonization process. It should also as an organization be able to regulate the internal differences created by the penetration of capital in the region, and which constitute the most frequent cause of failure of this kind of project.

Guidelines for an action policy

The need for effective community participation obliges us always to ensure compatibility between the project objectives and the expectations of the population. For this reason the final definition of aspects which the programme of community action should include must be established together with the community organizations themselves. The following are simply certain important areas of work, derived from the work already carried out, and intended as a general orientation for the project.

In global terms, the starting point is constituted by the most important problems faced by the region, especially those relating to health, technico-productive aspects and commercialization, which are the three central themes considered in the direct promotion work carried out with the population. From this basis, it would be sought to encourage gradually a greater awareness of the probable origin of the problems, and of their relation to national and international socio-economic processes.

As mentioned in the preceding paper, in the health field the main concern would be to encourage a new concept of health, in which disease is part of the general social condition, and thus the only viable control model is that of community action. As mentioned above, in the productive sphere, in order to diminish high ecological costs, it is sought to promote among migrant peasants a gradual intensification of the use of natural resources which at the same time conserves their fertility and richness. In order to achieve this, diversified resource use is proposed (forestry agriculture and livestock), as well as the use of appropriate technology. Linked closely to this, is the proposal to improve the terms of exchange with the wider society by means of the promotion of a collective instance of commercialization which would not only increase the effective income per hectare worked to the peasant, thus diminishing his need to clear new areas of forest in order to reproduce his life; but would also permit the choice of crop patterns more appropriate to the tropical forest such as cacao, coffee, achiote, palillo, etc.

Employing a broader perspective, and in terms of medium term objectives, it is sought to create awareness of the historico-social, regional, national and international context within which the colonization process takes place. Especial emphasis should be placed on
those aspects which appear to directly condition the specific situation within which the population finds itself.

Sectors Involved

At present the project involves eight communities. [The "communities" or "annexes" are associations of property holders with common civil authorities. Property in land is individual, though possession is in most cases, at present, precarious or illegal.] The population, around 2,000 inhabitants, represents 10% of the total population of Pangoa. In each of these communities a voluntary health promoter has been trained, with adequate knowledge of basic therapeutic techniques. It has also been sought to make there aware of the indispensability of community action for effective health control, as well as their principal dynamizing role in this organization. The nucleus of health organization in each community is the health committee, with 3 or 4 members, who, together with local authorities and the community as a whole in general assembly seek to specify priorities and develop specific control actions.

A broader level of organization has been encouraged, grouping together the eight communities of the microregion. This had gradually consolidated itself through effective community action with concrete results. Its establishment has permitted a reciprocal stimulation between the organizations of each community; by facilitating the interchange of ideas it has accelerated the process of becoming aware of the problem; furthermore by broadening its social base and its capacity to draw on community support it has increased possibilities for negotiation with capital and state or private organizations for social promotion. Finally, by centralizing the management of the programme the duplication of efforts is avoided, making possible a more efficient use of human resources and logistics.

Methodology

As specified in the preceding paper, action research is proposed as the essential methodological tool. The direct participation of the external agent is the social process of the community is the basis for the possibility of research, and at the same time the incorporation of the population in the research process is the basis for the programme of action for control.

The research component combines qualitative and quantitative techniques in order to specify in detail the complex spectrum of relations between the regional, national and international social context and the specific phenomenon studied — be this health, production or any other aspect. On the other hand, the most direct action component proposes emphasizing the organization as the indispensable basis for community action for control. The organization should be able to solve problems varying from immediate health or productive problems to the structural conditioning factors of the phenomenon: the processes of external centralization and internal regional differentiation.

If we understand it as a permanent exercise in search of greater collective awareness of social-health conditions and their origin,
education in its proper sense, "popular education", is both the discipline and the methodological technique most indicated in order to achieve the aims which have been put forward.

In the area of promotion, the methodological design for action is similar to that put forward for the health problem, and should be taken into account in addition to the direct social conditioning factors: the system of agricultural production and commercialization. Though preserving the concept of the unity of social problems, the training of a specialized voluntary promoter would be undertaken for each of the aspects to be taken into account. Also the formation of a production committee would be encouraged, and also in each community a commercialization committee.

The social science component, not linked so directly to promotion, would seek to attain a global vision of the process by means of a research perspective. In the first place, it would attempt to articulate in a single dynamic mechanism the relation between the different factors involved, both social (including health), economic and cultural. Then, it would attempt to specify the part played by the phenomenon within the broader context of conditioning factors. It would also seek to support the microregional and regional levels of organization and simultaneously to insert them within the national social movement.
SOCIAL EPIDEMIOLOGY OF LEISHMANIASIS IN THE CENTRAL JUNGLE OF PERU

R. Bartolini, E. Bedoya*, J. Calmet
M. Campos, E. Fernandez*, C. Mora* and L. Wahl*

INTRODUCTION

Leishmaniasis, which is second only to malaria as the most significant tropical disease in Peru, is associated in the central jungle of our country with occupation-related activities which have developed under precise social, economic, and cultural conditions of existence. The results of the research project described in this paper emerge from an innovative interdisciplinary research methodology which, we propose, may be fruitfully employed elsewhere. Its specific conclusions have implications for any future action-oriented project to be conducted in the area where research was carried out.

In the Peruvian Amazon, a critical incidence of leishmaniasis has been reported for different historical moments in diverse regions from the sixteenth century on. While it currently prevails among the colonizing population within this general context, its distribution continues to vary both over time and space.

Our investigating team thus found it necessary to explore, in the first instance, the factors that intervene in the uneven distribution of leishmaniasis and, secondly, the relationship between those factors and the colonization processes within which they are embedded. The present paper will thus cover both the socio-medical research tools which preceded and led to the methodology implemented in the above research process, and to the results thereby obtained. Emphasis will be placed on the primary significance for the productive development of any research or applied endeavor of who participates and how in the design of the work processes entailed.

SOCIAL EPIDEMIOLOGY AND POPULAR HEALTH

The role played by social factors in the definition of health problems has been gradually revalued throughout the second half of this century. This was initially associated with the discovery of social risk factors in the case of certain non-infectious diseases, such as heart disease and lung cancer and was later reinforced by the demonstration of relationships between the frequency of certain tropical disease and given social conditions, such as the construction of large infrastructural works like dams or highways. Furthermore, the insufficiency in practice of the eradicationist model led to the further weakening of the conceptual bases of the purer biologicist schools, and faced with this,

* The research received financial support from the World Health Organization through the Special Programme for Research and Training in Tropical Diseases - Social Economic Component.
investigators opted for an explicit reaffirmation of the primary role played by social aspects in determining sanitary conditions and of the necessity for the contribution of other sciences, especially the social sciences, to a full understanding of the problem.\(^3\)

An alternative orientation was developed here in Latin America from the 1960's onwards, drawing on historical materialism. Under the influence of the Cuban experience and in the context of the rapid evolution of popular movements, a closer relationship with lower income sectors of the population stimulated important groups of intellectuals, some linked to the Catholic Church, to progressively elaborate a new concept of health:

"Health was not viewed as an entity in itself but as interrelated with socio-economic conditions. Socio-economic conditions were not viewed as causes related to the disease but as 'determinants' of levels of health."\(^4\)

Whilst seeking initially to make explicit the social context of health phenomena, these thinkers gradually began to center their attention on the attempt to specify the modes of articulation between social and health fields, within a broader attempt to define the 'historicity' of the process:

"... this implies... both a solid understanding of the bionatural processes involved and of the economic, social and cultural ones within which these develop and, fundamentally of the character and dynamics of the essential interaction of both phenomena. And this latter is precisely the specific territory of social epidemiology..."\(^5\)

Social epidemiology postulates, then, the essentially social nature of the health process. Health is defined as the result—at a given moment—of the correlation of forces of distinct and contradictory interest groups. Thus it is proposed that the health problem as a typical social phenomenon may only be understood in an integral and dynamic way. The totality of factors, both health and social, are articulated with one another dynamically as part of a single mechanism which expresses and unlimited of relations of multiple reciprocal action.

Furthermore social epidemiology contains a specific methodological proposal. If the variation in health levels depends on changes in the correlation of forces of interest groups, the alternative for control implies an effective commitment on the part of the researcher, and his research, to immediate actions in support of efforts to attain changes which benefit the less favored social strata, within the perspective of the popular health prospect put forward by certain sectors of the Catholic Church.\(^6\) "Popular" in that the search for knowledge is part of a wider process of consciousness-raising among the population, within which the understanding of health in its articulation with social phenomena is a condition for the development of a model of community-based self-determining action for control. "Popular", too, in that it is only possible for the researcher to decode the 'logic' or 'rationality' of the socio-sanitary problem if he shares within the life of the community the effort to control disease. In short, we refer to an organic and committed
articulation of researcher and research with an integral development action, which constitutes a dynamic of permanent and reciprocal stimulus between research and actions for disease control.

It is beyond the scope of any one science to integrally understand the social nature of a phenomenon which also has a biological expression. Confronted with this, the interdisciplinary team would seem to be the most reasonable option. As a product of teamwork the alternative of collective and integrated action and expression is chosen, both for research and development activities. The criterion of interdisciplinary work is rigorously applied inasmuch as each one of the members of the team must personally incorporate the methodological and conceptual elements of the other disciplines involved in the project into his or her own work.

It is premature to state which is the social science which can contribute most to the elucidation of the complex problem of the social nature of the health process. This probably depends upon the context under study. Nevertheless, especially here in Latin America, anthropology—due to its greater capacity to evaluate findings relative to their specific context—seems to have the greatest contribution to make to programmes of action-research in health. In the first place, this is because this would seem to offer a better possibility of understanding economics like those of our countries which have important population groups only partially articulated with the market. In the second place, its methodological techniques permit a simultaneous level of relationship with the population which makes possible a greater degree of integration of the team with the community, and thus of the study itself with realistic measures of disease control.

METHODOLOGICAL CONSIDERATIONS

Methodologically, social epidemiology, as mentioned earlier, contains an implicit theoretical postulate regarding the unity of research and action for disease control. The search for knowledge has as a principal objective, the stimulation of immediate action, and vice versa.

Derived from the need for an interdisciplinary team, the methodological design of the research had as a principal general objective, the establishment of a balanced complementarity between methodological techniques, both qualitative and quantitative. In general, we preferred to use more sensitive qualitative and relatively unstructured instruments in the earlier states of fieldwork, leaving the more specific quantitative and structured ones for later stages. However, we consistently tried to transcend the limitations of rigid methodological design in order to establish a permanent open interchange with the population. The participant-action component had of necessity to be related to the expectations of the population. At first, we had to emphasize medical-recuperative attention, as an expression of the "sickness-individual" concept prevailing when we arrived. Later, leaving behind the 'biological' conceptions, the creation of a common open space for interchange and of a community organization for health made possible a continuous process of shared discussion and reflection which, in turn, gave rise to a progressive reorientation of these initial points of interest. Within
a perspective more oriented towards prevention, and revaluing the importance of the social, community-action based alternatives for the control of health problem, which at present include leishmaniasis, came to be revalued and consolidated.

Elaboration of the Hypotheses

In the attempt to embrace the diverse levels of analysis outlined earlier, hypotheses were put forward which ranged from the macrosocial politico-economic level to the communal and family microsocial level. We sought to avoid limiting ourselves to a mere description of the social context, and to specify precisely the probable articulatory links between the disease and its social determinants.

The global hypothesis began from two extreme starting points: the change in the prevalence of leishmaniasis and the historic-social context within which this change was occurring. From these, and articulating the two extremes, it was sought to identify the specific social determinants—direct and indirect—of the changes in the prevalence of the disease.

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SOCIAL CONTEXT ----> I.S.F. ----> D.S.F. ----> PREVALENCE
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Intensive case study

This represented the application of a typical anthropological or ethnographic technique, by means of which it is intended to reach an in-depth understanding of a single case. By reducing the size of the sample it was sought to intensify both in depth and detail each observation; attempting not only to include a wide spectrum of variables but also to discover possible relations of interaction between them. Methodologically, this stage was characterized by the need to employ more qualitative techniques. Highly unstructured instruments were employed.

Extensive Regional Study

The more precise understanding of the problem together with the closer relationship to the population under study, derived from previous stages of the research, made the application of the more quantitative techniques characterizing this phase of the project considerably more efficient. Within the framework of a rigorous statistical design, this was a regional study embracing a total of six communities. The methodological technique chosen was the structured interview; while the instrument applied was a totally closed, precoded questionnaire.

The central objective of this stage was to increase the sample size in order to seek statistical significance for certain correlations which in the previous stage did not meet the required standards of reliability.

Participant-action programme

In the field, a concrete return of direct benefit to the community
was an indispensable condition in order to obtain the effective collaboration of the population with the project.

In response to a basic principle of reciprocity, we sought always a balance interchange: on the one hand, we asked for a minimum of cooperation with the study, while on the other, we offered, as far as possible, support for the community and its needs. To incorporate ourselves in the daily life of the place, sharing its problems, and in some way participating in them, was in addition the only way of attaining a full understanding of the socio-sanitary process. This commitment to immediate action in support of the community represented in essence a form of exercising the conceptual principles which also govern us as individuals. This meant for us the abandonment of the possibility of the supposed neutrality of knowledge, and the adopting of a position with regard to the conflict of contradictory interests, attempting to place our knowledge and the power which derives from it at the direct service of less favored sectors. In other words, it translates the commitment to work with and for the community into a real attempt to change its living conditions.

Implicit within the conceptual option, the proposal for action postulates that the organization of the community will permit a better (greater) capacity for negotiation in the conflict with dominant interests, by making possible the accumulation of forces around a collective project. In explicit opposition to those who deny the possibility of changes in levels of health without accompanying changes in social structure, it is sought to transcend the level of individual negotiation, towards a broader common level in order to improve the possibilities of obtaining additional benefits in this permanent negotiation process. An integral action for development, not only in areas related to health aspects, but also considering the context of the total social, economic and cultural problem, was the only way to affirm in practice our conviction of the essentially social nature of health.

In our work, which in action, as well as in theory, was strictly interdisciplinary, we employed all available institutional resources. In the space created by the formation of a community health organization, it is health education, in its correct sense[^4], which is the discipline that has most to contribute to the action programme. Transcending the instrumental use of education, it seems to abandon the idea of the unidirectional transmission of knowledge, of educators and those who are educated, of wise and ignorant; proposing as an alternative an education which stimulated the formation of a critical consciousness on the part of the population of their social-health condition, promoting the rescue of the crucial self values as an indispensable condition for a community control programme, whose axis is the proposed unity of research and action, by control.

BACKGROUND

The peruvian jungle is located in the eastern part of our country. With a total of 72 million hectares, it occupies 65% of the national territory. Ecologically, it corresponds to a zone of tropical humid forest, with important differences in altitude, that divide it into two
big ecosystems: high jungle in the east side of the Andes, between the altitudes of 500-2000 m, and the low jungle with altitudes < 500 m. The general population is about 1.8 million inhabitants, which represents 10% of native amazonic populations that are distributed in 64 different ethno-linguistic groups. The remaining 85% consists largely of migrating rural population that comes from the adjoining Andes, those that, forming part of the process of internal migrations beginning in the 1950's, enlarged the demographic and economic frontier all the way to the amazonian zone.

This process of colonization could be explained, on one hand as an answer of the peasant families facing the population growth, the unfavorable rural-urban interchange terms, and, especially, the diminishing availability of land. It being almost impossible to maintain their living levels in their original communities, the option for the jungle has been made more attractive by the opening of new highways of penetration, the increase of the external demand for coffee, and the national economic crisis caused by the fall of international oil prices in the 1970's.

The forest is the home of 25% of rural families in Peru. The majority, are dedicated to agricultural activities. Thirty-three percent of the agricultural land of the nation is located in this region, especially in the high jungle, and produces 95% of the coffee and 50% of rice and hard yellow maize. In the low jungle the extraction activities are concentrated mainly on wood, oil and gold.

Generally speaking, the integration of the jungle has historically followed the rhythms of the extra-regional market demands; the international ones in first place, but also, the national urban demands. The rubber cycle was followed by furs, verbascum and, recently, by the wood, coffee, oil and gold. This process has been characterized, as in the national economy as a whole, by an external centralization of the production and its benefits, mainly through the effort to satisfy the international market demands, especially those of the developed countries. In a parallel and complementary way, the internal accumulation of capital has grown significantly in all the region, and has accelerated an internal process of social differentiation.

The colonization of the Amazon, including that of the central jungle region is not, however, a fixed event. While the concept of 'colonization' may be employed to refer to a wide range of social phenomena with diverse political and cultural implications. In the present study we employ it to refer to occupation of a given area, the Amazon region, on the periphery of the Peruvian nation-state and to the social characteristics of this occupation.

In the Peruvian Amazon, three principal expressions of the process of capital penetration may be observed. The first is characterized by the production of commercial crops and the significant demographic presence of people from other regions (colonists) with which is associated the development of intensive commercial agricultural practices. This mode of occupation extends in a dominant fashion along the routes of external communication which are required to transport agricultural products to
the market, whether by river or overland. The example par excellence of this mode of occupation is the central jungle.

A second type of occupation is based upon the extraction of highly profitable natural products, such as timber, oil, gold, etc. Even when some of these products can be produced, in principle, in a renewable fashion, that is, in such a way as to permit the regeneration of the areas exploited, they are rarely subject to this kind of resources management, since it is considered to be unprofitable in the short term. In terms of population densities, there is constant displacement away from those zones where resources have been exhausted and towards new ones still capable of yielding high profits. The articulation with indigenous populations in these zones is basically of mercantile order.

The third expression of the colonization process is the so-called 'refuge areas' which are considered of marginal economic value to the wider society and towards which flow the indigenous populations of the Amazon region who attempt to flee from the market economy and, hence, retain a degree of control over both their natural resources and productive processes. The regions to which these populations move are characterized, first, by the more sparse distribution of certain essential subsistence resources - for example, fishing is poor in their smaller streams and game resources are scarcer still than in other regions of the tropical forest. Secondly, by the susceptibility of such zones to be subject to rapid changes in their valuation by the wider society, especially due to the discovery of some mineral, hydroelectric potential, or other resource. This may then cause the sudden and drastic displacement, physical and cultural, of its inhabitants, often with tragic results.

While it is true that there exists different modes of the colonization process, a key underlying element in their diversity is the common factor of the attempt to reduce different production costs, i.e. maximize profits, at the expense of the natural and human resources of the region.

Thus, the generally high production costs of commercial crops underlie the series of responses outlined above, which attempt to cut down on these costs. The depredation of tropical soils is perhaps the principal strategy utilized. Another involves the reduction of the cost of labor power, which is the traditional limiting resource in Amazonian colonization (given the 'availability' of land), especially at harvest time. In the context of highland rural existence, this usually involves the intensification of family ties within the peasantry. These may provide, when necessary, material aid in the form of money or goods, and particularly in the form of labor, by means of different forms of reciprocity.

Leishmaniasis in the Peruvian tropical forest is a tropical disease of high prevalence among certain sectors of the population. Specific risk groups have been identified, such as workers employed in the extraction of oil, timber and gold, as well as considerable number of recent peasant migrants to the forest zones, who seek to expand their agricultural frontier. This latter is the case that concerns us here: that of leishmaniasis among the population of andean origin, who (as part of a wider process of colonization of the Amazon which dates from the 1950's) migrate to the adjoining forest zones and occupy the region.
according to a specific pattern of principally commercial agriculture (coffee, plantain, maize, etc.).

The project was carried out in the central tropical forest, in the Pangoa district, Satipo province, in the Department of Junin. The ecosystem of Pangoa corresponds to the high tropical forest type. The principal economic activity is commercial agriculture. Diverse annual crops such as maize, rice and plantain are produced for the internal (mainly urban) market, but permanent crops such as coffee and cacao are grown with an export orientation. Pangoa has the highest population density in the Province, with around 30,000 inhabitants; 30% of these are natives of the Campa-Nomatsiguenga ethnic group, belonging to the Arawack language family. The remaining 70% includes migrant populations of diverse origin, mostly from the Central Andes.

THE PROJECT

This work attempts to show that the activity of forest clearing, in this case for agricultural purposes*, is the most important direct factor which modifies the risk of disease. Secondly, we attempt to specify the principal motives which cause this intense clearing activity. We postulate that the principal cause of this active clearing process is the extensive agricultural system practiced in the region (see section on Agricultural System, Clearing and Leishmaniasis). Finally, we pay special attention in trying to identify possible structural determinants of agricultural systems which as we argue are related to the greater prevalence of the disease (see section on Historico-social content of colonization in the Peruvian Amazon).

Leishmaniasis and Forest Clearing

Since the team's experience in specific aspects of tropical pathology relating to this project was insufficient, we found it necessary to call upon the support of a specialized institution. This was the Alexander von Humboldt Institute of Tropical Medicine, based in Lima, which has collaborated closely with our work and helped us arrive at an adequate working definition of a clinical lesion of leishmaniasis which did not call for invasive techniques which would have jeopardized the initial relations with the community, which were crucial to the success of the project. Additionally, laboratory techniques for diagnosis, such as biopsies, imply high costs in terms of trained personnel, imported laboratory supplies, etc..

It was not easy to arrive at an adequate definition of the clinical lesion of tegumentary leishmaniasis, especially since, for our purposes, we required an operative definition which could be efficiently employed--

* In the Amazon, the forest is cleared for agricultural purposes by the "slash and burn" technique. The are is first cleared and the vegetation which has been cut is burned in order to transfer nutritive elements from the tree cover to the soil. Given soil fragility, this system requires prolonged fallow periods in order to regain fertility.
by a non-specialist professional. In conjunction with the Institute of Tropical Medicine we decided to attempt to initially identify all chronic aggressive ulcers, thus seeking only to exclude the group of non-leishmanial acute ulcers (usually bacterial) which are very common in an area like the one under study, with a high frequency of skin diseases (parasites, fungus infections, atopical dermatitis, wounds, etc.). We considered that the greater part of the lesions thus identified would be due to leishmaniasis, and that criterion would therefore be sufficient for the purposes of the initial stages of interdisciplinary work.

In addition to this operative definition, it was necessary to specify a more objective form of measurement in order to permit a more systematic analysis of variables. The period of activity of the lesion provided the most important objective diagnostic criterion. The average period of activity is 9±9.63 (0.5) months, with a range between 3 and 60 months.

In the case of active lesions, a further criterion which assisted in the definition of the aggressiveness of the lesion was a color photograph which was taken. The purpose of this was to specify precisely the size of the lesion, its depth, the involvement of surrounding parts, etc. In the case of lesions which were already at the stage of healing, the criterion adopted was to attempt to judge their aggressiveness indirectly by observation of the size of the residual lesion. Considering the refractory nature of the healing process in a chronic disease, the size of the scars found was relatively large, varying according to the part of the body affected and the age of the patient. The average maximal diameter of the lesion was close to 4 cm., with a range from 3 to 7 cm.

In the second stage, the clinical cases and the accompanying photographs of the lesions were discussed with a specialist in tropical medicine. The results of this discussion led us to reaffirm our initial idea that the majority of the pathology observed was due to leishmaniasis. Of the 44 cases occurring in the past three years, 18 were found to be active at the time of the interview. According to the opinion of the specialist, more than 60% of these cases fell within the 'classic' presentation of leishmaniasis, with little room for diagnostic uncertainty: a single ulcer with well-defined borders, round in shape, deep, with a fine granulated base. A further 30% of the lesions, although of less typical clinical presentation, were also classed as a probable origin due to leishmaniasis: the presence of multiple smaller lesions, imprecise borders and shapes, of similar depth to the former and accompanied by a significant inflammatory process.

Social Direct Determinant of Leishmaniasis: Deforestation

In accordance with current advances concerning the ecology of leishmaniasis, we considered this zoonosis to be a product of the permanent process of interaction between vector, parasite, host and environment. On this basis, we postulated that a preserved tropical forest would be the most favorable place for the reproduction of the zoonosis. This, at the same time, implied that ecological modifications, including the introduction of agriculture, would stop the transmission of leishmaniasis by destroying the environment required for its reproduction.
In so far as the primary forest constituted the most adequate environment for reproduction of the zoonosis and transmission would be interrupted by ecological modifications, it seemed likely that the very act of clearing the forest could be determining the increase in the rates of leishmaniasis by affecting man's exposure to the parasitic vector. As hypothesized, the relationship between forest clearing and leishmaniasis was indeed expressed by:

1. the higher exposure of cases over controls to forest clearing before acquiring the disease;
2. longer time of residence in the jungle region among controls;
3. higher incidence of leishmaniasis among those communities surrounding Naymlap where the colonization of a primary forest habitat is taking place; and
4. appearance of leishmaniasis beginning in the months of October and November, with a peak in January, about three months after forest clearing takes place.

Taking into account then, that it is during the act of clearing the forest that the most favorable moment for the transmission of the zoonosis to humans is produced, we believed it would be possible to develop and objective measure of this relationship by measuring the degree of exposure to active clearing. As we have already stated, in accordance with clinical criteria, 44 patients with a diagnosis of probable tegumentary leishmaniasis were identified. Their respective controls were then randomly selected based on two criteria: that of belonging to the same age groups (± 5 years) as the corresponding case, and that of having been in the region at the time the patient contracted the disease.

Both cases and controls were asked about their exposure to forest clearing during the three months prior to the development of leishmaniasis among cases. However only those who actually worked at clearing the forest were considered as having a 'direct exposure'. Women, children, and others who frequented those forest areas that had been recently cleared were considered as having been exposed 'indirectly'. Among such circumstances were those instances of people who approached the area regularly to bring food to the men working, went there to play, or passed through on their way elsewhere. 'Occasional' exposures were those where contact with forest clearing was of little significance, unforeseen, or of short duration. As Table 1 shows, 60% of the cases had been directly involved in forest clearing while 25% had been exposed indirectly. In contrast, among controls only 8% had been involved directly in deforestation activities. As can be observed, the difference is highly significant statistically.

The above findings are backed up by the greater tendency among cases to have spent less time in both the jungle region and the community where they currently reside. This is shown in Graphs 1 and 2. This finding reinforces the relationship posited between leishmaniasis and clearing, if we consider that the initial stages of colonization seem to be associated with an accelerated rhythm of clearing. This, however, would lead one to assume that controls would have been similarly exposed upon their arrival to the lowlands. Yet this is not the case, in so far as their exposure to forest clearing was less than that found among cases even
upon their arrival. Apparently, what seems to be the case is a lower exposure of controls to clearing itself, due to one or more of these associated conditions:

- greater use of non-family labor (see Indirect Social Factors).
- greater incidence of purchase of already cleared lands.
- use of better agricultural technology:
  . greater initial capital.
  . greater previous experience.

The distribution of cases in the general area of study strengthened not only our conclusion that leishmaniasis generally prevailed where the colonization process was being initiated, but that man himself played a further role in this in that only 5% of the native Nomatsiguenga had developed leishmaniasis over the past three years, in clear contrast to colonists who exhibited an incidence of 35%, while the rate for both groups together was of 22%, as may be observed in Graph 3.

We believed that the indigenous population was protected from contracting the disease because they managed the forest conservatively, and conversely that transmission was interrupted when ecological changes made the reproduction of the zoonosis difficult. The types of communities inhabited by cases and controls were classified according to their respective age and to their primary forest conservation. Type 'A' communities dated back more than 30 years with primary forest largely transformed, type 'C' communities had been colonized in the past 10 year and hence had substantial amounts of primary forest, and type 'B' communities were those in between. The incidence of cases among these communities was again statistically significant, even when considered by age groups, as may be seen in Graphs 4 and 5.

<table>
<thead>
<tr>
<th>Exposure to Forest Clearing for Agriculture Among Cases of Cut Leishmaniasis</th>
<th>Controls</th>
<th>Cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>none</td>
<td>28 (78%)</td>
<td>4 (11%)</td>
</tr>
<tr>
<td>circumstantial</td>
<td>2 (06%)</td>
<td>0 (00%)</td>
</tr>
<tr>
<td>indirect</td>
<td>3 (08%)</td>
<td>10 (27%)</td>
</tr>
<tr>
<td>direct</td>
<td>3 (08%)</td>
<td>23 (62%)</td>
</tr>
<tr>
<td></td>
<td>36 (100%)</td>
<td>37 (100%)</td>
</tr>
</tbody>
</table>

\[ p > 0.0001, \chi^2 \]
Table 2.
Degree of Exposure to Forest Clearing for Agriculture
Among Cases of Cutaneous Leishmaniasis

<table>
<thead>
<tr>
<th></th>
<th>Controls</th>
<th>Cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>low exposure</td>
<td>33 (92%)</td>
<td>14 (38%)</td>
</tr>
<tr>
<td>high exposure</td>
<td>3 (08%)</td>
<td>23 (62%)</td>
</tr>
<tr>
<td></td>
<td>36 (100%)</td>
<td>37 (100%)</td>
</tr>
<tr>
<td></td>
<td>(p &gt; 0.0001), x^2</td>
<td></td>
</tr>
</tbody>
</table>

Figure 3.
Distribution of Incidence by Age, and According to Degree
of Conservation of Primary Forest

<table>
<thead>
<tr>
<th></th>
<th>A</th>
<th>B</th>
<th>C</th>
</tr>
</thead>
<tbody>
<tr>
<td>0 - 14 years</td>
<td>0% (0/168)</td>
<td>8% (2/253)</td>
<td>60% (10/168)</td>
</tr>
<tr>
<td>15 - 39 years</td>
<td>29% (3/103)</td>
<td>46% (9/193)</td>
<td>87% (13/149)</td>
</tr>
<tr>
<td>40 years</td>
<td>0% (0/27)</td>
<td>18% (1/56)</td>
<td>29% (1/34)</td>
</tr>
<tr>
<td>Total</td>
<td>10% (3/293)</td>
<td>24% (12/502)</td>
<td>68% (24/351)</td>
</tr>
</tbody>
</table>

Table 3.
Monthly Distribution of Appearance of
New Cases of Leishmaniasis

<table>
<thead>
<tr>
<th>Cases</th>
<th>%</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Feb - Mar</td>
<td>12</td>
<td>32.4%</td>
</tr>
<tr>
<td>Apr - May</td>
<td>2</td>
<td>5.4%</td>
</tr>
<tr>
<td>Jun - Jul</td>
<td>3</td>
<td>8.1%</td>
</tr>
<tr>
<td>Aug - Sept</td>
<td>3</td>
<td>8.1%</td>
</tr>
<tr>
<td>Oct - Nov</td>
<td>6</td>
<td>16.2%</td>
</tr>
<tr>
<td>Dec - Jan</td>
<td>11</td>
<td>29.7%</td>
</tr>
<tr>
<td></td>
<td>37</td>
<td>100.0%</td>
</tr>
</tbody>
</table>
Finally, it was found that the appearance of new cases did not take place homogeneously throughout the year; 60% of the cases appeared in a period corresponding to 30% of the year, as Graph 6 and Table 3 show. Although in this region an agricultural calendar is not followed in the strict sense of the term, in so far as several crops may be planted at different times, this is not true of forest clearing activities. These must be carried out in the dry months of the year (between June and October), in a pattern typical of tropical slash and burn cultivation.

**Agricultural System, Forest Clearing and Leishmaniasis**

Having initially demonstrated a direct and causal relation between forest clearing and the existence of the disease, the central concern of the project has been to attempt to define precisely the specific social determinants (ISF: indirect social factors) of this forest clearing activity. We affirm that having developed these enquiries it is possible to construct an integral vision of the mechanism of articulation between the social context and the disease. The hypothesis, postulates that:

In the central tropical forest, leishmaniasis is a product of the activities of forest clearing, which in turn result from the agricultural system employed by colonist populations whose occupational, economic, social and cultural characteristics in the zone spring from the wider historical-social context, regional and inter-regional, within which the colonization of the Peruvian Amazon takes place.

It is postulated, then, that this intense clearing activity is a direct consequence of the form of utilization of land resources within the predominant agricultural system; which is subject to natural rainfall cycles with low levels of yields, predominantly annual crops, and inadequate technology. This land use, to summarize, is an expression of an extremely extensive type which it is only possible to maintain by means of aggressive clearing.

The Amazon region occupies the greater part of the Peruvian national territory. In spite of the fact that it shares with the rest of the Amazon the general characteristics of a humid topical forest, there exist important differences within the region itself, principally as a result of differences in altitude. The Peruvian tropical forest is classified according to altitude as 'high' (over 500 m above sea level) or 'low'.

The soils of the Amazon are extremely fragile, and their fertility depends almost entirely on the cycle of decomposition of leaves from the tree cover. The natural vegetation of the tropical forest, therefore, extends its roots horizontally rather than vertically, and at the same time any given species is almost always extensively distributed amongst others, permitting the establishment of an equilibrium between the nutrients exchanged between diverse species. The uneven topography, high rainfall and the destruction of the tree cover introduced by agriculture cause erosion, with serious and generally irreversible deterioration of the Amazon ecosystem and especially of soil fertility.

Under these specific ecological conditions, two alternative forms of soil use are employed. The first type is extensive, where the logic of
the system implies the increase of production by broadening the agricultural frontier. The other possibility is more intensive soil use. In general, stimulated by limited availability of land, it is sought to increase total production by increasing productivity by increased use of technology: irrigation systems, manure and fertilizers, insecticides, machinery or animal power.

Over the past decades and as a result of erroneous agrarian policies in Peru, the greater part of capital investment in agriculture ($80\%$) has been directed towards the expansion of the agricultural frontier.$^{(8)}$

In the specific case of the tropical forest, a sustained policy of stimulation of road construction has precipitated a massive affluence of migrants from the adjacent Andean region, who as we aim to show, make extremely extensive use of the soil.

**Pangoa: the extremely extensive use of soil**

The agricultural system of Pangoa depends exclusively on natural rainfall, and the technique for preparation of the soil is clearing and burning the vegetation which has been cut (slash and burn). The extremely uneven topography which characterizes the region, constitutes the limiting element for the diffusion of irrigation systems.$^{(10)}$

The predominance of non-irrigated cultivation is the principal determining factor in the low levels of yield obtained both for annual and permanent crops in Pangoa and in the high tropical forest in general (see Appendix 1). This is the case for maize and rice, whose production per hectare is considerably higher under irrigation. In the case of rice, this difference is up to 2-5 times. The same is true for coffee. In the coffee growing regions of the Northern Tropical forest, where irrigation systems predominate, the yield per hectare is as high as 22 quintals.$^{(8)}$ Thus, dry regime agriculture in Pangoa, to equal production in irrigation systems, needs to employ at least double the area of land. This is made possible by the greater availability of land here. In Pangoa the average extent of an agricultural unit is two to four times higher than in the Northern tropical forest.

This tendency for extensive land use under non-irrigated cultivation is notably accentuated in the case of Pangoa by the pattern of crops employed. We found half the agricultural surface to be occupied by annual crops, which as several studies have shown$^{(11,12)}$ cause greater erosion and intense lixiviation, finally resulting in accelerated loss of soil fertility and, as a consequence, obliging the farmer to constantly open up new areas in order to maintain stable yields.

The use of inadequate technology aggravates to an extreme the extensive pattern of land use. Due to major economic limitations, only one farmer in ten in Pangoa uses manure. In the case of annual crops, low crop diversification-associated with large extensions of adjoining deforested slopes-increases the fragility of the ecosystem and creates earlier soil exhaustion.
Sonomoro: Differences in extensive agricultural system and their relation to Leishmaniasis

The Sonomoro micro-region, the specific zone where research was carried out, is one of the micro-regions of the district of Pangoa. Pangoa is a district with special characteristics vis-a-vis other zones of the high tropical forest, but at the same time its multiple micro-regions, like Sonomoro, maintain their own internal dynamics as well as sharing a common articulating centre, which is the district capital, San Martin. A Network of tracks, mostly opened by timber workers, link this nucleus with secondary centres (Naymlap de Sonomoro), while paths connect these villages with the more distant and inaccessible zones (Centro Sanibeni). Each micro-region behaves as a productively and commercially articulated unit. We postulate that the internal dynamic characterizing the study zone is representative of the region as a whole. This dynamic is determined by a network of commercial relations between centre and periphery in each micro-region. These zones also have special productive characteristics which in the last instance express different forms of soil use.

San Martin de Pangoa, the Centre of articulation shared by all the micro-regions has received important migratory contingents over the last 30 years. Since that time, the adjoining territories were also gradually occupied. Centro Sanibeni, a recently occupied zone, has been colonized during the past ten years, while Naymlap de Sonomoro is intermediate between the two in terms of time of colonization. Population density gradually diminishes from centre to periphery, and the settlement pattern becomes more disperse. Likewise the control zones are characterized by a predominance of commercial activity, while in the peripheral zones a greater degree of conservation of ecosystem and soils is associated with agriculture as the fundamental economic activity.

While it is true that the micro-region shares a labor market, the flow of capital from centre to periphery seems to be the principal articulator of the regional economy. Though part of this capital is invested in the opening up of new areas in recent colonization zones, most of it is directed commercially to the bulk purchasing of agricultural produce by means of a series of successive "loans" which seem to constitute "usury" in the use of capital. All the agricultural production of the region is concentrated in San Martin, and from there directed to extra-regional markets. Places like Naymlap which are intermediate between centre and periphery have strategic importance for the continuity of the commercial circuit, since they are sites for the first instance of bulk accumulation of agricultural products of adjacent zones. In Naymlap are located the intermediaries who by means of the "loan" system are financed by the big buyers of San Martin. These intermediaries in turn directly finance the agriculturalists, assuring in advance, and at low prices, the produce of the future harvest.

*Andean migrations in the region date back to prehistoric times. Within the internal migratory process since 1940 the Satahipo zone reached its greatest growth rates only in the 1960's, unlike other high forest zones where colonization dates back to the 40's and 50's, and thus is a zone of relatively recent colonization."
In general the Sonomoro micro-region behaves according to the agricultural system which characterizes the region. There is high land availability, heavier concentration of annual crops, and very low use of modern inputs (see Appendix 2). However, there are important differences between the agricultural systems of the more central zones (Naymlap) and the peripheral ones (Centro Sanibeni) which allow us to explain more clearly the differing prevalence of leishmaniasis.

On the basis of a non-irrigated regime and inadequate technology we postulate that in Naymlap there is more intensive soil use, with a corresponding lower current rate of clearing while in Centro Sanibeni where use tends to be more extensive, there is a higher rate of clearing of primary forest and as a consequence a greater prevalence of leishmaniasis (see DSF section).

We attempt to show that in Centro Sanibeni there is more extensive soil use, and consequently more leishmaniasis, on the basis of the differences found in terms of greater total plot size, a high proportion of available primary forest, and behaviour in terms of crop systems.

As shown in Graph 8, the total average extension per family agricultural unit in Centro Sanibeni is twice that of Naymlap, while the area of conserved primary forest is three times greater. These conditions facilitate more extensive land use in Centro Sanibeni. At the same time, the availability of primary forest favours greater reproduction of the zoonosis, which also explains the prevalence of leishmaniasis found there.

Permanent crops are generally linked to relatively more intensive soil use. Nevertheless in Centro Sanibeni we find rather extensive use, due to the adoption of a strategy of gradually extending the plantation into available primary forest. As shown in Table 4, in Centro Sanibeni there is a higher percentage of agriculturalists who increase their plantations of coffee, the main permanent crop. Faced with the extremes fragility of soils and the uneven topography of the high forest, the extensive use of soil for permanent crops guarantees high productivity because it takes advantage of the initial fertility of new areas. The low production of coffee plantations in Naymlap (Table 5) is explained by the low increase in plantation size due to lesser availability of primary forest.

In the case of annual crops, Naymlap shows much more extensive soil use, with repeated re-use of previously used soils and reduced fallow periods. Relating the fallow areas to areas sown, we found that in Naymlap there is 1.26 hectare under fallow for each hectare under production, while in Centro Sanibeni the figure is 2.53. The difference becomes even clearer when we consider the relatively lesser age of fallow areas in Naymlap (see Table 6).

A final aspect which should be stressed is the differing proportion of pasture area in the two zones, which is 6% of the cleared area in Naymlap and 30% in Centro Sanibeni. The low energetic value of pasture lands in the humid tropical forest, and the vast ecological deterioration they cause (much more than that caused by agriculture) oblige the farmer
to clear large areas periodically in order to continue to feed his cattle. This also creates a higher clearing rate in Centro Sanibeni.

To conclude, in Centro Sanibeni soil use for both annual and permanent crops is more extensive compared to Naymlap. This necessitates more intensive clearing of the forest, which finally explains the greater proportion of the disease found.

In Naymlap, as a result of the limited availability of primary forest, more intensive soil use and inadequate technology have caused soils to deteriorate rapidly. The erosion caused by large-scale sowing of annual crops on steep slopes*, together with the lesser periods of fallow, further affect soils which already show serious outward signs of exhaustion. The response to this is a growing tendency to clear new lands in zones of greater availability of conserved primary forest. This permits the continued application of the extensive agricultural strategy which allows fertility to be recovered and guarantees global stable levels of yield. As a result of this, growing sectors (43%) of the population of Naymlap (see Table 7) are increasing their relative risk of the disease by moving to regions of more intensive transmission, thus increasing the total population at risk.

Table 4.

Coffee Growing Strategy, Percentage, for Naymlap and Centro Sanibeni (1986)

<table>
<thead>
<tr>
<th></th>
<th>Naymlap</th>
<th>Centro Sanibeni</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Do not sow</td>
<td>5 (21.7)</td>
<td>1 (3.6)</td>
<td>6 (11.8)</td>
</tr>
<tr>
<td>Do not increase</td>
<td>12 (52.2)</td>
<td>8 (28.6)</td>
<td>20 (39.2)</td>
</tr>
<tr>
<td>Do increase</td>
<td>6 (26.1)</td>
<td>19 (67.8)</td>
<td>25 (49.0)</td>
</tr>
<tr>
<td></td>
<td>23 (100.0)</td>
<td>28 (100.0)</td>
<td>51 (100.0)</td>
</tr>
</tbody>
</table>

Source: Survey ISF. CIPA/OMS 1985-86

* The surface under annual crops plus the fallow areas previously sown with these crops represent 63% of the area dedicated to agricultural purposes (excluding pasture land).
Table 5.

Hectare Production of Coffee in Centro Sanibeni, 1986

<table>
<thead>
<tr>
<th></th>
<th>Naymlap</th>
<th>Centro Sanibeni</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kg/Ha</td>
<td>644.0</td>
<td>920.08</td>
</tr>
<tr>
<td>qq/Ha*</td>
<td>11.5</td>
<td>16.43</td>
</tr>
</tbody>
</table>

1 quintal (qq) = 56 Kg.

Table 6.

Distribution by Year of Areas Lying Fallow in Naymlap and Centro Sanibeni, 1986

<table>
<thead>
<tr>
<th>Years</th>
<th>Naymlap</th>
<th>Centro Sanibeni</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>#</td>
<td>%</td>
</tr>
<tr>
<td>1 - 2</td>
<td>9</td>
<td>(60)</td>
</tr>
<tr>
<td>1 - 5</td>
<td>5</td>
<td>(34)</td>
</tr>
<tr>
<td>7</td>
<td>1</td>
<td>(6)</td>
</tr>
<tr>
<td></td>
<td>15</td>
<td>(100)</td>
</tr>
</tbody>
</table>

Source: Survey ISF. CIPA/OMS, 1985-86

Table 7.

Location for Holding For Cases and Controls in Naymlap, 1986

<table>
<thead>
<tr>
<th></th>
<th>Cases</th>
<th>Controls</th>
<th>Totals</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>#</td>
<td>%</td>
<td>#</td>
</tr>
<tr>
<td>Only in Naymlap</td>
<td>8</td>
<td>(57)</td>
<td>19</td>
</tr>
<tr>
<td>In Naymlap and in zone of recent colonization</td>
<td>6</td>
<td>(43)</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>14</td>
<td>(100)</td>
<td>19</td>
</tr>
</tbody>
</table>

Source: Survey ISF. CIPA/OMS, 1985-86
Specific Determinants of an Agricultural System

It is necessary to define the factors which condition the prevalence of the different crop patterns, annual and permanent, and the different agricultural systems, irrigated or non-irrigated, in the high tropical forest. The global determinant underlying this general process would seem to be the prevalent nature of the market economy and specifically its manifestations within the agrarian sector of the Peruvian economy. With regard to crop patterns, there are some principal variables which cause colonists to opt predominantly or exclusively for one or the other alternative.

The fact that colonist families in the tropical zone reproduce their character as productive/consuming units, leads the majority of producers to grow both permanent and annual crops on their holdings, for sale, self-consumption, and to maintain relations of reciprocity with relatives who live in Andean regions.

In addition, the fluctuations in international markets for export crops, such as coffee, created uncertainty among agriculturalists. In this regard productive diversification enables the avoidance of danger and unbalance to the family economy of the colonists resulting from sudden changes in international prices. Crops such as rice and maize function as a reserve in the face of unmanageable economic cycles. Furthermore, the presence of the monopsony in coffee, among colonists of the high forest, limits profits for this product and thus encourages the cultivation of other crops.

Another factor is the increasing national urban demand since the 1960's for food products e.g., rice and agro-industrial products, such as hard yellow maize. This has caused the number of hectares under these crops to increase in the entire high forest region.

We should also mention that productive diversification by combining annual and permanent crops permits varied harvesting calendars which, in turn, generates cash income at different times and consequently makes capital permanently available. At the same time this makes speculative maneuvers viable, assuring a more rapid rhythm of capitalization among agriculturalists and traders.

The distance from rapid and efficient means of communication; roads, highways and navigable rivers, definitively excludes the option for certain crops, such as plantains for commercial purposes, and favours the choice of coffee.

Finally, the length of time of residence in the colonization zone is another variable also associated with the relative predominance of annual or permanent crops. This is partly due to the vegetative growth periods of some permanent crops like coffee.

We would suggest that the adoption of one or other agricultural system is determined by the relationship between two groups of variables: on the one hand, diverse cultural factors constituting the set of technological knowledge with the colonist brings to the colonization process;
and on the other the availability of resources such as capital, labor and land to the colonist. The first refers to the experience or technological culture of the colonist or Andean migrant. In general terms the technological culture of the colonists of Satipo, Chanchamayo and other high forest zones only includes rudimentary knowledge of "seasonal" irrigation, dependent on rainfall, which is applied in the Andean zones.

In association with this, the greater availability of unexploited land in the high forest in comparison with high Andean zones has originated a return by Andean migrants to non-extensive systems of soil use, with prolonged fallow periods, above all, in the initial phases of colonization. In general terms, this is similar to the phenomenon which occurred when European migrants to North America returned to more extensive agricultural practices in new colonization zones, employing fallow periods much longer than they had in their countries of origin, where land was much scarcer.

The other important group of determining factors in the agricultural system is constituted by the resources possessed by colonists on arrival and throughout their experience on the colonization front. Such is the case of the money capital initially available to the colonist (capital sum or that derived from a favourable credit policy).

Another principal limiting factor is the availability of land. This is related not only to demographic pressure on available areas but also, and more importantly, to the agricultural potential of soils, which depends on topography, the chemical composition of soils, altitude, temperature and rainfall in each region. Finally, manpower would seem to be the other determining factor as regards the intensification of the agricultural system employed (13), especially for systems employing rudimentary technology where manpower is the most important investment in the productive process.

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Graph 1.

Graphic distribution of Residence Time in Community

Controls

Cases

<table>
<thead>
<tr>
<th>Log of time of residence</th>
<th>Controls</th>
<th>Cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>11</td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>2</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>4</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>6</td>
<td>1</td>
<td>25</td>
</tr>
</tbody>
</table>

controls: 25 cases
Graph 2.

Graphic Distribution of Total Residence Time in Tropical Forest

Controls

Cases

\[
p = 0.0331
\]
Graph 3.
Distribution of Incidence by Ethnic Groups

GRAPH 4
Incidence of CL in the General Population as Related to Degree of Conservation of Primary Forest
GRAPH 5

Incidence by Age Groups According to Degree of Conservation of Primary Forest
MONTHLY DISTRIBUTION OF APPEARANCE OF NEW CASES OF LEISHMANIASIS IN PANGOA DISTRICT, 1985-86

GRAPH 6
APPENDIX 1

Hectare Production of Maize, Rice and Coffee in Jungle Areas, 1979

<table>
<thead>
<tr>
<th></th>
<th>MAIZE Kg/Ha</th>
<th>RICE Kg/Ha</th>
<th>COFFEE Kg/ha</th>
</tr>
</thead>
<tbody>
<tr>
<td>total jungle</td>
<td>1748</td>
<td>2815</td>
<td>690</td>
</tr>
<tr>
<td>with irrigation</td>
<td>2012</td>
<td>4475</td>
<td>741</td>
</tr>
<tr>
<td>dry regime</td>
<td>1744</td>
<td>1916</td>
<td>689</td>
</tr>
</tbody>
</table>

Source: VERDERA, 1984

Hectare Production of Coffee in Amazonas and Junin, 1979

<table>
<thead>
<tr>
<th></th>
<th>Amazonas</th>
<th>Junin</th>
</tr>
</thead>
<tbody>
<tr>
<td>With Irrigation</td>
<td>Kg/Ha: 1192</td>
<td>Kg/Ha: 823</td>
</tr>
<tr>
<td>Dry Regime</td>
<td>Kg/Ha: 823</td>
<td>Kg/Ha: 14.7</td>
</tr>
<tr>
<td>qq/Ha*</td>
<td>21.3</td>
<td>14.7</td>
</tr>
</tbody>
</table>

Source: VERDERA, 1984 * 1 quintal (qq) = 56 kg.

APPENDIX 2

General Characteristics of soil use, for Naymlap and Centro Sanibeni (1986)

<table>
<thead>
<tr>
<th></th>
<th>Naymlap</th>
<th>Centro Sanibeni</th>
<th>Significance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intensity of soil use</td>
<td>0.72</td>
<td>0.76</td>
<td>0.45</td>
</tr>
<tr>
<td>Rhythm of increase (h. per year)</td>
<td>2.48</td>
<td>1.87</td>
<td>0.22</td>
</tr>
<tr>
<td>Agricultural use of soil</td>
<td>0.49</td>
<td>0.28</td>
<td>0.001</td>
</tr>
<tr>
<td>Area lying fallow/area with annual crops</td>
<td>1.26</td>
<td>2.13</td>
<td>0.15</td>
</tr>
<tr>
<td>Cleared Area</td>
<td>70.5</td>
<td>37.45</td>
<td>0.00</td>
</tr>
</tbody>
</table>

Source: Survey Health Project. CIPA/OMS, 1986.
### APPENDIX 3

**General Characteristics of the Average Holding for Naymlap and Centro Sanibeni (1986)**

<table>
<thead>
<tr>
<th></th>
<th>Naymlap (hectares)</th>
<th>Centro Sanibeni (hectares)</th>
<th>Significance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total Area</td>
<td>19.09</td>
<td>34.02</td>
<td>0.002</td>
</tr>
<tr>
<td>Area of Primary forest</td>
<td>8.5</td>
<td>23.69</td>
<td>0.01</td>
</tr>
<tr>
<td>Area of Purma</td>
<td>3.38</td>
<td>3.8</td>
<td>0.73</td>
</tr>
<tr>
<td>Area of Agricultural Surface</td>
<td>7.2</td>
<td>6.84</td>
<td></td>
</tr>
<tr>
<td>Area with Annual Crops</td>
<td>3.03</td>
<td>1.48</td>
<td>0.000</td>
</tr>
<tr>
<td>maize</td>
<td>0.88</td>
<td>0.5</td>
<td>0.025</td>
</tr>
<tr>
<td>plantain</td>
<td>1.27</td>
<td>0.6</td>
<td>0.018</td>
</tr>
<tr>
<td>yucca</td>
<td>0.23</td>
<td>0.36</td>
<td>0.037</td>
</tr>
<tr>
<td>rice</td>
<td>0.65</td>
<td>0.02</td>
<td>0.00</td>
</tr>
<tr>
<td>Area with permanent crops</td>
<td>3.75</td>
<td>3.29</td>
<td>0.32</td>
</tr>
<tr>
<td>coffee</td>
<td>2.03</td>
<td>3.24</td>
<td>0.041</td>
</tr>
<tr>
<td>cacao</td>
<td>1.71</td>
<td>0.05</td>
<td>0.00</td>
</tr>
<tr>
<td>Area with pasture</td>
<td>0.45</td>
<td>2.05</td>
<td>0.0007</td>
</tr>
</tbody>
</table>

Source: Survey ISF. CIPA/OMS 1985-1986
MATHIMATICAL MODELS AND THE EPIDEMIOLOGY OF LEISHMANIASIS

Miguel Campos

INTRODUCTION

Despite the seductive potential of these tools, mathematical models, in general, have had a limited use in the study of epidemiology. This presentation is an effort to make the case for continuing research in the development of adequate models of Leishmaniasis, as a complement to epidemiological work.

BASIC CONCEPTS

A mathematical model, in epidemiology, can be defined as a set of mathematical equations representing the epidemiology of a health problem.

The epidemiology of a health problem can be seen as composed of:

1. a structure with the different states a human being can have regarding the health problem, and the feasible transitions between states:

2. a description of the distribution of the problem in space, time and person; and

3. an analysis of the causal mechanisms driving the transitions between states.

A health problem is any defined condition affecting human beings and deserving a solution. This definition encompasses the concepts of disease, illness, physiological status, abnormal test results, and psychosocial disturbances.

A health problem, being an abstract concept in as much as is related to the real world, can be composed of a set of health problems inside it. This reversiveness will be very important in the epidemiological analysis.

The restricted definition of an epidemiological model given above excludes purely conceptual causal webs, statistical fits, algorithms, economic models, operational research models and the information system models applied to health problems. Epidemiological models, in this regard, are closer to algebras and formal theories than to systems of equations.

Within the frame of an epidemiological model, the process promoting the transition of human beings towards undesirable states is called propagation. The concept of control can be described as the (artificial) process of maintaining the minimum amount of human being time within undesirable states, optimizing the resources available.
The definitions given here are extensions and integration of the published definitions of problem, epidemiology and model.

USES OF A MODEL

Potential applications of epidemiological models in control can be discussed at both general and specific levels.

On a general level, models can provide the health manager with an integrated frame within which it is possible to zoom in to understand a specific aspect. The "health manager" many times is a team, rather than a single person. Models can help to provide a closer integration for the team, by giving a common language and a place to see where the particular interests of each member fit into the general objective. On a specific level, models can provide a help in designing measurement and intervention actions, by identifying the targets likely to be more productive, and those which are likely to waste efforts.

Apart from these direct effects, models are also helpful for supporting the general health system, mainly through teaching simulations.

These uses have been shown for malaria, measles, and ascariasis, and leishmaniasis has also been studied.

Any activity in public health requires some sort of conceptual model. Some of the models used are incredibly complex when expressed in formal terms. Mathematics provide only a formal symbolic representation; of those models and a set of pre-tested tools for handling the models. Thus, some degree of modelling (i.e. hypothesis building) is necessary, and it is likely that there is some expression of the same models in mathematical terms.

The by-products of the modelling process (most of which were excluded from the restricted definition in the previous section) are as important as the main products. Modelling can also be a by-product of other design activities.

MODELLING TOOLS

There are four approaches that can be used simultaneously.

- compartmental models
- deterministic models
- stochastic models
- multivariate models

To support the modelling process there are a number of techniques which are listed here in the appropriate order in which they are used.

1. Abstraction and decomposition
2. Modular development
3. Stability analysis
4. Sensitivity analysis
5. Validation
6. Optimization
7. Simulation

Modelling is not a routine activity; it requires a mix of science and art whose product, the model hopefully becomes a useful tool.

CHALLENGES OF MODELLING LEISHMANIASIS

Leishmaniasis is one of the more complex diseases whose epidemiology is not fully understood. Its structure involves the following transitions:

- exposure
- inoculation
- infection
- disease
- sequelae
- recovery

Factors involved range from the immunology and molecular biology to the sociology and ecology of the disease. All of them are important and difficult to exclude from models.

There are various characteristics of leishmaniasis which pose important problems for modelling efforts.

- leishmaniasis has many compartments, introducing the "cure of dimensionality"
- it is an heterogeneous disease inside any given country
- focality of parasite populations has been long recognized, introducing an element of aggregation
- almost all states in the epidemiology cover a spectrum of damage and duration which will affect the sensitivity analysis
- human populations have demographic patterns, notably migration, that can not be ignored
- measurement limitations provide very sketchy figures for even the simplest of the rates involved
- causal webs are almost unknown regarding social factors, which are determinates of incidence and recovery
- effectiveness of available interventions has not been adequately quantified, neither their cost nor feasibility have been measured
- in order to optimize decision-making, models should allow for conflicting interests

While at this stage models cannot yet provide a breakthrough in control, they reflect with a high degree of concreteness, the state of our knowledge regarding our objectives, whether they are directed toward control or something else.
COST OF MODELLING

Modelling often is seen as too costly or expensive. However, it does not consume special materials, and the main equipment in use is the human brain (preferably a relaxed one, however well qualified). Costs can be distributed in:

1. Personnel (usually epidemiology/statistics/computing group)
   - modelers
   - supporting consultants and experts
2. Equipment and Support
   - computing
   - libraries
   - publication
   - management
3. Field Testing (controversial)

These costs can be very high, especially if one thinks that the product is anything but material. In developing countries it may seem a luxury to support modelling, until we realize that these resources are needed for many other purposes in control.

It seems sensible to allocate resources from epidemiological teams to attempt modelling, if the efforts are well motivated.

CONCLUDING REMARKS

1. Epidemiological modelling is an essential part of any public health activity. It cannot be dispensed with.

2. Epidemiological models can be developed with more mathematical depth, but this requires a specific allocation of relatively sophisticated environment to pursue this option.

3. Efforts to include modelling (in formal terms) in longitudinal research projects should be encouraged. Progress in modelling reflects progress in general understanding.
EPIDEMIOLOGICAL MODEL:
LEISHMANIASIS IN AMERICA

SUSCEPTIBLE  EXPOSED  INFECTED  AFFECTED  RECOVERED

Box  =  group  of  human  beings  
Arrow  =  flow  of  human  beings

Jun 82  
May 87

Box size  =  population
Arrow width  =  flow rate
Arrow length  =  flow time
ROLE OF NATIONAL DATA CENTERS AND OBLIGATORY REPORTING IN CONTROL PROGRAMS

H. Guerra

It is well recognized that leishmaniasis cases are grossly under-reported worldwide. In the Andean area, leishmaniasis is so prevalent that parents expect it to occur in their children as a childhood disease. In the jungle areas the reporting may be better, but perhaps only in the patients who are covered by insurance systems. Otherwise the patients will continue working until the disease is so advanced it becomes crippling or highly disfiguring.

The data that is obtained in many countries is not reliable enough for many decision-making issues, but it is referential in nature, and may help to signal geographic areas and particular times for more detailed exploration. Some of the serious defects in the reporting system are:

-- that diagnoses are made solely on clinical grounds, and often non-medical personnel (health promoters).

-- that cases are often attributed to the place where they are clinically attended, rather than where the infection was acquired.

-- that when a patient seeks medical attention at more than one medical facility, a single case may be reported at each place.

-- number of patients per month will be only remotely related to actual time of infection.

-- ages of patients may not be properly recorded.

-- where migration is a significant factor, interpretation may be considerably complicated.

Making leishmaniasis a notifiable disease may not initially change the situation of underreporting and poor quality of the data, but improvement is bound to occur in both quantity and quality of the information received by the Ministry. The reporting of all cases within a country, even if diagnosis is not absolutely certain, will result in an increase in the relative importance of the disease and influence the attitudes of the public and of health authorities. Primary health care schemes may even take advantage of leishmaniasis as a target disease, since it had high visibility.

The quality of information may be much better if efforts are concentrated in a few selected areas, by provision of more complete diagnostic and reporting tools. This is the concept of "sentinel areas" put forward by Dr. J. Leeuwenburg. It is possible that in some countries where official notification is not obligatory, a system patterned on this idea would be set up and data extrapolated for other areas. Research institutions and universities which do not have capabilities for nationwide coverage could contribute in such a system.
Computerization has arrived in many Ministries of Health and social security systems, and individuals are assigned unique self-generated identification numbers, nationwide. Data bases for certain diseases, including the leishmaniasis, could make use of this system for rapid retrieval and processing of information.

To be of value, information which is collected cannot just remain in the records without use being made of it. The minimal products usually provided by the Ministry of Health are tables giving the number of cases per year occurring in large political divisions. Analysis for better localization of the localities where active transmission is taking place may not be feasible from this information. Processing of the information will provide rates for certain endemic areas, but will be distorted by delays in reporting and migration.

Processing of the data by age groups in small areas is important. This type of information should then be disseminated back to the smallest reporting areas, so that this feedback stimulates improvement of the activities developed. In order for this stimulus to be effective, the data should be presented in easily interpretable form, as graphs rather than tables, so that all health workers can use the information in their areas of responsibility.
INTRODUCTION

Diagnostic methods have been applied at various levels of leishmaniasis control and research. Some methods which may be appropriate as research tools in a national institution are not necessarily appropriate in a rural setting. Too often, for example, new serological tests are evaluated in a series of clinically suspect patients of whom a high proportion have the disease under investigation. Because of the high prevalence in such a series, the test shows a high predictive value of a positive test result. However, when the same test is applied to a community, where the prevalence is lower than in a clinical series, the predictive value (of a positive test) drops dramatically, whilst sensitivity and specificity remain the same.

The main diagnostic methods relevant to the epidemiology of the leishmaniasis include those used for patient diagnosis and follow-up, community assessment (potential for transmission in susceptible age groups), for parasite characterization, and for vector and animal reservoir studies.

CLINICAL DIAGNOSIS AT CLINICAL LEVEL

At the most peripheral level the health care worker, or often the patient himself, makes a presumptive diagnosis on signs and symptoms alone. In many areas the people have their own word for leishmaniasis, be it cutaneous or visceral. In Kenya, for example, people differentiate spleen enlargement likely due to malaria from the more chronic and cumbersome splenomegaly associated with kala azar and different names are given to those conditions. A diagnostic method which is still used in remote areas is the formol gel test which serves as an elementary screening test for kala-azar and which is often a reason for referral from the basic health care services to a higher level in the district, where facilities for a parasitological diagnosis may be available. Parasite demonstration is done by aspiration, staining, and sometimes culturing, of the parasite from material obtained from the spleen, bone marrow, liver, lymph glands, blood (Buffy coat) or skin lesions.

For VL, HO{sup 1} et al. compared the relative merits of sternum, spleen and liver punctures as early as 1948. Best results were obtained from splenic aspirates. The three techniques were compared in 121 patients. In 329 patients spleen and sternum aspirates were compared, also with better results by splenic aspirate (98% and 86% positive smears respectively). The splenic aspirate technique has been modified in Kenya and is carried out by medical staff in charge of health centres. A useful method of grading parasite density has also been proposed following a logarithmic scale, e.g. grade 3 density in splenic aspirates equals 1-10 parasites per 10 oil-immersion fields (magn.1000x) and grade 2 equals 1-10 parasites per 100 fields.(2) The literature on splenic aspirate as a
diagnostic technique for VL has been extensively reviewed by Kager and Rees,\(^3\) and Kager et al.\(^4\), including their own experience in Kenya. Although the technique of splenic aspiration has been used in Kenya for community-wide investigations (Leeuwenburg unpublished), less invasive methods are more appropriate under field conditions. Demonstration of either the *Leishmania* antigen or antibodies is another option. Samples should be preferably from capillary blood, which can be collected by non-medical staff with some additional training.

Several tests for antibody detection in kala azar have been developed and refined in recent years, such as the IFAT (indirect fluorescent antibody test),\(^5\) the CFT (complement fixation test),\(^6\) the ELISA (enzyme-linked immunosorbent assay),\(^6\)-\(^11\) and the DAT (direct agglutination test).\(^12\)

Ideally, a test is needed that can be taken to the patient (and not vice versa). Such a test would require an antigen of excellent stability in warm-climate conditions. Small volumes of, preferably capillary, blood would be needed and indeed a card-test with a rapid reading would be preferable. Such a CAT (card agglutination test) exists for gambiense trypanosomiasis from which a reading is obtained in 5 minutes. Such a test for visceral leishmaniasis would be a great step forward, particularly for its application at most rural health facilities or even for use in community-based surveys as a first stage screening method. A dot-ELISA for VL is actually already available\(^13\); the test however needs peroxidase-conjugated anti-human antibody, substrate and the use of microtitre plates.

For cutaneous leishmaniasis, serology often gives equivocal results. However, the often pronounced cell-mediated immunity in the cutaneous disease complexes can be demonstrated by the leishmanin skin test (Montenegro test), or in a more sophisticated fashion by a lymphocyte transformation test which correlates well with the leishmanin skin test.

**DIAGNOSIS AT COMMUNITY LEVEL**

The leishmanin skin test still provides a valuable epidemiological tool. It indicates delayed-type hypersensitivity to the leishmanin antigen and may denote past exposure to flagellates. A skin test profile by age provides evidence for an endemic or epidemic situation, as has been illustrated in Kenya,\(^14\)-\(^18\) and Italy.\(^17\) An age-specific profile for anti-*Leishmania* antibodies can also be useful since subclinical infection may be common.\(^18\) In addition, age-specific incidence of disease (as opposed to infection) is very important to determine the most vulnerable age group and to provide information at which age immunity by vaccination (a not too distant prospect for CL) should be achieved.

A number of diagnostic tests have been, or are being, developed and field tested using a technique for demonstrating the *Leishmania* antigen. They include the application of monoclonal antibodies and KDNA (kinetoplast DNA) probes. These techniques have a great potential for rapid and early diagnosis. They will certainly find research application, and, if simplified, (e.g. non-radioactive probes) also field application.
Another advantage is that they can be sub-species specific which may be very important, particularly in the American leishmaniases, notably the *Leishmania braziliensis* complex.

The indirect demonstration of the parasite is patients by xenodiagnosis is being tried in PKADL and can be useful in situations where culturing parasites from direct aspirates proves difficult. Such a method is time useful for parasite recovery and preservation, as well as for diagnosis.

**PARASITE IDENTIFICATION AND CHARACTERIZATION**

Parasite characterization methods are particularly important where sympathy exists and, of course, these methods are vital for any institute maintaining a *Leishmania* bank. Isolation from a patient, a vector, or reservoir host is always difficult under field conditions, since culture media are readily contaminated or overgrowth may occur, e.g. with *Crithidia*. If culture is successful, cryopreservation in a well equipped laboratory is needed. Recently many improvements have been achieved, such as better culture media and more dependable cryopreservation. Currently, the most common method of parasite identification is by isoenzyme electrophoresis, using cellulose acetate or poly-acrylamide gels. There is no agreement on the minimum number of enzymes required in a given geographic area, though claims are being made that 4 or 5 enzymes will suffice. Most commonly, for zymodeme analysis, up to 14 enzymes are applied. Other methods for parasite identification are Kinetoplast (KDNA) analysis and the use of monoclonal antibodies. The clinical data related to the isolate and its geographic location also remain important, together with its behavior in experimental animals.

The epidemiological importance of proper parasite identification is obvious. It is important, for disease control also, to know whether a parasite causing a given disease in a certain area is identical to parasites found in a suspected vector or animal reservoir host. Proper identification also, has implications for future vaccination strategies. Clinically-similar cutaneous lesions may be caused by different sub-species, and even species, of *Leishmania*.

**VECTOR IDENTIFICATION**

Identification of sandfly vector species has traditionally been carried out by collection by various methods and subsequent identification based on external and internal features. Infected flies are determined by dissection and microscopic examination for the presence of *Leishmania*. Practical rapid assays suitable for the field are needed. Some techniques have a potential for future application. Again KDNA probes or monoclonal antibodies could be applied to detect the presence of *Leishmania* parasites in wild-caught sandflies. A test exists for *Drosophila* species which uses monoclonal antibodies against soluble yolk proteins. A similar test design could be useful; for example, in differentiating females of the *Synphlebotomus* complex in Kenya.
Such studies can be done with methods similar to those described for human epidemiology. This applies both to studies in the natural habitat and to studies in experimental animals. Serology is widely used in canine leishmaniasis, with immediate application for VL control programmes. Identification of host blood meals in sandflies is an important additional way to determine which mammals may be potential reservoir hosts of leishmaniasis. There is a large variety of blood meal identification techniques, such as the precipitin ring test, countercurrent immunoelectrophoresis, passive haemagglutination inhibition, complement fixation, ELISA, gel-immunoprecipitation and, more recently, application of monoclonal antibodies, polyclonal antibodies, refinement of ELISA, dot-blot assays and reverse passive agglutination. It is within the realm of possibility that for a given sandfly one could carry out 3 tests simultaneously, one for bloodmeal analysis, one for sandfly species identification, and one for parasite identification.

From the foregoing brief review, it is clear that there exists a large variety of methods possible and available, for use in studying the epidemiology of leishmaniases, for disease diagnosis, community diagnosis and vector or animal reservoir epidemiology. Methods differ greatly in level of sophistication. Some, which are appropriate (acceptable and applicable under the circumstances) in one situation, may not be appropriate in another. It is clear that a need exists to make tools for epidemiological assessment available for workers in endemic countries, not only as research tools, but in particular as methods useful for the peripheral health worker, or for the field zoologist and entomologist. Diagnostic tests should be taken to where the patient lives or where he seeks primary care. It is often undesirable to refer the patient to a distant reference laboratory or hospital, where sophisticated diagnostic facilities may exclusively be available, without any simpler technology being offered at the primary echelons.
REFERENCES

IDENTIFICATION OF RISK FACTORS ASSOCIATED WITH 
CUTANEOUS LEISHMANIASIS IN COSTA RICA

Julio C. Rojas, Rodrigo Zeledon,* Juan Murillo,* Andrea Urbina*

In Costa Rica, as in other parts of the world where leishmaniasis is 
endemic, most of the epidemiologic studies done so far have been descript­
tive, where the main objective has been to estimate its prevalence and 
its geographical distribution, its vectors with their feeding habits and 
their distribution. Analytic epidemiologic studies on tropical diseases 
are scarce, specially in leishmaniasis.

The statistics from the Dermatology Department of the Ministry of 
Health of Costa Rica showed an important increase in the number of cases 
of leishmaniasis in the last five years. This increase has been more 
evident in children in the age group 0 to 9 years. In 1983, 37% of the 
total reported cases were in this age group (Table 1).

In Costa Rica, L. h. panamensis has been isolated on three occasions: 
from two specimens of Lutzomyia ylephiletor and one from Lu. 
trapidoi.11,12 In Acosta, a rural county of Costa Rica, Lu. youngi 
constitutes 93% of the sandflies captured using human bait, 95% of those 
captured using C.D.C. light traps, 64% of those captured inside the 
houses, but only 4% of the sandflies captured in the trees. The sandfly 
density increases during the dry months of the year, December through 
May. In spite of the data that suggest that this species could be the 
main vector in this region, we have not been able to isolate the parasite 
from this species. In Table 2 we observe the species of sandflies 
captured in Acosta. The information above leads us to believe that the 
epidemiology of this disease has changed in certain parts of the country 
and we now refer to it as a "domiciliary transmission".

A case control study was designed to explore which housing charac­
teristics and environmental factors around the house may be associated 
with the transmission of cutaneous leishmaniasis (CL). A second 
objective of the study was to illustrate the value and feasibility of 
this kind of epidemiological study to better understand this disease and 
other tropical diseases as well.

MATERIALS AND METHODS.

Area of study

The study was done in Acosta, a rural county in the province of San 
José. Acosta is 30 km. south-east of the city of San José, the capital 
of Costa Rica with an area of 342 square kilometers, and is divided into 
five districts. The use of the land is primarily agricultural and the 
main crops are (in order of importance): coffee, sugar cane, citrus 
fruits, corn and black beans. The altitude of the region ranges from 700 
to 1100 meters. The relative humidity in the summer (dry season), which 

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lasts 4 months is extremely low and in the winter (rainy season), which lasts 8 months is 80% to 90%. The mean annual precipitation is 2500 mm. (Data from the National Institute of Meteorology). The region is classified as a humid tropical pre-mountainous forest, but the primary forest has been completely destroyed. The temperature is stable throughout year and it ranges from 18 to 28°C.

Population

The total population of the county is 16,591 (1981) and is evenly distributed throughout the five districts (with a mean of 3,318 inhabitants per district). The population is white, and consists mainly of small-scale farmers who own their land. This condition makes the population stable, and migration is negligible.

Study Population

The unit of study was the house. A total of 41 houses, scattered in 12 small villages, were studied, 18 of which were considered cases and 23 were controls. The age and sex distribution of the cases is illustrated in Table 3.

Case Selection

The health post in Acosta was visited (one day of each month on announced days) and patients with diagnosed leishmaniasis were treated. The rural health workers were in charge of referring any suspected cases of cutaneous leishmaniasis to the health post. Personal data was collected as well as the exact place of residence. Biopsies were obtained from the borders of the lesions to make the final diagnosis by direct smear and culture. The time frame for the selection of cases was from September of 1983 to December of 1984.

A house was considered a case if at least one of its members had the following characteristics:

1. Presence of clinical signs suggestive of CL (active ulcers).
2. A positive smear or culture.
3. The patient had resided at least two years in the house.

By selecting cases with active ulcers we had incident cases only, and tried to control for any time sequence bias. Since the cases were new, there would be a smaller chance that any changes had occurred in the condition of the house since the infection.

Selection of controls

The criteria for the selection of controls was geographical, only those houses within 100 m of the case-house could be considered as potential controls. At the same time, a house had to have a resident of similar age to that of the case (±3 years). Finally, the residents of the control-house were not infected. This was determined by the following criteria:
1. An interview.
2. The absence of scars that would suggest past infection.
3. A negative intradermal-reaction using the Montenegro test.

The antigen for this test was prepared from a well-studied strain of *Leishmania mexicana mexicana* (OCR) cultured in Senekjie medium with a concentration of 5 mg/N/ml. This antigen was also tested and standardized in our conditions. A result was considered negative if the induration was less than 5 mm.

**Methods**

For each house that was selected in the study, a questionnaire was filled out, and the possible variables related to transmission within the house were noted. Furthermore, peri-domestic characteristics, such as the type of vegetation, and the presence of domestic animals were noted.

**Analysis**

The frequency of each variable was calculated and the information was organized in 2x2 tables. The estimated odds ratios were calculated by hand calculator and the exact 95% confidence intervals were found, using the method described by Mehta et al. For this purpose an IBM computer model 4341 OS VS 1 was used. Stratified analysis was performed in six variables (Table 4) to control for confounders and also to identify effect modifiers. Finally the summary odds ratios were calculated.

**RESULTS**

Information was collected on 22 variables related to the house and its surroundings. From these, 19 2x2 tables were constructed. Three variables were discarded because of incomplete information. In Table 4 is found the estimated odds ratio for the variables that were found to be associated with the transmission of the disease.

An odds ratio equal to or greater than 2 was considered to be important in the risk of being infected with cutaneous leishmaniasis. Our analysis showed four variables in this category:

1. Large number of members per house (equal to or greater than 5).
2. Low illumination.
3. Houses on stilts.
4. The presence of domestic animals inside the house.

We also found three variables with an odds ratio less than one that could have a protective effect. The presence of these variables suggest a decreased risk of being infected with *Leishmania*. These variables were:

1. Presence of flat ceiling.
2. The proximity of the house to the road.
3. Presence of hen-houses in the proximity of the house.
The variables that presented an odds ratio less than 2 and greater than 1 (unimportant effect) were: duration of residence in the area, type of floor, type of walls, distance to a river, type of windows, number of window, distance to the mountains, type of vegetation around the house, distance from the house to the hen-house, number of chickens, duration of residing in the house and the age of the house.

DISCUSSION

All the variables with an odds ratio greater than 2 and less than, or equal to 0.5, (Table 4) have a reasonable biological explanation. These variables indicate an increase or decrease in the risk of a person having contact with the sandfly responsible for the transmission of the disease.

The variable, "number of persons by household", presented the highest odds ratio, 6.6 (95% CI 1.06-70.3) for the houses which had 5 or more members (high) versus those houses with fewer than 5 members (low). This odds ratio is easily explained, since when the number of members in the house is high, the contact rate between the vector and the host is also high. This may also suggest that, independent of the type of house, if there are more residents in a house, the possibility of any of these persons contacting an infected sandfly will be also greater. This variable then, is related to other characteristics of the house (exposure) and at the same time to the disease (outcome). In this instance, this variable is a confounder of all the other variables. A stratified analysis was done to compare the cases and the controls within narrow ranges of the confounding variable. This allowed evaluation and removal of the confounder and also evaluation and description of any effect modification.14

The variable "low illumination", presented an odds ratio of 2.7. This variable after stratification by number of members, changed to an odds ratio of 3.05 for a high number of members and to 1.32 for low number of members. This illustrates how the variable high number of members is modifying the magnitude of the effect of the variable low illumination. This also indicates that in those houses with a high number of members and with low illumination, the risk of getting the infection increases to 3 times, but in those houses with low number of members and low illumination intensity, it decreases to about 1. In spite of this, it was considered useful to calculate the summary measure to illustrate the overall effect of the variable. Its summary measure was 2.2 (95% CI 0.32-13.6). It is well known that the parts of the houses with low illumination are the preferred resting sites for the sandflies. Several Lu. youngi females, with recent blood meals, were captured resting underneath the crib of one of the babies (unpublished data). At the same time it was observed that some sandflies were biting inside of a poorly illuminated case-house early in the afternoon.

Houses built on stilts compared with those not built on stilts presented an odds ratio of 2.4. This variable, when stratified by number of members, presented an odds ratio of 2.6 for high number of members and 5.0 for low number of members. Even though there was considerable variation between the strata, they maintained the same direction. This is
explained by the effect modification of the variable number of members in the house. The summary measure for this variable was 3.2 (95% CI 0.64-18.9). The space that is formed by the stilts is used as a storage place for crops and other materials which attract rodents and domestic animals that feed on the crops and use the space for shelter. Sandflies were frequently captured in the location. Here the rodents could be a source of infection for the sandflies, which later migrate into the house through the spaces between the wooden floor to where they can bite and infect humans.

The last variable that presented an odds ratio greater than 1 was "presence of animals inside the houses". This variable had an odds ratio of 6.0. After stratification by number of members in the house, a summary measure odds ratio of 7.0 (95% CI 1.2-53.4) was found. The more domestic animals were allowed to stay inside the house, the more likely the vector will be attracted into the house.

The variable proximity of the house to the road, presented an odds ratio of 0.55 for distance less than or equal to 100 meters and 0.44 and 0.43 when stratified by the number of members in the house. The summary measure was 0.45 (95% CI 0.06-0.91). The houses near the road tended to be cleaner and have less vegetation than those further from the road. This probably makes it more difficult for the sandfly to get in the house. Other authors showed the attraction of the vector Phlebotomus papatasi in the Jordan Valley, to certain types of plants for feeding and shelter. At the same time it was shown how sugar-feeding habits influenced the behavior and distribution of the sandfly in the field. Although not demonstrated in this study, we suspect that coffee trees are a source of sugar and shelter for the sandflies in this region of Acosta. Our observations support this theory, since these insects have been observed resting on the reverse of leaves of coffee trees, which are very common in this region. The high plant density and the high density of adult sandflies in the summer, indicate that coffee may serve as a refuge as well as a means of getting to the houses.

The presence of hen-houses near the houses presented an odds ratio of 0.33 and, after stratification, presented odds ratio of 0.16 and 0.28 (small effect modification of number of members). The summary odds ratio was 0.16 (95% CI 0.01-0.91). This variable presented the highest protective effect against infection with leishmaniasis. There are two possible explanations for this phenomenon. Other authors have demonstrated that the sandfly Phlebotomus papatasi is attracted by poultry, and poultry blood significantly reduced the L. major infection in the vector. This could also happen in our situation. The other possibility is that the poultry may act as a decoy, and the sandflies do not infest the houses as much. It has not yet been determined if the suspected vector Lu. youngi is attracted to poultry.

The variable, "presence of a flat ceiling", also was a protective factor, with a summary odds ratio of 0.42 (95% CI 0.05-2.49). It is thought that the presence of a flat ceiling may deprive the sandflies of adequate resting space after a blood meal, as compared with absence of a flat ceiling. Therefore, a flat ceiling may discourage the presence of the vector inside the house.
We are aware that many of these variables are correlated, and that at the same time respond to the socio-economic conditions of the families studied. The solution to this is to perform a multivariate analysis such as multiple regression to determine if associations observed in the crude and stratified analysis persist when multiple confounding variables are simultaneously controlled. Unfortunately, the sample size of the current data is not large enough to perform the necessary analyses.

The findings of this study are of practical importance and will lead us to design future studies and practical interventions that will have an impact on reducing the incidence of cutaneous leishmaniasis in Acosta and in Costa Rica in general. Finally, we strongly recommend the execution of this kind of epidemiological study in order to have a better understanding of the risk factors which influence the transmission of the disease.

REFERENCES
Table 1.
Cutaneous Leishmaniasis by Age in Costa Rica
Incident cases
Rates per 100,000 Persons - 1983

<table>
<thead>
<tr>
<th>Age (years)</th>
<th>Cases</th>
<th>Rate</th>
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<tbody>
<tr>
<td>0-9</td>
<td>851</td>
<td>137.9</td>
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<tr>
<td>10-19</td>
<td>649</td>
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<td>20-29</td>
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<td>50-59</td>
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<td>&gt; 60</td>
<td>134</td>
<td>96.6</td>
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<tr>
<td><strong>Total</strong></td>
<td>2,387</td>
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</table>

* Source: Department of Dermatology, Ministry of Health. Costa Rica

Table 2.
Anthropophilic Sandflies Captured in Acosta, San Jose
1984-1985

<table>
<thead>
<tr>
<th>Species</th>
<th>C.D.C. Light Trap</th>
<th>Endophilism</th>
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<tbody>
<tr>
<td>Lutzomyia youngi</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>L. shannoni</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>L. vlephiletor</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>L. sanguinaria</td>
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<td>+</td>
</tr>
<tr>
<td>L. ovallesi</td>
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<td>+</td>
</tr>
<tr>
<td>L. cruciata</td>
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<td>+</td>
</tr>
<tr>
<td>L. gomezii</td>
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<td>-</td>
</tr>
<tr>
<td>L. evansi</td>
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<td>-</td>
</tr>
<tr>
<td>L. trapidoi</td>
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<td>-</td>
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<tr>
<td>L. rosabali</td>
<td>-</td>
<td>+</td>
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<tr>
<td>L. odax</td>
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</tr>
<tr>
<td>L. serrana</td>
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<td>+</td>
</tr>
<tr>
<td>L. verspertilionis</td>
<td>-</td>
<td>+</td>
</tr>
<tr>
<td>L. pilosa</td>
<td>-</td>
<td>+</td>
</tr>
</tbody>
</table>
Table 3.
Age and Sex Distribution of Cutaneous Leishmaniasis Cases in Acosta, Costa Rica in 15 month period

<table>
<thead>
<tr>
<th>Age (years)</th>
<th>Male</th>
<th>Female</th>
<th>Total</th>
<th>% of Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>0-5</td>
<td>3</td>
<td>2</td>
<td>5</td>
<td>24</td>
</tr>
<tr>
<td>6-10</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>14</td>
</tr>
<tr>
<td>11-15</td>
<td>1</td>
<td>3</td>
<td>4</td>
<td>19</td>
</tr>
<tr>
<td>16-20</td>
<td>3</td>
<td>4</td>
<td>7</td>
<td>33</td>
</tr>
<tr>
<td>&gt; 20</td>
<td>2</td>
<td>-</td>
<td>2</td>
<td>10</td>
</tr>
<tr>
<td>Total</td>
<td>10</td>
<td>11</td>
<td>21*</td>
<td>100</td>
</tr>
</tbody>
</table>

* Total number of cases does not correspond to total number of house-cases, since two houses presented more than one case.

Table 4.
Odds Ratio Estimates for Seven Variables Associated with the Transmission of Cutaneous Leishmaniasis Acosta, Costa Rica - 1985

<table>
<thead>
<tr>
<th>Variable</th>
<th>Crude O.R</th>
<th>O.R. Stratified by High and Low # of Member by House (Exact 95% CI)</th>
<th>Summary</th>
</tr>
</thead>
<tbody>
<tr>
<td>High number of member/house</td>
<td>6.0</td>
<td>--</td>
<td>(1.06,70.3)</td>
</tr>
<tr>
<td>Low illumination</td>
<td>2.7</td>
<td>3.05 (1.32, 13.6)</td>
<td>2.2</td>
</tr>
<tr>
<td>Stilt-house construction</td>
<td>2.4</td>
<td>2.57 (5.0)</td>
<td>3.2</td>
</tr>
<tr>
<td>Animals kept inside house</td>
<td>6.4</td>
<td>8.1 (8.0)</td>
<td>7.0</td>
</tr>
<tr>
<td>Presence of flat ceiling</td>
<td>0.49</td>
<td>0.43 (0.42, 2.59)</td>
<td>0.49</td>
</tr>
<tr>
<td>House close to road (&lt;100m)</td>
<td>0.55</td>
<td>0.44 (0.43, 0.45)</td>
<td>0.55</td>
</tr>
<tr>
<td>Presence of hen-house</td>
<td>0.32</td>
<td>0.16 (0.28, 1.16)</td>
<td>0.32</td>
</tr>
</tbody>
</table>

Note: The table shows the odds ratio (O.R.) and its confidence interval (CI) for various variables associated with the transmission of cutaneous leishmaniasis in Acosta, Costa Rica in 1985. The summary column provides the confidence interval for the odds ratio.
IDENTIFICATION AND QUANTIFICATION OF RISK FACTORS ASSOCIATED WITH NEW WORLD CUTANEOUS LEISHMANIASIS

A. Llanos-Cuentas and M. Campos

INTRODUCTION

Descriptions of leishmaniasis in the New World go back to pre-Inca times. In 1586, Fray Rodrigo de Loayza referred the existence of a destructive disease affecting the nasal mucosa. He pointed out some factors that seemed associated with the disease, like occupation and geographical environment.

Since the leishmanial etiology was established in 1909 various Latin-American researchers have made excellent descriptions of the clinical and epidemiological characteristics of the disease in the different American countries. Those descriptions also quote some factors like age, sex, weather, altitude and occupation, all associated with a higher risk of acquiring the disease.

The first infected animal, a dog, was found by Pedroso in Brazil, and many others were later encountered in endemic foci.

Peruvian chronicles of the XVIII century suggest that leishmaniasis is transmitted by insects. Araujo was the first who demonstrated the transmission by sandflies. Important advances in the knowledge about vectors and reservoirs and their role in the epidemiology of leishmaniasis have been made. Despite these advances, no significant progress has been made in the determination of the real value (that is, their quantitation and their position in the causal web) of the risk factors, so as to permit the development of effective control measures. The limiting factor is likely to have been the complexity of the disease, in all its aspects, from biology to epidemiology. It is also important to recognize that, even now, most of the epidemiological studies on Leishmaniasis lack appropriate methodologies for specifically quantifying the risk factors.

This paper will attempt to summarize the known risk factors for Cutaneous Leishmaniasis in the New World, with special emphasis in the Peruvian experience.

THE DISEASE

New World Leishmaniasis (NWL) is a complex of clinical entities caused by a complex of Leishmania sub-species with various epidemiologic patterns in an heterogeneous distribution. The greater the variety of physical and geographical conditions, the greater the diversity of clinical and epidemiologic patterns.

All NWL forms are zoonoses (wild or domiciliated animals). Man acquires infection when entering the enzootic zones. To better understand the assessment of the epidemiology of leishmaniasis, it becomes
necessary to realize that, despite the wide distribution, it has focality (nidality), a hypothesis suggested by Pavlovsky and fully applicable to leishmaniasis in the USSR.\textsuperscript{28}

The tegumentary forms, Cutaneous Leishmaniasis (CL), Muco-cutaneous Leishmaniasis (MCL) and Diffuse Cutaneous Leishmaniasis (DCL) constitute the majority of cases of NWL.\textsuperscript{110} The clinical features are similar to those of Old World cutaneous leishmaniasis but the lesions tend to be more severe and chronic. Visceral Leishmaniasis (VL) is distributed in various countries, but it constitutes a public health problem only in the states of Ceará and Bahia (Brazil).

Two clinical forms of leishmaniasis exist in Peru.\textsuperscript{21} Andean leishmaniasis ("Uta") is classically described in the Western Andean and Interandean Valleys. This form is mainly cutaneous, with uncommon mucosal damage by contiguity and even more rarely by metastatic spread.\textsuperscript{122} Amazonian jungle leishmaniasis ("Espundia"), described in jungle regions, produces metastatic mucosal damage more frequently.

The epidemiologic factors that determine the transmission of infection, the development of disease and its evolution, and the distribution of disease in populations are not known with any precision.\textsuperscript{110}

THE RISK FACTORS

The concept of risk factor is close to the concept of causative factor. The main difference lies in the role of the first as a practical variable to be used without the technical and epistemological rigour required for the second.

It is important, however, to notice that the ability of a property to serve as a risk factor, in the practical sense of the word, is affected by (i) the instruments of measurement available, and (ii) its role in the causative mechanism operant in the setting of interest. The ability of the researchers to incriminate a particular characteristic as a risk factor is affected by (a) the statistical design employed and (b) the sample size.

Most of the known risk factors have been identified on the basis of statistical association, and observed or estimated incidence rates.

Leishmaniasis is a complex disease. Human beings do not oscillate between just two stages (healthy and ill) but distribute themselves among a number of different stages from susceptibility to sequelae (Fig. 1). These relations are probably changing with time. Each transition between compartments has a corresponding causative mechanism with its own risk factors.

For the transition between susceptible and exposed, the following risk factors can be proposed:
- age
- sex
- job activity
- socio-economic group

It would seem logical to propose that these four factors are the main characteristics driving the probability that a healthy susceptible person living in an endemic area becomes exposed to the places where the infected vector bites. The specific weight of each factor varies with the epidemiologic pattern. Other factors can be shown to be associated with these four, such as house locality, altitude, income and education. All these factors are either "naturally" or "artificially" dependent on the human beings.

The specific weight of each factor varies with two parameters: (i) intensity of transmission in the focus (hyperendemic, mesoendemic, hypoendemic) and (ii) evolutionary stage (epidemic, persistent, sporadic).

Latin American literature regarding the occupation as a risk factor is extensive. The people with higher risks for contracting NWL are the ones having activity in (a) deforestation, involved either in agriculture (slash and burn), road building or new settlements, extractive activities, like timber, oil or gold, (b) collection of wood, chicle, wild rubber, palm nuts and palm hearts, (c) hunters, fishermen, explorers, public health workers, and (d) other persons with occupations that introduce them into a sylvatic cycle of leishmaniasis in forested areas or areas with scarce vegetation.

Age and sex are factors closely related to job activities. For example in Peru, in areas of jungle leishmaniasis, the patients are commonly 20-40 years old, this being the group that is engaged in forest or recollection activities. When the activity is farming in agricultural projects, both sexes are affected in similar proportions. In the Andes, where the activity is predominantly agricultural, with limited raising of sheep, goats or beef, almost all members of the family participate in these activities. Thus adults and children (since very early) have a similar exposure and the disease appears in the same proportion in both groups. Children under age 10 are most affected.

In some geographic regions altitude is also a risk factor. In Peru, Uta occurs between 900 and 3000 m above sea level, but incidence rates are higher between 1800 and 2400 m. In Venezuela, Scorza also found different incidence rates by altitude.

Bray points out to house location as a risk factor, in Ethiopia. The people whose houses located near to rock cliffs and rock falls had an incidence 25 times greater than the others. This is probably related to being in proximity to the habitat of hyraxes, known reservoirs of Leishmania. Loyola, in Bajo Calima, Colombia, found that infection rates were higher in houses located near the periphery. Netto in Tres Bracos, Bahia, Brazil, found that 85% of the cases had their houses located in areas with "mata atlantica". It is possible that house location is also a risk factor in Uta areas.
FIG. 1. RISK FACTORS ASSOCIATED WITH NEW WORLD LEISHMANIASIS
The great majority of persons who acquire leishmaniasis have a low socio-economic status. The motives for remaining in an endemic zone are mainly economic. In Peru, the persons who acquire sylvatic leishmaniasis come from economically deprived Andean areas; their knowledge about the jungle and their cultural level are deficient. These facts determine an inadequate forest management, producing excessive deforestation and promoting and increase in the risk of acquiring leishmaniasis (Calmet and Bartolini, 1986, personal communication). Only rarely professional or people with a high economic level become infected, generally in relation with an uncommon activity.

For the transition between exposed and infected, the following risk factors can be proposed:
- vector species
- reservoir
- parasite strain
- physical environment
  . narrowness of the valleys
  . temperature and humidity cycles

Here we have a close relationship between environmental and ecological factors and the existence of certain vectors and reservoirs.\(^{17,18,31,32}\)

The risk of infection will depend essentially on two factors (i) the infection probability of the sandflies (depending on the infective doses) and (ii) the host/parasite relationships. Variations in weather will also affect transmission.

The "man-biting density" (vector capacity) of a population of a phlebotomine vector is an important factor affecting transmission.\(^{18}\) Population densities, biting rate, anthropophilic habit (food preferences), natural infection and places of man-vector contacts are essential for the understanding of the epidemiological cycles and the development of control strategies.

Intrinsic characteristics of the vectors can also have importance in control. Specific factors related with phlebotomine sandflies are important.\(^{15-33}\) Specially relevant are the length of the mouth parts, particularly the labrum length, and the trophic sensilla, whose arrangement and shape resemble the trichiod sensilla of mosquitoes which have a fluid-flow detector function.

The ecological system in which the parasite population is maintained indefinitely may be regarded as the true reservoir of a Leishmania species. The experience accumulating over the past two decades suggests that each species is not, as commonly supposed, randomly distributed in a miscellanea of sandfly and mammalian hosts, but that there are natural barriers limiting certain leishmanias to certain sandfly/mammalian combinations.\(^{14}\)

No successful attempts at reservoir control are known in America. Since most Leishmania species are maintained by wild animals in natural foci of infection this type of measure is unlikely to result in success, with the exception of restricted ecological niches, like in the Western Andean and Interandean valleys in Andean leishmaniasis.
The incrimination of domestic animals in cutaneous NWL is arguable. The dog was indicated as the reservoir of *Leishmania peruviana* but recently Cruzado and Miranda (1982, 1986, personal communications) have found rats and small wild mammals infected. Possibly the dog should be considered only an incidental host.

The physical environment is closely related with the vector and reservoir populations. Although as a factor it is not directly vulnerable, it can serve as an indicator or maker for high risk zones. For example, in Peru, the Andean leishmaniasis, endemic in the Western Andean and Interandean valleys, seems to be a more important health problem in narrow and deep valleys, where contact between hosts and parasites occurs with higher probabilities than in open valleys, where transmission is less likely.

The seasonal variations in the transmission of leishmaniasis, related to the weather (temperature and humidity), are well known. Possibly the density of sandfly populations is affected by climatic variations. Each sandfly species has specific humidity requirements.

It has been proposed that accurate taxonomy of the parasites is of great practical importance since the expansion of information concerning the parasite and the disease is possible only when new facts can be related to organisms that have been adequately characterized and named. Improved taxonomic knowledge could be important in solving the problems which at the present impede the control or eradication of the various leishmaniases. Progress has been significant, but no direct application of this knowledge to control can be envisaged.

For the transition between infected and affected (ill) person, the following risk factors can be proposed:
- parasite strain
- human genome
- immune response
- ethnic group
- past experience

It is admitted that only an unknown proportion of persons exposed to the bite of sandflies, will develop cutaneous leishmaniasis. With apparently equal exposure risks, some inequality appears among the individuals. Various hypotheses have been proposed to explain this variability: (a) differences in parasite virulence (b) differences in the skin "permeability" to sandfly bites; (c) a variation in individual genetic susceptibility (d) an individual differential attraction for phlebotomine sandflies.

It is commonly accepted that some species and subspecies of *Leishmania* producing NWL are more virulent than others, as it happens with *L. b. braziliensis*. Their biological behavior in "in vitro" cultures and in animal models also vary.

The hypothesis on skin permeability to sandfly bite was evaluated by Esterre *et al.*, in French Guiana. Characteristics such as local sweat output, cutaneous pH, armpit temperature, skinfold thickness,
epidermal thickness, dermal thickness and sweat gland density were assessed. They do not show any significant difference between the patients and controls. The results indicated that none of the factors studies appeared decisive in transmission. Other factors related to human attractiveness to sandflies such as CO₂ emission, thermal emission, skin humidity and blood steroids, remain to be studies. Unfortunately, no data are available about the possible genetic control of susceptibility of humans to leishmanial infection; on the other hand, it seems clear that resistance to L. donovani and L. major is genetically determined in mice. 

It has been proposed that immune and genetic factors related to the host would be the ones regulating the susceptibility, clinical course and severity of the complications. No demonstration of this hypothesis in humans exist. The experiments with mice and L. major infection agree with this suggested behavior.

Recently Antunes et al., while assessing the protective effect of a Leishmania vaccine, observed that the real protective effect was apparent in the reactors to the skin test. If this event were a natural phenomenon, the risk for the people to develop disease would have to be related to the degree of reactivity. Similarly, past experience is a protective mechanism within the same area; there seems to be no cross protection between the different Leishmania species. We have observed that patients with a history of having had Uta (scar) may develop active Amazonian jungle leishmaniasis (Espundia) in the jungle.

The control of leishmaniasis in mammals appears to be determined primarily by cell-mediated immune mechanisms. There are many clinical responses in the human, from a subclinical infection to fatalities, and this has led some researchers to suggest it as a "spectrum disease", comparable to leprosy. The considerable amount of information obtained in the last few years on the immune responses in experimental animals has made IMMLEISH conclude that vaccination against cutaneous leishmaniasis in man is not only desirable, but feasible.

The role of malnutrition is not known in NWL. Hypothetically, if there is any effect, it would have an impact on Espundia cases. In visceral leishmaniasis a greater proportion of destructive facial lesions in people of African origin, as compared with the native population. Previous and later studies could not verify this observation. Some native groups living in endemic areas shared with Andean settlers show a lower incidence of jungle leishmaniasis. The recent studies of Calmet and Bartolini (1986, personal communication) suggest that this difference may be due to the way these two populations interact with the forest in their agricultural practice, the settlers exposing themselves more to transmission.

Risk factors were calculated for the development of metastatic mucosal damage after having had a primary cutaneous lesion. Extensive and multiple skin lesions above the belt seem to be associated
with a greater chance of mucosal lesions. Campos\textsuperscript{43} in an ongoing prospective case-control study finds the size of the primary skin lesion is the main risk factor. Other important risk factors are having old lesions not treated with specific medicines. An additional factor is the speed of growth of the primary skin lesion.

It should be also clear that some of these factors behave like "black boxes", in the sense that they contain inside them complex interrelationships which deserve further study.

The use of the risk factors briefly discussed above could be directed along the following lines:

- as starting points for elucidating internal mechanisms in operation in particular cases:
  - social factors determining exposure to leishmaniasis in the Peruvian Central Jungle
  - geographical factors in Andean leishmaniasis, Uta.
- as markers for populations at risk, to become the targets of control efforts:
  - social action to change agricultural habits and treatment of the forest in the Peruvian Central Jungle
  - control activities to be intensified by human populations in the Andean valleys.
- as targets for direct intervention, so as to interrupt disease propagation:
  - destruction of identified reservoirs near human households (as in the example of hyraxes in Ethiopia)
  - attack on specific vectors in well defined environments, for example to concentrate attack on vectors in the geographical areas and micro-environments near human households identified in the Andean valleys.

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THE IDENTIFICATION OF RISK FACTORS ASSOCIATED WITH THE TRANSMISSION OF NEW WORLD VISCERAL LEISHMANIASIS

Roberto Badaró

INTRODUCTION

*Leishmania* is an obligate intracellular parasite. It has been shown that even in clinically cured patients or animals it is possible to cultivate viable parasites. In as much as the *Leishmania* lives almost exclusively inside the macrophage, the persistence of the parasite is related to the inability of the killing mechanism of these cells to function against this parasite. Despite the fusion of lysosomes to the parasitophorous vacuoles, and in vitro demonstration of the leishmanicidal ability of the macrophage by toxic metabolites produced during the respiratory burst, it is possible that some in vivo situations impair the effectiveness of the killing. Among such factors, one should mention temperature, a decrease in myeloperoxidase content, and capacity for triggering the respiratory burst during the differentiation of monocytes to macrophages. It is also possible to envisage difference of susceptibility among diverse parasite isolates. The host plays an important role in developing the disease after being infected.

The epidemiology, clinical patterns, and risk factors for visceral leishmaniasis were prospectively studied in an endemic area of Brazil. The prevalence of disease was 3.1% for children <15 years of age, and the annual incidence was 4.3 cases per 1,000 children. The number of children with disease fluctuated yearly and seasonally, and distribution of the disease varied within the endemic area. Risk factors included young age (median, three years), and malnutrition before the onset of disease. Seventy-eight percent of cases occurred in children less than five years old. The median age of the study population was 7.5 years. It should be noted that only four cases of leishmaniasis occurred in persons >15 years of age in the study area during the period 1980-1984. A 33 year-old patient was diagnosed in 1982, and three persons (20, 30, and 35 years old) were diagnosed in 1984. One adult (age 20) had had visceral leishmaniasis diagnosed at the age of 12.

Because the majority of patients with leishmaniasis were less than five years of age, we examined the census data of the 10 children with leishmaniasis who were five to 15 years old to determine whether migration into Jacobina predisposed the children to developing disease. We found, quite to the contrary, that nine of these 10 patients had lived in the area since birth, and only one patient had recently moved to the area.

RELATION BETWEEN LEISHMANIASIS AND NUTRITION

The relation of visceral leishmaniasis to nutritional status, as determined by anthropometric measurements, was also analyzed. Because anthropometric evaluation of nutritional status is most reliable in young children, this association was done only on children eight years of age...
or younger. We obtained anthropometric data on children in the study from 1981 to 1983 and determined the percentage of children with significantly reduced weight for their age and height. Growth data were determined on the basis of growth-rate charts for children in similar settings. The data indicate that 56% (725) of all children were malnourished; 45% with first-degree malnutrition, and 10% and 1% with second and third-degree malnutrition, respectively. When analyzed by height for age, 28% were malnourished. It is recognized that leishmaniasis itself is a significant contributor to negative caloric and nutrient balance. We therefore examined our census record for the nutritional status of patients the year before the onset of leishmaniasis. Among 22 cases of leishmaniasis for which anthropometric data were available, two to 12 months before the onset of symptoms, 77% had at least first-degree malnutrition and 45% either second or third-degree malnutrition (p < .001 for individuals with only second or third-degree malnutrition compared with patients with the same malnutrition and visceral leishmaniasis.) This finding suggested that poor growth due to malnutrition, or to other factors, contributed significantly to the occurrence of leishmaniasis.

Children in the study community with a history of moderate-severe malnutrition are 8.68 times as likely to develop classic visceral leishmaniasis as children not suffering this degree of malnutrition. These finding suggest that pre-infection nutritional status may influence whether Leishmania infections remain subclinical or develop into the classics, fulminating form of the disease.

GEOGRAPHIC CLUSTERING OF CASES

Eight families in the area had two or more members with leishmaniasis (range, two to five). There was no correlation between the position of the child in the family and the occurrence of leishmaniasis. The location of the houses of patients with leishmaniasis was mapped to determine whether houses located near a potential phlebotomine breeding area (such as a shaded area, an area with standing water, or a cave) was related to the occurrence of disease. No correlations could be made. This result may be due to the considerable movement of children throughout all sections or to the ubiquitous presence of large numbers of sandflies.

Intestinal parasitism, recent migration into the area, and house location within the area did not influence the progression of infection to disease. Serological testing indicated the 7.5% of children were infected with Leishmania each year and that the ratio of disease to infection was 1:18.5 for the whole area and 1:6.5 for the section with the highest prevalence of disease. Early diagnosis the therapy altered clinical patterns of the disease.

ACKNOWLEDGEMENTS

We are indebted to the Bahia-Cornell program that supported this work (NIH Grant AI-16282).
All information in this report has been previously published and is available in the following references:

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IDENTIFICATION OF LEISHMANIA: CRITERIA AND STATE OF THE ART

Nancy G. Saravia

INTRODUCTION

Characterization methods serve two fundamental purposes: 1) The identification of Leishmania stocks with respect to type or reference strains, so that phylogenetic relationships, pathogenic potential, response to treatment, recurrence rate, geographic distribution, transmission ecology and epidemiologic patterns may be defined for the corresponding taxa; and 2) the recognition of factors responsible for, or markers associated with, virulence, vector selectivity, tissue distribution, temperature sensitivity, drug resistance, etc. While identification allows organisms to be grouped on the basis of apparent relatedness, characterization is more concerned with discerning biologically important traits or molecules.

Historically, the different clinical forms of leishmaniasis have been attributed to infection by epidemiologically distinguishable organisms. However, the pathogenic potential and disease spectra of Leishmania are now known to overlap. For example, visceral disease can be caused by L. tropica and L. mexicana amazonensis as well as by L. donovani. Likewise destructive mucosal disease, classically associated with infection by members of the L. braziliensis species complex, can result from infection by members of the L. tropica and L. mexicana complexes. Although the aforementioned examples may represent exceptional observations, the frequency and importance of what appear to be aberrant infections can only be ascertained through the consistent identification of Leishmania stocks from the gamut of clinical situations.

The pleomorphic nature of Leishmania renders taxonomic discrimination based on morphologic criteria both tedious and unreliable. However, morphometric criteria may prove to be of particular value in distinguishing developmental stages, such as infective promastigotes.

Biological behavior in experimental invertebrate vectors and vertebrate hosts have broadly corroborated taxonomic divisions established on the basis of geographic, epidemiologic, and clinical aspects of disease occurrence. Nevertheless, the time factor, the participation of host variables in the outcome of infection, and the shared behavior of taxa separable by other criteria qualify the utility of biological approaches to parasite identification. It should be noted however, that the full characterization of Leishmania ultimately depends upon the recognition of biological correlates of intrinsic markers and the establishment of appropriate biologic indices of pathogenicity.

METHODOLOGIES FOR IDENTIFICATION

The shortcomings of clinical, morphologic and biologic criteria in resolving the identity of Leishmania stocks have prompted the development of methods that focus on stable inheritable differences. These probe
both the genetic material of the nucleus and kinetoplast, and discrete gene products, for readily detectable and reproducible differences. One of the first methods to be explored, DNA buoyant density, is disproportionately expensive and technically demanding to be of practical use in parasite identification, since an analytical ultracentrifuge is the key instrument. Moreover, based on the few stocks examined, the resolving power of this approach was insufficient to consistently distinguish between *L. tropica* and/or *L. aethiopica* and *L. donovani* or among the *L. braziliensis* subspecies.\(^{(13)}\)

Isoenzyme electrophoresis has been particularly revealing as an identification tool for Old and New World *Leishmania*\(^{(14-18)}\) and is amenable to widespread use, including laboratories in endemic areas. Several genetic loci can be assessed and the resulting patterns of electrophoretic polymorphisms can be intuitively compared or subjected to numerical taxonomic analyses. Depending upon the enzyme panel and matrix employed, identification of *Leishmania* based on isoenzymes can be more of less complex, costly, and time consuming. We have found four enzymes (G6PDH, SOD, NH, and G6PD) to be useful in distinguishing *L. braziliensis* subspecies in Colombia and the region.\(^{(19)}\) Appropriate enzyme panels can be devised according to the regional species and intraspecies diversity and the intended application, i.e., identification of characterization.

Genetic engineering methodologies provide powerful alternative approaches to conventional identification and characterization methods. However, practical issues surrounding their routine applicability such as sensitivity, specificity, and affordable non-radioactive detection systems remain to be resolved. Nevertheless, the feasibility of in situ identification of *Leishmania* in tissue samples is now clearly evident.\(^{(20-22)}\) Technical refinements involving the exploitation of highly conserved regions of genomic (nuclear) DNA, in situ gene amplification (Cetus) and the possibility of targeting probes to ribosomal\(^{(23)}\) or other abundant forms of RNA promise further progress in the design of nucleic acid probes applicable to the rapid etiologic diagnosis of leishmaniasis and the simultaneous identification of the subspecies involved.

Monoclonal antibodies offer several advantages over all other currently available identification methods: simplicity, sensitivity, specificity, and cost (after the initial investment in a light or fluorescence microscope). Although some subspecies are not yet consistently defined by existing monoclonal panels\(^{(19)}\), the potential of the approach has been well documented.\(^{(24-30)}\) Additional reagents will have to be included\(^{(19)}\), either to detect uniform conserved subspecies-specific determinants, or to define other subspecies markers that can substantiate the identity of stocks unreactive with the subspecies-specific monoclonals developed and described by McMahon-Pratt and colleagues.\(^{(32)}\) Until more sensitive, non-radioactive nucleic acid probes become available, monoclonal antibodies offer the most cost-effective and technically simple approach to *Leishmania* identification. Constraints on the universal applicability of monoclonal antibodies are:

1. Lack of established reference panels or pool of monoclonal antibodies (tailored to regional needs).
2. The lack of a consensus on, and the interpretation of, inter- and intraspecific variation based on any of the widely used marker systems, i.e., isoenzymes, schizodeme analyses, and monoclonal antibody reactivity.

3. The adaptation of an immunoenzyme method for use with light microscopy; conjugated monoclonals may be used directly to achieve greater specificity and simplicity. Alternatively, a dot-blot assay might be developed that would eliminate the need for microscopy.

METHODOLOGIES FOR GENETIC CHARACTERIZATION

The need for characterization of stocks for purposes beyond routine identification quickly emerges as information on parasites and their corresponding hosts is accumulated. Thus, questions such as whether vector restriction occurs among phenotypically distinguishable members of a given taxon, the endogeneous or exogeneous origin of recurrent lesions, the ability to track the geographic or epidemiologic origin and extension of individual outbreaks require more highly resolving methodologies. DNA restriction mapping, based on the predictable and reproducible site specific cleavage of particular DNA sequences, has been applies to both kinetoplast\(^{32,33}\) and nuclear\(^{34}\) DNA of Leishmania. The accessibility, limited size, and rapidly evolving mini-circle component of kinetoplast DNA render this extrachromosomal DNA of particular utility; species-, subspecies-, and strain-specific patterns of fragments generated by a variety of restriction endonucleases permit different levels of discrimination applicable to the aforementioned questions.

Further insights may be gained by restriction analyses of nuclear DNA in combination with southern blot hybridization using cloned probes, as has been reported by Beverley and collaborators. The physical separation of chromosomes in pulse field gradient gels\(^{35-37}\) has also allowed genes to be mapped in situ by direct hybridization of probes containing the sequence coding for particular genes. These, and other, technical advances predict that genes responsible for any predetermined character will eventually be able to be localized, selectively screened for, and correlated with, other information on Leishmania strains, such as virulence, drug resistance or epidemiologic indicators.

Different problems require and benefit from distinct approaches. Methods that are most suitable for identification can also be employed in characterization. High resolution methods, in contrast, are generally not practical as methods of identification. However, new taxonomic markers are likely to derive from detailed characterization.
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Leishmaniasis is not a single disease entity, but rather a complex of disease syndromes caused by a variety of different members of the genus Leishmania. It is therefore extremely important that in any case of leishmaniasis the causative organism is identified. As the various leishmanias are not easily distinguishable one from another using simple morphological and clinical criteria, more sophisticated identification techniques have to be employed. These techniques almost always require more parasite material than can be directly obtained from either the vertebrate host or the sandfly vector, so *in vitro* cultivation techniques are usually employed to increase the available material.

Unfortunately we still lack a universal culture medium in which all leishmanial organism will grow and it is extremely difficult to predict whether or not a particular leishmania will grow in one medium or another. Indeed, there are some occasions where it proves impossible to isolate the organism from parasitologically positive cases of leishmaniasis. Despite these difficulties, considerable strides have been made in the field of Leishmania identification and characterization over the last 10 years; isoenzyme techniques and the more recently introduced monoclonal antibody and DNA hybridization technologies all having played major roles.

Before any realistic strategies to control an outbreak of leishmaniasis can be devised it is essential to know something of the epidemiology of the disease in the area. Which organism is causing disease in man, is there animal leishmaniasis in the area and if there is, is it caused by the same organism as the human disease? The same applies for leishmanial organisms found in potential vectors. This is where leishmaniasis reference centres can be of great help:

(i) they should be able to offer advice on the most suitable methods for parasite isolation and transportation;
(ii) to receive and cultivate the organisms;
(iii) compare the organisms with reference strains of *Leishmania*,
    (a) for identification and
    (b) detailed characterization;
(iv) to cryopreserve the organisms for future reference and for possible redistribution to other interested parties;
(v) to collate these data and integrate them into the overall picture of leishmaniasis in both local and global contexts.
PARASITE MODIFICATION IN RELATION TO VIRULENCE AND TRANSMISSION: IDENTIFICATION AND CHARACTERIZATION OF 'METACYCLIC' PROMASTIGOTES

David L. Sacks

INTRODUCTION

Leishmania species are known to multiply as intracellular amastigotes in macrophages of their vertebrate hosts and as extracellular promastigotes in the midgut of their sandfly vector. An equally elementary aspect of the developmental cycle of Leishmania parasites has only recently been investigated. This concerns the question of whether or not sandfly promastigotes differentiate into an infective stage. If there is an infective stage of Leishmania in invertebrates, it does not appear to have a readily distinguishable morphological identity, unlike other hemoflagellates. This paper briefly reviews the evidence demonstrating the existence of infective stage of metacyclic promastigotes, and describes the preliminary studies on the molecular characterization of these developmental stages.

DEMONSTRATION OF INFECTIVE STAGE PROMASTIGOTES

The first experimental evidence of transmission of leishmaniasis by the bite of sandflies was by Shortt et al.\(^1\) in 1931, who observed transmission of L. donovani to hamsters by the bite of Phlebotomus argentipes. The first transmission of leishmaniasis to man by sandflies was proven by Adler et al. in 1941.\(^2\) Both investigators believed that there is one particular form of promastigote in the sandfly which is adapted to life in the vertebrate. Morphological differences between dividing midgut forms and those found anteriorly have been described,\(^3\) but until recently there has been no evidence that these changes reflect development of promastigotes into an infective stage. By comparing directly the infectivity of promastigotes as they developed temporally within the fly, we have been able to demonstrate that promastigotes undergo sequential development from a noninfective to an infective stage during growth within the midgut.\(^4,5\) Clones of L. major and L. mexicana promastigotes that were recovered from midguts of P. papatasí and L. longipalpis, respectively, 3 days after fly infection were avirulent in BALB/c mice, whereas midgut promastigotes that were recovered on days 4-7 after infection were progressively more virulent. The generation of optimally infective parasite populations shortly after bloodmeal passage coincides with the time at which another meal is sought by the fly. The generation of infective promastigotes during, and indeed as a consequence of their early growth within the midgut, clearly means that they are infective prior to their invasion of the mouthparts. This means that the low numbers of highly characteristic forms found within the mouthparts are not necessarily required for transmission, and that if the more abundant parasites found posterior to the mouthparts can be regurgitated forward and deposited on the skin during feeding, then this would be a highly effective means of transmission since these populations will be comprised of infective stage promastigotes.
We and others have chosen to term this infective promastigote stage 'metacyclic' promastigotes, by analogy with the term used to devote the infective invertebrate stages of other hemoflagellates.

CHARACTERIZATION OF METACYCLIC PROMASTIGOTES

There is considerable evidence that identical developmental events accompany the growth of promastigotes within axenic culture. In early studies, investigators found a correlation between the age of *L. donovani* in culture and their infectivity for experimental animals. We found more recently that cloned promastigotes of *L. major* taken from logarithmic (log) phase cultures were unable to establish intracellular growth within mouse peritoneal macrophages *in vitro*, and they were relatively avirulent for normally susceptible BALB/c mice. As cultures approached the stationary phase, the virulent behavior of the promastigotes progressively increased, both *in vitro* and *in vivo*. The discovery of both noninfective and infective stages of *Leishmania* within cultured populations was an important step toward identifying those specific developmental changes that are associated with the ability of these parasites to adapt to and survive within the vertebrate host.

While the metacyclogenesis of *Leishmania* promastigotes is not accompanied by any obvious morphological change, we have been able to identify a biochemical surface marker for metacyclic promastigotes of *L. major*. These organisms fail to be agglutinated by the lectin peanut agglutinin (PNS) at concentrations which agglutinate all noninfective promastigotes. These results indicate that metacyclogenesis involves changes in surface carbohydrates, and the lectin can be used to both enumerate and purify metacyclic *L. major* promastigotes from culture. We have since determined that PNA binds to previously described *L. major* glycolipid, also referred to as excretory factor, or EF, which is the major surface and released glycoconjugate of these cells. The loss of PNA binding during growth appears to be due to a carbohydrate modification of the glycolipid which accompanies the differentiation of promastigotes into metacyclics. Thus, the *L. major* glycoconjugate is expressed in at least two developmental forms, and the expression and release of the metacyclic specific form of the molecule is consistently associated with the ability of promastigotes to initiate infection. We have found that one role which the modified form of the glycolipid might play in promoting intracellular survival is influencing the nature of the cellular receptors on the host macrophages which are used by the parasite to attach to and gain entrance into the cell. It will be of interest to determine whether the lipid containing glycoconjugates which are produced by other *Leishmania* species also display developmental polymorphisms, and whether these changes also influence the nature of the parasite-target cell interaction.

METACYCLOGENESIS AND LEISHMANIA VIRULENCE

The observation that promastigote populations are not necessarily uniform with respect to infectivity means not only that their heterogeneity must be taken into account in molecular and antigenic
studies, as has been just described, but also in comparative studies of *Leishmania* virulence. Differences in virulence between leishmanial promastigote strains and clones have been repeatedly described. These differences become difficult to interpret since until recently, metacyclic promastigotes could not be distinguished from noninfective stage and therefore, the size of the 'effective' inocula may not have been comparable. This point is clearly demonstrated in recent studies in which we have used the loss of agglutination with PNA as a phenotypic marker for metacyclic promastigotes of *L. major* in order to compare the degree to which metacyclogenesis occurred for different strains and clones during growth. We found that there was considerable variation in the efficiency of metacyclogenesis between different strains and clones, and even within the same clone when promastigotes propagated for different lengths of time in culture where compared. For example, a previously described virulent clone (10) generated 20-30% metacyclics during stationary growth, in contrast to a reportedly avirulent clone, (10) for which on closer examination we found metacyclogenesis to be extremely inefficient (less than 1%) and delayed until very late stationary cultures. Those metacyclics which could be recovered from these aging cultures were virulent for BALB/c mice. The loss of virulence associated with frequent subculture could also be attributed to a drastic diminution in metacyclogenesis potential over time, and a clone which yielded over 90% metacyclics during growth within its first passage, by the 100th passage generated fewer than 10% metacyclics during growth. Thus, metacyclogenesis does not appear to be stable for even cloned lines of *Leishmania* promastigotes, and virulence comparisons between different strains and clones can only be meaningful if the metacyclic populations contained within the respective inocula are determined.

REFERENCES

STUDIES AND CRITERIA FOR THE INCRIMINATION OF VECTORS AND RESERVOIR HOSTS OF THE LEISHMANIASES

R. Killick-Kendrick

INTRODUCTION

The control of leishmaniasis must be preceded by an analysis of the focus to identify the parasite(s), vector(s) and reservoir host(s). With data on the incidence of the disease in man and this minimal information, a judgement can be made of the feasibility and cost-effectiveness of control. If control depends upon attacking the vector(s) or reservoir host(s), information is needed on (a) their basic biology and (b) seasons of transmission.

In the present paper, criteria for the incrimination of vectors and reservoir hosts are given with notes on, and references to, the methods of study currently in use.

INCRIMINATION OF VECTORS OF LEISHMANIASIS

There is broad agreement on the information needed and the methods to study to incriminate vectors of arthropod-borne diseases. Different workers, however, may put a different emphasis or order on the steps it is necessary to take. In practice, the approach to leishmaniasis is determined mainly by operational limitations, such as the staff available and levels of training, equipment and transport, rather than by scientific judgement.

Barnett\(^1\) in 1961 listed the following criteria which, although drawn up as a guide to the incrimination of vectors of arboviruses, are equally relevant to the vectors of the leishmaniasis.

1. Demonstration that the suspected arthropod species feeds upon man or otherwise makes potentially effective contact with man under natural conditions.

2. Demonstration of a convincing biological association in time and space of the suspected arthropod species and the occurrence of clinical or subclinical infection in man.

3. Repeated demonstration that the suspected arthropod species, collected under natural conditions, harbors the completely identified infectious agent in the infective stage or state.

4. Demonstration of transmission of the completely identified infectious agent by the suspected arthropod species to suitable hosts under controlled conditions.

In a report on a workshop to consider the incrimination of vectors and reservoir host of the leishmaniasis, Killick-Kendrick and Ward\(^2\) in 1981 suggested grading the degree of certainty of the role of a vector in
ascending order of the difficulty of investigation. Their suggestions were not meant to "pigeon-hole" vectors but were given as a practical guide to the field worker. They proposed 5 grades, namely:

1. A sandfly which is anthropophilic and frequently bites man in the focus.

2. A sandfly with a distribution in accord with that of the disease in man.

3. A sandfly which, with certain qualifications, harbors the same parasite as the isolated from man.

4. A sandfly which is shown to support the flourishing development of the parasite found in man.

5. A sandfly which is shown to transmit the parasite found in man by biting a susceptible animal.

Neither the definitions of Barnett (1) nor Killick-Kendrick and Ward (2) are completely satisfactory. For example, the experimental transmission of leishmaniasis by the bite of a suspected vector is not only technically difficult, but may also give inconclusive results. Laboratory transmission by an undisputed vector is not always successful and, even when achieved, it does not necessarily mean that the sandfly is a vector in nature. Furthermore, the emphasis by Killick-Kendrick and Ward on the importance of infections in the proboscis of the sandfly needs modification in view of recent evidence that it is not essential for the mouthparts to be infected for successful transmission by bite. (3) Revised criteria for incrimination of a vector are given below, based on Barnett (1) and Killick-Kendrick and Ward (2).

Criterion 1. Feeding habits.

A vector must be anthropophilic and also feed on the reservoir host(s).

Methods of study. In practice, in spite of the risks, man-biting has usually been studied by catching sandflies at night as they come to feed on man. Alternatively, the bloodmeals of wild-caught sandflies can be identified by immunological methods (4). Knockdown catches in rooms where people sleep, using non-persistent insecticides, are useful with endophilic species of sandflies.

Observations to discover which anthropophilic sandflies feed on a reservoir host are usually made with animal baited traps. With small animals, workers in South and Central America have mainly used Disney traps which are metal or plastic trays smeared with castor oil on which the caged animal is placed. (5, 6) Flies attracted to the animal are caught on the tray. These traps have also been used in the Old World where the host preferences of P. perfiliewi and P. perniciosus were studied in Italy. (7, 8)
Tests with larger animals can be made with tent traps constructed from bed nets and fitted with a standard sized opening. Flies entering to feed on the animal rest inside the net are collected at dawn.

When a series of traps is set up, some may be in a more favorable position than others. Experiments must therefore be replicated with the bait animals being rotated from one trap location to another.

Bloodmeal analysis will reveal the families or genera of host animals. There are, however, practical difficulties in determining comparative preferences of many species of sandflies which may feed on a wide range of animals; the results may simply reflect the availability of different animals within flight range of collection places.

Comments. In suitable weather and at the right time of year, some proven vectors of leishmaniasis (e.g. Phlebotomus papatasi, P. ariasi, Lutzomyia longipalpis, Lu. umbratilis) may be highly abundant and come to bite man in large numbers. Others, however, (e.g. P. martini, Lu. flaviscutellata) sometimes appear to be so scarce or to bite man in such low numbers that it is difficult to understand how he ever becomes infected. In some foci, an assessment of the roles of the anthropophilic sandflies is obscured by wide variations in population sizes. Thus, in the Iraqi focus of visceral leishmaniasis between the Tigris and Euphrates, P. papatasi greatly outnumbers P. alexandri; but, a view supported by evidence that P. alexandri is almost certainly the vector of the same disease in the Xinjiang-Uygur Autonomous Region of China.

Criterion 2. Carrier of the parasite.

Strong evidence of the vectorial role of a sandfly is given by the repeated isolation from wild-caught sandflies of the same Leishmania as that found in patients.

Methods of study. Stocks of Leishmania are first isolated from patients and identified. Methods for identification include, inter alia, cultural characteristics, course of infection in laboratory animals, isoenzyme characterization, DNA hybridization and observations with monoclonal antibodies.

These observations are essential because parasites found in sandflies may be mammalian Leishmania which do not infect man, Sauroleishmania of lizards or a variety of other trypanosomatids of no medical importance. The preliminary work with isolates from patients gives the baseline against which parasites from sandflies must be compared.

The commonest current method identifying Leishmania and other trypanosomatids is by isoenzyme analysis which necessitates the isolation of the parasite in culture. For this, wild sandflies are best caught alive - from bait animals, by active searches or the use of CDC miniature light traps - rather than with sticky papers. The female flies are narcotized with CO₂, ether or chloroform and are washed in normal saline (0.85% w/v) containing a small trace of detergent. The gut is dissected out in culture medium, containing antibiotics, on a microscope slide under a dissecting microscope. Dissecting needles, slides and culture
media are sterilized before the dissection during which the fly and the gut are passed from drop to drop of medium to reduce risks of contamination.\(^{15}\) The terminalia are cut off and examined to identify the fly. (It may also be necessary to examine the head for this identification.) The dissected gut, free from all unnecessary parts, is transferred with a needle to a final drop of sterile culture medium. It is then examined with \(x\ 29\) and \(x\ 49\) phase-contrast objectives of a compound microscope and, if flagellates are seen, it is sown into culture medium with sterile precautions.

In spite of the expertise of a worker, in some conditions a greater or lesser proportion of cultures may be lost by contamination. With some sandflies, this may be because the guts are naturally infected by bacteria or yeasts\(^{16}\) or it may be because of technical failure. An alternative method of isolation to reduce this loss is to inject the parasites into laboratory animals (hamsters or BALB/c mice, depending on the parasite isolated from patients). Parasites are then cultured from the animals when the infections is apparent.

Neither of these methods is ideal. Both require experience and facilities which are not always available. Furthermore, the dissection of, perhaps, many hundreds of sandflies for a few isolates is labour intensive and time consuming: the culture from guts carries the risk of loss of isolates by contamination: inoculated animals not infrequently remain negative either because they are not susceptible to the Leishmania found or because the parasites were, perhaps, not Leishmania. There is a need for further development and refinement of methods of direct examination such as DNA hybridization or staining by tagged monoclonal antibodies so that parasites fund in sandflies can be identified in smears or squashes of infected guts on microscope slides or nitrocellulose sheets.

Comments. Failure to compare parasites from sandflies with stocks isolated from patients has led to poorly founded suggestions that several species of Sergentomyia in the Old World are vectors of leishmaniasis of man (e.g. \(^{17}\) S. arpakakensis; S. baghdadis; S. garnhami). At the moment, no species of Sergentomyia is a proven vector of mammalian Leishmania, although several species will commonly bite man. (The majority are lizard-feeders.). Similarly, the discovery of flagellates in P. papatasi in India has given rise to the suggestion that this species, as well as the proven vector, P. argentipes, may play a part in the transmission of kala azar. Simply seeing flagellates is, however, insufficient evidence to incriminate a sandfly as a vector of leishmaniasis.

If isolation of the parasite is impossible, a smear of the gut should be made and be stained with Leishman's of Giemsa's stain so that at least the morphology of the parasite can be seen. If epimastigotes are present the parasite is not Leishmania; if only promastigotes are seen, the parasite may be a Leishmania which may or may not be a parasite causing disease in man.

Killick-Kendrick and Ward\(^{2}\) in 1981 pointed out that the best time to find Leishmania in sandflies is when the highest proportion of the population is relatively old and has, therefore, taken one or more bloodmeals. This is generally as the population falls towards the end of
Another important point is that the discovery of a Leishmania in a sandfly with no blood in the midgut is more significant than in one with a partially digested bloodmeal. The reason is that a Leishmania may develop in the bloodmeal of a fly which is not a vector but be lost when the remnants of the meal are passed as faeces. Examples are L. donovani in P. mongolensis (Hindle, 1928) and L. infantum in P. sergenti.\(^\text{17}\)

Criterion 3. Distribution.

A vector has a distribution which agrees with that of the infection in man and reservoir host(s).

**Methods of study.** Inventories are made of the species of sandflies in a focus and the distribution of the different species is mapped and compared with the distribution of cases and infected reservoir hosts.

**Comment.** While the vector will obviously occur in places where there is transmission, the distribution of a vector is greater than that of the disease.

If the parasite causing the disease in man has been found commonly in an anthropophilic species of sandfly this time-consuming step may be considered unnecessary.

Criterion 4. Vector competence.

A vector will readily support the development of the parasite and will efficiently transmit it by bite.

**Methods of study.** A general picture of the development of a parasite will be gained by the examination of infected wild-caught specimens. Peripylarian species of Leishmania will be seen in the hindgut of the fly and elsewhere. In flies which are true vectors, both Peripylaria and Suprapylaria will give rise to massive infections of the stomodaeal valve.

If, however, no naturally infected sandflies can be found, an assessment of the ability of the species in a focus to support the growth of Leishmania can be made experimentally. Batches of wild-caught flies are fed on laboratory animals infected with strains isolated from man, or on naturally infected animals the parasites in which have been characterized and found to be the same as those in man. The flies are then tubed individually, fed on sucrose and maintained at the temperature of their habitat. Depending upon the combination of parasite and fly, and the temperature of incubation, the flies should be dissected and examined 4 - 10 days after the infecting feed. As they are dissected, they are identified by examination of the spermathecae and, if necessary, the cibarium and pharynx.

If infected flies can be induced to feed a second time, it is possible to attempt transmissions by bite to animals known to be susceptible to the parasite.
Comments. Flourishing infections in experimentally infected flies with migration of parasites to the stomodaeal valve, and even to the foregut and proboscis, show that the species is capable of supporting the development of the parasite. It does not, however, prove that the fly is necessarily a natural vector. Negative results, or infections which die out in the fly, are evidence of the inability of a fly to support the growth of the parasite and, therefore, that the species is not responsible for transmission. The equivocal results and difficulties of interpreting experimental transmissions by bite are discussed in the paragraph on incrimination, above.

INCRIMINATION OF RESERVOIR HOSTS

Bray gives 5 major characteristics of a "good" reservoir host of leishmaniasis (other than man himself), namely:

1. It will have a fairly constant contact with man via the vector.
2. It will be susceptible to infection.
3. It will continuously 'present' the parasite to the vector.
4. It will rest and breed in a place suitable for the vector to feed.
5. It will be a major blood source of the vector.

Investigations to incriminate reservoir hosts are not done necessarily in the order suggested by this list. Nevertheless, Bray's points are useful in defining the target animal.

Criterion 1. Carrier of parasite.

As with sandflies, strong evidence of the role of a wild or domestic animal as a reservoir of leishmaniasis is the repeated isolation of the same Leishmania as found in patients.

Methods of study. Representatives samples of wild animals are shot or trapped and examined for Leishmania. Rare infections probably represent 'dead ends' and are in animals which play no true part in the maintenance and circulation of the parasite. Clearly, to calculate the prevalence and, therefore, the significance of the findings, large samples of animals should be examined whenever possible. There are three methods. Firstly, stained smears or sections of skin, liver, spleen and bone marrow can be examined for the presence of amastigotes. The results may give some indication of a reservoir host but have the serious limitation that the parasites cannot be identified. This method can be recommended only when no facilities are available for the isolation of the parasites.

The second method is to culture the tissues and, if parasites are isolated, to compare them with Leishmania from patients (see paragraph on vector carriers).

Some parasites are difficult to culture and are more easily isolated by inoculating either hamsters or susceptible lines of laboratory mice with triturated tissues.
Bray suggests that a point prevalence of infection of 10% or more makes a "good" reservoir the major host of the disease.

As with the identification of parasites from sandflies, the requirement that Leishmania must be cultured for identification limits the number of animals which can be examined. Again, there is a need for the refinement of methods of identification such as DNA hybridization or monoclonal antibody tests so that parasites can be examined on smears on slides or nitrocellulose sheets without the need to culture. Although "non-target" leishmaniae might be missed, parasites identical to those isolated from man could readily be identified.

Repeated isolations from animals of parasites identified as the same as those in patients is enough evidence to incriminate that animal as a reservoir host. If, however, only few infections are found, or even none at all, some indications might be given by observing the susceptibility of suspect animals to the "target" Leishmania and the course of infection. Another approach is to study which species of animals are strongly attractive to the vector, if known.

In searching for infected animals, serological tests would be useful, particularly because infections may be totally inapparent. The IFAT followed by a clinical examination and, if isolates are required, lymph node puncture is performed under local anaesthetic.

Criterion 2. Contact with vector.

A reservoir host will be a major source of bloodmeals for the vector.

Method of study. Contact between the vector and domestic animals can be studied by catching sandflies coming to feed. With wild animals, baited traps are used. Additional information is obtained by collecting sandflies from animal holes or burrows by means of stick traps, electrically operated aspirators, or active searches.

Comments. Although bloodmeal analyses may be of some use, this method is limited by (a) the difficulty of collecting large numbers of engorged females of some species, (b) the limitations of current techniques to identify the species of animal on which a fly has fed and (c) the possibility that, by chance, few of the engorged flies may have fed on the reservoir animal immediately before the period of collection (e.g. Neotropical sandflies which transmit Leishmania of sloths).

Criterion 3. Presentation of parasite.

The course of infection in a reservoir host is such that the parasite is readily picked up by the vector.

Method of study. Female sandflies are fed on an animal with a natural infection and are then dissected 4 - 10 days later (see paragraph on vector competence). Alternatively, sandflies which are caught in a tent trap bated with a naturally infected animal are collected and later
dissected for infection. This second method is useful with sandflies which do not feed readily in the laboratory.

Comments. Observations on the "pick up" of parasites by sandflies were made by Gradoni et al., in studies on the role of Rattus rattus in the epidemiology of visceral leishmaniasis in Italy.\(^{16}\)

The proportion of a vector species which becomes infected after feeding on a reservoir host may vary according to the severity of the disease. Thus, Rioux et al.\(^{21}\) showed that the percentage of sandflies (P. ariasi) which became infected after feeding on leishmanial dogs (L. infantum) was directly related to the clinical condition of the dogs; those with severe disease infected higher proportions of flies than those with only mild signs.

SUMMARY

Vectors.

Essential observations to incriminate a species of sandfly as a vector of leishmaniasis of man are (a) the demonstration that the fly is anthropophilic and (b) the repeated isolation and identification of Leishmania from wild-caught sandflies showing that the fly carries a parasite identical to that isolated from patients in the same focus.

Supplementary observations which support the conclusions are: (a) the demonstration that the sandfly is attracted to, and commonly feeds on, the reservoir host(s), (b) a distribution of the sandfly which agrees with that of the parasite in man and in the reservoir host(s) and (c) confirmation that the fly supports the growth of the parasite and can transmit it by bite.

Reservoir hosts.

The essential observation to incriminate an animal as a reservoir host of leishmaniasis of man is the repeated isolation and identification of Leishmania from animals with natural infections showing that a high proportion are carrying a parasite identical to that isolated from patients in the same focus.

Supplementary observations which support the conclusions are (a) a demonstrable close association between reservoir host and vector and (b) a course of infection in the reservoir host which readily "presents" the parasite to the vector when a bloodmeal is taken.
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ANIMAL RESERVOIR SAMPLING METHODS IN LEISHMANIASIS SURVEILLANCE,
WITH SPECIAL REFERENCE TO LEISHMANIA BRAZILIENSIS (s.l.)

Bruno Travi

INTRODUCTION

Despite the complexity of the ecological factors involved in American tegumentary leishmaniasis, some fundamental concepts were established in the past decade\(^1\) which facilitate current epidemiological research with regard to the selection of the most probable animal reservoirs of the disease.

Surveillance of suspect reservoirs in the New World encompasses basically three Orders of mammals: Rodentia, Marsupialia, and Edentata. Within the latter groups several species have been incriminated in the transmission cycles of leishmaniasis (Table 1).

METHODS

Reservoir sampling methods include the techniques utilized for animal trapping as well as the procedures influenced to isolate the parasite from its tissues; both aspects will be considered herein.

While rodents represent the terrestrial component of the reservoirs, sloths are the strictly arboreal members of the transmission cycle. A third group is constituted by marsupials, which are characterized by their dual arboreal-terrestrial behavior. Since the majority if not all of the mammals involved in leishmaniasis transmission are crepuscular or nocturnal, traps need to be set up just before dusk and collected at dawn. Invariably, ants will invade the bait if traps are set too early, or even attack trapped specimens if they are not promptly removed in the morning. If diurnal mammals such as squirrels are considered of interest traps can be set during the day but need to be checked frequently, particularly in tropical climates. Weather conditions are also important and may have a strong influence on the trapping success. A heavy rain could easily wash the bait off or even activate the trap. This is particularly frequent in tropical forests where a good number of Leishmania surveys are carried out.

Trapping

When planning the time necessary to collect a pre-determined number of specimens for an epidemiological study, several considerations should be made, among them, calculating the trapping success (TS).\(^4\) The latter is given as the percentage of the traps that produce specimens per night. This figure is subjected to great variation according to the habitat, type of trap, and population densities. Unfortunately TS is generally lower in the tropics than in regions of temperate climate (in the latter, 10% is considered a reasonable TS), probably due to a greater availability of food.
Collection of mammals may be accomplished with a wide variety of home-made or commercial traps. The study of Leishmania reservoirs ideally requires live specimens from which "fresh" samples may be taken under appropriate conditions in a central or field laboratory. For this purpose, commercially available collapsible traps seem to yield the best results. For marsupials (Didelphis spp., Marmosa spp., Philander spp.) and rodents (Proechimys sp., Oryzomys sp.), different sizes of National-type traps are especially useful. These welded wire traps have either one or two doors and are activated by a bait pan in the center of the trap. Most rodents and marsupials will fall in a 30 x 16 x 16 cm trap, while small carnivores will need a 60 x 17 x 17 cm trap. Small species of rodents and marsupials may also be trapped in 23 x 9 x 9 cm Sherman-type traps, made of galvanized sheet iron or aluminum. A large number could be transported to the field if the folding variety is acquired. In our hands the National-type traps are more efficient than Sherman traps in collecting small and medium size mammals. In the former, visualization of the specimen facilitates handling and, if necessary, the trap can be used as a transport cage when adequately provided with food and water.

Edentates (sloths and anteaters) are trapped "by hand" after cutting branches of trees during the day or at night with the aid of a blinding flashlight to approach and capture the animal.

Seasonal food or substances entirely new to the animals are used as bait. Sweet meals attract rodents whereas insectivores are caught with small quantities of meat, fish or bacon. Most carnivores will be attracted to canned dog food or fish while herbivores require fruits or vegetables. Usually, natives of the area under study are familiar with the best baits to be used in each case, which are mainly composed of local fruits or small animals.

Selection of the trapping area depends upon the objective of the study. In an endemic focus of leishmaniasis, attention is drawn to those places where human activities overlap with the home range of suspect reservoirs. In new developing areas, sampling of primary undisturbed forests may have a predictive value, according to the density of suspect mammals and their infection rate. Distribution of traps in intensely modified ecotopes is usually accomplished in the peridomicile where most of the plantations (plantain, coffee, etc.) are intermingled with secondary forest. If possible, both primary and secondary forests should be evaluated simultaneously with respect to the potential to support transmission of leishmaniae to human populations.

Changes in the dynamics of transmission were observed by Arias, et al. in Amazonas state, Brazil, when comparing two areas of a forest reserve. The L. b. quyanensis infection rate of opossums was much lower in undisturbed forest than in the modified areas of the same reserve. This was attributed to the withdrawal of the primary hosts (sloths, anteaters) due to environmental changes.

Upon arrival at the laboratory, animals are sacrificed in accordance with the methods recommended by recognized institutions such as the
American Veterinary Medical Association.

Ether, chloroform, halothane, and other nonflammable inhalant anesthetics are recommended for medium and small size species. Barbituric acid derivatives (i.e., pentobarbital 60 mg/kg) are also acceptable. If euthanasia should be practiced in the field, gunshot, although esthetically unpleasant, is acceptable, when directed to the brain to produce immediate unconsciousness and death. Decompression to produce hypoxia, electrocution, or curariform drugs should be avoided because of their unreliability. Finally, application of microwave irradiation has been reported as a procedure for killing small rodents. The special device used in these cases inactivates the brain instantly and death occurs painlessly within 2-4 seconds.

Several years ago, when the first epidemiological studies on leishmaniasis were undertaken, the sampling of reservoirs was somewhat biassed by the concept that some clinical evidence of disease should exist. Herrer et al. observed a high rate (19%) of L. b. panamensis infection in Choloepus hoffmanni; all of them without lesions but with detectable parasites in the skin and viscera. Lainson and Strangways-Dixon in studying the reservoirs of L. m. mexicana noted that the infected rodents (Ototylomys phyllotis, Heteromys desmarestianus and Nyctomys sumichrasti) had inconspicuous lesions locate mainly on the base of the tail, and that the parasites were restricted to the skin. In the same way, infection was usually inapparent in Proechimys guyannensis infected with L. m. amazonensis. In the Republic of Panama only 7% of 230 sylvatic animals infected with dermatotrophic leishmaniae showed typical lesions. Consequently, a clear picture emerged that parasite detection in wild vertebrate hosts should be carried out not only from suspicious lesions but from normal appearing skin and viscera.

Culture of Parasites

Recovery of parasites from feral mammals and experimentally inoculated animals is currently accomplished through hamster inoculation and culture in acellular media. In our laboratory, as in many others, small samples of normal skin, usually from depilated areas such as snout, lips, ears and tail, as well as spleen and liver, are disinfected with PVP-Iodine and rinsed with sterile water. The samples are then introduced into vials containing sterile phosphate buffered saline (PBS) with the addition of antibiotics (Penicillin-Streptomycin, 250 U/ml -250 g/ml) and maintained for 24 hours at 8°C in the refrigerator. Triturates of the different tissues in small volumes (3 ml) of PBS are then seeded in Senekjie's medium and inoculated subcutaneously in the snout or hind foot of hamsters. Although with this procedure L. b. panamensis was isolated from Choloepus hoffmanni in our laboratory, subsequent studies failed to demonstrate Leishmania in more than 370 mammals of the Pacific Coast of Colombia. The focus of cutaneous leishmaniasis in this region (Tumaco, Nariño) is characterized by a high proportion of L. b. panamensis (>87%) compared with L. b. braziliensis (<12%) in the infected human population. As was mentioned before, trap setting was oriented to those places where man-mammal contact is frequent, mostly in modified secondary forest dedicated to agriculture. As judged by our entomological studies, transmission is taking place outside the domiciles, and as no primary forest is left, the source of parasites for the vectors should be confined to the described area. Rodents and
marsupials are abundant whereas Bradypus variegatus is not frequent, and C. hoffmanni is virtually absent. For this reason we tend to believe that the former mammals still should be regarded as the "first choice" candidates to screen, but applying a methodology in which other organs or tissues are studied.

In our laboratory we observed that subcutaneous inoculation of hamsters with $5 \times 10^6$ promastigotes of *L. b. panamensis* in the nose and hind foot resulted in local lymph node invasion as early as three days after infection. At this point in time, no parasites were recovered from distant lymph nodes, spleen, liver, or bone marrow, although 30 days post-infection, *Leishmania* were widely disseminated. Parasites were most frequently isolated from lymph nodes. Interestingly, bone marrow was comparable to spleen and liver in its frequency of infection.

In view of these results, we decided to include in our cultures and inocula to hamsters, samples of lymph nodes which drain the tissues exposed to the sandfly bites, as well as bone marrow aspirates. On the other hand, our failure to detect *L. b. panamensis* in the blood of infected hamsters from day 4 to 30 post-infection by hemocultures at 4 day intervals, made us believe that parasite isolation by this method is quite improbable.

Searching for other reasons to explain our inability to isolate leishmaniae from the mammals of the Pacific coast, we designed a short experiment to see up to what extent trituration of tissues could impair parasite growth. Senekjie's medium was simultaneously used in culture tubes, Petri dishes and in 96-well flat bottom microplates. Three-day old promastigotes of *L. b. panamensis* were suspended in triturates of hamster spleen, liver and snout, and 0.1 ml aliquots containing approximately 20 promastigotes were seeded in each of the different culture systems. Results after seven days of incubation at 27°C showed that the standard culture tubes were unable to support development, while the control inoculum (promastigotes + PBS) was positive. On the other hand, the Senekjie-Petri dish system yielded positive cultures with each of the triturates used. Microplate cultures were negative but in further experiments we observed that this was due to an excessive volume of inoculum. In fact, we were able to detect growth starting with 20 promastigotes suspended in 0.05 ml of liver and nose triturates. With the latter method it was suggested that spleen was the most inhibitory tissue used in these experiments. Interestingly, the Petri dish system without any liquid overlay was the most sensitive method in detecting a low number of parasites in the presence of tissue triturates. This method, though subjected to a higher risk of contamination, should be explored as a suitable culture system for field material.

An encouraging method to apply in reservoir sampling is that proposed by Monjour et al.\(^1\) in which tissues are homogenized and mixed after centrifugation with $2 \times 10^6$ sarcomatous cells (TG 180). This mixture is injected intraperitoneally into BALB/c mice and amastigotes readily multiply within 8 days of incubation. Parasites may be harvested from the ascitic fluid by aspiration and subsequently subcultured, or inoculated into other laboratory animals.
Trapping of suspected mammals in an endemic focus, followed by their experimental infection with Leishmaniae prevailing in that area, may yield useful information on parasite behavior. Identifying the most commonly infected tissues may save time and effort during the field studies, facilitating reservoir detection.

It is clear that an improved methodology in the sampling of Leishmania reservoirs will increase the knowledge of certain epidemiologic situations (i.e., L. b. panamensis in Columbia; L. b. braziliensis in Brazil), which is basic for the application of control measures.

It is believed that, in the American continents, reduction of the mammals involved in Leishmania transmission is difficult and ecologically unacceptable. Selective trapping of proven reservoirs may temporarily reduce the source of parasites for the sandfly vectors. However, under normal conditions repopulation of the area by other specimens will reinitiate the transmission cycle, due to the abundance of infected animals or to the existence of infected phlebotomines.

Probably a selective trapping of animals, together with rapid modification of the environment where agriculture is practiced, could decrease sandfly populations and reduce transmission below critical levels.

REFERENCES

### Table 1.
RESERVOIRS OF HUMAN TEGUMENTARY LEISHMANIASIS
IN THE NEW WORLD

<table>
<thead>
<tr>
<th>Parasite subspecies</th>
<th>Host</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>L. m. mexicana</td>
<td>Heteromyys desmarestianus, Myctomys sumichrasti</td>
<td>Lainson and Strangways-Dixon, 1962, 1964</td>
</tr>
<tr>
<td>L. m. amazonensis</td>
<td>Primary host: Proechimys guayanensis. Others: Oryzomys capito. Also includes other rodents, marsupials, and foxes</td>
<td>Lainson and Shaw, 1973</td>
</tr>
<tr>
<td>L. m. pifanoi</td>
<td>Heteromyys anomalus</td>
<td>Torrealba E, 1972</td>
</tr>
<tr>
<td>L. m. venezuelensis</td>
<td>Unknown</td>
<td></td>
</tr>
<tr>
<td>L. b. braziliensis</td>
<td>Primary reservoir: Unknown Suspected hosts: Choloepus didactylus, marsupials, Rattus sp., Oryzomys concolor</td>
<td>Lainson, 1983</td>
</tr>
<tr>
<td>L. b. panamensis</td>
<td>Primary host: Ch. hoffmanni Others: Bradypus griseus, Aotus trivirgatus, Saguinus geoffroyi</td>
<td>Herrer et al., 1969, 1973 Zeledon et al., 1975</td>
</tr>
<tr>
<td>L. b. guayanensis</td>
<td>Primary host: Ch. didactylus Others: Tamandua tetradactyla, Proechimys sp. Potos flavus, Didelphis marsupialis</td>
<td>Lainson et al., 1981b,c Le Pont et al., 1980 Gentile et al., 1980 Arias et al., 1981</td>
</tr>
<tr>
<td>L. b. peruviana</td>
<td>Suspected primary host: dog Others: Probably wild rodents</td>
<td>Herrer, 1951</td>
</tr>
</tbody>
</table>
TAXONOMIC CRITERIA AND NEW METHODS IN PHLEBOTOMINE IDENTIFICATION

David G. Young

INTRODUCTION

Taxonomic research on phlebotomine sandflies requires no justification when viewed in relation to epidemiological investigations of the leishmaniases. Because of their role as vectors, these insects are better known than the nonbiting psychodids in other subfamilies. Present knowledge of the diversity of sandfly taxa is based largely on the morphology of the adults, especially after 1926 when Adler and Theodor first pointed out the utility of the female spermathecae and cibaria as diagnostic characters. These and other structures have also provided a basis for grouping sandflies into supraspecific categories, the number and concepts of which vary according to author.

In the present paper, we are more concerned with the criteria and methods used in identifying species and subspecies of Phlebotominae. Examples are given for members of Phlebotomus and Lutzomyia, the two genera that contain proven vectors of leishmaniasis in the Old and New Worlds, respectively. More than 500 species have been described in these two categories.

TAXONOMIC CRITERIA

Species Definition

Following the biological species concept, a sandfly species may be defined as a "group of interbreeding natural populations that are reproductively isolated from any other such groups." It is necessary to apply one or more criteria to determine the taxonomic status of individuals in these populations.

Morphology And Coloration Of Sandflies

Classical taxonomy has relied heavily on adult morphology and, to a lesser extent, external coloration to distinguish extant and extinct phlebotomines. General taxonomic reviews of Phlebotomus and Lutzomyia illustrate the importance of these criteria. Nevertheless, slight or no discernible changes in the phenotype of an undetermined number of species occurred during speciation, and there is a broad spectrum of structural diversity among these insects, including vectors.

At one extreme, it is likely that different species exist that are morphologically indistinguishable in both sexes. Preliminary studies of two populations of P. ariasi in France indicate, for the first time, that such species pairs may occur in Phlebotominae. Differences in behavior, ecology, and physiology of individuals in sympatric populations provide clues suggesting that two or more distinct taxa are present.
There are reports of other sibling species or morphospecies in the subfamily that can be structurally distinguished with certainty in one sex or the other, usually the male. Examples among sympatric vectors include *Lu. wellcomei* and *Lu. complexa* in Brazil and *P. martini*, *P. vansomeranae* in Kenya.

Attempts to differentiate morphospecies by structure or other means begin with examining known individuals of each species from individual rearings in the laboratory or by obtaining wild caught specimens in localities where no more than one morphospecies exists. Close comparisons of this material may lead to previously overlooked structural differences such as the relative lengths of the antennal ascoiids, recently shown to be reliable for separating *P. papatasi* and *P. bergeroti* females. The use of detailed morphometric analysis was first applied to sandfly taxonomy by Lane & Ready who attempted to distinguish females of *Lu. wellcomei* and *Lu. complexa*. Not all females could be determined by these methods but their use should be expanded to include other species complexes.

New advances in rearing phlebotomines will no doubt aid these and other studies pertaining to the morphology and number of chromosomes. There is a paucity of data on cytogenetics of sandflies. Examination of the polytene chromosomes in the salivary glands of larvae and of brain cells (R. Kreutzer, unpub. data) has shown that the chromosome number varies according to species (e.g., 2N = 6 for *P. argentipes*, *P. colabensis*, *Lu. trapidoi*; 2N = 8 for *Lu. longipalpis*, *P. papatasi*; 2N = 10 for *P. perniciosus*).

The intensity and/or distribution of external pigmentation may vary interspecifically and can be used in species diagnosis. The discovery of dark specimens of "*Lu. carrerai*" in parts of Bolivia, Peru, and Brazil (J. Arias, pers. comm.) prompted other studies that confirmed the hypothesis that the dark individuals were not conspecific with that species. Further examination showed that the dark species, *Lu. yucumensis*, could be separated by slight, but consistent, structural differences. Coloration alone is used to distinguish males of *Lu. shawi* from those of *Lu. richardwardi* in Brazil and provides an easy way to distinguish one-spot and two-spot forms of *Lu. longipalpis* males, the status of which has not been resolved.

Variation in coloration or structure between individuals of allopatric populations, such as the one- or two-spot forms of *Lu. longipalpis* can be problematical when the differences are minor. Additional information from cross-breeding experiments, behavior, electrophoresis, and other studies may help shed light on the taxonomy of such forms.

Nomenclatural decisions regarding the status of these variants are somewhat subjective without additional knowledge. Some vectors such as *Lu. olmeca* in the neotropics are regarded as polytypic, with two or more named subspecies. In contrast, *P. langeroni* and *P. orientalis* and several species in the verrucarum group related to *Lu. townsendi* are treated as distinct species. The names used for these taxa, whether specific or subspecific, is not especially important from the
epidemiologic standpoint as long as the distinguishing features are unambiguous and the individuals can be correctly identified.

BIOCHEMICAL METHODS IN TAXONOMY

Enzyme Electrophoresis

Buth (19) reviewed electrophoresis data in relation to biosystematics in general, but the concepts and analysis apply to phlebotomine taxonomy as well. Enzyme electrophoresis for estimating genetic variation was first applied to insects (Drosophila) in the late 1960's (5) and to phlebotomines about a decade later. (22) Enzyme variants may be species-diagnostic and are therefore useful for detecting for distinguishing sibling species. For example, diagnostic enzyme profiles served to separate Lu. carrerai and Lu. yucumensis -- two morphologically similar species in Bolivia. (23) Ready & Silva (23), on the other hand, did not find enzyme variants (allozymes) that could distinguish Lu. wellcomei from Lu. complexa females in Brazil but only 11 enzyme systems could be successfully resolved. Intraspecific variation of some sandflies has also been investigated or revealed by electrophoretic data. (24-29) An increasing number of laboratories in endemic areas of leishmaniasis are using these methods to characterize Leishmania and it would take relatively little effort and expense to use the same methods for phlebotomines.

Cuticular Hydrocarbon Analysis (CHA)

Cuticular hydrocarbon analysis, introduced as a taxonomic tool for studying vectors in 1979 (30), has been used to distinguish adults of sibling phlebotomines in Brazil (31) and two populations of P. ariasi in France. (6) In the latter study, it was shown that the CH profiles of P. ariasi larvae differed from those of conspecific adults. Sandflies collected in the field can be stored dry at ambient temperatures until processed. (32) Moreover, the technique, unlike that of enzyme electrophoresis, does not destroy the insects so that voucher specimens can be saved for additional taxonomic studies.

DNA Probes

New technology in developing specific DNA probes for distinguishing organisms, including insects (33-35), has not yet been applied to phlebotomines. A probe for identifying females or males of the Anopheles gambiae complex is used routinely in one laboratory. (34) DNA, extracted from whole or parts of mosquitoes, provides sufficient material for assays. Preliminary data suggest that the probe is equally effective for immature stages as well. (34)

Computer Assisted Taxonomy

Analyzing data from taxonomic studies is efficiently accomplished with the aid of computer-based technology. It is possible to accurately measure the size and shape of insect structures with computers and electronic measuring equipment. (36) There are many statistical programs
available for microcomputers that are now available in most parts of the world. Furthermore, computer-aided identification programs are available ('37-41'), one of which allows the user to identify sandflies of French Guiana ('42). Such a program, when broadened geographically, would be an excellent method for training nonspecialists in sandfly identification.

CONCLUSIONS

The methods and criteria used in sandfly systematics continue to change as new information becomes available. The search for new taxonomic characters and new ways of analyzing known characters that distinguish taxa and show relationships among them, is an important continuing objective in biosystematics. Computer-aided taxonomy will no doubt play a more important role in the future but classical methods will not become obsolete.
REFERENCES

VECTOR SAMPLING METHODS AND LONGITUDINAL STUDIES IN LEISHMANIASIS SURVEILLANCE

J. E. Pérez R.

INTRODUCTION

The sampling methods used to collect the adults of the sandfly vectors of leishmaniasis (Diptera: Psychodidae: Phlebotominae) are almost the same as those commonly used for the nocturnal Diptera in general; the principles are the same, having been conditioned to the particular behavior of sandflies and the habitats to be sampled. Very specific data are now sought, and the strategy focuses on suspicious point moments or loci during long periods, and sampling methodology has been designed to investigate facts that are important in the transmission of the disease. The best trap, for example, can be successful for only a part of the species (or only one sex) occurring in one place. Therefore we must use a combination of 2 or 3 different sampling methods to obtain a greater and more representative global sample, with both quantity and diversity.

METHODS

A brief listing of the most commonly used sampling methods to capture sandflies is presented in the following table:

<table>
<thead>
<tr>
<th>Diurnal collection:</th>
<th>Search in resting places</th>
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<tr>
<td></td>
<td>Flight traps</td>
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<td></td>
<td>Man-biting collection</td>
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<table>
<thead>
<tr>
<th>Nocturnal collection:</th>
<th>With attractant (bait)</th>
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<tbody>
<tr>
<td></td>
<td>1. anthropophilic collections.</td>
</tr>
<tr>
<td></td>
<td>2. tent traps.</td>
</tr>
<tr>
<td></td>
<td>3. Disney trap.</td>
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<td></td>
<td>4. sticky traps.</td>
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<tr>
<td></td>
<td>5. CDC light traps.</td>
</tr>
<tr>
<td></td>
<td>Modified with UV light, white light.</td>
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<tr>
<td></td>
<td>6. Chemical: CDC light trap with CO₂</td>
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<tr>
<td></td>
<td>7. Plants as attractant in CDC light trap.</td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>Without attractant</th>
<th>1. flight traps.</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>2. sticky traps.</td>
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</table>

Search in Resting Sites

As sandflies have mainly nocturnal activity, they spend the day in places that can offer suitable conditions of temperature and relative humidity similar to those they prefer when they are active outside. These conditions are found in tree holes, caves, crevices, animal burrows, human bedrooms, etc. In Andean localities they also rest in
crevices in rocky fences ("pircas") built as nocturnal animal yards, and in chicken coops, which are made of adobe and always closed to avoid the entrance of predators. In tropical environments sandflies can be found in tree buttresses and manual aspirators are used to capture them. Sometimes the Damasceno trap is also used for tree buttresses but it is best used in animal burrows, covering the whole entrance.

Flight Traps

The purpose of these traps is to intercept the flight of the insects, that then climb by the central wall of the trap until they fall into the collector flasks. A very widely used model is the Malaise trap. This trap works very well in tropical forests. Successful diurnal collections were made in the South East Jungle of Peru (Pérez unpublished data) where some species of sandflies are active during the day because of the suitable microclimatic conditions provided by the permanent tree shadow. These traps are used for long periods, but primarily for fauna surveys, since in the large number of insects collected, sandflies represent only a small part.

Man Biting Collections

Man is often used as bait to attract the sandflies; this method is used everywhere, including the tropical areas and also at different levels above the ground in suitable tree platforms. As some sandflies have diurnal activity, these collections are also made during the day in localities with the conditions for their activity, as in the primary tropical forests and large caves.

Tent Traps

These traps are in the form of a tent, made with white cloth or fine mesh. A very popular trap is the Shannon trap that has no floor, and is suspended at 30 cm or less from the ground; the size of the trap should permit two persons to work inside. If an animal is to be used as a bait, it is placed inside. For anthropophilic collections, the human bait may use a fine mesh protection to avoid sandfly bites, while another person collects the insects attracted and within the trap with manual aspirators. A minimum use of flashlights is recommended to avoid the light attraction of the sandflies.

Light Traps

The type of trap most used to capture sandflies is the CDC model that uses yellow light; the insects attracted to the trap are suctioned by a fan into a fine mesh bag where they cannot escape. This trap is used within the tropical forest at different levels from the ground, but not in open areas. In Andean places where the lower vegetation permits the wind to disperse the sandflies, successful attempts using light traps have been made in protected spots.

Other kinds of lights (lightsticks) are also used to test the specific light attraction preferences of sandflies. Ultraviolet light also gives good results in the tropics.
Disney Traps

This trap consists of a tray with castor oil and a caged animal as bait in the center. Different small animals are used to determine the feeding preferences of the sandflies. These traps are very useful in the tropics although they need a protection against the rain.\(^{(12,13)}\) Specific collections can be made using a particular bait. The same principle, but in the forest floor and with a static system, was assayed in Panama with oiled trays in front and separated thirty centimeters under the animal cages.\(^{(14)}\)

Sticky Traps

These traps consist of square pieces of paper or plastic film coated with castor oil and fastened to a structure to avoid folding. The combination with light gives the best results for collecting sandflies\(^{(15,16)}\). The two types are used indoors and outdoors and in resting places such as caves (always in dry areas), operating all night, but they are not convenient in the tropical forest. In Andean regions transparent plastics are conveniently used in open windows to investigate penetration into houses during the night. (Pérez, unpublished)

Plants as Attractants

Experiments replacing the bulbs from CDC light traps with plant branches were reported by Schlein and Yuval\(^{(17)}\) to test the preferences of Phlebotomus papatasi. These preferred plants can be the source of sugar meals, and repellent principles can be sought among non-attracting plants.

Chemical Attractant

Carbon dioxide in the form of dry ice is added to the light traps, thus combining two insect attractants\(^{(18)}\). Collections were made in Panama with a slow liberation system for the CO\(_2\). More females were captured, while there were no great specific differences with other methods. This method is used only for surveying fauna in places not disturbed by wind.

LONGITUDINAL STUDIES IN LEISHMANIASIS SURVEILLANCE

In respect to vectors, this type of study attempts to detect factors affecting high incidences of leishmaniasis through the study of the events which determine this situation. Complete studies must cover all these events as much as is possible. The following points must be considered:

1. The search for naturally infected sandflies.
2. The determination of sandfly anthropophilic activity.
3. The search for the man-vector contact places and situations.
4. The sandfly population density.
5. The use of sentinel animals.
6. The study of reservoir hosts.
The role played by sandflies in the natural history of the leishmaniasis is determined and modified by the influence of external factors which affect their life. It is extremely important to have a good knowledge of the ecological factors of the area under study; the flora, fauna, soil and especially, climatic elements must be recorded in the study area.

Search for Naturally Infected Sandflies

The individual dissection technique\(^\text{(19)}\) is the most useful way to search for natural infections. The sandflies are killed in a detergent solution and dissected in an antibiotic solution, removing the head and tugging the final abdominal segments to remove the gut which is then examined under the microscope. If a sandfly is infected, the mouth parts and pharynx must be observed. The infected gut is crushed in the antibiotic solution to liberate the parasites, and this material inoculated into hamsters and culture media.\(^\text{(20)}\)

Regular monthly captures of live sandflies must be made for this purpose to determine the time of the year that infected sandflies appear in nature.

Anthropophilic Activity

To transmit the disease to humans sandflies need to be anthropophilic. As the females are the vectors, a collecting method must be oriented to determine the anthropophilic fauna of a study area. The tent traps are very useful for this, and, as was described above, they can be used with protection for the human bait. Occasional feeders can also be captured. All-night hourly collections with this method are made to determine the time of night that transmission must occur, by observing the highest sandfly densities. By performing these collections at regular intervals during the year it is possible to determine the existence of any specific modification or replacement in anthropophilic preferences. The presence of cattle in some periods of the year can offer a preferred source of blood to the sandflies, and their densities in tent traps and collections in human households would decline. The results obtained are also an expression of the population and is recorded in number of species by night by month.

Search for Man-Vector Contact Sites

The places which are common to sandflies and humans must be determined. One of these is houses. Many species of sandflies are very well adapted to be indoors, and seek a source of blood at the time that the people sleep, e.g, Lutzomyia verrucarum and L. noguchii. (Pérez unpublished) Human modifications in their natural habitats determine domiciliary changes in the sandflies. In the rural areas where the houses are widely dispersed, the sandflies can also enter by accident (as L. noguchii). In Andean localities the shepherds sleep in temporary shelters or huts with no doors or windows, openly exposed to bites; these houses are also resting places for sandflies.
In tropical areas it is possible to find active sandflies during the day, with Malaise trap collections, when the people are working within the primary forest (fruit collection, wood extraction). Fishermen and hunters also walk in the forest, especially from sunset through the night and at dawn, at the same time that the major activity of the sandflies occurs. Many bites are produced by active sandflies in caves used as shelters and in other dry areas when it rains in the tropics.

Population Densities

The purpose of these studies is to determine the time of the high densities of the sandfly population during the year, that is, the most probable period to contract the disease. The abundance can be the cause of a greater possibility to be bitten by infected sandflies. At least two collection methods must be used in these studies. Relative estimates of the population densities depend on space and time, expressing also a measurement of the activity of the sandflies. Man-biting collections give very good results but their use is declining because of the possibility of contracting the disease with the large exposure time of the collectors. Working with a previously immunized person as bait is recommended.

Collections in resting sites are beginning to be used to measure sandfly populations. Results of daily collections made in the same resting sites in Andean places do not differ much each day, the changes appearing with seasons, but there need to be more studies. Murillo and Zeledón made collections of sandflies in tree buttresses in the tropical regions of Costa Rica, and expressed their results as number of specimens captured in 30 minutes of a day by month, to provide estimates of annual relative densities.

Light traps are very good devices for sandfly capture in tropical forests. Light is an excellent attractant for sandflies in the darkness under the forest canopy. Extensive collections were made by Penny and Arias in Brasil; the sandfly populations had a peak within the dry season, and the results were expressed as the average of specimens collected with four traps, four nights by month (see also Christensen and Herrer, 1980). Collection of sandflies with CDC light traps set at different heights in Brazil disclosed a separation of the populations of L. wellcomei and L. complexus by height stratification.

Sticky traps are used very often in the Eastern Hemisphere to measure sandfly populations. They are placed around specific productive (in number of specimens captured) habitats during the whole night. The results are expressed as number of sandflies per trap each month of sampling, or by m² by month.

The parameters that various authors use to express their sampling methods are very diverse, and because of this the results are not a clear reflection of the real sandfly populations involved. A more precise indication of true populations could be obtained by designing methods that would provide complete numbers, and an approximation is possible if thorough descriptions and exact trapping methods are standardized in time and location.
Sentinel Animals

Sentinel animals are used in endemic areas with two purposes: to obtain (indirectly) a sample of the leishmanial parasites transmitted by the local sandflies and to determine the time of appearance of the disease in the study area. Dogs, hamsters, birds, and sylvatic rodents are used in these studies. If different animals are used, the preferences of the sandflies will show a specific tendency toward a frequent host. The sentinel must be susceptible infection by Leishmania, and problems can arise with particular species or strains. Different exposure times are assayed and after a period of observation (approximately 2 months) the sentinels are studied and cultures or inoculations in hamsters are made from skin and internal organs. A system that can retain living sandflies attracted by sentinels for their dissection is a recommended adjunct to these studies.

Study of Reservoir Hosts

One approach is to search for infected wild and domestic animals by dissection and attempts to isolate leishmanias. Another is to first determine which are the preferred species by bloodmeal analyses from engorged female sandflies. The bloodmeal analysis precipitin test is a very useful tool for this objective. Antisera against the majority of the animal species occurring in a study area are needed. The sandfly species known to be anthropophilic have priority to be processed by this method. Bloods other than human may give an idea of the preferred host of the sandfly, reducing the spectrum of the possible sources of blood and also of the natural infections by Leishmania. This abbreviated and more directed approach may become more popular in the future.

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FACTORS RELATED TO THE VECTOR COMPETENCE OF SANDFLIES IN LEISHMANIA TRANSMISSION

Yosef Schlein

INTRODUCTION

This report is not intended to cover the inter-relation between the Leishmania and the vector, but to present the results of some investigations on factors involved in the establishment of infection and those affecting the transmission by bite.

Other aspects have been considered in the recent and most comprehensive review of the biology of Leishmania in phlebotomine sandflies by Killick-Kendrick.¹

The development of Leishmania in its sandfly vector is restricted to the alimentary canal, hence, the subsequent stages of parasites are exposed to a varying medium consisting of the ingested food, induced secretion of enzymes and products of the digestive processes. The interacting factors governing the vector's competence can thus be classified into two categories: the innate capability permitting the development of a given Leishmania that results from physiological specificities, and the composition of the food taken.

EFFECT OF SANDFLY MEALS ON LEISHMANIA

The resistance of vectors unable to support the growth and transmission of Leishmania other than the one they transmit naturally has been described several times and recently reviewed by Killick-Kendrick.² However, there has only been one early study³ which was aimed at investigating the phenomenon and which demonstrated that components of the blood-meal induced vector selectivity. Adler, using artificial feeding, showed that a non-transmitted Leishmania could survive in the sandfly following infective meals of erythrocytes and saline, whereas following meals of serum and saline, the number of flies with parasites was inversely proportional to the amount of serum.

In the sandfly gut, the levels of proteases rise after the ingestion of blood and they could be the effectors of Leishmania selection. We compared the effects of the naturally transmitted L. major and of L. donovani on the gut enzymes of Phlebotomus papatasi, using gut homogenates of artificially infected flies and uninfected controls as enzyme preparations. The digestion of C¹⁴ labelled globin substrate by preparations from flies fed 24 hrs earlier on serum containing L. major was about a third less than that of controls, while that from flies infected with L. donovani was about one third greater. When added to control homogenate, in vitro, promastigotes of both species promoted proteolysis.⁴ Similar preparations of flies fed on rabbit blood were used in further experiments, in which the relative quantity of trypsin-like enzymes was measured at different times after the infective meal.⁵
The overall amount of the enzymes in *L. major* infections was reduced to 58% and 34% of the controls, 20 and 30 hrs post-feeding and increased to 184% at 52 hrs. The general levels measured for flies infected with *L. donovani* did not vary considerably from the controls, however, the quantities of different enzymes that were measured from gel-electrophoresis by densitometry were different. The greater effect of *L. major* leads to the suggestion that the massive manipulation of gut enzymes by this species represents its defence mechanism against enzymes of its vector. To substantiate this assumption, it was necessary to demonstrate that the trypsin-like enzymes of *P. papatasi* were harmful to *L. donovani*. This was confirmed by adding 1% soybean trypsin-inhibitor to infective meals, which resulted, 3 days later, in 63% of the flies harboring *L. donovani* compared to 10% in the controls.

All the experiments to investigate the fit between vector and pathogen were carried out using the blood of one host, the rabbit. However, there is evidence that the choice of host can also alter vector competence, as shown by the death of *L. major* in *P. papatasi* that fed on turkey before or after the infective meal. Chicken blood given 24 hrs following an infective meal of parasites in saline had a similar effect and no parasites were observed in flies dissected 3 days later. As with *L. donovani*, it appeared that trypsin-like enzymes were responsible for the vector's resistance, since the infection succeeded in 63% of the flies, when 1% soybean trypsin-inhibitor was added to the chicken blood-meal (unpublished data). According to these results, it appears that even the adaptation of *L. major* to *P. papatasi* is limited and it cannot cope with the composition of trypsin-like enzymes elicited in this sandfly by avian blood.

The establishment of *Leishmania* infections in the vector takes place during the digestion of the blood meal and further developments occur in the presence of frequently taken sugar meals. Sugar meals are necessary for transmission of *Leishmania* by bite, as was shown by the successful transmission of *L. donovani* by *P. argentipes* fed on raisins. Laboratory diets of sandflies apparently lack some of the components which allow optimal transmission. This point was demonstrated by the limiting of *L. infantum* to the midgut of *P. ariasi* in the laboratory; whereas flies infected in the laboratory that had been released and recaptured, had parasites in the fore-gut and had, thus, become potential transmitters. There is no information on the actual sources of natural sugar meals of sandflies, except for the observation that, in the laboratory, *P. papatasi* feeds selectively from plants and on honeydew. However, since plant sap and honeydew contain amino acids, the effect of protein on the transmission of *L. major* by *P. papatasi* was investigated. Transmission was evaluated by counting the parasites ejected into capillaries during forced feeding. The location of the parasites in the gut was similar whether the flies had been fed sugars alone or sugar and albumin. However, the percentage of transmitting females was significantly higher, following feeding on the latter. Some of the flies were unable to engorge fully from; the capillaries and transmission was positively correlated with the apparent inability to engorge.

The promotion of transmission by the coarse imitation of natural diet can probably be improved by feeding the sandflies on natural diets. Such
experiments should be carried out with food plants which occur in the biotope of the vector. It could be that some plant diets, like the effect observed with avian blood, will be harmful to the Leishmania.

ACKNOWLEDGEMENTS

Studies by the author reported here received support from the leishmaniasis component of the UNDP/World Bank/WHO Special Programme for Research and Training in Tropical Diseases, the Project on Epidemiology and Control of Vector Borne Diseases in Israel (REP-NIH-NIAID-AI 126688) and AID grant CDR C5-136.

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HOST-PARASITE RELATIONSHIPS: LEISHMANIA IN SANDFLIES

R. Killick-Kendrick

INTRODUCTION

Over the past 15 years, the establishment of colonies of sandflies in many laboratories in different parts of the world has been accompanied by a re-examination of the life-cycles of Leishmania spp. in the invertebrate host. Notable advances have been made by:

a) the use of the electron microscope, particularly in revealing the attachment of parasites to the internal surfaces of the alimentary tract of the sandfly.\textsuperscript{[1-3]}

b) the demonstration of a form of promastigote adapted for life in the vertebrate host (the "infective" or "metacyclic" form)\textsuperscript{[4-15]}, and

c) studies on the effect of the parasites on the production of digestive proteases in the midgut of the sandfly leading to a new hypothesis explaining patterns of susceptibility and insusceptibility of sandflies to different species of Leishmania.\textsuperscript{[16-12]}

PARASITE FORMS

Leishmania has two principal morphological forms, the amastigote in the vertebrate host and the promastigote in the sandfly. A third form the paramastigote, in the foregut and hindgut of sandflies may be considered as a variety of promastigote or as an "amastigote with a flagellum". According to the sites of development in the sandfly, the Leishmania have been divided into two groups, namely, the Suprapylaria with development confined to parts of the alimentary tract anterior to the pylorus (Fig. 1), and the Peripylaria with development both anterior and posterior to the pylorus. The life-cycles of these two groups, which have recently been given new subgeneric names\textsuperscript{[13]}, are considered separately below.

Peripylaria

At the moment, all species of Leishmania in this group are considered to be phylogenetically related to L. braziliensis. Their development in the sandfly differs from that of all other Leishmania by their multiplication in the pylorus and ileum followed by an anterior migration to the thoracic midgut, stomodaeal valve and foregut. In the hindgut the principal form is a paramastigote which attaches to the cuticular intima by the tip or side of the flagellum accompanied by the presence of hemidesmosomes inside the flagellar sheath.\textsuperscript{[14]}

The detailed life-cycle of Peripylaria after the multiplication in the hindgut has not been described and there are no published accounts of laboratory transmissions of these important parasites by the bite of experimentally infected sandflies.
Suprapylaria

This group includes all Neotropical leishmaniae except the braziliensis group and all mammalian Leishmania of the Old World.\(^{18}\)

In the sandfly, the development of these parasites is confined to the midgut and foregut. Soon after taking blood, the meal is encased in a peritrophic membrane within which the parasites develop. Amastigotes taken up by the female sandfly when taking a bloodmeal divide once, perhaps twice\(^{18}\), and change to elongate promastigotes with a single anterior flagellum arising from a basal body near the kinetoplast. On escaping from the peritrophic membrane, the parasites attach by inserting the flagellum between microvilli lining the midgut. Division is, firstly by the production of a daughter flagellum shorter than the existing one followed by replication of kDNA unaccompanied by division, then division of the nucleus, kinetoplast and body, in that order.\(^{12}\) The parasites continue dividing and, after a few days, move forwards to the stomodeal valve. At this point, two types of promastigotes are seen in the L. mexicana group. One, a nectomonad, is long, slender and electron dense; the other, a haptomonad, is broad and electron lucid. The change in form appears to be related to modifications of the flagellum associated with attachment to cuticular surfaces by the tip.\(^{17}\) By the electron microscope the mechanism of attachment is again seen to be by the formation of hemidesmosomes inside the sheath of the flagellum. Attachment may be mediated by electrical charges probably associated with binding sites on the flagellum and cuticle. Available evidence suggests that promastigotes of some species stop dividing at this point of development whereas others continue.

In flies with heavily infected valves, the infection commonly spreads forwards into the short oesophagus, where the duct of the diverticulum (= crop) enters. This move is accompanied by a change in form to a paramastigote, with the kinetoplast at the side of the nucleus. Paramastigotes in the foregut attach to the intima by the tip of the flagellum but, unlike promastigotes in the abdominal midgut, they are immotile and do not divide. Infections of this form may, however, be absent or they may spread forwards into the pharynx and, exceptionally, into the cibarium. The relevance of attached parasites in the stomodeal valve and foregut to transmission is not known, but it has been suggested that "their presence in large numbers may be crucial".\(^{3}\)

From as early as the third day of the infection in the midgut, perhaps earlier, morphologically characteristic promastigotes arise which are stages adapted for life in the vertebrate host. Those of the best studied species, L. major, are smaller than other promastigotes with, typically, a short body about 10 \(\mu\)m in length, and a flagellum twice the length of the body.\(^{18}\) They are highly motile and neither attach to the wall of the alimentary tract nor divide. This stage moves forward into the oesophagus\(^{3}\) and even as far as the mouthparts\(^{18}\) where they are put into the skin of the vertebrate as a bloodmeal is taken. Heavy infections interfere with feeding behaviour and the flies commonly probe many times, often failing to take a full meal.\(^{17-19}\) This may result in infective forms being flushed forwards into the skin from the foregut and
it is probably not essential for parasites to be in the proboscis for transmission to take place.\(^8\)

**RECENT OBSERVATIONS ON FACTORS AFFECTING THE LIFE-CYCLES OF LEISHMANIAE IN THE SANDFLY**

*Food other than blood.* See Schlein.\(^8\)

The introduction of the cold anthrone test for fructose to studies on the biology of sandflies has confirmed the importance of sugars in their natural diet\(^{21,22}\) and has stimulated work on the sources of food other than blood taken by sandflies in nature with special reference to the possible influences of these foods on the development of leishmaniae in the sandfly.

In the laboratory, Schlein and Warburg\(^{23}\) showed that *P. papatasi* of both sexes pierces the leaves or stems of plants and takes sap. In addition, the flies will feed on honeydews of aphids and coccids, even on plants which are otherwise inedible. Killick-Kendrick and Killick-Kendrick\(^{24}\) found no evidence that *P. ariasi* pierced plants but showed that honeydew of an aphid of oak trees is avidly taken. Sugars typical of honeydews (melezitose and turanose) were then demonstrated in wild-caught specimens of *P. ariasi* caught in an oak tree heavily infested with aphids.\(^{25}\)

Sugar tests on female flies at different stages of engorgement suggested that, having taken a bloodmeal, the females stop taking sugar until the meal is completely digested.

Warburg and Schlein\(^8\) examined the production of promastigotes of *L. major* infective to vertebrates in sandflies (*P. papatasi*) maintained on sugar with serum (as a source of amino-acids) and found that the numbers were higher in these flies than in flies kept on sugar alone. It is noteworthy that, in addition to a range of sugars, honeydews contain significant amounts of several amino-acids, including proline, which is important in the metabolism of trypanosomatids.

**Bacteria and yeasts.**

Although it is generally assumed that the intestinal tract of sandflies is normally sterile and it has been suggested that the crop contains an antibacterial factor\(^{28}\), high rates of infection of bacteria and yeasts have been reported in *P. tobbi* from Greece and *P. papatasi* from the Jordan valley. It was suggested that such infections may reduce the capability of sandflies to support the growth of leishmaniae and, thus, the transmission of leishmaniasis.\(^{28}\)

**Digestive proteases of sandflies.**

The pattern of natural vectors of leishmaniae of the Old World suggests that there is an "evolutionary fit" between vectors and parasites. The picture is less clear in the New World, although, where the vectors are known, all parasites of the *mexicana* group appear to be
transmitted by sandflies of the \textit{flaviscutellata} group. Perhaps the most puzzling aspect of the associations between parasites and sandflies is the frequent inability of a vector of one parasite readily to support the growth of another.\textsuperscript{128}

Schlein et al.\textsuperscript{111} and Schlein and Romano\textsuperscript{112} suggested that the explanation may be in the effect of parasites on the production of digestive proteolytic enzymes in the gut of the sandfly. Experiments were reported in which the production was depressed when \textit{P. papatasi} was infected by \textit{L. major}, a parasite this fly transmits, whereas it was enhanced when the fly was infected with \textit{L. donovani}, a parasite not proven to be transmitted in nature by this sandfly. The production of proteases was, moreover, shown to be enhanced or suppressed in flies fed on spent medium in which the respective parasites had been grown. One interpretation of these findings is that increased levels of digestive enzymes destroy a "foreign" parasite and that the partial suppression enables a "natural" parasite to become established (see Schlein, 1986b). It is, however, difficult to reconcile these observations with the recent successful laboratory transmission of \textit{L. infantum} by the bite of \textit{P. papatasi}.\textsuperscript{127} Possibly it is relevant that the experimental sandflies were fed on a suspension of $10 \times 10^6$/ml promastigotes\textsuperscript{112} and thus took a much larger number of parasites than a sandfly would normally ingest, and at a different stage. Schlein and Romano\textsuperscript{112} point out that their observations may not apply to New World sandflies and parasites; some Neotropical parasites have been found to grow well in flies which are not their natural vectors.

**The life-cycle and the epidemiology of the leishmaniases.**

Three gaps in knowledge of the life-cycle are relevant to quantitative studies on the transmission of the leishmaniases for which it is necessary to estimate the expectation of life and the probable number of bloodmeals of the female fly in relation to (a) the time from an infecting bloodmeal to an infective bite, (b) the likelihood of an infected female delivering a minimum infecting dose of promastigotes every time she feeds and (c) the possibility that the infection shortens the life of the sandfly. These facets of the dynamics of transmission need to be investigated.

**The life-cycle and vaccination.**

The recognition of promastigotes of \textit{Leishmania} in the sandfly (and cultures) which are uniquely adapted for survival in the vertebrate host reveals the form against which man should be protected by vaccination. It seems probable that an antigenic analysis of these forms will be rewarding. Furthermore, in challenges of experimentally protected animals, these forms alone should be used. It is no longer reasonable to give a challenge of $1 \times 10^6$ promastigotes most of which are non-infective but which, when inoculated, may act as a booster.
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INTRODUCTION

In recent years significant changes have taken place in the health field in Costa Rica, brought about by measures that could not have been taken without the resolve of successive governments to preserve health, as a matter of policy, even in times of economic crisis. According to UNICEF, in 1985 Costa Rica was among the thirty countries with lowest infant mortality and longest life expectancy at birth even though it had a lower per capita income than any of them. The guiding principles of health policy in Costa Rica are provision of health services to the entire population without any distinction whatever; promotion of health and prevention of disease are paramount priorities.

JUSTIFICATION FOR A NATIONAL CONTROL PROGRAM

Cutaneous/mucocutaneous leishmaniasis is common in Costa Rica. The number of cases is high, and they are widely distributed over the entire nation. This infection currently occupies the seventh position among obligatorily reportable diseases (Table 1) and represents a significant economic problem. The disease produces disabilities which lower national productivity, and the only specific treatment is very expensive. The cost of the drug to treat the 3,000 case encountered annually is estimated to be $US 210,000. Additionally, the prolonged treatment with injections over a 3-4 week period places heavy demands on the time of medical personnel and health facilities which pre-empt their availability for other urgent health problems.

In addition to the direct financial cost to the government, it is also a special problem because of its strong socio-economic impact and high incidence in the child population. Infection affects the patient both mentally and physically; lesions which reduce capacity to work occur particularly among the rural population least able to afford reduced productivity. The permanent facial mutilations caused by espundia can deny the opportunity for a normal life. This is obviously a public health problem which urgently requires action to mitigate heavy demands on national resources and to alleviate human suffering.

The immediate future offers no new methods for a solution to the problem, not for management of patients, nor for prevention of infection. It is not acceptable simply to await developments in leishmaniasis control in other parts of the world which will solve or alleviate the problems of Costa Rica. A national leishmaniasis control program offers a means to:

*Departamento Dermatologia Sanitaria, Ministry of Health
a.) achieve improved treatment for patients without an increase in financial resources, by raising the efficiency of the health services.

b.) Advance the development of new methodologies, test and adopt new methods developed elsewhere.

c.) Take the first steps to reduce the number of infections.

There already exist in the country a multitude of activities related to control of the disease, such as medical attention at all levels, obligatory reporting of cases, epidemiological surveillance, analysis of data, research on vectors and reservoirs, and clinical and epidemiological investigations. In sum, these activities represent a greater and more effective effort than some, so-called, national control programs of other nations. These activities, now partially carried out at different levels in the health services, and jointly with other involved institutions, represent the necessary elements for a national program. To unite all of these activities under the direction of the Ministry of Health (MOH), would effectively create a program which could utilize the national resources (financial, institutional, personnel) with maximum efficiency. Central planning and coordination could avoid duplication of effort and advance the program toward the goal of control of the disease. A plan for a National Leishmaniasis Control Program was designed in conformity with this goal, in consonance with the national philosophy of providing health care to all equally, and within the economic constraints of the current economic crisis. It is currently under consideration for implementation.

GOALS AND CONCEPTS

The program has two primary objectives:

1. Bring the capability for adequate diagnosis and treatment to the primary health care level in the areas where the cases occur.

2. Initiate preliminary measures to reduce the number of cases.

The concept of the program is based upon the following principles:

a) It will be a horizontal program carried out entirely within the organization of existing Health Services and collaborating national entities and with resources currently available. No new organizational elements or personnel to be required.

b) All efforts to apply control measures against vectors and reservoirs will be within the framework of a pilot project which will assure adequate baseline information and ongoing studies to evaluate the results.

c) Research efforts will emphasize projects designed to improve existing techniques for management of the disease and methodologies for control of reservoirs and vectors. Projects which
promise practical results to improve the situation will be given priority.

d) Coordination of all elements involved in various aspects of the program will be carried out to achieve maximum efficiency and full utilization of financial and material resources available.

e) Collaboration of institutions and individuals outside of the MOH with the training and ability to contribute to the program will be fostered and encouraged to take full advantage of human and institutional resources available in the country.

STRATEGY

Patient management

a) Establish the detection of suspect cases at level 1-2 of the pyramidal system of levels of health care [fig 1.] over the entire country. Refer these cases to level 3. for diagnostic procedures.

b) Make the diagnosis, according to standards of the program at the primary health care level (level 3) over the entire country.

c) Carry out treatment according to program standards at the primary health care level (level 3) for cases of uncomplicated cutaneous leishmaniasis. Refer problem cases to higher levels in the health care system, according to the grade of difficulty.

Training of personnel

Conduct training of auxiliary and professional personnel in reference to the methods, standards, and goals of the program. Maintain a continuing education program.

Anti-vector and anti-reservoir campaign

Initiate efforts against vectors and reservoirs within a pilot project which combines operations and investigation in an area with high level of transmission. This project will be carried out by the National Malaria Eradication Service, (SNEM) with support of other departments of the MOH, and other collaborating institutions.

Research

By means of the Advisory Council, select research goals which will serve to improve the measures utilized in the program. Promote investigations related to real problems.
PROGRAM DESCRIPTION

1. Responsibility for the national program will reside with the MOH. Activities will be coordinated interinstitutionally and between different departments of the MOH, by the Department of Sanitary Dermatology, which will have the collaboration of an Advisory Council in establishing the standards and goals of the program. The program will be carried out within the framework of existing Health Services and collaborating institutions. It will be structured in such a manner that the activities will be distributed to utilize all levels of the Health Care System available in the country; the intent being to bring diagnostic and treatment facilities to the rural areas where they are most needed, and difficult cases to specialized centers.

   The program will promote scientific investigations with practical goals directed at solving current problems. It will attempt to take advantage of all human and institutional resources available for these investigations.

   All attempts to control vectors and reservoirs will be within the Pilot Control Project under control of SNEM, but with support of other institutions, to insure adequate evaluation of the measures taken and incorporation of a research component.

2. The Advisory Council of the program will provide consultation to the Department of Sanitary Dermatology in specialized branches of leishmaniasis, to take advantage of the great experience and specialized knowledge which exists in the country and keep up with developments in other regions. The Council will be comprised of members who represent each of the following entities: Department of Sanitary Dermatology, Division of Epidemiology, Division of Program Regions, Costa Rican Social Security, and Zoonosis Project (Veterinary School, National University). This composition of the Council will be subject to change according to necessities of the program and opportunities to include new sectors with special experience or expertise.

3. Distribution of functions within the Health Care Services will be made to take advantage of all available facilities. At the level of operations, functions of the program related to patient management will be distributed in all levels of the pyramidal plan of levels of health care [Fig 1] with the intent to offer diagnosis and treatment in rural areas.

   3.1 Functions at Operations level

   Level 1-2 (Rural Health and Community Health Auxiliaries, Health Posts.)

   -Detection of suspect cases
   -Referrals to Health Center
   -Supervision of compliance with required treatment
   -Surveillance for recurrence in treated cases
   -Community education
Level 3-4 (Health Center, Peripheral Hospital, Outpatient Clinics)

- Parasitologic diagnosis by smear
- Diagnosis by leishmanin skin test, when considered necessary
- Treatment of uncomplicated cutaneous leishmaniasis cases
- Case follow-up
- Referral of mucous involvement and other complications to appropriate level
- Hygiene education
- Obligatory reporting of cases

Level 5,6 (Regional, National Hospitals)

- Parasitologic diagnosis by smear and culture
- Diagnosis by leishmanin skin test if necessary
- Treatment of any clinical form of leishmaniasis
- Case follow-up
- Hygiene education
- Obligatory reporting of cases
- Specialized support services
  (Ear, nose & throat, Ophthalmology)

3.2 Functions at Policy (standards) level

MOH-Division of Epidemiology
(Department of Sanitary Dermatology)

- Direction and coordination of national program
- Establish standards for program, with guidance of Advisory Council
- Interpretation of epidemiological data
- Planning of emergency measures in event of epidemic outbreaks

Department of Epidemiologic Surveillance

- Receiving and analysis of data of reported cases
- Improvement of reporting

Department of Control of Arthropods and Rodents (SNEM)

- Direction and execution of Pilot Control Program
- Provision of serology service (immunofluorescence)
- Surveys and investigations of phlebotomines and reservoirs

MOH-Division of Program Regions

- Review and evaluation of the execution of the actions of the program

Department of Health Laboratories

- Review and evaluation of activities of health laboratories
- Training and continuing education in techniques of program
Figure 1.
PYRAMIDAL SYSTEM OF LEVELS OF HEALTH CARE IN COSTA RICA

VI. Specialized Hospital Care
   National Hospitals

V. Regional Hospital Care

IV. Care in Peripheral Hospitals and Out-Patient Clinics

III. Care in Integrated Health Clinics

II. Care in Health Posts in Each Community

I. Direct Home Care

TYPE OF PERSONNEL IN SERVICE
   Professional-Auxiliary-Other

   Professional-Auxiliary-Other

   Professional-Auxiliary

   Other

   Auxiliary

   Auxiliary
Costa Rican Social Security

- Control activities of program in SS medical facilities at levels 3, 4, 5, 6 of the pyrimidal plan of health care
- Maintain training and continuing education program related to program

4. Pilot Project.

Studies carried out by the Zoonosis Project of the Veterinary School of the National University under the direction of Dr. Zeledón in a zone of high incidence of leishmaniasis in Canton, Acosta, have indicated the presence of vectors with domiciliary and peridomiciliary habits. This focus is reasonably well studied, and reasonable baseline epidemiological information is available. This situation appears to offer an opportunity to carry out a pilot project with the primary goal of lowering transmission by spraying dwellings with insecticides. This would be carried out by SNEM, which has the most experience in this activity, with the support of other departments and institutions, to provide ongoing investigation to determine the reservoir and possible measures against this link and an adequate evaluation of the measures taken.

Table 1.

Obligatorily reportable diseases of greatest incidence
Costa Rica, First Semester of 1986

<table>
<thead>
<tr>
<th>Disease</th>
<th>No. cases</th>
<th>Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>per 10,000</td>
<td></td>
</tr>
<tr>
<td></td>
<td>inhabitants</td>
<td></td>
</tr>
<tr>
<td>1. Influenza</td>
<td>11,201</td>
<td>420.30</td>
</tr>
<tr>
<td>2. Venereal diseases</td>
<td></td>
<td></td>
</tr>
<tr>
<td>a) Blenorragia</td>
<td>3,796</td>
<td></td>
</tr>
<tr>
<td>b) Syphilis</td>
<td>733</td>
<td></td>
</tr>
<tr>
<td>c) Soft chancre</td>
<td>519</td>
<td></td>
</tr>
<tr>
<td>d) Chancre w/o specified aetiology</td>
<td>31</td>
<td></td>
</tr>
<tr>
<td>Total:</td>
<td>5,079</td>
<td>190.58</td>
</tr>
<tr>
<td>3. Chicken pox</td>
<td>2,296</td>
<td>86.27</td>
</tr>
<tr>
<td>4. Haemorrhagic conjunctivitis</td>
<td>1,962</td>
<td>73.62</td>
</tr>
<tr>
<td>5. Hepatitis</td>
<td>1,537</td>
<td>57.67</td>
</tr>
<tr>
<td>6. Parodititis</td>
<td>903</td>
<td>33.88</td>
</tr>
<tr>
<td>7. Leishmanias</td>
<td>767</td>
<td>28.78</td>
</tr>
<tr>
<td>8. Measles</td>
<td>456</td>
<td>17.11</td>
</tr>
<tr>
<td>9. Malaria</td>
<td>310</td>
<td>11.63</td>
</tr>
<tr>
<td>10. Bacterial meningitis</td>
<td>186</td>
<td>6.82</td>
</tr>
</tbody>
</table>

Source: Dept. of Epidemiological Surveillance
Ministry of Health
August 1986
FEASIBLE CONTROL ACTIVITIES AGAINST THE SAND FLY VECTORS OF LEISHMANIA IN THE NEW WORLD

Jorge R. Arias

INTRODUCTION

Even though most cases of human leishmaniasis respond well to a variety of chemotherapeutic agents, the prevention of the disease is more desirable, and in certain cases more economical.

The prevention of leishmaniasis can be approached by: A) control of the vector species, B) control of reservoir hosts, C) prophylaxis against the parasite by vaccination or leishmanization or D) a combination of two or more of these measures, to such an extent that it interrupts the transmission cycle of the parasite to human populations.

Control methodologies against the sandfly vector of Leishmania parasites can be divided into two major categories depending on the epidemiology of the disease:

A. In those cases where the disease is an anthroponosis or a peridomestic zoonosis (primarily in the Old World), direct attack on the phlebotomine sandfly by means of residual insecticide spraying of houses, barns and stables has proven effective. Examples of this type of activity can be appreciated in the results obtained from antimalarial programs that have greatly reduced visceral leishmaniasis (kala-azar), oriental sore (due to Leishmania tropica tropica) and sandfly fever in India, Italy, Greece, USSR and Israel.\(^1,2,3\) The only New World residual insecticide control programs which have had an effect on the incidence of human leishmaniasis were carried out in Peru, where DDT spraying of houses to control the sandfly vectors of Bartonellosis (Carrion's disease) noticeably reduced the incidence of Uta (due to Leishmania braziliensis peruviana).\(^4\)

B. In those cases where leishmaniasis is a zoonosis and transmission occurs outside the houses, control is more complex and a successful effort may depend on a combination of several methods. In the New World, most cutaneous leishmaniasis is contracted in tropical rain forests, which are very complex ecosystems. Vector control in these cases may have restricted success and some methods are impractical. Nevertheless, the control of sylvatic zoonoses can be further subdivided into two approaches:

1) Protection of specialized groups for limited periods of time (e.g. military personnel on maneuvers, road or bridge construction crews, oil drilling or exploration teams, neo-colonization projects) or,

2) Protection of residents of endemic areas whose generations become infected; and the area is stable as far as development is concerned.
Protection efforts of specialized groups against the sandfly vectors has been attempted in several occasions, particularly in Neotropical forests. Floch sprayed 5% DDT in kerosene indiscriminately on the bases of trees and in burrows in the ground in French Guyana. After having found no sandflies in the treated areas for six consecutive weeks, he claimed success. No control plots or sandfly identification/quantification was made prior to the study, so his exact results are hard to ascertain. Chaniotis et al., utilizing malathion as a 2% EC spray (on the tree bases) and 95% ULV fogging bimonthly, achieved an average reduction of 30% of the anthropophilic sandflies in a 9 month period. Finally, Ready et al., treated tree trunks with 2 gm DDT/m² in a 200 x 200 meter plot in a multi-storied primary rain forest. They found that for 21 days the sandfly population resting on the tree bases was significantly reduced. However, if any reduction was observed in CDC light trap catches or human bait captures in the treated plot.

The limited success of these three trials in tropical rain forests show the possibilities offered by this type of control methods, and suggests that a better system can be developed.

Utilizing a different technique, that of habitat destruction, French workers were able to reduce the human infection rate in the village of Cacao in French Guyana. These authors showed that by clearing a 400 m forest zone around a human settlement they could eliminate human infection.

In a study conducted under similar conditions in the recently settled area of Cidade Nova (Manaus, Brazil), we found that Lutzomyia umbratilis could be found in houses up to 500 m from the forest edge, but most were collected in or around houses located within 300 meters of the forest. Human infection rates of leishmaniasis in the housing project followed these collection patterns; the more removed the houses were from the forest edge, the less was the incidence of leishmaniasis in the people who lived in them.

An undocumented reduction of cutaneous leishmaniasis in another relocation housing project was also noted. In the Bairro of São José (Manaus, Brazil), the low income people who were moved into lots given by the government were not allowed to enter the area for several months after the forest had been felled. The incidence of NWCL was lower than in previous groups who had entered the same area prior to tree felling activities in earlier phases of the project.

It can be concluded that more control methods need to be tried in all areas where leishmaniasis is a problem. Habitat manipulation and human population control programs that are well coordinated with entomological and epidemiological findings have proven to be the most successful in the New World. These, in association with other feasible methods, such as individual personal protection as well as reservoir host reduction, could substantially reduce leishmanial infections in man. It is of fundamental importance that the parasite, vectors, reservoirs and epidemiology of leishmaniasis in the different regions be known in order to be able to correctly implant control activities, as well as to properly assess the changes that occur.
SUMMARY

Sandfly vector control approaches can be divided into two major categories depending on the epidemiology of the disease:

A. When the disease is an anthroponosis or a peridomestic zoonosis and residual insecticidal activities have proven useful.

B. When the disease is a zoonosis, in which the control strategies could be:

1. Insecticide spraying of endemic areas.
2. Habitat management by forest removal.
3. Human population protection with netting, clothing and/or repellents.
4. Human population relocation, or
5. Delaying the human population from entering recently deforested areas.

A single approach to leishmaniasis control is easier to evaluate than integrated control activities. A combined effort of several methodologies, applied simultaneously, could result in controlling the disease yet would not permit the measurement of the individual control efforts.

REFERENCES

RESERVOIR HOSTS OF LEISHMANIASIS AND THEIR CONTROL

R. W. Ashford

INTRODUCTION

There is an almost universal acceptance that the best approach to communicable disease in man is the prevention of infection. This is rarely matched by research efforts and very rarely by the provision of health funds which are usually directed more towards the diagnosis and cure of disease. Indeed it is not uncommon to find resistance among medical practitioners who fear a loss of business if infection rates are reduced. The recent advances in epidemiological knowledge on the leishmaniases clearly indicate situations where control is possible but also some where control is inappropriate and the detection and treatment of cases is more appropriate. Occasionally the avoidance of natural habitats or personal protection are the only solutions. Frequently, when effective preventive measures are indicated, these are ignored with consequent disastrous results. This is particularly true of development projects and resettlement schemes, where political pressures have demanded ill-considered invasion of previously unexploited areas by large numbers of susceptible people.

With few exceptions the study of Leishmania reservoir hosts has been carried out by medically oriented people with little appreciation of mammal taxonomy or ecology. Some of the important reservoir hosts such as the hyraxes, Arvicanthis, Proechimys and Meriones are in taxonomic and therefore ecological confusion; there is a need to attract mammalogists to solve many of the specific problems which have arisen.

HOSTS AND METHODS

The six (or more) species of Leishmania which infect man have an extraordinary array of reservoir hosts quite limited in number but covering a wide spectrum of mammalian forms, belonging to isolated species or genera in the primates, carnivores, hyraxes, edentates and rodents. The main characteristic shared by Old World reservoir hosts is a high population density, often associated with gregarious behaviour and sedentary life in burrows, caves or houses. This does not seem to be true of the New World reservoir hosts which, therefore, present additional problems of control.

Man: Despite recent searches there is no indication that Indian kala azar in the main areas is transmitted other than man to man. Bloodmeal analysis shows that P. argentipes does not feed on dogs. The elimination of the reservoir is therefore synonymous with case detection and treatment. It is less certain that the same is true in East Africa but persistent work has failed to demonstrate animal reservoir hosts in either the epidemic or endemic areas. Similarly man is recognized as the reservoir host of L. tropica.
Case detection and treatment belong to other chapters, in particular details of the direct agglutination test being developed for screening potential patients in the field for VL.

The detection of PKDL cases has been intensified in India (Nandy, pers. comm.) on an informal basis; this activity is particularly important when cases of VL are rare, and should be incorporated into the primary health care programme in the post-epidemic period.

Case detection and treatment as a control measure for L. tropica infection can be successful if applied intensively and combined with insecticides, as shown in USSR. In Kabul and other parts of Afghanistan the programme has been disrupted by administrative problems. Kabul being, apparently, a "dependent" focus in which transmission is limited to those years of high sandfly abundance presents opportunities for quantifying the parameters necessary to spark an outbreak.

**Dog:** The domestic dog is the reservoir host for L. d. infantum from China, to the Mediterranean basin and South America. Dog control has been used in China and in Ceara Province, Brazil but details of the measures and the results are not readily available. The work of Rioux's team shows that the parasite can persist even though only some 2% of dogs are infected in an area of low dog density. This indicates that drastic reduction in dog populations is required and that the screening and elimination of infected dogs may be inadequate unless accompanied by the elimination of all strays as well. Dog control is, of course, a matter whose significance extends beyond leishmaniasis.

Particular problems may be presented by the packs of wild dogs which roam parts of Italy and other Mediterranean nations, though L. donovani has not been demonstrated in these dogs.

It would be interesting to hear details of the Soviet experience in Kzyl Orda where dog control seems not to have eliminated the infection.

Despite encouraging results of experiments in the use of liposome-encapsulated drugs for treatment of dogs, there is no effective treatment available so case detection and treatment cannot yet be applied to dogs. This raises problems in communities where dogs have considerable social or monetary value.

**Other canidae:** At least four species of fox, jackals and the Raccoon dog have been found naturally infected. Though the parasites have not always been identified and one of the early Brazilian foxes was infected with a parasite different for L. d. infantum most are certainly L. d. infantum or close relatives. It is intriguing to think that a related non virulent strain may even be maintained in foxes in Tuscany and may immunise people; in such a situation fox control would even be counter-productive.

The evidence that L. d. infantum is maintained by canids other than domestic dogs is not convincing and control of these animals is not indicated.
Rodents: The VBC division of WHO has recently produced an excellent annotated slide set on rodent control. Unfortunately among those rodents implicated in leishmaniasis maintenance only *R. rattus* has great significance outside leishmaniasis and is the only one covered in detail by this visual training aid.

Rats: Apart from some ambivalent serological results and an isolated occurrence *R. norvegicus* has not been implicated in leishmaniasis maintenance. *R. rattus* however has been shown possibly to have a role. However, this is in areas where dogs are probably the primary hosts and the reasons for deratisation only include leishmaniasis as an afterthought.

*Rhombomys opimus*: The great gerbil maintains *L. major* in Soviet Central Asia and in eastern Iran and northern Afghanistan. Generally this is a harmless rodent which plays an integral and essential role in the life of its semi-desert habitat and should be left in peace. Personal protection of visitors can include staying behind fine mesh nets at night or camping well away from *Rhombomys* colonies.

Where development projects necessitate a serious attempt to reduce the possibility of transmission, especially during the construction phase of the project, measures such as ploughing, poisoning and environmental barriers have proved cheap and effective. These are briefly described in WHO (1984) and at slightly more length in WHO (1980).

*Psammomys obesus*: As with *Rhombomys*, it is only under special circumstances that *Psammomys* requires control. Despite serious effects of *L. major* infection on development projects in much of N. Africa and Arabia, there seems to be no research on the control of *Psammomys*. While the colonies are readily detectable and identifiable control may be more difficult than for *Rhombomys* as *Psammomys* does not readily eat grain so cannot be fed anti-coagulants or zinc phosphide. Vegetation clearance should starve them and was applied with apparent success in a badly affected Canadian contractors' camp in Saudi Arabia. Ploughing should also be good and, where materials are readily available, an explosion under the burrow network should collapse the burrows and suffocate the animals.

*Meriones*: At least four species of *Meriones* have been credited with the maintenance of *L. major* but the role of these rodents has been firmly established only in S. Morocco and USSR. Some *Meriones* spp have minor agricultural or stored products significance and those in Morocco were abundant inside villages where they fed largely on human excrement. *Meriones* spp do take grain readily and can be poisoned. One man with a sack of poisoned corn and a long applicator could keep the environs of a village or work site free of this rodent indefinitely. The problem is to identify the time and place where *Meriones* control is required. These rodents have enormous population fluctuations which are rarely recorded and poorly understood. At least in Morocco, the human leishmaniasis outbreak seemed to follow a peak in the *Meriones shawi* population but this conclusion was by anecdotal hearsay and cannot be used predictively.
Arvicanthis: The role of Arvicanthis has been more or less established in maintaining L. major in Senegal and possibly L. donovani in southern Sudan. In the current massive outbreak of L. major infection in Khartoum, specimens of Arvicanthis are said to have been found infected by this is not published and preliminary. Again, anecdotally, there does not seem to have been a great increase in Arvicanthis recently. Arvicanthis spp are predominantly herbivorous rather than granivorous and may or may not be susceptible to normal rodent control methods.

Hyraxes: No one has had good reason for controlling hyraxes except in South Africa where the destruction of carnivores has led to excessive numbers. Indeed in some countries a special permit would be required to destroy them.

It has frequently been predicted that removal of hyraxes from the environs of Ethiopian villages would reduce L. aethiopica transmission. So far this has not been tried. One individual working with a shotgun for a couple of hours each day could keep a village "clean".

CONCLUSION

Reservoir host control is the method of choice for reducing leishmaniasis transmission only in certain specific situations. This method has rarely been tried and even more rarely properly evaluated.

Specific research is required on the taxonomy in relation to ecology of a number of reservoir genera. There are really no predictive guidelines to show to what extent reservoir host populations should be reduced in order to interrupt transmission. Control methods specifically adapted for Psammomys, Meriones and Arvicanthis are required to be developed; the latter is particularly important if the suspicions raised in Khartoum are confirmed.

REFERENCES

INTEGRATION OF LEISHMANIASIS CONTROL IN PRIMARY HEALTH CARE:
PROS. AND CONS.

P. de Raadt

INTRODUCTION

Leishmaniasis and primary health care (PHC) are both highly variable entities. The former is not a single disease, but a group of at least six different diseases, each caused by different parasites, involving different reservoir hosts, transmitted by different vectors, and occurring under a wide variety of ecological conditions. As a consequence, each requires a tailored-to-measure control approach. PHC involves a health delivery principle based on community involvement which likewise varies depending upon different sociological characteristics such as religion, traditions, and several other strictly local factors. At the same time other factors such as economics, levels of education, and administrative infrastructure play a role. As a consequence, implementations greatly differ from country to country and, within countries, from one locality to another. It is readily apparent that the possible relationship to these two entities can result in an infinite number of variations. However, these are basic relationships common to most situations which are important considerations.

Primary health care is a realistic solution for permanent access to health services for the entire population, in spite of chronic shortfalls in skilled personnel, logistic facilities and finances. However, certain technical compromises have to be accepted and the amount of time required to make the system work is often underestimate.

CONSIDERATIONS

Only a few programmes exist for the control of communicable diseases though primary health care, for instance in malaria, schistosomiasis, and African trypanosomiasis. Efforts in leishmaniasis are even more scarce and modest. Examples are the vector control programme in China and the small-scale experimental pilot trials in Bolivia, Israel, Peru and Venezuela. The following discussion, therefore, will be mainly based on lessons learned in other fields, such as in malaria and African trypanosomiasis. The main issues to be taken into account are:

Local responsibility: Primary health care does not mean mobilizing the local population as cheap manpower for bush clearing or for hunting animal reservoir hosts. In order to achieve a long-term commitment by the communities, community members must have a clear understanding of the advantages they individually may expect from the control measures envisaged.

Appropriate communications: A regular dialogue between the population and the professional health personnel is essential, whereby the latter must be prepared to "step down" and support and guide the communities in their share, rather than give orders. A good way to
attain a genuine commitment from the community is through the community health committees.

Realistic operational level: The tasks given should be within the reach of the local capacities and not be over stretched for the sake of the PHC principle. For example, treatment of visceral leishmaniasis or African trypanosomiasis should not be done by the PHC worker, since diagnosis needs to be confirmed in the laboratory first, and adverse side effects can not be handled at village level. However, the PHC worker can be very useful in referring suspected patients to an appropriate referral centre for treatment, and after their return, stimulate patients to go for follow-up examinations. Also, certain preventive measures, such as vector and animal reservoir control can often be made a responsibility of the PHC worker. An example of a possible breakdown of activities for community participation in leishmaniasis control is given in Table 1.

The time factor: The time needed for attaining an adequate level of motivation amongst the population is generally underestimated by health professionals. Communities need time to get used to the idea of sharing the responsibility for their health care. "The greatest enemy is rush".

Since each individual has his own priorities in health matters, usually a package deal is more interesting for the community than projects concerning the control of a single disease. The package should be defined in such a way that most members of the community can clearly recognize their personal interest in the programme objectives.

For instance, in tsetse control for the prevention of African trypanosomiasis, the communities apply simple traps or screens impregnated with insecticides. It appeared that the communities became very keen to participate, and in most cases such programmes proved a great success until the time came when the fly density dropped below 10%. Initially, the population was easily convinced and ready to adopt the system. However, their motivation was not inspired by the desire to control Sleeping Sickness, but rather to reduce the fly nuisance. When tsetse traps were introduced in Congo, it was necessary for some of the communities to combine the fly trapping programme with other local health issues, such as appointing a midwife in a nearby health centre, or guaranteeing the supply of certain drugs (Lancien personal communication).

When considering the "Pros" of leishmaniasis control as part of primary health care, there are obvious advantages in that a wider geographic coverage of control activities can be obtained. A second advantage would be the potential continuity of such activities, since the responsibility and implementation rests in the hands of the population at risk themselves. Moreover, the PHC approach, for instance fly control, could be done at relatively low cost. The "Cons" include the compromise in the technical quality of the programme. For instance, epidemiological analysis and evaluation, will rarely be done as it is in the specialized programmes. There is also the higher risk of technical errors. Finally, introduction of the system will be time-consuming and require organizational changes and a heavy training programme for many years to come.
Table 1.
Examples of level of implementing activities in Leishmaniasis Control in a Primary Health Care Programme

<table>
<thead>
<tr>
<th>Level</th>
<th>Activity</th>
</tr>
</thead>
</table>
| Community | - Identify suspects
           | - Follow up treated patients                                             |
|           | - Sampling of                                                             |
|           | - Identifying high transmission sites                                     |
|           | - Spraying                                                                |
|           | - Traps, impregnated curtains etc.                                        |
|           | - Animal reservoir control                                                |
|           | - Treatment of cutaneous leishmaniasis                                   |
| Dispensary| - Diagnosis, parasitological and serological                              |
|           | - Treatment, cutaneous leishmaniasis only                                 |
|           | - Treatment follow-up                                                    |
| Hospital  | - Diagnosis confirmation                                                 |
|           | - Treatment of both visceral and cutaneous leishmaniasis                  |
|           | - Active surveillance                                                    |
|           | - Data collection                                                         |
| Ministry  | - Define national strategy and control plan                               |
|           | - Financing                                                               |
|           | - Supplies                                                                |
|           | - Distribution and technical information                                  |
|           | - Propaganda-Radio/T.V./posters, etc.                                     |
|           | - Technical support                                                       |
|           | - Data collection and analysis                                            |
|           | - Evaluation                                                              |

Table 2.
Advantages/Disadvantages of Leishmaniasis Control under a Primary Health Care System

**Pros:**
- availability
- continuity
- community involvement
- cost saving

**Cons:**
- technical compromise
- risk mistakes
- training/refresher course = heavy
- slow
RESEARCH AND SPECIALIST TRAINING FOR NATIONAL CONTROL PROGRAMS

Rafael A. Cedillos

INTRODUCTION

The appropriate organization of preventive and control measures of leishmaniasis, as well as of other vector-borne diseases, depends on several closely related factors: 1) adequate knowledge of the epidemiological, sociocultural and economic factors involved in its transmission; 2) existence and effective utilization of trained personnel; 3) sufficient financial resources; and 4) a political decision by the government to confront the problem.

Of these elements, the human resource is the most critical due to the deterioration observed in their training in the last two decades, and the need to implement new strategies of prevention and control of these diseases into the general health services and within the context of Primary Health care. Therefore, it is important to analyze briefly the strategic approach being promoted to combat these diseases and the structure and organization of the general health service in order to understand the need and orientation of training for public health personnel.

CONTROL STRATEGIES FOR LEISHMANIASIS

The establishment of mechanisms for intrasectoral cooperation (within the Ministry, i.e., with other programs for vector control, maternal and child care, social security services) and intersectoral cooperation (other ministries, e.g. Agriculture and Defense) constitutes the basis of the strategy of control of leishmaniasis and other vector-borne diseases. The final objective is to promote health as an integral part of the social and economic welfare of the affected communities (Primary Health care strategy). This multisectoral approach is perhaps more feasible against leishmaniasis than in other vector-borne diseases because the ecological characteristics of its transmission immediately rules out any vertical approach to its control. The search for combined control activities in areas under increased transmission and health risk should be explored within the primary health services and with active participation of the community.

Emphasis should be given to applied field research for a better understanding of the epidemiology of the disease in general and the specific local problems implicated in its distribution and incidence. For this purpose, the national health programs should have the capacity to carry out parasitological studies in man, reservoirs and the vector, entomologic studies to identify the most important vectors and their ecology, as well as socio-economic surveys to determine working and living conditions of the affected population and at risk of infection.
Basically, it is necessary to promote the capacity to develop the following supplementary activities in the health services: a) an information and reporting system based on a reliable diagnosis, adequate treatment and follow-up cases; b) epidemiological research oriented to characterize the transmission foci; and c) implementation of a dynamic and timely surveillance system.

**ORGANIZATION OF THE GENERAL HEALTH SERVICES**

The development of human health resources should be planned and programmed coherently in relation to the needs of established health priorities of the Health Services, and the availability of human and financial resources.

Traditionally, the General Health Services have had two different components: a basic component, oriented basically to curative medicine; and an epidemiological component, responsible for prevention and control actions. The first component, structured into service institutions (public and private hospitals, health units) is hypertrophied and absorbs a substantial percentage of the health budget. The second, weak and without resources, has been structured into epidemiology units, oriented to the collection and general analysis of data, and into vertical programs to combat important vector-borne diseases (malaria, Chagas' disease, schistosomiasis).

The current trend in most of the countries of this Region is toward integration of both components into a single administrative structure, as is outlined in Figure 1. The objective is to promote greater participation of the epidemiological component in the formulation and execution of the health policy, especially in countries where communicable diseases are highly prevalent, and to plan rational use of multifunctional resources in the campaign against these diseases. Even the most specialized component, vector control, should be integrated into the structure at central, regional, and local levels in order to promote participation of the rest of the health personnel in the programming, execution, and evaluation of control and of epidemiological surveillance activities.

**THE NEED FOR, AND ORIENTATION OF, TRAINING**

The overall vision of the strategy of vector-borne disease control and the integrated organization of the health services poses the need to organize two types of training for health personnel (Figure 1): the first, directed toward the training of professional and research personnel for the central and regional levels (physicians specialized in public health, epidemiologists, medical entomologists, parasitologists); and the second, oriented to the training of professional personnel and auxiliary technicians in specific methodologies for the study, prevention and control of given vector-borne diseases (malaria, leishmaniasis, Chagas'disease, etc.).

1. Organization of the first type of training (postgraduate) should be oriented to the training of professionals for: 1) planning, organizing,
FIGURE 1. ORGANIZATION COMPONENTS and TRAINING NEEDS OF A HEALTH SERVICE

HEALTH DELIVERY & TRAINING

S S S

G H S

TRAINING

Un. & R I

SKILLS NEEDED

- Management
- Data Collect. & Analysis
- Control & Surv. Methods
- Study design
- Teaching Skills
- Management
- Data Collect. & analysis
- Control & Surveillance
- Laboratory
- Principles field research
- Control & Surveillance
- Techniques
- Health Education
- Communication Skills

TRAINING ACTIVITIES

- Post-graduate studies
- Sem. & Workshops
- In-service training
- Courses
- Workshops
- On-the-job training
- Courses
- Workshops
- On-the-job training

G H S = General Health Service
S S S = Social Security System
Un. & R I = Universities & Research Institutes

Physicians
Epidemiologists
Medical Entomologists
Parasitologists
Physicians
Nurses
Health Inspectors
Health Educ.
Laboratorists
Field Workers
Laboratorists
Community Participants

COMMUNITY

PREVENTION AND CONTROL

Epidemiology and Research Component

Health Delivery
Training
developing, supervising, and evaluating complex interventions regarding control and epidemiological surveillance of vector-borne diseases, and 2) designing, carrying out, and supervising applied field research for the development of effective prevention and control measures. The basic training of these professionals is obtained in higher learning institutions through intensive programs of applied research on communicable diseases in general and of vector-borne diseases in particular. The multifunctional characteristic of this type of professional is achieved only through tutorial, participatory, and dynamic teaching of health problems. The participation of the General Health Services in this program is fundamental in incorporating the experience of field of specialized personnel and, in addition, demonstrating the importance of this cooperation in the development of educational, service, and research activities at the national level.

In this Region, the activities to strengthen the Special Program for Research and Training in Tropical Diseases of the UNDP/World Bank/WHO have constituted a valuable element in promoting the training of research personnel in priority health problems and, indirectly, promoting technical cooperation between the favored institutions and the General Health Services. Taking into account the institutional impact achieved in this field, the Program of Tropical Diseases of PAHO analyzes the possibility of setting up an Multinational Inter-Institutional Network for Strengthening Research and Training Capacity in Tropical Diseases, whose purposes would be the following:

1) To strengthen research and training capacity in tropical diseases (exchange of educators and investigators; development of courses and seminars; etc.)

2) To promote optimum use of available resources at the regional and subregional levels

3) To strengthen the transfer of knowledge and appropriate technologies among the Institutions

4) To reconcile viewpoints on the use of biomedical technologies for diagnosis, control, and epidemiological surveillance.

It is an excellent idea that would favor less developed institutions and could be financed with regular PAHO funds, TDR research grants, and financial support from other international agencies. This project could also constitute a solution to two problems inherent in the training of multifunctional and specialized personnel: a) the structuring of programs for continuous education at the national and subregional level; and b) the adequate utilization and the maintenance of human health resources at the national level.

The scarcity of medical entomologists in the programs for vector control in most of the countries of Latin America and of the Caribbean poses the need to train personnel through courses at the intermediate and masters level. In 1983, a masters program in Medical Entomology began in the University of Panama with the support of PAHO/WHO and WHO/TDR. So far, three Panamanian students have been graduated, another four students
from Panama, Guatemala, Honduras, and Venezuela will complete their requirements this year, and a third group will begin its studies in September 1987. There is interest in developing similar programs in Mexico, Venezuela, Colombia, and Brazil.

Of course, training of this type of personnel already is posing problems of absorption and maintenance in the health services; problems that require study and immediate solution.

2. On the other hand, training for professional personnel and auxiliary technicians should be directed toward the learning of data collection and analysis methodologies (at the programming level) and the proper organization of control and evaluation measures. The characteristics of this training are shown in Figure I. Training is the responsibility of the General Health Services, but the participation of national teaching and research institution should be promoted.

TRAINING ON LEISHMANIASIS PROMOTED BY PAHO

In relation to leishmaniasis, PAHO is developing a program for training health personnel through workshops oriented to standardization of methods of study, diagnosis, and treatment of patients for the purpose of:

a) better defining disease prevalence and incidence
b) determining the factors that influence their transmission
c) isolating and characterizing the parasites
d) identifying vectors and reservoirs
e) developing an expeditious and timely system of supply of specific drugs
f) establishing a reliable system of registering and reporting of cases, and
g) organizing an epidemiological surveillance system.

This type of training is being promoted at the subregional level (Figure 2) to take advantage of the human and technical resources of the most developed countries. In 1983, the first seminar-workshop in Mexico was held with the participation of this country and the countries of Central America and Panama. During 1987 workshops have been held at the country level in Argentina, Costa Rica, Ecuador, Guatemala, Mexico and Paraguay.

The purpose is to hold a workshop at the central level for the professional and technical personnel of the General Health Services responsible for prevention and control actions regarding this or other vector-borne diseases and to support the subsequent holding of other workshops at the regional and provincial level until a system of diagnosis, treatment, and information is established at the national level. Each workshop has a duration of five days and costs approximately US $10,000 to finance the participation of one regional adviser, 25 to 30 national students, and the purchase of some essential laboratory materials.
FIGURE 2. INTERCOUNTRY COOPERATION ACTIVITIES ON PREVENTION AND CONTROL OF PARASITIC DISEASES

- Leishmaniasis
- Onchocerciasis
- Malaria
- Chaga's Disease
- Schistosomiasis

Map showing the distribution of these diseases across the world.
The program covers the following topics:

- *Leishmania* and leishmaniasis and their importance in public health.
- Leishmaniasis as a national health problem (country headquarters).
- Taxonomy of *Leishmania*. Identification. Reference strains - Reference Centers of WHO.
- Clinical forms. Presentation of cases.
- Diagnosis of leishmaniasis. Practical work for the preparation of smears, biopsies, cultures. Taking of samples in the field.
- Serology.
- Treatment. Regimens recommended by WHO. Alternative treatments.
- Visits to an endemic area.
- Control and surveillance activities.
- Discussion. Recommendations.

In Table 1, the specific activities concerning training and surveillance activities promoted by the Communicable Diseases Program are listed as well as the indicators selected for evaluation.

**CONCLUSIONS AND RECOMMENDATIONS**

The development of human health resources should be planned and programmed coherently in relation to the needs of the national health services, the already established health priorities, and the availability of human and financial resources.

The establishment of mechanisms for intrasectoral and intersectoral cooperation constitutes the basis of the strategy of control of leishmaniasis and other vector-borne diseases. The final objective is to promote health as an integral part of the social and economic welfare of the affected communities. Emphasis should be given to applied field research for a better understanding of the epidemiology of these diseases in general and the specific risk factors implicated in their distribution and incidence.

This strategy of vector-borne disease control poses the need to organize two types of training activities for health personnel: the first, directed toward training of professional and research personnel for the central and regional levels for: 1) planning, organizing, developing, supervising, and evaluating control interventions and epidemiological surveillance of vector-borne diseases; and, 2) designing, carrying out, and supervising applied field research for the development of effective prevention and control measures. The second is oriented to the training of professionals and auxiliary technicians in specific methodologies for the study, prevention and control of a given vector-borne disease (malaria, leishmaniasis, Chagas disease, etc.).

For economic reasons some of these professional and research personnel (medical entomologists, epidemiologists, parasitologists) can be located in national academic and research institutions. In such a
case, strong cooperative activities should be promoted between these institutions and the General Health Services.

For leishmaniasis, it is basically necessary to promote the capacity to develop the following supplementary activities in the health services:

a) an information and reporting system based on a reliable diagnosis, adequate treatment and follow-up of cases;

b) epidemiological research oriented to characterize the transmission foci; and

c) implementation of a dynamic and timely surveillance system.

REFERENCES


Table 1.

Leishmaniasis Activities and Indicators for Evaluation in the PAN0 Communicable Diseases Program Parasitic Disease Component

<table>
<thead>
<tr>
<th>Activity areas</th>
<th>Specific activities</th>
<th>Indicators for evaluation</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Training</td>
<td>1. Organization and coordination of courses and seminars at central level on diagnosis,</td>
<td>- Reduction of the number of cases in the population at risk</td>
</tr>
<tr>
<td></td>
<td>2. Promotion of workshops at regional an provincial levels on diagnosis, treatment, prevention and control</td>
<td>- Number of laboratories with capabilities for diagnosis of leishmaniasis.</td>
</tr>
<tr>
<td>2. Epidemiological surveillance</td>
<td>3. Assisting the countries to evaluate the leishmaniasis problem to determine areas and groups under risk of infection</td>
<td>- Number of trained laboratory and other health personnel for diagnosis and prevention and control of the disease.</td>
</tr>
<tr>
<td></td>
<td>4. Assisting the countries to obtain baseline data and in elaborating methodologies for monitoring and evaluating control activities</td>
<td></td>
</tr>
</tbody>
</table>
EMERGENCY PROCEDURES AND SPECIAL MEASURES FOR DEALING WITH OUTBREAKS AND EPIDEMICS

Philippe Desjeux

INTRODUCTION

Outbreaks and epidemics of cutaneous or visceral leishmaniasis are consistently reported around the world. Long-standing endemic foci can suddenly erupt into epidemics, or new foci may appear where leishmaniasis was never reported before. In both cases, there is an upsurge in the number of cases, reaching epidemic proportions.

Control measures in case of outbreaks or epidemics can be proposed, but they need to be based upon previous information and conditions to adequately adapt to local conditions.

EMERGENCY MEASURES

When an epidemic starts, some emergency measures are needed to try to stop the transmission and dissemination of the disease. Among these are:

(1) Release of funds: financial resources must be immediately released by health authorities, for the purchase of drugs, chemicals, insecticides, transportation, salaries, et cet., which implicates the previous definition of priorities and the concommitant availability of funds.

(2) Prompt involvement of infrastructures:

- When specific leishmaniasis units do not exist, existing health infrastructures should be used, for example malaria eradication organizations. In Afghanistan, there was a network of leishmaniasis control units, associated with malaria control units, which allowed the insecticide spraying of 31 tons of DDT and the protection of 369,000 people during the first 6 months of 1982.¹

- Mobilization of institutions and groups of persons likely to participate should be attained: primary health care units (if they exist), local sanitary agents, community workers, teachers, et cet.

- A network of diagnosis and treatment centers should be involved or rapidly organized. Prompt and effective treatment of human cases is essential, especially for anthroponotic cutaneous leishmaniasis and visceral leishmaniasis, so as to stop the extension of the epidemic (man being the main source of infection).

- Involvement and training of the staff of hospital and health centers should be practiced, on the following topics: sample-taking, transportation of samples, serodiagnosis techniques, basic knowledge on the focus,... by the organization of training courses, workshops and
demonstrations for doctors and physicians (pediatricians, dermatologists, haematologists).

(3) Certain specialized medical supplies are essential and should be made rapidly available: drugs, reagents, bone-marrow needles, stains, et cet. In this aspect, the problem is that all the material needed for parasitological diagnosis is usually dependent on outside assistance.

(4) Standardized reporting and recording systems should be implemented, with use of special forms.12)

One of the best examples is how India faced the epidemic of 1977 in North-Bihar.13 Prompt control measures initiated by the Government were made efficient by the presence of an adequate health infrastructure (reaching the most remote corners) which had been developed over the last 40 years, and which could be mobilized to meet specific needs of the epidemic. Simultaneously, adequate drugs were manufactured and made available. The prompt control was primarily made possible by the detection of all cases through annual house-to-house searches carried out by the health services.

(5) Information campaigns:

Sensitization of opinion should be made by all means (press and leaflets, radio, television, posters, educational programs) and at all concerned levels (health centers, hospitals, diagnosis and treatment centers, communities where the outbreak occurs). The message should contain instructions to the population at risk such as: consulting a doctor at an early stage of the disease, location of diagnosis and treatment centers, epidemiological data practical control measures, et cet.

(6) Restrictions on the movements of people are not always practicable: avoidance of sandfly infected areas can be suggested, as well as restrictions for people without health certificates to enter the epidemic area (immigrants, new settlers, road workers, nomads, soldiers, et cet.) However, evacuation of all human population from potential transmission areas is not feasible for political and socio-economical reasons.

(7) Retrospective or simultaneous investigations on specific aspects of the epidemiological situation should bring information on:

- prevalence: during epidemics of kala azar, the risk population can be defined when an accurate recording system is kept of the residence of patients, household members, neighbors: this population should be revised serologically at bi-monthly intervals for at least 6 months.14)

- affected area: a precise mapping is necessary to appreciate the exact geographical area involved.

- origin of epidemic (autochthonous or not?): some data are needed on the severity of outbreak, on the form of the disease. Parasitological diagnosis will permit the isolation of parasites (culture medium or
hamster) and permit later identification of the causative agent by iso-
enzyme characterization, DNA, or monoclonal antibodies.

- knowledge of human ecology and cultural practices, and of vector(s)
  (incrimination of vectors, precise transmission periods and sites) and
  reservoirs.

(7) Control measures for vectors and reservoirs should be implemented
where there is sufficient information about their epidemiological cycle.

Insecticide spraying is a rather simple and rapid measure, which
could be applied immediately before the next transmission season, indoor
if vector is endophilic, outdoor in other cases (breeding and resting
sites).

In the case of visceral leishmaniasis, a synthetic pyrethroid
(Deltamethrin) was recently used, with a long residual effect (more than
400 days); the evaluation of this control method in a VL focus of the
Yungas valleys of Bolivia is in process. Houses and hen-houses were
sprayed and, after 4 months, Lu. longipalpis could no longer be found (Le
Pont, personal communication). No significant side-effects were noted on
people or the environment. The same product is being tested by the
Bolivian Health Ministry in a cutaneous leishmaniasis and malarial focus
of Northern Bolivia, in the form of impregnation of mosquito nets
(120,000 nets treated in 1986).

CRITERIA OF CHOICE FOR EMERGENCY MEASURES

Besides the criteria of the type of leishmaniasis (VL, ACL, or ZCL),
the following aspects should be taken into consideration:

(1) availability of funds, importance of budgets,
(2) health priorities defined by Governments,
(3) degree of health education among the people,
(4) existence of trained personnel, adequate infrastructures, public
health services,
(5) existence of information on some aspects of the epidemiological
context; if no relevant information is available, it is better
not to attempt control strategies. Complete data are necessary
to ensure good chances of success and avoid wastage and future
resurgence of cases.

FURTHER RECOMMENDATIONS

(1) A coordinated use of multiple measures should often be imple-
mented (for example in VL foci: treatment of human cases, elimination of
dogs, DDT spraying) which, in case of emergency, sets the problem of
sequencing, timing, and interaction between measures;
(2) After solving the acute situation, another condition for success would be to evaluate costs and benefits, to detect changes in the effect of the program, and to implement permanent research, as epidemiology is a dynamic process in constant evolution.

REFERENCES

INTRODUCTION

Leishmanization is not vaccination in the true sense, because in most cases it produces sores similar to those seen in natural infections, and some of these last for long periods, up to a year or more, and require treatment. However, there are still some situations in which this is the only feasible way of controlling cutaneous leishmaniasis.

PRESENT PROGRAMME

Many foci of zoonotic cutaneous leishmaniasis are found in Iran, but in one of them, situated in the southwestern part of the Central Salt Desert adjacent to the city of Isfahan, the endemicity is so high that almost 80% of the rural population contract the disease before the age of 10 and essentially all non-immune newcomers moving to this part of the country become infected. Various control measures in the past have failed to control the disease or to permanently decrease the number of cases. In a limited field trial which was carried out in a small town north of Isfahan and lasted three years, it was shown that leishmanization was really effective and reduced the number of cases by 80%. Therefore, the Department General of Health in the province of Isfahan decided to put the whole rural population of the infected areas under this programme. This decision was implemented in 1982, and continued since.

The plain areas of the provinces of Khuzistan and Ilam in the southwestern part of Iran were known to be infected with zoonotic cutaneous leishmaniasis, but the disease has always had low endemicity. When war broke out between Iran and Iraq, hundreds of thousands of soldiers and paramilitary men were sent to the war front, living for months right in the middle of these infected areas. Thousands of cases appeared in these troops. Spraying of the fox-holes (in which soldiers were living for months) and distribution of repellents was completely ineffective in decreasing the number of cases. Therefore a decision was made in the army to start a programme of leishmanization in newly recruited soldiers, so that a few months after their training period most become immune for the rest of their service. The programme in the army has been implemented since 1983.

Apart from these two big programmes, leishmanization was also conducted in some war refugee camps during the first three years of war, and in other military bases in Isfahan and Baluchistan.

Local authorities of other infected areas in the country repeatedly have requested that this programme be implemented in their areas as well.

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However, because of lower endemicity of the disease and the possibility of control by other means, such as insecticide spraying, their requests have not been accepted.

**Parasite Inoculum**

The "vaccine" is prepared by culturing a strain of *L. major* isolated from *Rhombomys opimus* in the Isfahan area in 1964, and maintained thereafter in the central laboratories of the Institute of Public Health Research in Teheran by regular passage in out-bred laboratory mice.

For each round of leishmanization, parasites isolated from these infected mice are cultured in simple NNN medium, and after several passages in new culture tubes, with a 10-15 day interval between each two passages, the fifth passage is made in large 500 ml screw-top containers. The promastigotes from these are used for inoculation when the culture is 10-15 days old.

Early in the morning on the day of vaccination (wherever it is taking place), the culture is examined microscopically to make sure it is suitable for use, and is not contaminated with bacteria or fungi. The liquid phase is then aseptically transferred into sterile 20 ml vials which are given to vaccinators. At the end of the working day, these used vials are brought back to the distribution centre and, once again, they are tested to be sure that parasites have remained viable and have not been killed by mishandling.

The size of the inoculum is 0.1 ml containing approximately 200 to 300 thousand parasites. The inoculation is done intradermally on the upper arm on one side only.

**Timing**

In Isfahan, the leishmanization programme is carried out once a year in January or February. These dates are selected because the maximum transmission takes place in August and September and it is hoped that by that time the majority of vaccinated people have become immune.

For military recruits, leishmanization is done once a month in several training centres scattered over the country. The training period is about 3 months, and by the time these soldiers are sent to the front, most have some immunity.

**Programme Implementation**

In the last six years, about 160,000 persons have been inoculated in the Isfahan area. In the military, in the last five years, more than 1,250,000 soldiers have been inoculated. About 60,000 civilians (war refugees) were also inoculated in Khuzistan in the first three years of war; therefore the total number of leishmanizations carried out in the Islamic Republic of Iran is about 2 million.
Impact of the Programme

The following data provides some information about the impact of the programme:

1. During 1983 and 1984, a total of about 8,000 cases of the disease have been reported from Isfahan; less than 100 of which were among inoculated persons, although the population of inoculated persons exposed to the bite of sandflies has been greater than the non-inoculated. However, this does not mean that the incidence in the inoculated group was this low. There have been many other cases in the inoculated group, but the sores are small and heal spontaneously in one or two months, so the patient does not seek treatment.

2. An evaluation study was carried out in 1983-84, in children under five years of age in fifteen randomly selected villages in the area under the programme in Isfahan. There had been 530 children inoculated in 1982 ("takes" 77%, "non-takes" 23%), 961 children inoculated in 1983 and 1,716 children non-inoculated. The incidence of the disease for the Iranian year 1362 (21 March 1983-20 March 1984) in children inoculated in 1982 was 2.6% (14 cases), and in non-inoculated group was 14.5% (250 cases). The incidence in the second group was not calculated because they were inoculated in January-February 1983 and it was too early to include them in the evaluation.

3. In another evaluation study, more than 1,000 inoculated children were skin-tested in January 1985 in fourteen villages in the infected area. Among the "takes", more than 93% were skin test positive, while among the "non-takes" the rate was 54%. A total of 84% of inoculated persons were skin-test positive.

As for the complications of leishmanization, the following points should be mentioned:

1. About 2-3% of inoculated persons develop large lesions which are troublesome and should be treated like other active cases of cutaneous leishmaniasis.

2. Some sores (very exceptionally) last for more than two years, probably because of some deficiencies in the immune response of the person (we have seen five or six such cases in Isfahan).

3. A few cases of severe allergic reaction at the time of inoculation were seen, but all recovered after a few hours with, or without, treatment. The total number of such cases so far does not exceed ten.

Needless to say, sores of 5-10 mm of diameter lasting 4 to 6 months are not considered as a complication, because this is the natural consequence of leishmanization in most cases.

In conclusion, although not recommendable everywhere for the control of cutaneous leishmaniasis, it seems that this method of control is advisable for hyperendemic areas and also under conditions where the probability of becoming infected is extremely high, such as soldiers who
live in fox-holes and trenches for many months in infected areas during the active season of sandflies.

When the war ends the leishmanization programme in the army will end, as well. In the Isfahan area, there are plans to test the effectiveness of non-living crude vaccine. If positive results are obtained the Department General of Health may change its control programme and shift to this crude non-living vaccine. However, until then, provincial health authorities are recommending the continuation of this leishmanization programme.
EXPERIENCE WITH VACCINATION AGAINST LEISHMANIASIS IN BRAZIL
Carlos M. de F. Antunes

INTRODUCTION

The first suggestion of the possibility of using killed promastigotes of Leishmania as a vaccine against New World Cutaneous Leishmaniasis (NWCL) was published in Brazil in the late 1930s, following the observation of antibody development after intravenous parasite injection. It was speculated, at that time, that those antibodies would provide an effective protection against this disease.

Immediately after this initial suggestion, an uncontrolled field trial was carried out at a highly endemic area for NWCL; the observations were made on 1,127 participants, of whom 527 had been subcutaneously vaccinated with 3 doses given at one week intervals, of phenol-saline suspension of heat killed Leishmania promastigotes (600-700 million organisms). After 20 months of follow-up, the NWCL infection rate was 3.2/100 among the vaccinated participants, statistically different when compared to 18.0/100 observed in the non-vaccinated group (Table 1). However, despite these encouraging initial results, no further attempts were made in Brazil for almost 40 years to investigate prophylaxis via vaccination to control NWCL.

RECENT EXPERIENCE

After these pioneer efforts, the first real progress obtained was the corroboration of the original observation of leishmanin skin test conversion following the inoculation of non-living parasites in men, an indication of the development of delayed hypersensitivity. An uncontrolled field trial was then conducted in order to evaluate the efficacy of this vaccine, consisting of pooled killed Leishmania promastigotes of 5 stock isolated from different parts of Brazil (none from the actual trial area), containing 120 µg/ml of protein nitrogen and 1:10,000 buffered merthiolate phosphate solution. Unfortunately, this trial did not permit any definitive conclusions, because no cases of NWCL, in either control or vaccinated groups, were diagnosed during the trial period.

This same vaccine as used again as an emergency measure in an attempt to confine an epidemic of NWCL occurring in east Brazil. Although the vaccination campaign was neither planned nor organized as a randomized vaccine trial, the results obtained showed a statistically significant difference between the infection rates of the vaccinated group (2.2/100) when compared to the non-vaccinated participants (8.9/100), after 2 years of follow-up (Table 2). However, the high migration rates observed in this area during the trial period (16.7 and 23.7/100 among the vaccinated and non-vaccinated groups, respectively), made the interpretation of the results in relation to the vaccine efficacy quite difficult (Table 3). Nevertheless, information about the storage and the administration...
schedule of the vaccine was obtained which served as a baseline in planning future randomized trials.

Two controlled double blind field trials were conducted in 1981 and 1983 in northern Brazil. Brazilian Army conscripts were randomly assigned to the vaccine or placebo groups and tested during their training in the Amazon jungle, a high risk area for NWCL. The vaccine used in these trials differed slightly from the one used in previous experiments: one of the original stocks was replaced by a stock of Leishmania of the braziliensis complex; the doses contained 240 μg/ml of total nitrogen. The placebo consisted of phosphate buffer pH 7.4 plus merthiolate 1:10,000. The participants received 2 doses of 1.5 ml (of either vaccine or placebo), by deep intramuscular injection, at one week interval. The results obtained, after one year of follow-up (each trial) showed: (1) no significant differences between the vaccine and the placebo groups with respect to a number of characteristics (age, race, previous contact with the jungle, etc.); (2) no significant differences between the participants who got, and who did not get, NWCL during the trial, with respect to length of exposure, contact with the jungle, etc. and (3) a reduction of 67.3% (22.2/100 to 2.9/100) and 85.7% (1.3/100 to 0.2/100) in the annual incidence rate of NWCL, in 1981 and 1983 respectively, among those vaccinated who had converted to a positive leishmanin skin test as compared with the placebo groups (Table 4). It has to be pointed out that the difference between incidence rates of the disease in vaccinated and control groups in the 1983 trial was not statistically significant; because the disease frequency in the area was assumed to be around 10% in estimating sample size, these two groups may have been too small to detect any protective effect of the vaccine. During the 1981 trial, two unexpected results were observed: (1) an abnormally low conversion rate of the leishmanin skin test among vaccinated participants and (2) a high incidence rate of NWCL observed in a specific sub-group. Immunosuppression due to a concomitant yellow fever vaccination during this trial appears to be a plausible explanation for both results; in the 1983 trial, where the yellow fever vaccine was given 120 days before the NWCL vaccine, similar phenomena were not observed (Tables 5 and 6).

Another field trial, using the same methodology and conducted in the same area in 1984 had the objective of testing the NWCL vaccine with an added adjuvant (Corynebacterium parvum). Several problems have been identified concerning the trial execution - (1) the reading and interpretation of the leishmanin skin test done after vaccination; (2) the parasitological confirmation of Leishmania infection in participants who have been diagnosed with clinical NWCL and (3) the low incidence rate of NWCL during this period. The results obtained (one year follow-up) when the analysis was carried out ignoring the skin test conversion after vaccination and including only those participants who had a confirmed parasitological diagnosis, showed a 54.3% reduction (4.6/100 to 2.1/100), (not statistically significant) in the incidence rate of the group who received the vaccine plus adjuvant when compared to the rate among participants who received the placebo. No difference was detected between the incidence rates of those who received the vaccine without the adjuvant and those who received the placebo (Table 7). Similar results were observed when the analysis was restricted to a random sample of participants whose skin test after vaccination was confirmed (Table 8).
conclusion, despite all the problems which have occurred, it was possible
to detect a trend towards vaccine efficacy in preventing NWCL, as
indicated in previous trials; however, these results must be confirmed
especially the suggestion of an increased vaccine efficacy when an
adjuvant was added.

A similar field experiment is now in progress, in an attempt to
confirm the suggestive findings of the 1984 trial; the results should be
fully analyzed by mid-1988.

REFERENCES

10. Antunes, C.M.F. et al., New World (in press)

Table 1.

<table>
<thead>
<tr>
<th>Groups</th>
<th>Yes</th>
<th>NWCL No</th>
<th>Total</th>
<th>Incidence Rates (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vaccinated</td>
<td>17</td>
<td>512</td>
<td>527</td>
<td>3.2</td>
</tr>
<tr>
<td>Non-vaccinated</td>
<td>108</td>
<td>492</td>
<td>600</td>
<td>18.0</td>
</tr>
<tr>
<td>Total</td>
<td>125</td>
<td>1002</td>
<td>1127</td>
<td></td>
</tr>
</tbody>
</table>

X² = 101.6, p < 0.05

Source: Pessoa SB, 1941. Rev Paulista Med 19:1
Table 2.

Vaccination against New World Cutaneous Leishmaniasis in Brazil

Incidence rates of NWCL among vaccinated and non-vaccinated groups, Espírito Santo, Brazil, 1978-1980

<table>
<thead>
<tr>
<th>Groups</th>
<th>Yes</th>
<th>NWCL</th>
<th>Total</th>
<th>Incidence Rates (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vaccinated</td>
<td>4</td>
<td>176</td>
<td>180</td>
<td>2.2</td>
</tr>
<tr>
<td>Non-vaccinated</td>
<td>18</td>
<td>185</td>
<td>203</td>
<td>9.8</td>
</tr>
<tr>
<td>Total</td>
<td>22</td>
<td>361</td>
<td>383</td>
<td></td>
</tr>
</tbody>
</table>

$X^2_{gl} = 60.6 \quad p < 0.05$


Table 3

Vaccination against New World Cutaneous Leishmaniasis in Brazil

Migration rates of NWCL among vaccinated and non-vaccinated groups, Espírito Santo, Brazil, 1978-1980

<table>
<thead>
<tr>
<th>Groups</th>
<th>Included in the Trial</th>
<th>Migration 1st year</th>
<th>Migration 2nd year</th>
<th>Total</th>
<th>Migration Rates (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vaccinated</td>
<td>216</td>
<td>19</td>
<td>17</td>
<td>36</td>
<td>16.7</td>
</tr>
<tr>
<td>Non-vaccinated</td>
<td>266</td>
<td>33</td>
<td>30</td>
<td>63</td>
<td>23.7</td>
</tr>
<tr>
<td>Total</td>
<td>482</td>
<td>52</td>
<td>47</td>
<td>99</td>
<td></td>
</tr>
</tbody>
</table>

$X^2_{gl} = 3.18 \quad NS$

Table 5.

Vaccination against New World Cutaneous Leishmaniasis in Brazil

Number of cases and incidence rates of NWCL during the trials period

Manaus, Amazonas, 1981 and 1983

<table>
<thead>
<tr>
<th>Trial</th>
<th>NWCL</th>
<th>Group I</th>
<th>Group II</th>
<th>Total</th>
<th>X²</th>
<th>gl</th>
</tr>
</thead>
<tbody>
<tr>
<td>1981</td>
<td>Yes</td>
<td>60</td>
<td>9</td>
<td>69</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>No</td>
<td>511</td>
<td>692</td>
<td>1243</td>
<td>47.74</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Total</td>
<td>611</td>
<td>701</td>
<td>1312</td>
<td>p&lt;.001</td>
<td></td>
</tr>
<tr>
<td>1983</td>
<td>Yes</td>
<td>6</td>
<td>6</td>
<td>12</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>No</td>
<td>529</td>
<td>733</td>
<td>1262</td>
<td>.32</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Total</td>
<td>535</td>
<td>739</td>
<td>1274</td>
<td>NS</td>
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</tr>
</tbody>
</table>

Incidence Rate (%) 1.1 0.8 0.9

Table 6.

Vaccination against New World Cutaneous Leishmaniasis in Brazil

Number and proportion of conversion of leishmaniasis skin test among vaccinated participants

Manaus, Amazonas, 1981 and 1983

<table>
<thead>
<tr>
<th>Test</th>
<th>Vaccinated</th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>1981 Group I</td>
<td>Group II</td>
<td>1983</td>
<td>Total</td>
<td></td>
</tr>
<tr>
<td>Positive</td>
<td>104</td>
<td>124</td>
<td>416</td>
<td>644</td>
<td></td>
</tr>
<tr>
<td>Negative</td>
<td>207</td>
<td>214</td>
<td>195</td>
<td>616</td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>311</td>
<td>338</td>
<td>611</td>
<td>1260</td>
<td></td>
</tr>
<tr>
<td>Proportion of positives</td>
<td>0.33</td>
<td>0.37</td>
<td>0.68</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Scores</td>
<td>0.49</td>
<td>0.54</td>
<td>1.00</td>
<td></td>
<td></td>
</tr>
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</table>

X²gl = 137.03  p < 0.0001

Orthogonal Comparisons

1981 Group I x Group II  X²gl = .80  NS

Vaccinated 1981 x Vaccinated 1983:  X²gl = 136.23  p < .0001

Linear trend analysis (proportion of skin test conversions):

b = 0.68

Z = 11.7  p < .0001

Table 7.
Incidence rates of NWCL among vaccinated and placebo groups (cases with parasitological diagnosis)
Manaus, Amazonas, 1984

<table>
<thead>
<tr>
<th>NWCL</th>
<th>Vaccine</th>
<th>Vaccine + Adjuvant</th>
<th>Placebo</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yes</td>
<td>20</td>
<td>9</td>
<td>19</td>
<td>48</td>
</tr>
<tr>
<td>No</td>
<td>439</td>
<td>421</td>
<td>394</td>
<td>1254</td>
</tr>
<tr>
<td>Total</td>
<td>459</td>
<td>430</td>
<td>413</td>
<td>1302</td>
</tr>
</tbody>
</table>

Incidence Rates (%) 4.4 2.1 4.6

$X^2 c 2gl = 4.0$ NS  Source: Antunes, et al., (in press)

Table 8.
Incidence rates of NWCL among vaccinated and placebo groups adjusted by skin test conversion cases with parasitological diagnosis
Manaus, Amazonas, 1981 and 1983

<table>
<thead>
<tr>
<th>NWCL</th>
<th>Protected(^{(1)})</th>
<th>Unprotected(^{(2)})</th>
<th>Placebo</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Vac</td>
<td>Vac+Adj</td>
<td>Vac</td>
<td>Vac+Adj</td>
</tr>
<tr>
<td>Yes</td>
<td>10</td>
<td>2</td>
<td>5</td>
<td>5</td>
</tr>
<tr>
<td>No</td>
<td>107</td>
<td>98</td>
<td>136</td>
<td>130</td>
</tr>
<tr>
<td>Total</td>
<td>117</td>
<td>100</td>
<td>41</td>
<td>58</td>
</tr>
</tbody>
</table>

Incidence Rates (%) 8.6 2.0 12.2 7.9 9.7

$X^2 c 4 gl = 5.6$ NS

\(^{(1)}\) Vaccinated protected = DID convert the skin test after vaccination

\(^{(2)}\) Vaccinated unprotected = DID NOT convert the skin test after vaccination

Source: Antunes, et al., in press
EXPERIENCE WITH VACCINATION AGAINST CUTANEOUS/ MUCOCUTANEOUS LEISHMANIASIS IN BRAZIL

Mayrink, W., Antunes, C.M.F., da Costa, C.A.¹, Melo, M.N.², Dias, M.³, Michalick, M.S.M.², Magalhaes, P.A.⁴, Oliveira Lima, A.⁵, Williams, P.², Nascimento, E.², Tavares, C.A.P.⁶, Afonso, L.C.C.⁶

INTRODUCTION

The current studies on a vaccine against American cutaneous leish­maniasis (ACL) in Brazil have their origins in observations made almost 50 years ago. Salles Gomez¹¹ inoculated killed promastigotes of Leishmania into individuals with active cutaneous lesions and reported that responses varied according to the method of administration. Intravenous inoculation led to a regression of lesions and suggested that the dead promastigotes were promoting the production of antibody. He thought that killed promastigotes could provide an effective prophylactic vaccine against ACL, but was unable to develop this line of investigation.

The feasibility of a vaccine against ACL was then explored by Pessoa and Pestana¹², Pessoa¹³ and Curban.¹⁵ The vaccine tested at that time was a phenol-saline suspension of the culture forms of a strain of Leishmania isolated in the State of São Paulo, in one of the six localities where the field tests were carried out. The trials were conducted in areas that had recently been deforested, and were character­istic of endemic areas of ACL in São Paulo during the 1930s and 1940s. By the end of 20 months, 18.0% of 600 controls had developed cutaneous lesions whereas only 3.2% of 527 vaccinated individuals did so. The difference in the prevalence rates of the two groups was statistically significant. It was thought that the few vaccinated subjects who devel­oped lesions had become infected either immediately before, or during, administration of the vaccine.

The promising results obtained by the late Samuel Barnsley Pessoa and his associates were ignored for more than 30 years, when it was decided to prepare a similar vaccine and test it in an endemic area in the State of Minas Gerais. Modifications were made in the preparation of the vaccine. Promastigotes were mass-produced in LIT medium¹⁶, harvested after seven days and concentrated by centrifuging. Organisms in one half of the concentrate were disrupted ultrasonically, those in the other half were left intact. The two were then mixed and the concentrate was diluted with buffered merthiolated phosphate solution to give a vaccine containing 120 µg/ml of protein nitrogen and 1:10,000 merthiolate.

The vaccine prepared for the Minas Gerais test was made by pooling promastigotes of five strains of parasites. Because this was in the days

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⁶ Departamento de Bioquímica e Imunologia ICB/UFMG
before biochemical methods were introduced for the identification of Leishmania, selection of strains was based on the clinical condition of the patients from whom the parasites were isolated. Thus, one strain originated from a case of diffuse cutaneous leishmaniasis in the State of Bahia; another came one of mucocutaneous leishmaniasis in the State of Ceará; the third was from a case of simple cutaneous leishmaniasis either in the State of Goiás or the State of Mato Grosso; and another was from a case of multiple cutaneous lesions on a patient in the State of Minas Gerais. To complete the "cocktail", the vaccine incorporated stock PH8, isolated by Dr. Ralph Lainson from a sandfly collected in the State of Pará.

As well as assessing the vaccine by comparing prevalence rates in vaccinated and control groups, it was decided that observations on changes in response to Montenegro antigen would be a useful and simple means of assessment. For this purpose, it was necessary to standardize the preparation and administration of Montenegro antigen and to have a uniform method for reading responses to the skin test; this was done by Melo et al. It perhaps needs to be emphasized that this Montenegro antigen, though now widely used in Brazil and elsewhere for diagnostic purposes, was developed as an essential part of the vaccine studies.

The vaccine was first field tested in Correia de Barracão in the Município of Caratinga, in the eastern part of the State of Minas Gerais. In contrast to the São Paulo trials, carried out in recently deforested areas, the landscape ecology at Caratinga is stable and has been so for many years. The land is used mainly for cattle rearing or agricultural/horticultural purposes and undisturbed woodland is chiefly confined to hill tops. In this mainly man-modified environment, ACL is still common. During the two years immediately before the use of the vaccine, 22 new cases occurred in Barracão.

No one could have predicted that ACL would disappear from the study area, but that is what happened. None of the 1,588 participants in the study (614 vaccinated, 974 controls) developed the disease in the three years following the first use of the vaccine. (ACL has since returned to Barracão). Despite this setback, useful information emerged from the Caratinga study.

The second time that the vaccine was used in the field was at Viana, not far from the coast of the State of Espírito Santo. Here, 53 new cases of ACL occurred in an eight-month period compared with 35 cases over the preceding four years. The outbreak of the disease was not associated with recent deforestation and the landscape ecology at Viana, as at Caratinga, is stable. Europeans came to the region in the 17th/18th centuries and the early settlers were engaged in timber extraction and subsistence farming. After extensive deforestation, coffee plantations were established until the 1950s and 1960s, when bananas became the main crop. No major environmental changes have taken place at Viana in recent years.

The vaccine used at Viana had the same composition as that used in Caratinga. Indeed, some tests were carried out using vaccine stored for the five years since the Caratinga studies. Opportunity was taken in
Viana to determine the number and size of doses of the vaccine. Otherwise, procedures in the two studies were similar. A preliminary screening was made with Montenegro antigen to eliminate those already with positive responses. Children under two years of age, pregnant women, people with signs of cardiac or renal disease, and those with active ACL were excluded from the study.

Of a population of 606, scattered in four rural communities, 483 were available; 216 were vaccinated and 267 were controls. Depending on the type of vaccine and its method of administration, 84-90% of the vaccinated group became Montenegro positive within 40 days. After two years, 1.7% of the vaccinated group and 8.9% of the controls had developed ACL. The differences were statistically significant. The individuals in the test group who became infected gave either negative or weakly positive reactions to Montenegro antigen 40 days after vaccination.

An unexpected factor in the Viana study was the instability of the human population. In two of the communities, 25-34% of the inhabitants moved away from the area during the two years of observations. This population movement did not involve single individuals; whole family groups suddenly packed up and disappeared. Again, useful information emerged from the field study at Viana. As emphasized by Mayrink et al., the studies were neither planned nor organized as a controlled clinical trial.

Controlled field trials were carried out amongst army conscripts undergoing jungle training near Manaus in the State of Amazonas. A preliminary note of these trials was published by Mayrink et al. and complete details were given by Antunes et al. The randomly chosen vaccinated and placebo groups matched each other by age, race, previous contact with forest, and incidence of other parasitic infections. Unlike the participants in the field studies at Caratinga and Viana, and also those in the original trials in São Paulo, the soldiers were at risk to infection in mainly undisturbed forest and, because they were involved in a training programme, they were at risk for definable periods. In the trials carried out in 1981 and 1983, the annual incidence of ACL was lower in the vaccinated group than in controls.

Once again, however, an unexpected difficulty arose. In the 1981 trial, only 33% of the test group showed a change in Montenegro responses within 35 days of being vaccinated. This was less than half of the conversion rates recorded at Caratinga and Viana. Unlike the civilians, the soldiers had received yellow fever, typhus and tetanus inoculations about the same time that the leishmaniasis vaccine was given. The low conversion rate was attributed to immunosuppression following yellow fever vaccination. Laboratory observations with inbred mice showed that measles vaccine could also induce immunosuppression. In the 1983 Manaus trial, the anti-leishmaniasis vaccine was given 120 days after yellow fever inoculation; Montenegro conversion rates returned to levels comparable with those recorded at Caratinga and Viana.

Further trials, still in progress or in the follow-up stage, have been organized amongst conscripts at Manaus. The main objective of these
trials is to evaluate the effects of incorporating an adjuvant (*Corynebacterium parvum*) into the vaccine. Other field work, already in progress or in the planning stage, is directed towards finding out about the long term effects of vaccination by assessing the current immune status of participants in all studies carried out to date.

Field work with the vaccine is being supported by laboratory studies. Costa et al. used *Leishmania mexicana amazonensis* infections in C57BL/10 mice to study the utility of incorporating adjuvants into the vaccine and to follow immunohistological changes following vaccination. A convenient laboratory model for *L. braziliensis braziliensis* infections is not available but Michalick et al. have found that such infections in dogs give rise to lesions that are histologically, pathologically and immunopathologically comparable with those found in man. The immunogenic properties of this parasite can, therefore, be studied in dogs. The vaccine itself is being analyzed. Nascimento et al. reported that a monoclonal antibody, obtained by immunizing BALB/c mice, recognized an antigen (molecular weight 65KDa) in the crude vaccine and in the membranes of promastigotes of all its constituent strains of *Leishmania*. The same antigen was recognized in the sera of vaccinated individuals and of patients with ACL. Afonso et al. studied the vaccine and sera of vaccinated individuals by immunoprecipitation using 125-I labelled material followed by SDS-polyacrylamide gel electrophoresis and autoradiography. A protein of 94-97KDa was recognized in the soluble fraction of the vaccine and in sera of patients with ACL but not in persons with negative Montenegro reactions. Taxonomic characterization of the five strains of *Leishmania* included in the vaccine is also in progress. However, on the basis of isoenzyme analyses and other methods, Melo et al. have failed to establish the identity of two of the strains.

ACKNOWLEDGEMENTS

This investigation received support from "Financiadora de Estudos e Projetos" (FINEP), from "Superintendencia de Campanhas do Ministerio da Saude" (SUCAM), from the Pan American Health Organization (PAHO), from "Conselho Nacional de Desenvolvimento Cientifico e Tecnologico" (CNPG), from "Ministerio do Exercito" (Comando Militar da Amazonia - CMA) and from the Research Strengthening Component of the UNDP/World Bank/WHO Special Programme for Research and Training in Tropical Diseases.

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FUTURE LEISHMANIA VACCINE DEVELOPMENT


INTRODUCTION

In human populations, any evidence that resistance to reinfection follows from natural or drug-induced cure of a parasitic disease augurs well for the development of a vaccine against that disease. A steep decline with age in infection rate, or intensity of infection, may indicate development of solid resistance in endemic areas. Also of value in the pursuit of a "natural antigen" vaccine is any demonstration that resistance to reinfection follows resolution of disease in a model system. As is well known to "leishmaniacs", the above encouragements for vaccine development exist in the case of zoonotic or Old World cutaneous leishmaniasis caused by Leishmania major. Additional encouragement to pursue the molecular vaccine objective may come from a demonstration in a well-controlled clinical trial, or in model systems, that protective immunity follows exposure to a crude antigen preparation or an attenuated organism. No doubt we will hear in this Workshop of studies on protective immunization trials in man. The bulk of the data from which discussion in this article derive, come from the mouse model of Old World cutaneous leishmaniasis caused by L. major. However, in regard to certain features of vaccination in mouse models, there may well be close parallels between L. major and at least L. mexicana amazonensis (e.g. 7).

POSSIBLE CANDIDATE VACCINES

Of course, vaccination to prevent infection or disease need not be based on natural antigens detected through analysis of immune responses induced during or after natural infection. Novel antigens that by definition are poorly, if at all, immunogenic in the majority of susceptible host genotypes, may provide attractive alternative strategies to vaccine development. In other words, useful vaccines may not only come from analysis of high titered, aggressive "inflammatory" immune responses that occur naturally during infection of hosts and that, because they are obvious, are usually the first to be studied. For example, using crude promastigote and amastigote antigen mixtures, genetically-susceptible BALB/c mice are high responders in vitro to L. major promastigote antigens in contrast to genetically-resistant C57BL/6 mice that respond rather poorly, particularly to amastigote antigens; analysis of the latter may be more useful in terms of identification of host-protective immune responses. If molecules of poor immunogenicity are contemplated for incorporation into a vaccine, they must be checked for cross reactivity with self, and induction of autoimmunity; poor immunogenicity may reflect partial tolerance to self-like epitopes in the molecule.

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In the selection of antigens that are naturally immunogenic for purposes of vaccination, it is necessary to be cautious in those parasitic diseases that have a major immunopathologic component. This is the case in some helminth infections, namely schistosomiasis, lymphatic filariasis and onchocerciasis. It may well also be a consideration in the leishmaniases, because of compelling evidence in murine cutaneous leishmaniasis, that immune responses dependent upon T cells of a certain phenotype (termed L3T4+, Ly2- T_M cells) actually exacerbate disease (10-13). The mechanism of disease-promoting immunity remains unknown, but does not appear to be due to anti-leishmania antibodies or T cells of the classical suppressor phenotype (i.e. Ly2+). One target of this immunity has been shown to be the carbohydrate antigens of L. major that are recognized by the monoclonal antibody WIC-79.3. These antigens are found in promastigote culture supernatants that have been termed excretory factor (EF), and that as a component of EF, have been used for the serotyping of L. major. Clearly, in vaccination to prevent disease, no opportunities must be given to the immune system of the sensitized individual to progress along pathways that promote disease or facilitate parasite survival.

In the recombinant DNA era of vaccination that involves production of near-native molecules, protein antigens are sought. Proteins and genes encoding them are also sought for purposes of antigen delivery in recombinant viruses (e.g. vaccinia) and bacteria (e.g. attenuated Salmonella). However, relevant antigens and epitopes involved in host-protective immunity may not be proteins. Whether carbohydrate, glycolipid and other non-protein epitopes of either T_M or B cell responses can be mimicked (in a manner useful for vaccination) by synthetic peptides or anti-idiotype antibodies remains to be established in natural host-parasite relationships. Nevertheless, the synthetic mimotope approach of Geysen et al. is of special interest in leishmaniasis for two reasons: (a) several carbohydrate-rich molecules that are immunogenic appear to have particular importance in leishmania infections and (b) T_M cells that are unequivocally involved in host-protective immunity in leishmaniasis, probably through macrophage activation only, are known to recognize chemically-synthesized peptides efficiently, though they do not recognize only peptides.

Studies by Handman and colleagues have established that an amphipathic glycolipid antigen on the L. major promastigote surface is one of the important parasite recognition structures involved in receptor-mediated "facilitated phagocytosis" by macrophages. This molecule, purified by WIC-79.3 antibody affinity chromatography, or sequential solvent extraction combined with hydrophobic chromatography, (McConville, M.J., unpublished) is rich in mannose and galactose and will vaccinate mice against cutaneous disease. The effectiveness of this experimental vaccine presumably relies upon expression of the glycolipid antigen at the surface of the infected macrophage, although this is not proven.

As in the case of cruder preparations of leishmania antigens which require intraperitoneal (IP) and intravenous (IV) injections to achieve effective vaccination, severe constraints on the route of injection of the glycolipid are evident. IP injection together with the adjuvant,
**Corynebacterium parvum**, is an effective method of vaccination of mice, although results are certainly more impressive in mouse strains that are not at the extreme of susceptibility to disease (e.g. BALB/c). Why subcutaneous (SC) injections are ineffective remains to be established, but may relate to decreased stability of the glycolipid in SC sites and cleavage to the disease-promoting hydrophilic carbohydrate form of the antigen. Newer methods of extraction of promastigote antigen, and serological analyses with monoclonals, have uncovered the existence of other molecules besides the glycolipids containing the target epitope(s) of the WIC-79.3 monoclonal that have protective effects. (McConville, M.J., unpublished)

As discussed in some detail recently, vaccines involving antigens that are lipophilic, and that have a relatively high affinity for membranes in general, are likely to benefit from the use of vehicles (e.g. liposomes and ISCOMS) that concentrate vaccine antigen into cells for MHC-restricted recognition by T<sub>H</sub> cells. These cells are involved in a variety of immune functions, such as help for antibody production by B cells, localized delayed-type hypersensitivity reactions, and macrophage activation. The latter function is presumably critical for destruction of intracellular leishmania, but it is not known as yet whether a particular lymphokine, a particular combination of lymphokines, and particular T<sub>H</sub> cell subpopulations, are involved in activation of macrophages that are already infected, in the process of being infected, or about to be infected. All evidence indicates that the lipid in the glycolipid is simply involved in orientation of the molecule and presentation of carbohydrate epitopes at the surface of the antigen-presenting cell. T cell clones will be required to establish that T<sub>H</sub> cells see carbohydrate epitopes, the issue of T cell recognition of carbohydrate epitopes still being controversial.

As indicated above, when the carbohydrate form of the protective glycolipid antigen is used for immunization prior to promastigote challenge, disease progression can be aggravated with lesion persistence.\(^{12,30}\) The most dramatic results have been obtained after subcutaneous injection of the carbohydrate in Freund's complete adjuvant, and variation seen amongst mouse strains, presumably reflects the differential ability of anti-carbohydrate T<sub>H</sub> cells to respond. The carbohydrate is derived from the glycolipid by treatment with phosphatidylinositol-specific phospholipase C and is found in large amounts in the supernatant of some, but certainly not all, *L. major* promastigote cultures. This carbohydrate has affinity for macrophage cell surfaces and presumably binds to the same ligand as the glycolipid does when it is displayed on the promastigote surface and used for macrophage recognition.\(^{28,34}\)

Will man respond to *L. major* carbohydrate antigen in a counterproductive way? Much would be learned on the point of whether the phenomena described in mice are pertinent to humans, by carefully-designed skin tests and *in vitro* T cell response analyses in endemic areas. Individuals to be examined would include those currently infected, compared with those recently recovered from known infection and apparently resistant to reinfection. Longitudinal studies would be the most instructive if the change in T cell responsiveness to glycolipids...
and derived carbohydrates is followed in individuals as their disease resolves spontaneously.

Production of glycolipid antigens for vaccination of man present numerous problems, although it is hoped that large-scale synthetic methods for carbohydrates will become available soon, just as they are available for peptide synthesis. Adjuvants such as *E. parvum* are out of the question, as are IV and IP routes of injection. What then of the future?

One approach would be to conjugate the carbohydrate portion of the glycolipid to immunogenic B cell-binding peptide epitopes through a stable linkage, and hope that this form of antigen presentation (as distinct from that probably provided by macrophages, and involving an unstable linkage to lipid) is better at recruitment of appropriate TH cells. If the disease-promoting effects of free carbohydrate immunization are dependent upon binding of the antigen to molecules on the surface of (uninfected) macrophages, then modification of the carbohydrate to alter this binding may be beneficial.

Whilst membrane-oriented *L. major* glycolipids have been implicated in macrophage recognition by promastigotes, and in TH cell recognition of infected macrophages, the far more relevant molecules must be those utilized by amastigotes in invasion of a macrophage after release from another, and thereby facilitating the progression of disease either locally or systemically. If these molecules are also expressed on infected macrophages, then opportunities for TH cell-dependent interruption of disease progression are increased. Whether vaccine-induced (or naturally occurring) antibodies can inhibit reinvasion by amastigotes is unknown, but seems most unlikely. It could occur if the antibody response can be restricted to some isotype that does not bind to macrophages through its Fc portion and thereby facilitate internalization of the opsonized organism into the macrophage. It is possible though not proven that some antibody specificities or isotypes may alter the access route of the amastigote (or promastigote) so as to prejudice establishment in the macrophage. Quantitative aspects of the respiratory burst, production of free oxygen intermediates, and other mediators of anti-parasite effects, could well depend on the route of access taken by the parasite (see discussion in 32). Virtually nothing is known about molecules at the surface of released amastigotes and this information is required urgently if their candidacy as vaccines is to be assessed.

Another promastigote molecule touted as a candidate vaccine in leishmaniasis is the dominant, and apparently ubiquitous, antigen gp63. However, no published results on vaccination efficacy of the isolated molecule are available to date. Because of the reasons outlined above, protein antigens are preferred over all others in the present state of development of biotechnology. If it evolves that promastigote/amastigote invasion cannot be impaired by antibodies, and that there are only glycolipid rather than protein antigens available to macrophage-activating TH cells at the surface of infected cells, then the mimotope approach referred to above may provide the best opportunity of eventually using a recombinant DNA or synthetic protein strategy for a leishmania vaccine. Depending on progress made in the identification of
candidate protective antigens of the multitude of Old World and New World leishmania over the next 3 to 5 years, it may be that well-characterized attenuated organisms offer some hope of a leishmania vaccine in the short term, whilst we wait for the molecularly-defined products that will be quite some time in coming, on present indications. This fact, in the case of L. major, is a little sobering, bearing in mind the very high degree of protective immunity induced in most humans by infection (and the availability of an excellent mouse model) compared with other helminth and protozoa parasites, including some other leishmaniases. A start in the experimental use of mutagenized leishmania (L. braziliensis) has been made. Much controversy centres around the value of using crude antigen mixtures or attenuated organisms in trial vaccination of man. Despite all the negative aspects of live organism vaccines, a factor in favor of attenuated organisms in establishing unequivocally that vaccination against a particular leishmanial infection is possible in man, is the likely low cost and feasibility of production locally. There might well be as many risks in the widespread use of powerful adjuvants that will be necessary for stimulation of Tc cell responses by molecular vaccines, as there are in the use of attenuated organisms.

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CONCLUSIONS AND RECOMMENDATIONS
OF WORKSHOP PARTICIPANTS

INTRODUCTION

Selection by the participants of priority needs to be recommended for control of the leishmaniases was one of the concluding activities of the workshop.

Recognizing that each clinical/epidemiological form has special characteristics which differ from the other forms so that general recommendations for control approaches are not feasible, four disease groups were considered separately:

A.) Visceral leishmaniasis (L. donovani)
B.) Infantile visceral leishmaniasis (L. infantum, L. chagasi)
C.) Old World cutaneous leishmaniasis (L. tropica, L. major, L. aethiopica)
D.) New World cutaneous/mucocutaneous leishmaniasis (L. braziliensis complex, L. mexicana complex).

For each of these, three major areas of knowledge, important for control efforts, were identified and recommended as priorities. The pertinent needs/tools were listed for each priority. It was considered that limiting the number of recommendations in this manner would emphasize the importance of the priorities selected by consensus. However, in one group, secondary priorities were identified as well, which were considered to merit special attention because of their importance to any future control activities. The priorities and needs/tools for each of these sections are listed here in summary form.

RECOMMENDATIONS

Visceral leishmaniasis.

Priorities

1. Detection of cases (clinical and subclinical).

   Needs/tools:

   a) Application of useful available serological tests (FA, ELISA, Direct agglutination) and leishmanin skin tests.
   b) Development of improved methods for diagnosis, especially those which can be used at the PHC level.

2. Identification of reservoir host(s) - especially in India.

   Needs/tools:

   Cheaper, quicker, less cumbersome methods for demonstrating amastigotes.
3. Establishment of vector spectrum and development of integrated control program.

Needs/tools:

a) Longitudinal studies (including infectivity rates).

b) Transmission experiments.

c) Field trials of control methods.

**Infantile Visceral Leishmaniasis**

Priorities

1. Control of canine reservoir.

Needs/tools:

a) Development of rapid diagnostic procedure (for field use).

b) Pilot studies to evaluate dog control as means to reduce human infections.

2. Establish role of wild animal reservoirs (canids, rats, others).

Needs/tools:

a) Studies utilizing existing methods to find infected species.

b) Development of new technology (e.g. sensitive antigen detection method).

3. Determine role and importance of man as a reservoir (symptomatic, asymptomatic, and oligosymptomatic cases)

Needs/tools:

a) Serology

b) Skin test

c) Evaluate xenodiagnosis.

**Old World Cutaneous Leishmaniasis**

Priorities

1. Protection on large scale (vaccination/oral prophylactic drug)

Needs/tools:

a) Studies to assess baseline quantitative epidemiological data; need analytical epidemiology capability [identification of population at risk.]

c) Candidate vaccine/drug (based on laboratory studies) for field trials.
2. Pilot studies on vector and reservoir control methods in relation to human disease.

Needs/tools:

a) Method acceptable in terms of environmental protection standards.
b) Means to evaluate results.

3. Better knowledge of reservoir hosts and vectors in many areas. (Khartoum outbreak suggests human reservoir of L. major).

Needs/tools:

Capability for longitudinal and in-depth studies on reservoirs and vectors.

Additional priorities; (not necessarily in order).


Tools/needs:

a) Field trials of current candidates.
b) Development of more effective new compounds.

5. Establish parasite identification capabilities in endemic areas.

Needs/tools:

a) Establish of national and regional centres for identification, with funding for operations.


7. Initiate socio-economic research (identify target groups for control projects, socio-economic factors to improve program acceptance, and factors to insure community involvement).

Needs/tools:

Personnel cross trained in bio-medical and socio-economic fields.

New World Cutaneous /Mucocutaneous Leishmaniasis

Priorities

1. Detection of cases and identification of high risk groups.

Needs/tools:

a) Trained personnel at all levels, from PHC upwards.
b) Optimization of technologies (e.g., develop more reliable culture techniques).
c) Analytical epidemiology by Ministries of Health (dependent upon obligatory reporting of cases).

d) Socio-economic research to define factors of significance.

2. Development of vaccines.

Needs/tools:

a) Animal model for chronic disease state; (espundia and DCL)
b) Human trials in sites selected from epidemiological data from studies which constitute Priority 1.

3. Identification of elements of transmission (vector, reservoir).

Needs/tools:

Studies to clarify complexities of *L. braziliensis*-complex foci and differences between foci.

ANALYSIS OF PRIORITY OF RECOMMENDATIONS

One of the major purposes of this Workshop was to identify priority needs for studies and methodology research which are directly related to control efforts. Because available resources for research support are invariably inadequate for needs, a ranking by priority has always been an important consideration for funding agencies. Toward that end, a rudimentary analysis was attempted in order to achieve an overall priority ranking of the needs which were identified.

Recommendations were made for each disease group by a separate committee. The participants were assigned to a committee according to the area of their major experience and expertise. It should be explained that the recommendations were made by the separate committees without the opportunity for a following plenary session to achieve uniformity of terminology. Consequently, there was some difficulty in defining the categories of needs. For example, the same third priority was selected by three committees. This concerned the need to obtain better knowledge of the vectors involved in transmission; but was expressed in a different manner by each, viz.

"Establishment of vector spectrum..."
"Better knowledge of ... vectors"
"Identification of elements of transmission (vector, ...)"

Longitudinal studies as the means for obtaining the needed information was specified by only one group, but for purposes of analysis, this was classified as "Longitudinal vector studies" for all, since it is obvious that this is the most appropriate means of obtaining such information. Other categories of studies and research were not always this clear, and might have been interpreted and defined differently by another person. Although, in most cases, the discussion of the Recommendations to be adopted provided a good basis for determining the intent and thinking of
the participants, the convenor must accept responsibility for determining and selecting the categories used in this analysis, and therefore, for any errors in the order of priority.

Methods

The recommendations made by the four committees for the various disease forms were reviewed, and categorized in a list of studies and research topics. For these categories, each mention in a Recommendation was listed with the number of the priority assigned. To obtain the Priority Index for each category recommended, a weighting factor was assigned, as the reciprocal of the three priorities, or a value of $0.5$ for any priority beyond the primary three priorities, viz.

<table>
<thead>
<tr>
<th>Priority</th>
<th>Factor</th>
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<tr>
<td>1</td>
<td>3</td>
</tr>
<tr>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>3</td>
<td>1</td>
</tr>
<tr>
<td>4-7</td>
<td>$0.5$</td>
</tr>
</tbody>
</table>

Results

The relative priority of the studies and methodology research which are embodied in the Recommendation of the Workshop are shown in Table 1. The highest priority identified was for improved diagnostic methodologies, since this was involved in recommendations for VL, Infantile VL, and New World CL/MCL. It should be explained that the high index resulted, at least in part, from including antigen detection techniques, culture methods, and procedures for parasite identification in animals in this category. However, it is clear that improved methods for detecting parasites (diagnosis) in man and animals is a high priority need, and would have many useful applications.

Additionally, there was a category which did not fit this classification scheme, and therefore not included in the table. This involved recommendations for the establishment of support services. One recommendation was for establishing a quantitative epidemiology capability in the Ministries of Health; which had a Priority Index of $3.0$, since it was identified as part of a first priority. The second service recommended was the establishment of national and regional parasite identification centers with adequate funding; with a Priority Index of $0.5$ as part of a secondary (beyond 3) priority.

A recurring theme of discussion during the Workshop was the concern for a more effective and feasible means of treating existing cases. The fact that, the great majority of cutaneous leishmaniasis sufferers in most parts of the world never receive treatment because repeated injections over an extended period are simply not feasible for most patients, was addressed in many papers, and mentioned frequently in discussions. It is, therefore, rather surprising that a Recommendation for a more practicable treatment regimen was made only for Old World CL, as an additional priority, with an Index of $0.5$. 

Table 1.
Priority Index of studies and research recommended

<table>
<thead>
<tr>
<th>Categories</th>
<th>*Recommendation/ Priority</th>
<th>Score</th>
<th>Priority Index</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Studies</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Basic human epidemiology</td>
<td>C-1, C-6</td>
<td>3+.5+</td>
<td>8.5</td>
</tr>
<tr>
<td>(Identification of high risk)</td>
<td>D-1, D-2</td>
<td>3+2  =</td>
<td></td>
</tr>
<tr>
<td>Serological and skin test</td>
<td>A-1, B-2</td>
<td>3+2+</td>
<td>7.0</td>
</tr>
<tr>
<td>surveys (human &amp; reservoirs)</td>
<td>B-3, C-3</td>
<td>1+1  =</td>
<td></td>
</tr>
<tr>
<td>Pilot control (vector,</td>
<td>A-3, B-1</td>
<td>1+2+</td>
<td>6.5</td>
</tr>
<tr>
<td>reservoir)</td>
<td>C-2, C-4</td>
<td>2+.5=</td>
<td></td>
</tr>
<tr>
<td>Establish reservoir (animal)</td>
<td>A-2, B-2</td>
<td>2+2+</td>
<td>6.0</td>
</tr>
<tr>
<td>Longitudinal, vector</td>
<td>A-3, C-2</td>
<td>1+2+</td>
<td>5.0</td>
</tr>
<tr>
<td>Role of human reservoir</td>
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<td>2+1+</td>
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<td>Socio-economic</td>
<td>A-3, C-3</td>
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<tr>
<td>Determined vector</td>
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<td>1</td>
<td>1.0</td>
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<tr>
<td>Transmission</td>
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<td>1</td>
<td></td>
</tr>
<tr>
<td><strong>Methodology research</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Improved diagnosis</td>
<td>A-1, A-2</td>
<td>1+2+</td>
<td>13.0</td>
</tr>
<tr>
<td></td>
<td>B-1, B-2, D-1</td>
<td>3+2+</td>
<td></td>
</tr>
<tr>
<td>Vaccine antigen</td>
<td>C-1</td>
<td>3</td>
<td>3.0</td>
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<tr>
<td>Non-environmental polluting insecticide</td>
<td>C-2</td>
<td>2</td>
<td>2.0</td>
</tr>
<tr>
<td>Animal model of chronic disease</td>
<td>D-2</td>
<td>2</td>
<td>2.0</td>
</tr>
<tr>
<td>(MCL and DCL)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Skin test</td>
<td>B-3</td>
<td>1</td>
<td>1</td>
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<tr>
<td>Xenodiagnosis</td>
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<td>1</td>
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<tr>
<td>Topical treatment drug</td>
<td>C-4</td>
<td>.5</td>
<td>0.5</td>
</tr>
</tbody>
</table>

*A- VL, B- Infantile VL, C- Old World CL, D- New World CL/MCL
1-4 Priority assigned in Recommendation
Another recurring subject of discussion, was the danger of the current popularity of research on a vaccine which is resulting in neglect of research on methodologies for control measures against vectors and reservoirs. Although there is almost unanimous agreement that an effective vaccine would be the single most effective measure for control of many forms, the consensus of opinion was that there is no great likelihood that one would be generally available in the near future, and that alternative measures should not be abandoned in favor of vaccine development. This view is probably reflected in the relatively low Priority Index given to vaccine development in the Recommendations.

DISCUSSION OF PREVALENCE AND INCIDENCE

One of the major constraints on an understanding of the global importance of the leishmaniases has always been the paucity of information regarding the true prevalence and incidence. For several years one of the most cited figures for world-wide occurrence of leishmaniasis was that of 400,000 cases per year, usually (and incorrectly) attributed to WHO. Actually, this was a "guess-estimate" made at the 1974 meeting of the Scientific Working Group on the Epidemiology of the Leishmaniases of the UNDP/World Bank/WHO Special Programme for Research and Training in Tropical Diseases. Recognizing that the then available figures were completely inadequate, the members of the SWG each made their own estimate of the areas with which they were familiar and these were combined to arrive at a global estimate, which was published in the report of the SWG. As incomplete and inaccurate as it was, this proved to be very useful, and provided an impetus for gathering more accurate information. Although many countries where leishmaniasis is endemic have now made it an obligatorily reportable disease and the knowledge of the occurrence is much improved, it is generally considered to be grossly underreported in most official government reports.

This Workshop provided the rare opportunity of a gathering of persons with current personal knowledge of endemic areas and foci in many areas of the world, and therefore an opportunity for a similar exercise which might yield an update of the current knowledge of the disease and efforts for control. Many participants had misgivings about providing answers concerning their country while relying only on their memory, without access to records or references, but considered that the result would be of interest and everyone participated. As an aid in this process, questionnaires were distributed which asked for:

a) the population at risk
b) average number of new cases occurring yearly
c) age group and occupation of majority of patients
d) the identity of the parasite, if known
e) government requirement to make leishmaniasis notifiable
f) current control activities

The figures in the following Table represent "best-guess" estimates by the workshop participants according to the restricted and incomplete information available to them.
Guess estimates on Leishmaniasis risk and approximate numbers of new patients reported per year

<table>
<thead>
<tr>
<th>Country</th>
<th>Millions at risk</th>
<th>CL</th>
<th>MCL</th>
<th>VL</th>
<th>A/S</th>
<th>V/C</th>
<th>A/R</th>
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<tr>
<td>*Afghanistan</td>
<td>10</td>
<td>8,000</td>
<td>-</td>
<td>100</td>
<td>-</td>
<td>+</td>
<td>-</td>
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<tr>
<td>*Algeria</td>
<td>10</td>
<td>6,000</td>
<td>-</td>
<td>200</td>
<td>-</td>
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<tr>
<td>Argentina</td>
<td>10</td>
<td>-</td>
<td>?</td>
<td>&gt;1</td>
<td>-</td>
<td>-</td>
<td>-</td>
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<tr>
<td>Belize</td>
<td>?</td>
<td>100</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>*Bolivia</td>
<td>0.4</td>
<td>1,500</td>
<td>-</td>
<td>10</td>
<td>+</td>
<td>+</td>
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<tr>
<td>Brazil</td>
<td>60</td>
<td>15,000</td>
<td>1,800</td>
<td>+</td>
<td>+</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>*China</td>
<td>1</td>
<td>-</td>
<td>-</td>
<td>100</td>
<td>+</td>
<td>+</td>
<td>-</td>
</tr>
<tr>
<td>*Colombia</td>
<td>?</td>
<td>2,000</td>
<td>120</td>
<td>100</td>
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<td>+</td>
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<tr>
<td>*Costa Rica</td>
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<td>?</td>
<td>-</td>
<td>+</td>
<td>-</td>
<td>-</td>
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<td>*Ecuador</td>
<td>6</td>
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<td>10</td>
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<tr>
<td>Ethiopia</td>
<td>4</td>
<td>250</td>
<td>10</td>
<td>150</td>
<td>+</td>
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</tr>
<tr>
<td>Honduras</td>
<td>?</td>
<td>350</td>
<td>-</td>
<td>10</td>
<td>-</td>
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<td>-</td>
</tr>
<tr>
<td>*India</td>
<td>20</td>
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<td>-</td>
<td>3,000</td>
<td>+</td>
<td>+</td>
<td>-</td>
</tr>
<tr>
<td>*Iran</td>
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<td>70</td>
<td>+</td>
<td>+</td>
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<tr>
<td>*Iraq</td>
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<td>1,000</td>
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<tr>
<td>*Israel</td>
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<td>3</td>
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<td>+</td>
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<tr>
<td>*Italy</td>
<td>?</td>
<td>1-10</td>
<td>-</td>
<td>1-10</td>
<td>-</td>
<td>-</td>
<td>+</td>
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<tr>
<td>*Kenya</td>
<td>1</td>
<td>10</td>
<td>-</td>
<td>300</td>
<td>+</td>
<td>+</td>
<td>+</td>
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<tr>
<td>Malta</td>
<td>?</td>
<td>20</td>
<td>-</td>
<td>100</td>
<td>?</td>
<td>?</td>
<td>?</td>
</tr>
<tr>
<td>Morocco</td>
<td>10</td>
<td>1,000</td>
<td>-</td>
<td>20</td>
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<tr>
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<td>500</td>
<td>-</td>
<td>10</td>
<td>-</td>
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<td>-</td>
</tr>
<tr>
<td>*Panama</td>
<td>?</td>
<td>1,200</td>
<td>-</td>
<td>-</td>
<td>-</td>
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<td>-</td>
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<tr>
<td>Paraguay</td>
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<td>550</td>
<td>-</td>
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<tr>
<td>Peru</td>
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<td>2,350</td>
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<td>+</td>
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<tr>
<td>Portugal</td>
<td>?</td>
<td>-</td>
<td>-</td>
<td>20</td>
<td>?</td>
<td>?</td>
<td>?</td>
</tr>
<tr>
<td>*Saudi Arabia</td>
<td>4</td>
<td>15,000</td>
<td>-</td>
<td>200</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>*Spain</td>
<td>?</td>
<td>2,900</td>
<td>-</td>
<td>20</td>
<td>+</td>
<td>-</td>
<td>+</td>
</tr>
<tr>
<td>*Sudan</td>
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<td>-</td>
<td>500</td>
<td>-</td>
<td>+</td>
<td>+</td>
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<tr>
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<td>800</td>
<td>-</td>
<td>10</td>
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<td>-</td>
</tr>
<tr>
<td>*Tunisia</td>
<td>8</td>
<td>5,000</td>
<td>-</td>
<td>50</td>
<td>+</td>
<td>+</td>
<td>+</td>
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<td>Turkey</td>
<td>4</td>
<td>-</td>
<td>-</td>
<td>20</td>
<td>-</td>
<td>-</td>
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</tr>
<tr>
<td>Venezuela</td>
<td>?</td>
<td>2,900</td>
<td>-</td>
<td>20</td>
<td>+</td>
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<td>-</td>
</tr>
</tbody>
</table>

* countries where leishmaniasis is compulsorily notifiable

**Legend**
- ? = no data available
- CL = Cutaneous leishmaniasis
- MCL = Mucocutaneous leishmaniasis
- VL = Visceral leishmaniasis
- A/S = Active surveillance of human population + Rx
- V/C = Vector control
- A/R = Animal reservoir host
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