# Update
# Le point

*Articles in the* **Update** *series give a concise, authoritative, and up-to-date survey of the present position in the selected fields, and, over a period of years, will cover many different aspects of the biomedical sciences and public health. Most of the articles will be written, by invitation, by acknowledged experts on the subject.*

*Les articles de la rubrique* **Le point** *fournissent un bilan concis et fiable de la situation actuelle dans le domaine considéré. Des experts couvriront ainsi successivement de nombreux aspects des sciences biomédicales et de la santé publique. La plupart de ces articles auront donc été rédigés sur demande par les spécialistes les plus autorisés.*

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# The control of leishmaniases*

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*Human leishmaniases are caused by at least 13 different species and subspecies of parasite of the genus* Leishmania. *These parasites are transmitted to man from other infected persons or mammals by sandflies when taking a blood meal. Leishmaniases have been reported from about 80 countries and probably some 400 000 new cases occur each year. Clinically the leishmaniases can be divided into three major groups: visceral leishmaniases, which are usually fatal if untreated; cutaneous leishmaniases, which often produce permanent facial disfigurement; and mucocutaneous leishmaniasis of the New World, which produces severe mutilation by destruction of the naso-oro-pharyngeal cavity and sometimes death. Since the various forms of leishmaniasis differ substantially from each other in their epidemiology, the strategy for control must be adapted to the local situation in each endemic area, after thorough ecological and epidemiological studies of the vectors, the hosts, and the landscape. If insufficient baseline information is available, failure of haphazardly applied control measures can be expected. Peridomestic insecticide spraying together with treatment of patients is effective in certain foci of anthroponotic cutaneous leishmaniasis, urban visceral leishmaniasis, and uta. Extensive programmes to eradicate desert rodents, combined with land reclamation, resulted in a considerable decrease in the incidence of zoonotic cutaneous leishmaniasis in vast areas of the USSR. Since control of zoonotic cutaneous/mucocutaneous leishmaniasis of the New World is hardly feasible at present, the only rational approach to prevent some of mucosal lesions is early diagnosis and radical treatment of patients with the rather unsatisfactory drugs at present available.*

The term leishmaniasis includes many different diseases that have very little in common, except for the morphology of the causative parasites. In fact, in some cases, the diseases have different clinical manifestations and epidemiological features and the approaches to their prevention and control are quite different.

The present paper will deal separately with the following forms:

**Visceral leishmaniasis (VL)**—caused by *Leishmania donovani donovani* in India and Bangladesh, by *L. donovani infantum* in the Mediterranean area and probably other parts of the Old World, by *L. donovani chagasi* in the New World, and by *L. donovani* s.l. in

* A French translation of this article will appear in a later issue of the *Bulletin*.

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some other countries such as the Sudan. The clinical picture of the disease is similar in all countries, although sometimes the duration of the disease seems to differ. However, *L. donovani infantum* and *L. donovani chagasi* are most commonly seen in infants and young children whereas *L. donovani donovani* is equally common in older children and young adults. The disease is characterized by insidious onset of irregular fevers, sometimes a fever that remits twice daily, progressive spleno-hepatomegaly, increasing anaemia and thrombocytopenia, often accompanied by an excellent appetite. Sometimes hyper- or hypopigmentation is seen. In the later stages cachexia develops, and sometimes purpura. In the absence of treatment, death ensues within a few months after onset of symptoms.

Post-kala azar dermal leishmanoid is commonly observed only in India. The dermal lesions appear one to several years after treatment, and respond poorly to specific treatment. In the Sudan, *L. donovani* s.l. is probably responsible for the mucosal lesions occasionally seen in adult males and the pure dermal lesions seen on rare occasions.

With the exception of India and Bangladesh, and probably East Africa and Iraq, canines are the main reservoir of the subspecies of *L. donovani*. Transmission occurs usually under rural conditions but sylvatic and occasionally urban epidemics sometimes occur.

Since VL is a hidden but killing disease it is of great public health importance.

**Anthroponotic or urban cutaneous leishmaniasis (ACL)**—caused by *L. tropica* (syn. *L. tropica minor*). The disease is known from southern Europe and northern and western Africa, and it is common in Asia, from Turkey to western India; but it has been practically eradicated from the USSR. *L. tropica* produces painless ulceration of the skin often leading to disfiguring scars. Ulcers usually heal spontaneously after a year or more. The lupoid or tuberculoid chronic form of the disease, which may last for several years and respond very poorly to treatment, occurs frequently in ACL. Lesions of the face and fingers are often painful and disfiguring.

With the possible exception of Afghanistan and Iran, where the dog is suspected, no animal reservoir exists. Transmission occurs from man to man in urban areas and occasionally in rural villages.

**Zoonotic or rural cutaneous leishmaniasis (ZCL)**—caused by *L. major* (syn. *L. tropica major*). The disease is common in part of southern USSR, Iran, Pakistan, and most countries of Middle Asia, including Saudi Arabia and Yemen. The disease occurs also in North and West Africa and probably in other parts of Africa.

The uncomplicated skin lesions are painless and self-healing in less than six months. Lesions are numerous and sometimes confluent, and often leave disfiguring scars. Different genera of desert rodents act as a reservoir. Transmission occurs under rural conditions in dry areas.

**Diffuse cutaneous leishmaniasis (DCL)** and **cutaneous leishmaniasis**—caused by *L. aethiopica* in the highlands of Ethiopia and Kenya. Usually DCL does not respond well to treatment but occasional cases are responsive. Hyraxes of two genera are the reservoir hosts. Transmission occurs in defined foci when people enter the territory of the reservoir host, usually near cliffs or large fig trees.

**Cutaneous leishmaniasis of the New World (CLNW)**—a zoonosis caused by numerous species of *Leishmania*:

*L. braziliensis guyanensis* has been reported from northern South America. The painless lesions of "pian-bois" are usually single and dry, sometimes with metastasis along the lymphatic system. Spontaneous cure often occurs in about nine months. The reservoir is probably the spiny rat, which is found in the dense forests where most transmission occurs.

*L. braziliensis panamensis* occurs in most countries of Central America. The skin lesions are sometimes painful, especially when localized near the lips, and the ulcers are usually of the wet type. Occasionally spread occurs along the lymphatic system. Lesions do not heal spontaneously. The reservoir hosts are sloths, monkeys, kinkajou, coati, the spiny pocket mouse, and the cotton rat. Transmission occurs deep in the forest.

*L. mexicana mexicana* occurs in the northern part of Central America and causes "chiclero's ulcer". The painless ulcer often heals spontaneously within a few months, but sometimes chronic progressive lesions develop and destruction of part of the ear is not uncommon. Most lesions are single and 60% are located on the ear. Several wild rats and mice constitute the reservoir in dense tropical forests where transmission occurs.

*L. mexicana amazonensis* has been reported from the Amazon region of Brazil. About 30% of patients develop the disfiguring and incurable form of DCL. The remainder develop skin ulcers that seldom heal spontaneously. The disease is rare in man but common in numerous forest mammals such as rats, mice, oppossums, foxes, and pacas. Transmission occurs in marshy forests along river terraces.

*L. mexicana pifanoi* has been reported from Venzuela and causes disfiguring and incurable DCL. The reservoir is thought to be a forest rodent of the genus *Heteromys.* Transmission occurs in agricultural or forest areas.

*L. peruviana* has been described from the western slopes of the Andes mountains in Peru and Argentina. "Uta" disease mainly affects children. The single or few painless ulcers usually heal spontaneously in about four months. Dogs are also frequently infected and may play a role as a reservoir. Transmission occurs in villages located at a high altitude where vegetation is scarce.

*L. garnhami* has recently been described from a mountainous part of western Venezuela. The painless lesion heals spontaneously in about six months. The reservoir host is not yet known. Transmission occurs in rural and urban populations living in agricultural areas at elevations of 800–1800 m.

Of the New World leishmaniae mentioned above, only *L. b. panamensis* and *L. m. mexicana* infections constitute significant public health problems, since *L. b. guyanensis*, *L. peruviana*, and *L. garnhami* cause rather mild and self-healing lesions, while *L. m. pifanoi* and *L. m. amazonensis* infections, although extremely severe, are very rare in man.

**Mucocutaneous leishmaniasis (MCL)** in the New World is caused by *L. braziliensis braziliensis* and is widespread in western and northern South America and Brazil and is a very grave public health problem. Sporadic cases have also been reported from various parts of Central America.

The skin ulcers are similar to those produced by *L. b. panamensis*, but they are sometimes more painful and extensive. Aberrant clinical cases may resemble numerous other skin diseases. Most cases do not heal spontaneously, and in those that do, healing usually takes more than a year.

Frequently mucosal lesions ("espundia") develop simultaneously with the skin lesions. More often, the mucosal lesions appear many years after the skin ulcers have disappeared. The progressive mucosal ulceration, often accompanied by hyperplasia of surrounding tissues, slowly destroys the nasal septum, the palate, the vocal chords, and other structures of the oro- and/or nasopharynx and produces very grave facial mutilation. Death is frequently due to secondary bronchopneumonia. So far there is no firm evidence that *L. b. guyanensis* is associated with nasopharyngeal lesions.

The MCL cases reported in the Sudan are probably caused by *L. donovani.* Fortunately the lesions progress slowly and respond well to treatment.

In South America, the reservoir hosts are various forest rats and mice. Transmission occurs under sylvatic conditions in areas of dense tropical forest.

## PRINCIPLES OF CONTROL

The principles of leishmaniasis control are dictated by the need to take action against the causative agent, its sandfly vector, and the reservoir host. The opportunities for leishmaniasis control and the most appropriate methods vary in different parts of the world since the various forms of leishmaniasis differ substantially in their epidemiology.

Effective control measures have been reported from only a few places. Campaigns in the USSR have been carried out with success against visceral leishmaniasis (VL) and against anthroponotic cutaneous leishmaniasis (ACL) and with less success against zoonotic cutaneous leishmaniasis (ZCL). Other small-scale campaigns have been successful against VL in restricted areas of Brazil, France, and India.

ACL is now virtually eradicated from the USSR. In Uzbekistan, eradication was the result of a campaign against malaria, and in Aškabad city control was related to sandfly fever control. The elimination of ACL from the cities of Kirovad and Barda in Azerbaidjan was the result of a planned campaign to detect and treat all human cases of ACL and of DDT spraying in the homes of the sick.[a, b]

In many countries, malaria control campaigns led to reduction in sandfly densities and in leishmaniasis morbidity, while resurgence of leishmaniasis morbidity was observed in numerous areas after cessation of these campaigns. In some parts of Italy, Portugal, and Yugoslavia either anti-malaria campaigns did not interrupt transmission of leishmaniasis or the incidence soon returned to the pre-spraying level. Malaria control measures have almost no effect on the morbidity from ZCL, the vectors of which have little or no connexion with human dwellings. Certain endophagous sandflies may bite and infect man inside a house without coming in contact with sprayed surfaces of the house. This can occur when infected reservoir hosts are found near to human dwellings.

Leishmaniasis foci can be cleared only if a combination of measures is used. To determine the best strategy it is essential to study the cycle of the parasite under the local conditions.

The biology and ecology of the reservoir host, the leishmaniae, and their vectors, the nature of the flora, the composition and moisture content of the soil, the meteorological data, and the habits of people must all be studied thoroughly before economic and rational measures can be carried out against the zoonotic types of leishmaniasis. New evidence exists that dogs may also be involved in VL transmission in Kenya, and in ACL transmission in Afghanistan and Iran. If this animal is indeed a reservoir of importance in these countries, all types of leishmaniasis should be regarded as zoonoses.

The isolation and subsequent biochemical typing of *Leishmania* strains from man is of prime importance for differentiating between *L. tropica* and *L. major*, since control measures are different, especially in Middle Asia, including Arabia, where the clinical differences between lesions produced by these two causal agents are less defined than in the USSR. Nevertheless it should be remembered that infection with a particular parasite does not always result in the same clinical condition: for example, *L. donovani infantum* may, in some cases, cause cutaneous or even mucocutaneous lesions in man and *L. tropica* may occasionally visceralize.

To be able to evaluate the effect of a pilot control programme, it is important to determine the intensity of transmission both before and after the measures are applied. This is difficult in the case of non-epidemic VL, since this "hidden" disease is patchy in distribution and often misdiagnosed. Since cutaneous leishmaniasis produces stable

[a] NADZAFOV, A. JU. Leishmaniasis incidence and control in Azerbaidjan SSR. *Medicinskaja parazitologija i parazitarnye bolezni*, 35: 463-700 (1966) (in Russian).

[b] SERGIEV, V. P. *Control measures against cutaneous leishmaniasis.* In: *Ecologie des leishmanioses*, Montpellier, 1977, pp. 321-323. (Colloques internationaux du CNRS N° 239).

resistance to reinfection, the morbidity from the disease does not reflect the real intensity of transmission in endemic conditions. However, Beljaev[c] has proposed a method for quantitative determination of the degree of endemicity that is a modification of the model of malaria transmission proposed by Moškovski.[d]

In Latin America, the exposure of sentinel mammals in the field has been used to estimate the level of transmission of cutaneous and mucocutaneous leishmaniasis.

The selection of particular control methods and decisions concerning their application depend to a large extent on the conditions under which human subjects come into contact with the local strains of leishmaniae and on the economics of the operation. Before planning large-scale campaigns, small pilot programmes should be carried out. Once the incidence of leishmaniasis has increased it is usually too late for immediate control actions since the transmission will have occurred many months previously.

The migration of non-immune populations or persons harbouring leishmaniae is of considerable importance in the establishment of new epidemic outbreaks or of stable new foci of leishmaniasis. Health authorities should constantly be alert to the potential dangers associated with the movements of, for example, nomads, pilgrims, harvest workers, expatriate workers, and new settlers, and with war and famine and should be prepared to take preventive measures.

## Control of sandflies

In many endemic areas, the identity of the vectors remains unknown or, at least, unproved. The target species must be identified and their biology studied before control measures are planned. This requires:

— collection and identification of the local sandflies
— observations on anthropophily and endophily
— dissection of female flies for detection of promastigotes (leptomonas) and inoculation of these flagellates into hamsters for subsequent identification by other methods
— host identification of the bloodmeals of dried sandflies
— age-grading when possible
— searching for resting and breeding places of peridomestic and sylvatic flies
— studies on sandfly population fluctuations and dispersion range throughout the year by using a variety of trapping methods
— study of the influx of the vector into houses and the reflux flow to animal burrows
— longitudinal assessment of the effect of measures taken in pilot programmes, as well as study of the effect of anti-malaria or anti-locust measures, on sandfly densities.

The only known way of controlling sandflies is by the proper application of insecticides. The optimal timing of application depends largely on the seasonal abundance and longevity of the vector, the duration of the life cycle (usually 1–2 months) and diapause period, the number of bloodmeals per gonotrophic cycle, autogenous behaviour of the fly, and many other factors.

Sandflies are highly susceptible to insecticides but some resistance to DDT and dieldrin has been reported in northern Bihar in India[e] and also from Brazil. Nevertheless, aerial fogging of towns, desert areas, or forests with insecticides should not be encouraged. Little, if any, effect on sandfly densities was observed after fogging an endemic area in central

[c] BELJAEV, A. E. System of epidemetric magnitudes for investigation of geography of zoonotic cutaneous leishmaniasis. In: *Research in medical geography*. Moscow, Moscow branch of the Geographical Society of the USSR, 1973, pp. 7-9 (in Russian).

[d] MOŠKOVSKI, S. D. *The main natural laws of malaria epidemiology*, Moscow Academy of Medical Science of the USSR, 1950 (in Russian).

[e] KAUL, S.M. *Preliminary observations on the susceptibility of* Phlebotomus argentipes *and* Phlebotomus papatasi *in two districts of north Bihar*. Unpublished WHO document WHO/VBC/79.715 (1979).

Sudan.[f] Soviet scientists observed that sandflies avoid agricultural areas sprayed by insecticides. Biological and genetic methods of control of sandflies have not yet been developed.

For other non-specific methods see page 818.

### Control of wild and domestic reservoir hosts

In areas where dogs are the reservoir of VL caused by *L. donovani infantum* or *L. donovani chagasi*, infected animals should be treated or eliminated and stray dogs destroyed. Diagnoses can be made by the indirect immunofluorescent test (IFT), by enzyme-linked immunosorbent assay (ELISA), or by the less specific aldehyde test of Napier. Control of wild canines, especially foxes and jackals, is considerably more difficult but attempts should be made.

The control of sylvatic mammals in the New World is not practical since most types of leishmaniasis are transmitted in dense humid forests. Similarly the eradication of the hyraxes that are the reservoirs of *L. aethiopica* in Ethiopia and parts of Kenya seems hardly feasible.

In areas where desert rodents are the reservoir hosts of ZCL, the control of leishmaniasis by attack on these mammals might be effective when the terrain is suitable. In areas of Middle Asia, where the relatively sedentary *Rhombomys opimus* is the principal reservoir of ZCL, rodent control is of paramount importance. Somewhat more difficult is control of the migratory *Meriones libycus erythrourus* in Asia.

Control of gerbils is likely to be more stable when other control measures are followed by deep ploughing (0.5–0.7 m) and land levelling in combination with an appropriate agricultural system.

Rats of the genus *Rattus* have been found infected with leishmaniae in four continents. If rats were found to be an important reservoir, rodent control measures should be considered in selected areas. However, it should be realized that the finding of a few infested specimens of a certain animal species, does not necessarily imply that the species is of epidemiological importance.

## RECOMMENDED APPROACHES TO CONTROL

### Control of visceral leishmaniasis (VL)

In India and Bangladesh control should be based on:

(*a*) Detection of cases and rapid treatment of patients. In man, IFT or ELISA should be used to detect VL (but in Latin America serological cross-reactions occur with *Trypanosoma cruzi* and probably also with the apathogenic *T. rangeli*). The well-established IFT, when carried out routinely under optimal conditions, may give more reliable and comparable results than the less internationally standardized ELISA test for leishmaniasis. When serological tests are done on whole blood collected on filter paper, corrections should be made in severely anaemic patients, when the serum dilutions are calculated. Also, the samples should be kept dry during transportation, since antibodies will deteriorate under conditions of high humidity and high temperature.

(*b*) Control of the specific vector in and near human dwellings by periodic spraying of

[f] HOOGSTRAAL, H. & HEYNEMAN, D. Leishmaniasis in the Sudan Republic. 30. Final epidemiologic report. *American journal of tropical medicine and hygiene*, **18**: 1091-1210 (1969).

insecticides. Animal houses and pens and nearby stone walls or caves should also be sprayed. DDT, dieldrin, or diazinone solution sprayed on walls up to a height of 1.5 m from the floor level, using DDT at a dose of 3.2 g/m$^2$ of surface, will provide several months' protection against most sandflies. The residual effect of most insecticides is considerably shorter under certain conditions, for example, when the temperature of the sprayed surface is excessively high.

(*c*) Repair of cracks in mudwalls and removal of rubbish around houses. This involves public health education.

(*d*) Organization of good reporting and recording systems for VL. Public health education by press, posters, radio, and television is valuable here.

In East Africa, the measures outlined above for India are appropriate and, in addition, it is valuable to spray with insecticide the ventilation shafts of termite hills that are close to human settlements, especially when the hills have been abandoned and become eroded.

In other countries, in addition to all the above measures, when it is proved or suspected that canines constitute a reservoir, it is important that infected dogs be detected and treated or destroyed, and that wild canines be destroyed. Limited changes in the landscape may also help to decrease the density of the vector in some Mediterranean areas.

### Post-kala azar dermal leishmanoid (PKDL)

Since chronic patients are a source of infection for sandflies, they should be encouraged to use fine-mesh netting around the bed, to screen the house against sandflies and to use an insect repellant. Efforts should be made to localize and treat patients with a pentavalent antimony compound or even with amphotericin B.

### Anthroponotic cutaneous leishmaniasis (ACL) caused by *L. tropica*

Control of this disease should be based on:

(*a*) Detection and treatment of human cases. House-to-house visits and surveys in schools should be considered since many people prefer local methods of treatment. Physicians should be encouraged to treat all cases with a pentavalent antimony compound.

(*b*) Control of the sandfly vector by insecticide spraying of daytime resting places and peridomestic breeding places.

(*c*) Aerial fogging may occasionally be indicated in selected places before mass meetings and pilgrimages.

(*d*) Elimination of infested dogs in countries like Afghanistan and Iran.

### Zoonotic cutaneous leishmaniasis (ZCL) caused by *L. major*

The most important elements in the control of this disease are:

(*a*) Detection and treatment of human cases.

(*b*) Control of the sandfly vector by application of insecticide in the breeding places, such as rodent burrows—preferably over a radius of not less than 1 km around human settlements—and by spraying of the daytime resting places inside and around houses.

(*c*) Eradication of all desert rodents over a radius of 2–3 km around the focus.

When the incidence of ZCL is 1/10 000 or less, the detection and treatment of cases alone should suffice.

The suppression of endemic foci on a national basis involves studying the structure of the

foci, using the method of large-scale mapping. When maps have been drawn up, preferably with the aid of aerial photography, a record is made of the spatial distribution and numbers of wild desert rodents and sandflies thought to be important as reservoirs and vectors, respectively, and also the extent to which they are infected with the causal agent of the disease. The incidence of fresh lesions in man should also be recorded. In the course of these investigations, light is shed on the connexion between links in the epizootic chain and particular types of landscape.

Mapping will show up the sectors where transmission is most intense and where the epidemiological risk is greatest. Attention must be concentrated mainly on these sectors when control measures are undertaken. By vigorous application of well-tested control procedures, dramatic reduction of the disease can be achieved in certain areas.

In the absence of sufficient information on the reservoirs and vectors, failure of control measures can be expected. Despite the destruction of rodents within a radius of 3 km of certain foci in the USSR, no interruption of ZCL transmission was obtained. In Iran, the use of insecticides or poisons in rodent burrows within a radius of 300 m around houses was also ineffective.

The most effective way of clearing foci of ZCL near human settlements is by ecological control of the reservoir animals by making radical changes in the natural landscape, for example, by construction of 5–7-m wide irrigation canals, and the establishment of a wide belt of cultivated crops and constant supervision to avoid reappearance of wild mammals. Russian workers obtained excellent results by 50-cm deep ploughing of all rodent colonies in the Golodnaja Steppe. However, land reclamation and environmental changes are tools that can be put into practice by only a limited number of countries.

The importance of the physico-chemical characteristics of the soil, and its degree of moisture, in regulating the territorial distribution of the reservoirs and vectors was shown by Safjanova.[g, h] For long-term planning of control measures, methods must be based on sound knowledge of the natural biocoenoses of which the *Leishmania* foci form a part.

Rodent control measures should consist of killing all desert rodents within a radius of 3 km of each focus. The holes of certain rodents are often 2.5 m deep and provide a good microclimate for the breeding of sandflies. It is advisable first to close the burrows. Those that are reopened can then be considered as active microfoci, and poisoned bait can be placed deep in them. After baiting, the holes should be closed again and those that are reopened again rebaited, until all rodents are killed. A suitable poisoned bait consists of 15 g of wheat containing 120 g of zinc phosphide per kilogram and some vegetable oil for application. Russian workers now apply anticoagulant bait to the burrows five days before using the zinc phosphide.

Simultaneously, sandflies can be attacked by placing 0.5 g of 75% DDT in the entrance of each burrow, which should then be left open. If the sand is very loose, insecticide powder may rapidly become covered, and in these cases, ultra-low-volume spraying of burrows may be more effective. However, when Russian workers blew exhaust gas mixed with DDT into animal burrows a residual effect was observed for only 24 hours. Recently, good results have been obtained in the USSR by distributing many small pieces of cloth impregnated with insecticide near the burrows of desert rodents (*Rhombomys opimus*). The rodents take the pieces of impregnated cloth into the burrows, and thus eliminate the sandflies. The sole use of 0.5-m deep ploughing of all rodent colonies has recently given excellent results in permanent eradication of *R. opimus* and sandflies in certain parts of th USSR. Treatment of burrows with insecticide should be continued at least monthly until only a few sandflies are obtained in funnel traps placed over the holes. In many areas, sandflies are abundant

[g] SAFJANOVA, V. M. The principles of characterization of foci of leishmaniasis. In: *Ecologie des leishmanioses*, Montpellier, 1977, pp. 279-284 (Colloques internationaux du CNRS N° 239).

[h] SAFJANOVA, V. M. The peculiarities of the structure and existence of zoonotic cutaneous leishmaniasis foci in the south of the USSR. *Ibid.* pp. 237-260.

only for two or three months of the year. Under such circumstances, rodent and sandfly control should be initiated several weeks before the peak sandfly density is expected. If there are two annual peaks, sandflies should be attacked at least twice a year.

In certain areas, 6000 or more animal holes can be found per square kilometre. In these areas, unless they are relatively small, rodent and sandfly control seems not to be economically justified. Very small holes are usually those of lizards and do not need to be treated. Nevertheless five workers were able to eradicate all the gerbils from 700 $km^2$ in one year in the USSR.

By careful study of the terrain and the mammal population, it is sometimes possible to find areas that are densely infested by desert rodents but surrounded by natural barriers where the main reservoir species is absent or rare. For example, certain species of *Meriones* are nearly absent from areas where the soil contains many stones or where the sand is very fine, or where certain liquid-containing halophyte plants or sedges are absent, or where certain agricultural activities are practised. When such natural or artificial barriers are present, rodent control is often feasible, but in their absence the treated area will soon become reinfested by rodents from the surrounding untreated area.

When housing, industrial, or agricultural projects or road constructions are planned in areas infested by infected desert rodents, health authorities should take anti-rodent and anti-sandfly measures to protect people against acquiring ZCL. Authorities should also discourage the construction of widely scattered houses in potentially dangerous areas of transmission.

### Cutaneous leishmaniasis of the New World (CLNW) (with the exception of uta)

As described in the introduction, cutaneous leishmaniasis in the Americas is caused by *L.b. guyanensis* (pian-bois), *L.b. panamensis*, *L.m. mexicana* (chiclero's ulcer), *L.m. amazonensis*, and *L. garnhami*. *L.b. braziliensis* also produces cutaneous lesions, but this entity will be dealt with under mucocutaneous leishmaniasis. Cases of CL should be treated with a pentavalent antimony compound.

This type of leishmaniasis is even more difficult to control than is ZCL of the Old World, since it is principally a disease of wild mammals in the dense forest, and numerous reservoir hosts are arboreal. The various known or suspected species of sandfly of the genus *Lutzomyia* usually breed in the organic material of the forest floor. Hence, in most endemic areas, reservoir and vector control is almost impossible.

Aerial fogging of insecticides over large forested areas would affect only some species of canopy-dwelling sandfly, and could have catastrophic effects on other animal populations. Natural food chains would be disrupted, causing long-term disturbance of the forest ecosystem.

In most endemic areas there are no permanent, naturally occurring barriers to the spread of sandfly vectors, and it is not feasible to construct artificial ones on a wide scale. However, researchers in Panama observed that cleared forest areas planted with grass for cattle raising and occupied by settlements provided an effective barrier against the forest-inhabiting *Lutzomyia trapidoi* vector of *L.b. panamensis*.[i]

Elimination of all possible mammalian reservoirs of *Leishmania* species is neither possible nor desirable. There are far too many mammalian species involved and their importance in the total forest community is too great. Some people believe that selective elimination of sloths in certain parts of Panama could reduce the incidence of leishmaniasis caused by *L.b. panamensis*.

[i] HERRER, A. ET AL. Epidemiological patterns of cutaneous leishmaniasis in Panama. II. Incidental occurrence of cases in non-epidemic settlements. *Annals of tropical medicine and parasitology*, 70: 67-71 (1976).

Destruction of tropical forests to eliminate leishmaniasis is equally undesirable. Lainson & Shaw[j] discussed the possible consequences of deforestation and pointed out that, while this might control one type of leishmaniasis, there was a risk of encouraging a worse form. For example, control of the rather mild pian-bois in the dense forest could lead to establishment of the vector of the often incurable DCL caused by *L.m. amazonensis*, and destruction of the forest could create open dry areas favourable for transmission of *L. donovani chagasi* by *Lutzomyia longipalpis*.

Unfortunately, there are, as yet, no methods for biological control of sandflies or for preventive vaccination of people at risk. This leaves only one alternative for the control of human cutaneous leishmaniasis in most parts of the neotropics, i.e., the evacuation of the entire human population from potentially dangerous forested areas. For political, socioeconomic, and logistic reasons, however, such a measure is inconceivable.

When more epidemiological data become available about the many species of New World leishmaniae, their vectors, and reservoir hosts, it may be possible to develop rational means of control. Until this is achieved or a vaccine is developed, little can be done to prevent most cases of non-visceral leishmaniasis in this part of the world.

### Uta caused by *L. peruviana*

In the event of an increase in the incidence of uta, which is a relatively benign and rapidly self-healing type of leishmaniasis, the following measures are recommended:

— peridomestic spraying with insecticide
— detection and treatment of human cases
— use of serological techniques to detect infected dogs, which often do not have visible skin lesions (such animals should be destroyed since it is not feasible to treat them)
— elimination of stray dogs.

Leishmaniasis was recently found in rodents in an area previously known to be endemic for uta, and this needs further investigation.

### Mucocutaneous leishmaniasis (MCL)

Although the existing drugs are unsatisfactory, radical early treatment is the only practical way to prevent severe mutilation or death.[k] When isolates from the primary dermal lesions fail to grow well in blood agar medium, treatment of patients should be monitored by observation of antibody levels. If these do not decrease considerably, individuals should continue to receive treatment.

#### *Problems involved in the control of MCL*

Although treatment of individuals is at the moment the only rational means of attack for MCL, the following examples illustrate the difficulties involved.

*L.b. braziliensis*, whether treated or not, can persist unrecognized in man after the disappearance of the primary dermal ulcer, and may subsequently appear many years later as a severely mutilating mucosal infection. Diagnosis of mucosal lesions is usually made late.

Few patients can afford a long absence from work to undergo treatment, and many cases

[j] LAINSON, R. & SHAW, J. J. Epidemiology and ecology of leishmaniasis in Latin America. *Nature (London)*, 273: 595-600 (1978).

[k] UNDP/World Bank/WHO Special Programme for Research and Training in Tropical Diseases, unpublished WHO document TDR/LEISH/MCL/79.3.

do not respond well to the drugs available.

Although it would be desirable to identify the subspecies of *Leishmania* from all patients with CLNW, this is usually impossible. Because of the failure of most isolates of *L.b. braziliensis* to grow in culture, inoculation in hamsters is necessary. However, evolution of the parasite in hamsters takes many months, and final biochemical typing of the isolate is not yet done routinely. Consequently, all patients with cutaneous leishmaniases should be considered as possible future victims of mucosal lesions due to *L.b. braziliensis.*

To avoid these grave later consequences it is essential to give intensive treatment in the early stage of the disease. Until better diagnostic facilities are routinely available in the endemic areas, efforts should be made to grow the *Leishmania* spp. from the skin lesions in NNN media. If the parasites do not grow or cannot be maintained in culture, the patient should be given intensive treatment. Such treatment should be continued until IFT or ELISA tests for antibodies become negative or until the serum antibody titres decline 6–8-fold over a period of 6 months. Serological cross-reactions in mixed infections with *Trypanosoma cruzi* and possibly also with *T. rangeli* should be considered in individual cases.

Preventive methods against MCL are as difficult to apply as are those against CLNW, since transmission occurs when man enters the deeper forest regions. Even though man can occasionally acquire infection from a sandfly in the domestic habitat, the vectors are probably infected by wild animals in the forest. Unlike Old World sandflies, many sylvatic New World species of the genera *Lutzomyia* and *Psychodopygus*, some of which have partly arboreal habits, frequently bite during the daytime when man enters the fly's biotope.

**Diffuse cutaneous leishmaniasis (DCL)**

DCL is found in Venezuela (caused by *L. mexicana pifanoi*), in parts of Brazil (caused by *L. mexicana amazonensis*), and Ethiopia (caused by *L. aethiopica*), and has recently been observed in the Dominican Republic (Walton, personal communication, 1980). Sporadic cases have also been reported from several other Latin American countries, Iraq, Kenya, the United Republic of Tanzania, and Zambia. The control of the disease is essentially based on early case detection and attempts to treat patients.

Since parasites are often abundant in the skin, sandflies can become infected by biting chronically ill patients. *L. mexicana amazonensis* is common in certain forest mammals, and man only becomes infected during certain seasons when visiting the swamp-forest. The vector, *Lutzomyia flaviscutellata*, does not usually bite man and this is perhaps the most important factor limiting the human disease.[l]

*L. aethiopica* is a parasite of hyraxes of the genera *Procavia* and *Heterohyrax* which is occasionally transmitted to man by two species of sandfly in the highlands of Ethiopia and Kenya. Transmission takes place mostly near the cliffs where the hyraxes live, and infected persons occasionally develop DCL.

As a consequence of the comparative rareness of DCL, large control campaigns are not recommended, but infected people should obviously be treated.

In Venezuela, patients respond well to treatment with sodium stibogluconate, while patients in Ethiopia respond well to pentamidine dimethansulfonate or to amphotericin B.[m] DCL patients in Brazil do not respond to any type of treatment, although short-term relief may be obtained by taking frequent, extremely hot baths over a period of several months.

[l] LAINSON, R. & SHAW, J. J. The role of animals in the epidemiology of South American leishmaniasis. In: Lumsden, W. H. R. & Evans, D. A., ed., *Biology of kinetoplastida*, London, New York, San Francisco, Academic Press, 1979, pp. 1-116.

[m] BRYCESON, A. D. M. Diffuse cutaneous leishmaniasis in Ethiopia. II. Treatment. *Transactions of the Royal Society of Tropical Medicine and Hygiene*, **64**: 369-393 (1970).

## GENERAL PROPHYLACTIC MEASURES

The following measures are applicable to the control of all forms of leishmaniasis:

(*a*) Use of fine-mesh nets around rooms and beds.

(*b*) Use of repellents such as *N*, *N*-diethyl-*m*-toluamide and hexamethylene benzamide. Both measures are especially useful for personal protection of visitors to endemic areas.

(*c*) Removal of rubbish and any kind of organic matter from around dwellings, since this may facilitate breeding of sandflies, and of bricks, firewood, or other material on which sandflies may settle.

(*d*) Health education to encourage the active participation of the public in measures to eradicate sandflies from urban areas.[n]

## CONCLUSIONS AND RECOMMENDATIONS

— Control of certain types of leishmaniasis is possible in defined foci when measures are carefully applied after thorough epidemiological investigations. Examples of such types of leishmaniasis are VL in India and Kenya, typical ACL in Europe, Middle Asia and North Africa, and uta in Peru and Argentina.

— Reduction in mortality from zoonotic VL is possible in countries where health services and recording systems are well organized, and where IFT or ELISA diagnostic tests can be done.

— Reduction in morbidity from Old World ZCL can be achieved in restricted areas, but this requires considerable financial investment and sufficient trained, permanent field workers and scientists for various types of epidemiological investigation in the foci. More positive long-lasting control can be expected with land reclamation and environmental measures.

— No rational control measures are available for use against CLNW and MCL of the New World, although improved treatment may ease suffering.

— Some types of leishmaniasis, or particular clinical manifestations, are too rare to justify extensive control campaigns, e.g., ZCL in remote areas or among nomads, DCL in general, and MCL in the Sudan.

— No recommendations on control can be given for countries that do not have up-to-date information.[o]

— Control measures should be based on long-term epidemiological studies of the foci and sound ecological knowledge, and should initially be applied in small pilot projects with careful monitoring of the results.

— Wherever insecticides are applied as imagocides for the control of malaria vectors or locusts, the impact of such campaigns on sandfly vectors and leishmaniasis transmission should be simultaneously assessed.

— Countries should be encouraged to collaborate on a regional and subregional basis, in epidemiological studies and control measures. Standard protocols would permit comparative analysis of data, and exchange and dissemination of information should be encouraged. In this context, WHO can play an important role as coordinating body.[o]

— Although vaccination against ZCL and ACL with live virulent strains of *L. major* has shown promising results in the USSR and Israel, there is still a great need for the development of an effective, standardized, and safe vaccine producing long-lasting immunity against all types of leishmaniasis.

— There is also a great need for more effective and safer drugs for treatment of leishmaniasis.

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[n] SAFJANOVA, V. M. Leishmaniasis control. *Bulletin of the World Health Organization*, **44**: 561-566 (1971).

[o] ZAHAR, A. R. *Studies on leishmaniasis. Vectors/reservoirs and their control in the Old World. General review and inventory*. WHO unpublished document VBC/79-749.