CONTROL OF TROPICAL DISEASES

THE LEISHMANIASES

RLD HEALTH ORGANIZATION

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THE LEISHMANIASES

WORLD HEALTH ORGANIZATION
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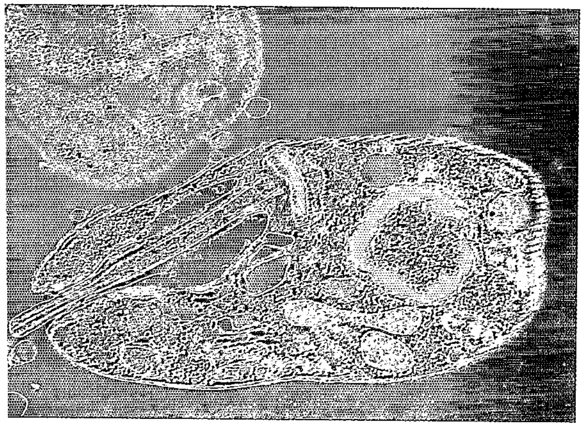

The parasite *Leishmania* X7600

THE LEISHMANIASES

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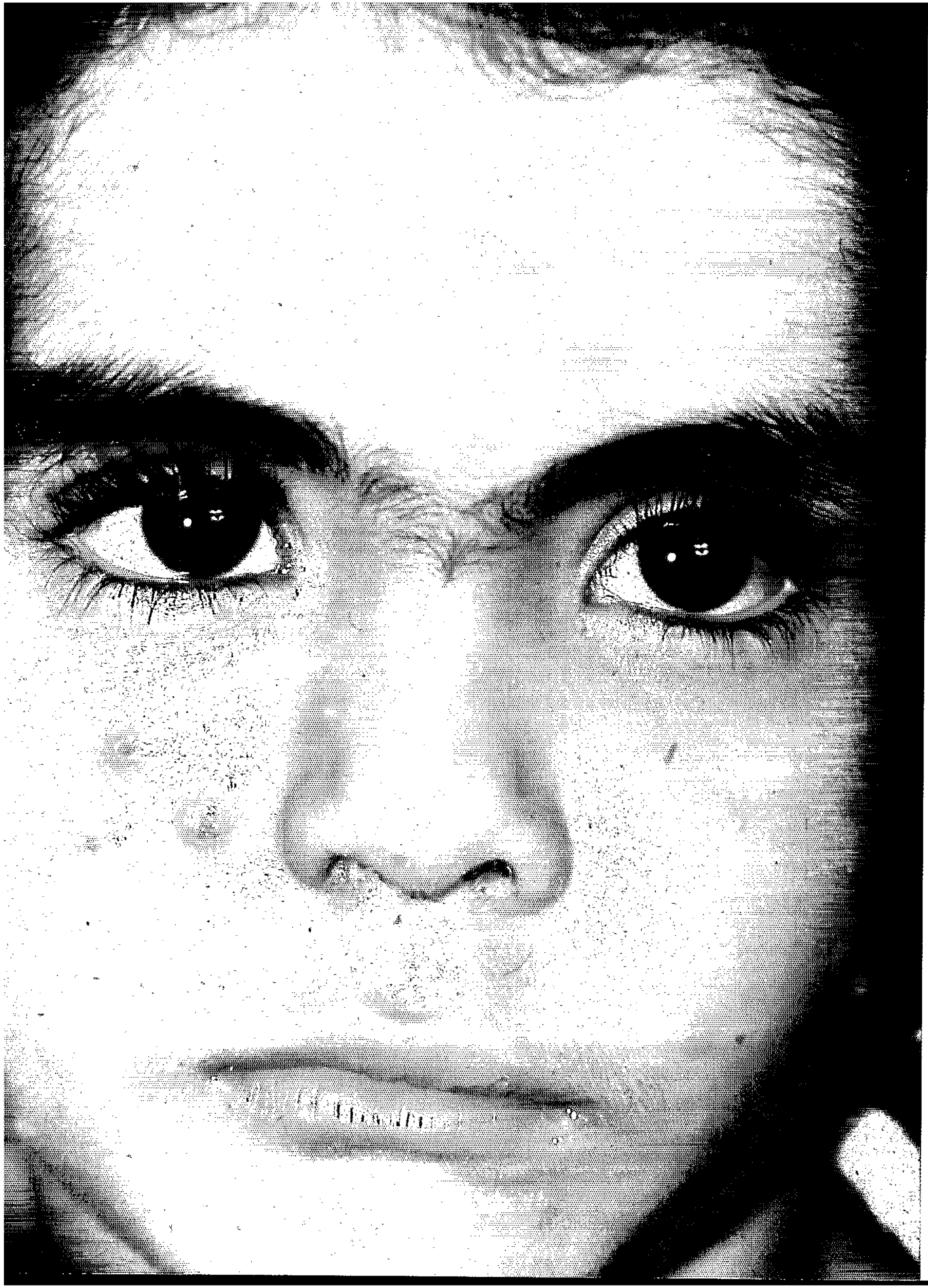
Cutaneous leishmaniasis.



THE DISEASE

The leishmaniases and the suffering they cause are threatening 350 million men, women and children in 88 countries around the world; 12 million of these people are already affected by the disease which, in its worst form, is fatal.

The leishmaniases are parasitic diseases with a wide range of clinical symptoms: cutaneous, mucocutaneous and visceral.

- **Visceral** leishmaniasis – also known as *kala azar* – is characterized by irregular bouts of fever, substantial weight loss, swelling of the spleen and liver, and anaemia (occasionally serious). If left untreated, the fatality rate can be as high as 100%.
- In *mucocutaneous* forms of leishmaniasis, lesions can lead to partial or total destruction of the mucose membranes of the nose, mouth and throat cavities and surrounding tissues. These disabling and degrading forms of leishmaniasis can result in victims being humiliated and cast out from society.
- *Cutaneous* forms of the disease normally produce skin ulcers on the exposed parts of the body such as the face, arms and legs. The disease can produce a large number of lesions – sometimes up to 200 – causing serious disability and invariably leaving the patient permanently scarred, a stigma which can cause serious social prejudice.

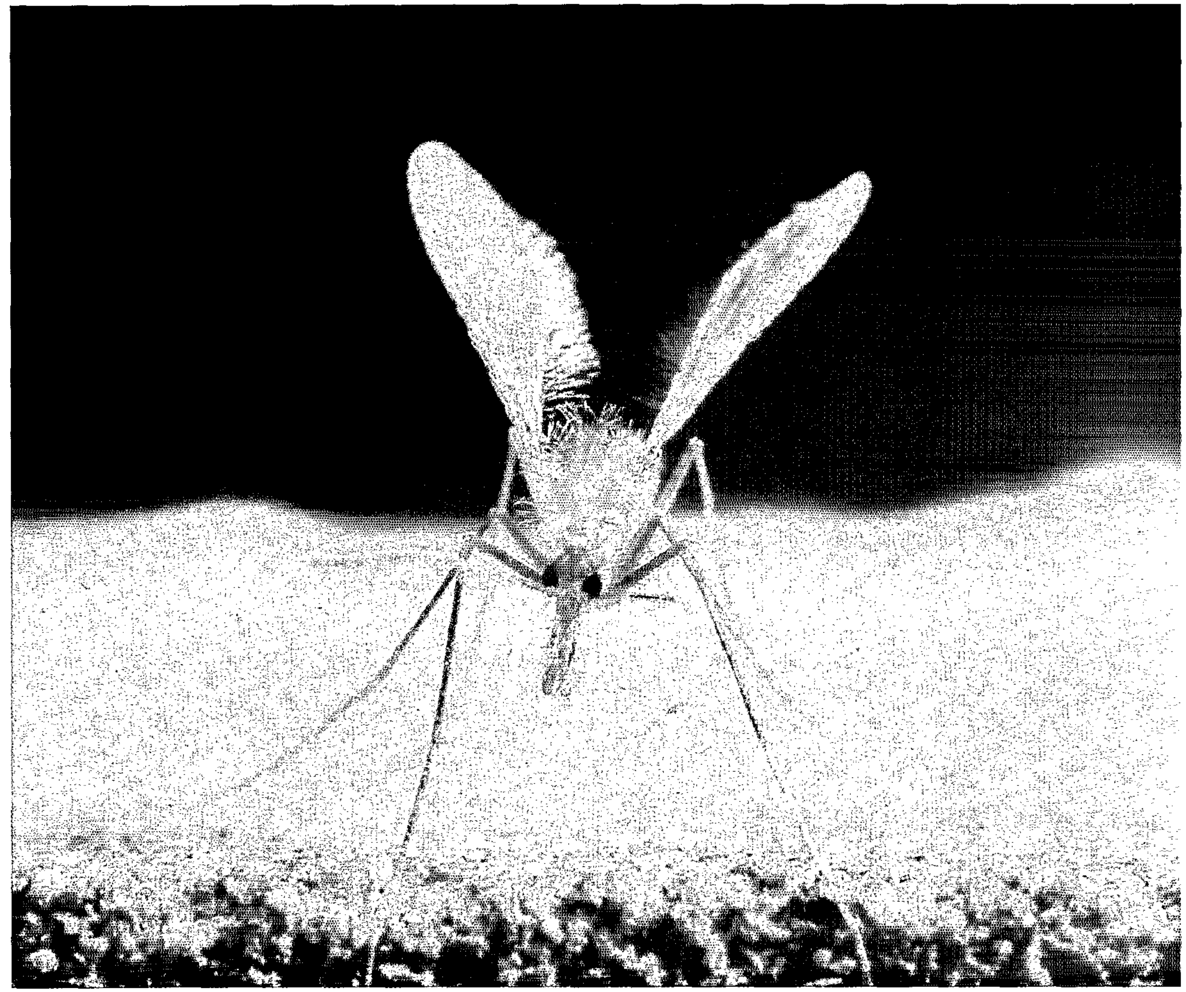
The leishmaniases are caused by different species belonging to the genus *Leishmania* a protozoa transmitted by the bite of a tiny 2 to 3 millimetre-long insect vector, the phlebotomine sandfly. Of the 500 known phlebotomine species, only some 30 of them have been

"Oriental sore" or "Aleppo boil" designates, in Syria, cutaneous leishmaniasis.

positively identified as vectors of the disease. Only the female sandfly transmits the protozoan, infecting itself with the *Leishmania* parasites contained in the blood it sucks from its human or mammalian host in order to obtain the protein necessary to develop its eggs. During a period of 4 to 25 days, the parasite continues its development inside the sandfly where it undergoes major transformation. When the now infectious female sandfly feeds on a fresh source of blood, its painful sting inoculates its new victim with the parasite, and the transmission cycle is completed.

The insect vector of leishmaniasis, the phlebotomine sandfly, is found throughout the world's **inter-tropical and temperate regions.** The female sandfly lays its eggs in the burrows of certain rodents, in the bark of old trees, in ruined buildings, in cracks in house walls, and in household rubbish, as it is in such environments that the larvae will find the organic matter, heat and humidity which are necessary to their development. In its search for blood (usually in the evening and at night), the female sandfly covers a radius of a few metres to several hundreds around its habitat.

For a long time, little was known about the transmission cycles of the disease, but over the last few years, field research and the application of molecular biology have enabled substantial progress to be made in understanding the different links in the transmission chain. Moreover, simple new diagnostic techniques have recently been developed which are practical, reliable and inexpensive. These techniques are available to concerned countries for the early detection and rapid treatment of the disease.



Phlebotomine vector of leishmaniasis, *Phlebotomus ariasi.*

IMPORTANT DATES

Although cutaneous leishmaniasis can be traced back many hundreds of years, one of the first and most important clinical descriptions was made in 1756 by *Alexander Russell* following an examination of a Turkish patient. The disease, then commonly known as "Aleppo boil", was described in terms which are still relevant: *"After it is cicatrised, it leaves an ugly scar, which remains through life, and for many months has a livid colour. When they are not irritated, they seldom give much pain... It affects the natives when they are children, and generally appears in the face, though they also have some on their extremities... In strangers, it commonly appears some months after their arrival... very few escape having them, but they seldom affect the same person above once."*

Representations of skin lesions and facial deformities have been found on pre-Inca pottery from Peru and Ecuador dating back to the first century AD. They are evidence that cutaneous and muco-cutaneous forms of leishmaniasis prevailed in the New World as early as this period.

Texts from the Inca period in the 15th and 16th centuries, and then during the Spanish colonization mention the risk run by seasonal agricultural workers who returned from the Andes with skin ulcers which, in those times, were attributed to **"valley sickness"** or **"Andean sickness"**. Later, disfigurements of the nose and mouth became known as **"white leprosy"** because of their strong resemblance to the lesions caused by leprosy.

In the Old World, Indian physicians applied the Sanskrit term *kala azar* (meaning **"black fever"**) to an ancient disease later defined as visceral leishmaniasis. In 1901, *Leishman* identified certain organisms in smears taken from the spleen of a patient who had

"Espundia" shown on a pre-Columbian pottery of Peru.

died from **"dum-dum fever"**. At the time, dum-dum, a town not far from Calcutta, was considered to be particularly unhealthy. The disease was characterized by general debility, irregular and repetitive bouts of fever, severe anaemia, muscular atrophy and excessive swelling of the spleen. Initially, these organisms were considered to be trypanosomes, but in 1903 Captain *Donovan* described them as being new. The link between these organisms and *kala azar* was eventually discovered by Major *Ross*, who named them *Leishmania donovani.* The *Leishmania* genus had been discovered.

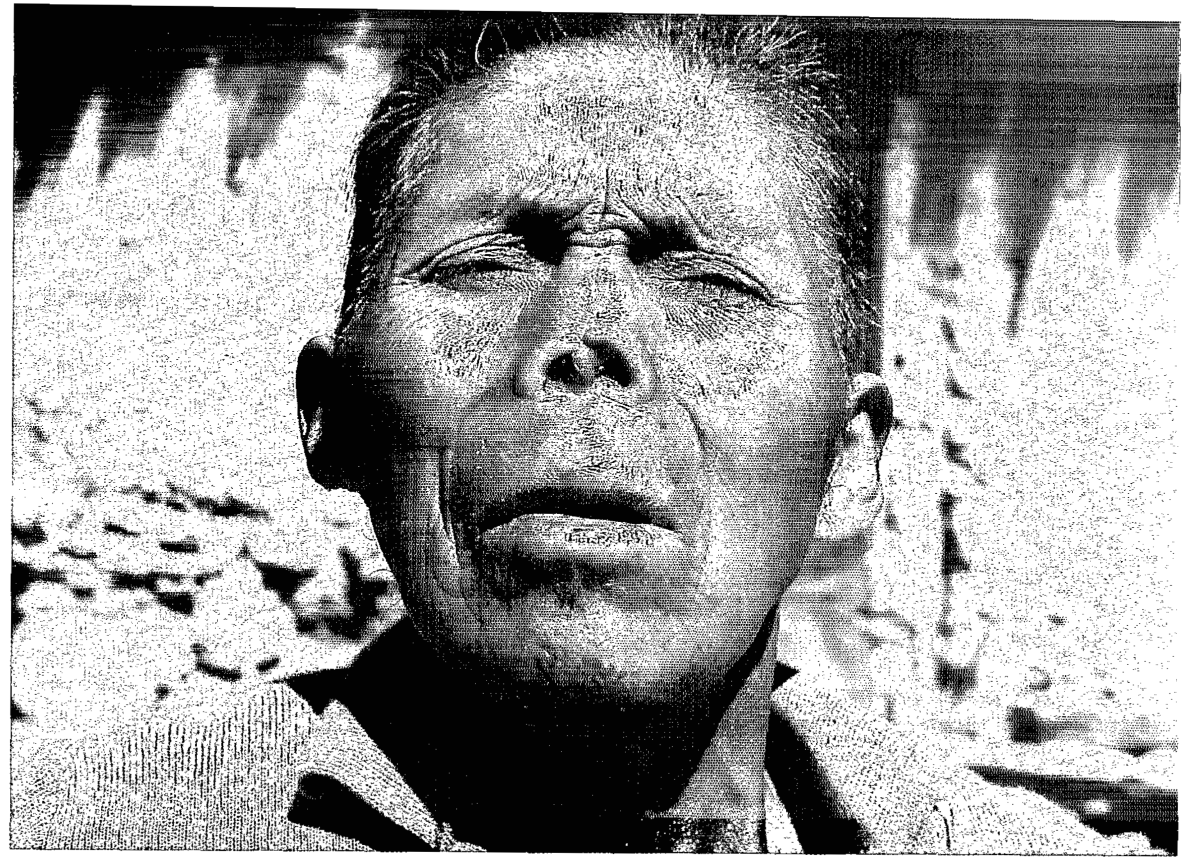
For many years, it was not realized just how serious the leishmaniases were. We now know that they are prevalent in **88 countries** around the world.

- 90% of all *visceral* leishmaniasis cases occur in Bangladesh, Brazil, India and the Sudan;
- 90% of the cases of *mucocutaneous* leishmaniasis occur in Bolivia, Brazil and Peru;
- 90% of *cutaneous* leishmaniasis cases occur in Afghanistan, Brazil, Iran, Peru, Saudi Arabia and Syria; in Saudi Arabia, cutaneous leishmaniasis is so widespread, it has been named "little sister". In the Andean valleys of Peru, the disease is so commonplace that parents consider it to be an infantile disease.

Over the last ten years **endemic regions have been spreading further afield** and there has been a **sharp increase in the number of recorded cases of the disease.***

Of the 2 million new cases of leishmaniasis** estimated to occur annually, only 600,000 are officially declared.

As declaration is obligatory in only 32 of the 88 countries affected by leishmaniasis, a substantial number of cases are never recorded:



"Espundia", mucocutaneous leishmaniasis in Bolivia.

- in the Indian State of Bihar, where 38 out of 42 districts are affected, between 250,000 and 300,000 cases were estimated in 1992 – five times the official figure.

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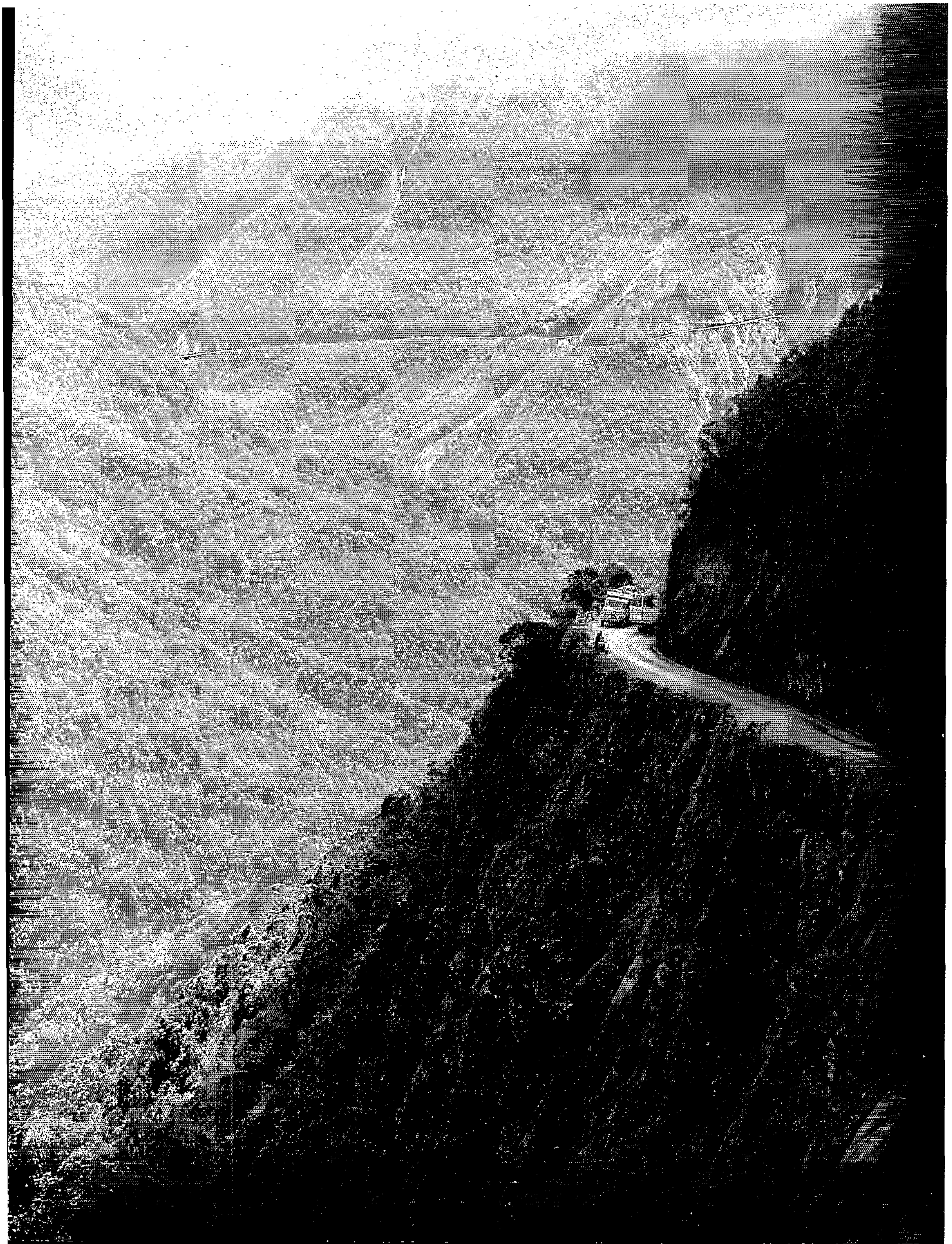
* In Tunisia, 1300 cases of cutaneous leishmaniasis were reported in 1983. In 1991, the figure had reached 6000. In the Northern States of Brazil, 2000 cases were reported in 1980, and 9000 in 1990.

** including 1.5 million cases of cutaneous leishmaniasis and 0.5 million cases of visceral leishmaniasis.



THE CURRENT SITUATION

Incidence of the leishmaniases is increasing at the same time as the world is experiencing an economic crisis. The disease is seriously hampering productivity and vitally needed socio-economic progress. The economic impact of the leishmaniases is far more serious than might be imagined from the number of cases recorded. Epidemics have significantly delayed the implementation of numerous development programmes, particularly in Saudi Arabia, Morocco, the Amazon basin and the tropical regions of the Andean countries.

In these latter countries, it is thought that the impact of diseases such as leishmaniasis, malaria and yellow fever on the new settlers is responsible for the partial failure of programmes aimed at transfering people to new development areas where these diseases prevail.

The leishmaniases mainly affect countries and populations facing serious economic difficulties. Of the 88 countries concerned, 76 are developing countries and 13 of these are among the world's least developed countries*.

Within these countries, the disease claims its victims among the most impoverished members of the community. Medical costs and the cost of transport to health centres for these people, caught up in the vicious circle of poverty and misery, are too high to be borne

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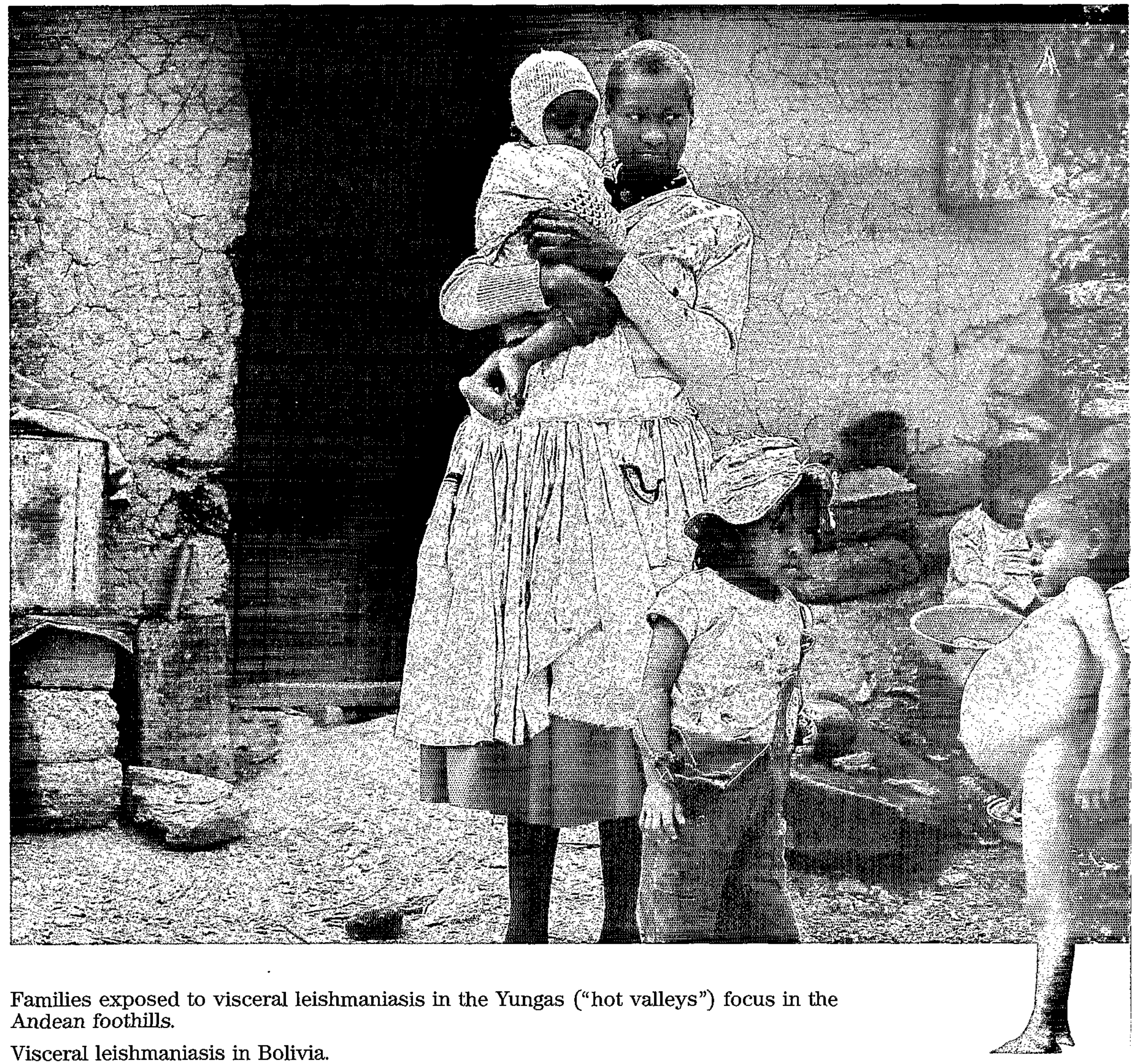
* The least developed countries (LDC) are currently made up of 47 countries, representing a population of over 550 million. This group of countries is the weakest segment of the international community. In 1990, the gross domestic product (GDP) of the LDC was between $US 473 and $US 567 per inhabitant per year.

Migration towards the Amazon basin.

borne by the family. The loss of many work hours in order to receive uncertain treatment only exacerbates their poverty.

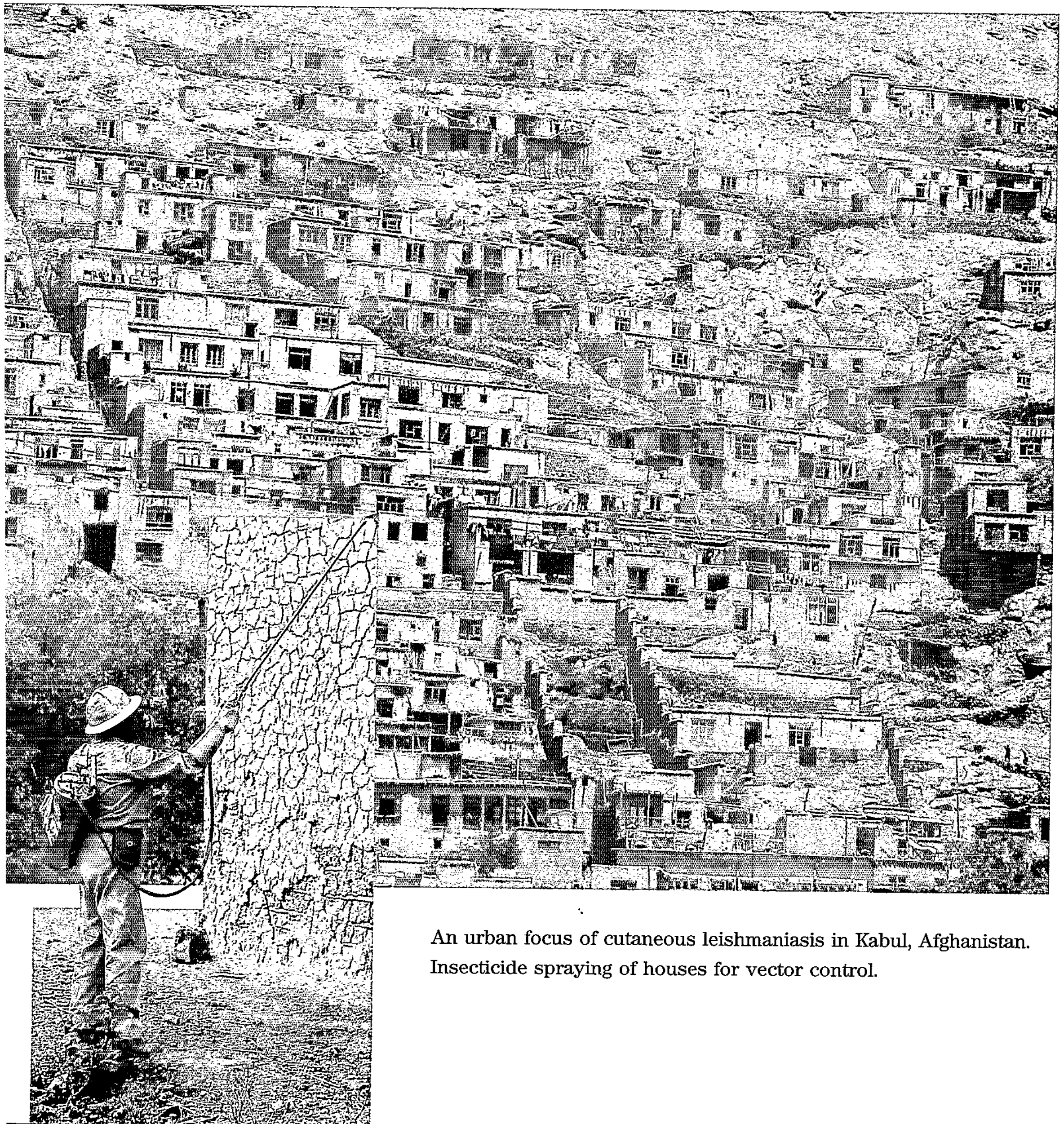
Paradoxically, certain social and economic development activities, if not planned and implemented in collaboration with the health authorities, can encourage fresh outbreaks of the leishmaniases and other diseases:

- in the Andean countries, the **settling** of new regions – as a possible means of resolving the problems brought on by the relative overpopulation and the lack of arable land in the high plateaux – is enciting entire populations to migrate towards the tropical plains where there is an extremely high risk of transmission;
- in the countries of Indian subcontinent and the Arabian Peninsula, **transnational movements of the workforce** are favouring the spread of the disease;
- the implementation of **development programmes:** road networks, all types of prospection, exploitation of forests, tourism and military activity are bringing an ever-increasing number of unprotected people into contact with the vectors, thus increasing the spread of the disease;
- the **haphazard growth of major urban centres** and the subsequent disastrous effect on socio-economic development, especially in insanitary areas, is increasing the risk of transmission;
- **ecological upheavals:** dams, hydro-agricultural development, deforestation, roads, new urban centres, etc., create conditions favourable to the proliferation of vectors and animal reservoirs and bring people into contact with disease vectors;
- the winding down or **halting of malaria control campaigns** using insecticide spraying has led to a resurgence of the leishmaniases in Bangladesh, Colombia, India, Peru and Mediterranean countries.



Families exposed to visceral leishmaniasis in the Yungas ("hot valleys") focus in the Andean foothills.

Visceral leishmaniasis in Bolivia.



An urban focus of cutaneous leishmaniasis in Kabul, Afghanistan. Insecticide spraying of houses for vector control.

ACTION

The well-known **success** of the control campaigns in certain countries shows that the fight against the leishmaniases can be won. In China, visceral leishmaniasis has been eliminated from the country's vast north-eastern plains. In Azerbaijan, Israel, Kazakhstan and Turkmenistan, cutaneous leishmaniasis has been eliminated from the urban areas. In the north eastern regions of Brazil, the incidence of visceral leishmaniasis was reduced by 68% between 1959 and 1963.

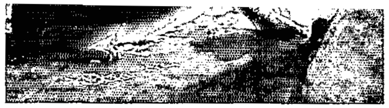
The tools to control the leishmaniases exist but they should be made available to any country that needs them.

The leishmaniases can be treated, but treatment must be given early;
- in the case of visceral leishmaniasis, because the disease can be fatal if left untreated;
- in the case of cutaneous leishmaniasis, if the patient is the reservoir and therefore likely to infect the biting vector, or if there is a risk of subsequent lesions in the mucosae.

Moreover, *it is possible to restrict the transmission of the leishmaniases* to humans by applying relatively simple prevention methods:

a) **Vector control,** using the following methods:
- personal protection using insect repellants applied to the skin, and insecticide-impregnated bednets or curtains;
- the spraying of residual insecticides inside and around house;
- the destruction of the sites (used for resting and breeding) of certain species of sandfly vectors.

b) **Control of animal reservoirs of the parasite:**
- Dogs are the main reservoirs of visceral leishmaniasis: a simple blood test will identify an infected dog. If the animal is found to be positive, it is either treated or put down.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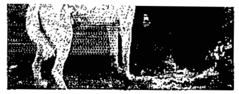
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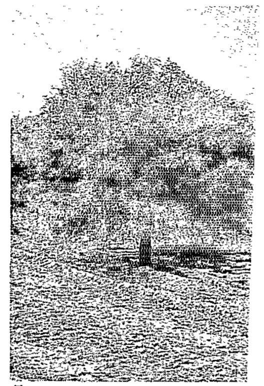
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– Rodents are reservoirs of cutaneous leishmaniasis. The control techniques are therefore tied in with agricultural activities: poisonous baits and anticoagulants are placed in rodent burrows; deep ploughing is used to destroy their burrows; the plants on which they feed are eliminated, etc.

c) **Modifications of the environment:**

– cleaning and sanitation operations in dwellings and household environments to eliminate sandfly reproduction sites in surrounding urban areas;

– land clearance around villages combined with insecticide spraying. In the Amazon basin of Brazil and French Guiana, deforestation must be of 300 metres around villages in order to isolate the villages from parasite vectors and reservoirs. This measure has substantially reduced and at times halted leishmaniasis transmission in villages.

With the support of WHO-sponsored technical assistance and supervision, health development programmes using traditional control methods in association with new control tools are now being implemented in the following countries:

- In **Bangladesh** and **India** (in visceral leishmaniasis foci) and in **Afghanistan** and **Syria** (in urban cutaneous leishmaniasis foci) where humans are the reservoirs, the following measures are being taken simultaneously:

– early detection,

– treatment using antimonials,

– residual insecticide spraying inside and around houses,

– and, more recently, the use of bednets impregnated with residual insecticide of the pyrethroïd family, currently being assessed for its effectiveness.

- In **Jordan** and **Tunisia,** in rural cutaneous lesihmaniasis foci where rodents are the reservoirs, the measures taken include;

– detection of patients by parasitological examination,

– treatment of severe forms of the disease,

and targeted control of the rodent *Psammomys obesus* by deep ploughing of their burrows, elimination of the goosefoot (of the genus *Chenopodium)* – the only plant they eat, and, more recently in **Tunisia,** rapid reforestation of land to prevent the resurgence of goosefoot.

- In **Iran,** the control of human and canine zoonotic visceral leishmaniases combines the following measures:

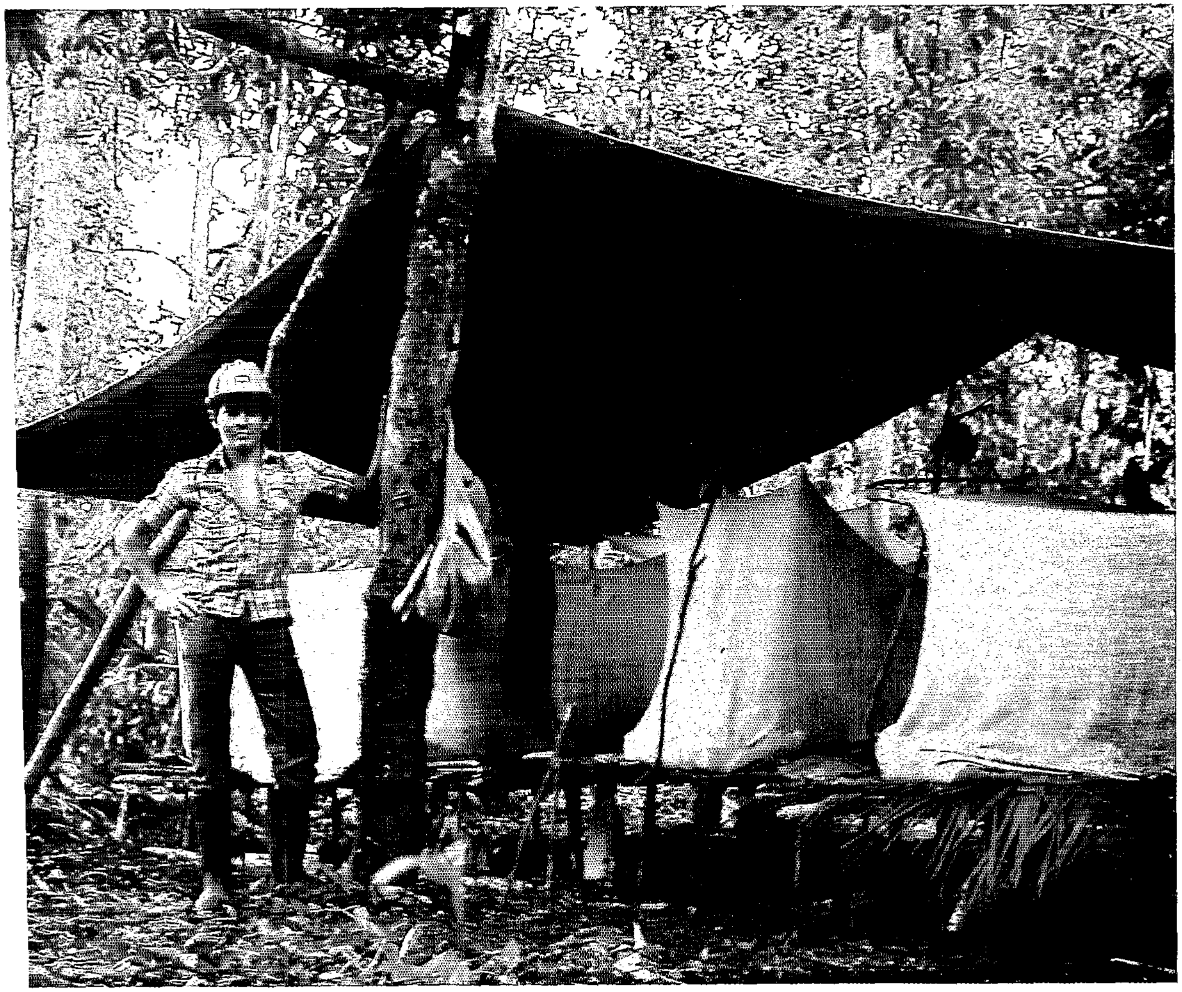
– detection of patients by serological and parasitological examination,

– treatment of patients,

– elimination of infected dogs,

and antivectorial control inside and around houses.

1. The hyrax, *Heterohyrax brucei,* a wild animal reservoir of cutaneous leishmaniasis in Ethiopia and Kenya.
2. The ant bear or great anteater, a wild animal reservoir of cutaneous leishmaniasis in South America.
3. The sloth, a wild animal reservoir of cutaneous leishmaniasis in Central and South America.
4. The dog, a domestic animal reservoir of visceral leishmaniasis.
5. A new control method is currently being evaluated. It would seem that the planting of acacia trees offers an indirect means of controlling *Psammomys obesus,* a rodent reservoir of cutaneous leishmaniasis. These trees apparently prevent the resurgent growth of the *Chenopodium* goosefoot, on which *P. obesus* feeds.



The camp of oil prospectors in the Amazon basin of Bolivia.

In order to optimize investments in personnel and equipment in mixed endemic regions, WHO advocates (whenever the epidemiological situation allows it) an **antivectorial campaign integrated with other public health activities,** for example:

- in **Brazil,** where visceral leishmaniasis control is frequently combined with malaria and Chagas disease control;
- in **Bangladesh** and **India,** where visceral leishmaniasis control is combined with malaria control;
- in **Mediterranean countries,** where canine visceral leishmaniasis control can be combined with rabies and hydatid control.

The challenges and funding

At the request of the countries concerned, the World Health Organization is coordinating the extension of control campaigns, ideally hoping to cover all 88 endemic countries.

The following **challenges** must be met by these countries:

- the reinforcement of **decentralized health structures;**
- the fostering of **awareness** and **commitment** on the part of the populations and political authorities;
- the **training** of health personnel;
- the provision of **qualified field personnel** on a full time basis;
- the **permanent supply,** in the field, of vital products such as health care equipment, drugs, reagents, insecticides and mosquito nets.

These activities require human and financial resources to back up the disease control capabilities of each country.

For example: the treatment for a patient infected with leishmaniases is based on antimonials. In the case of visceral leishmaniasis, this treatment lasts for one month with a minimum cost of $US 100 per patient if the required drugs are imported by the endemic country. Peru spent $US 2 million on 538,000 ampoules of antimonial drugs in the 4 years between 1987 and 1991. In India, however, where antimony products are manufactured, the local cost of medication is estimatd at $US 20 per patient. The overall "medication" budget for the 250,000 cases in India is in the order of $US 5 million.

Treatment costs also include:
- consultations,
- laboratory tests,
- health care,
- hospitalization (x number of days).

These costs vary according to the epidemiological and economic situation of the country:

- in French Guiana, the cost of treatment of cutaneous leishmaniasis for one patient in 1991 was estimated at $US 600, 80% of which was spent on hospitalization and the other 20% on treatment;
- in Saudi Arabia, the cost of treatment of cutaneous leishmaniasis per patient was estimated at $US 450 (1979),
- in southern Sudan, the cost of treatment of visceral leishmaniasis is estimated to be in the order of $US 250 per patient (1993).

In certain countries, the amount of money needed to treat leishmaniasis would exceed the total public health care budget. For this reason, WHO gives priority to establishing "minimum control initiatives" in order to ensure at least the early **detection, early treatment** and **notification** of leishmaniasis cases. These "minimum control initiatives" require constant availability of specific

The outskirts of Manaus in Brazil, a focus of cutaneous leishmaniasis.

to the

first-line drugs along with other essential drugs in all health centres including the most remote. In a good many cases, the international community is called on to assist in this urgent phase. The aim is to reduce the disease as quickly as possible to such a level that each country can integrate control and surveillance activities, at both technical and economic levels, into their overall health development activities.

Control strategies coordinated by WHO are designed to fit in with each country's approach to social and economic development. Whenever an agricultural, urban, industrial or other scheme is planned in a region where leishmaniasis or any other disease is a threat, simple measures must be immediately implemented to prevent the situation getting out of hand. Given the high cost of treatment, it is more feasible, in economic terms, to prevent the disease by applying vector control strategies. In the Indian State of Bihar, for example, 4000 tonnes of DDT are needed to spray the houses of 29 000 villages (60 million inhabitants). This corresponds to an "insecticide" budget of approximately $US 12 million, i.e. $US 0.2 per inhabitant protected. The investment is all the more efficient as it also covers malaria control.

The viability of development project is dependent on **health imperatives.** Funds allocated to disease control activities at an early stage quickly prove to be negligible in the light of the resultant social and economic benefits. Modest expenditure on health development ultimately proves to be a **productive investment.**

CONCLUSION

The leishmaniases, which are diseases closely linked to underdevelopment, are a scourge hampering the social and economic development of many countries. Failure to effectively promote health development will ultimately prove far more costly to the international community than the implementation of disease control programmes.

Some 12 million patients throughout the world are suffering from the leishmaniases. It is the duty of all of us to help relieve their suffering.

For all these reasons, the World Health Organization, in accordance with its mandate, is inviting all willing partners to participate in initiatives to foster health development based on the right of each and every person – including the world's underprivileged – to good health.

"Not an empty hope, but a real future."

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