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# Ecological Interactions in the Transmission of the Leishmaniases [and Discussion]

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# Ecological interactions in the transmission of the leishmaniases

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Epidemiological studies on the leishmaniases are disclosing a multiplicity of *Leishmania* species infecting a wide range of wild mammalian hosts, from marsupials to monkeys. In the primitive, silvatic habitat these parasites are transmitted by an equally wide variety of phlebotomine sandfly species (Diptera: Psychodidae: Phlebotominae). Transmission is not haphazard, however, and available evidence points to the existence of environmental barriers that normally limit the different *Leishmania* species to specific sandfly vectors, transmitting to certain mammalian species, within distinct ecotopes. In this situation, humans may become infected by a variety of leishmanial parasites when intruding into the different enzootics, if the sandfly vectors are anthropophilic. Many are not, however, and their parasites rarely, if ever, make contact with the human host. Natural or man-made ecological changes may result in modification of the epidemiological pattern of leishmaniasis, leading to either a reduction or an increase in the human disease.

## 1. Introduction

Species of the genus *Leishmania* Ross, 1903 are parasitic Protozoa placed, with the trypanosomes, in the family Trypanosomatidae. With a few possible exceptions, the leishmaniases are zoonoses, with a variety of reservoir-hosts in wild and (less frequently) domestic animals. Most infections in wild mammalian hosts are benign and inapparent, but in unusual hosts, such as man, dogs and equines, the parasites usually produce ugly skin lesions or a generalized visceral disease which is lethal unless it is adequately treated. Second only to malaria in importance among the protozoal diseases of man, the leishmaniases are not only the cause of death and mutilation on a large scale, but result in a heavy loss of man-working-hours, thus hampering development programmes in many countries. The diseases are widely distributed through most of tropical and subtropical America, Africa, India and parts of eastern Asia, Central Asia, the Mediterranean basin and some neighbouring European countries. Strangely, leishmaniasis has not been recorded in Australasia, although some sandfly species are known there. Transmission of *Leishmania* is limited, as far as is known, to the bites of a variety of blood-sucking phlebotomine sandflies (Diptera: Psychodidae: Phlebotominae). For detailed reviews on the biology and classification of the leishmanias, and the epidemiology of the leishmaniases, see Lainson & Shaw (1979), Lainson (1983*a*, 1988) and various authors in Peters & Killick-Kendrick (1987).

Early attempts to explain puzzling variations in the epidemiology of leishmaniasis in different geographical regions were hampered by a failure to appreciate the existence of a multiplicity of different species within the genus *Leishmania*. Most text-books, firm in the erroneous belief that all leishmanial parasites are indistinguishable, tended not to classify the organisms themselves, but rather the disease-states they produce in man. In general, they were loath to accept species other than *Leishmania tropica* (Wright, 1902) as the cause of Old World

cutaneous leishmaniasis, *L. braziliensis* Vianna, 1911, producing New World cutaneous and mucocutaneous leishmaniases, and *L. donovani* (Laveran & Mesnil, 1903), responsible for both Old and New World visceral leishmaniasis. The name *L. braziliensis* continued to be used for the aetiological agent of all forms of the dermal disease in the Americas until as recently as 1952, with the occasional acceptance by some of *L. peruviana* Velez, 1913 for the parasite causing 'uta', a form of cutaneous leishmaniasis occurring high up in the Peruvian Andes. Many workers even regarded both of these names as synonyms of *L. tropica* which, they suggested, had been introduced into the Americas in post-Columbian times.

Although most clinicians steadfastly clung to this highly restrictive classification, some workers with broader epidemiological and biological experience were clearly finding it difficult to force square pegs into round holes, and new names, mostly at subspecific level, began to appear for leishmanias associated with distinctive epidemiological features. In addition, the description of new species found in animals, and seemingly unassociated with human leishmaniasis, raised the question as to whether or not a whole host of other leishmanias might not exist, in specific relation with a wide range of mammalian hosts.

By the mid-1960s few could deny the existence of many more species and subspecies of *Leishmania* than had been previously supposed, and concern over the difficulties this posed for the epidemiologist led to a number of publications on their identification, classification and life cycles. The nomenclature used in the following discussion is that of the most recent review (Lainson & Shaw 1987), in which the genus *Leishmania* has been divided into the two subgenera *Leishmania* Saf'janova, 1982 and *Viannia* Lainson & Shaw, 1987, and the subspecific names raised to specific rank.

Once the multiplicity of *Leishmania* species was appreciated and more reliable means of identifying them became available, epidemiological peculiarities began to make much more sense, not only in widely separated geographical regions, but frequently in the same ecotope. Host and vector specificity are common features among parasites and, although several mammalian and phlebotomine sandfly species may be experimentally infected in the laboratory, there is evidence suggesting that in natural habitats ecological barriers maintain a relatively strict mammal–sandfly–parasite relation among the different species of *Leishmania*. As no two mammal–sandfly-vector combinations are likely to share exactly the same ecological niche, we can expect a wide variation in the influence that any modification of the environment may have on the prevalence or incidence of human leishmaniasis in a given region.

## 2. The man–reservoir-host–sandfly-vector contact

With some apparent exceptions, discussed below (§§ 3*b*, 3*c* (ii) and 3*c* (iii)), the dynamics of any form of human leishmaniasis will depend on population fluctuations at any point of an 'epidemiological triangle' formed by man, the reservoir-host(s) and the sandfly vector(s).

In addition to increase or decrease of the human population due to favourable or unfavourable local conditions, there are changes related to migration. The development of uninhabited or sparsely populated areas, for example, is usually accompanied by the introduction of work-forces and may lead to future colonization of those areas: conversely, there may be migration away from adverse conditions such as drought, famine and disease (including leishmaniasis). In an enzootic region where the human population remains sparse – as in some Old World deserts, and neotropical forests – the public health importance




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of leishmaniasis will be small. With the invasion by a large population of non-immune persons at some point within the region, however, the disease may well become a major problem. Such 'hot-spots' of leishmaniasis are often attributed to unknown ecological peculiarities, when they are simply due to greatly increased human contact with the sandfly vector. There are numerous examples of such focality of human leishmaniasis, of which the most outstanding are discussed below.

Provided the *Leishmania* species of a given enzootic is infective to man, the risk of acquiring leishmaniasis to individuals penetrating that area will be high (*a*) if the mammalian host is abundant and commonly infected, (*b*) if the vector is highly anthropophilic, and (*c*) if the vector feeds on man during daylight hours. Fluctuations in the populations of the vertebrate and invertebrate hosts may be natural ones (of which, in general, very little is known) or man-induced. The latter may result from deliberate attempts to control a given form of leishmaniasis, or it may follow entirely unassociated human activities that are either favourable or detrimental to the natural transmission cycle.

## 3. Leishmaniases of the Old World

### (*a*) *Rural, zoonotic cutaneous leishmaniasis due to Leishmania* (*L.*) *major Yakimoff & Schokhor*, 1914 *emend. Bray et al.*, 1973

This form of leishmaniasis is found throughout vast areas of the more arid regions of the Old World, including North Africa, the Middle East, and middle and eastern Asia.

Outbreaks of the disease are most often associated with the introduction of new populations into the enzootic areas during development programmes in agriculture or rural building schemes, or during massive troop movements. Thus 'Balkh' or 'Sart' sore is said to have affected up to 85% of the Russian troops concentrated in the Murghab district of Tadzhik, S.S.R., during border disputes with Afghanistan in the late 1880s, and similar outbreaks were noted among French troops during the Algerian invasion of 1830–1848, particularly in the Hafsah and Biskra oases (Petriščeva *et al.*, undated). In Saudi Arabia over 1300 cases were recorded during 1981 in the Hofuf region alone. The disease became such a problem among German engineering technicians and their families, who had been contracted to work in different parts of the country, that many of them demanded to be returned to their home country. It was estimated that the loss suffered due to the virtual collapse of the project was in the region of U.S.$6M (Killick-Kendrick, in Lainson (1983*b*)).

The causative organism, *L.* (*L.*) *major* is found in the skin of a variety of burrowing rodents (particularly gerbils), among which it is transmitted by certain burrow-dwelling sandfly species. In northwest China, Turkmenian and Usbek S.S.R., Mongolia (Gobi desert), north Afghanistan and northeast central Iran, the principal host is the 'great gerbil', *Rhombomys opimus*, with the 'red-tailed jird', *Meriones libycus*, involved in some areas. The sandflies *Phlebotomus papatasi*, *P. caucasicus*, *P. andrejevi* and *P. mongolense* have been indicated as vectors among the rodents: of these, *P. papatasi* is the most anthropophilic and considered to be of greatest importance in transmission to man. Different rodent–sandfly-vector combinations occur elsewhere in the geographical range of the parasite. Thus in Senegal the rodent hosts are *Arvicanthis*, *Tatera* and *Mastomys* species, and the vector *P. dubosqi*; in east Saudi Arabia, Israel and Libya, *Psammomys obesus* is an important host.

Nowhere has the ecological interrelation between the vertebrate and sandfly hosts of a




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leishmanial parasite been more intensely studied than in the epizootic foci of *L.* (*L.*) *major* in southern Russia (Neronov & Gunin 1971; Petriščeva 1971; Saf'janova 1971).

Colonies of *R. opimus* are most frequent where there is soft, sandy soil stabilized by vegetation, and the junction between different types of soil seems to be particularly attractive to them. Colonies may reach very large proportions and frequently overlap, to cover several acres. They consist of a labyrinth of underground runways, of two or three layers, and constructed at a depth of about 50 cm to 2 m; there are specific nesting, food storage and toilet compartments.

The microclimate in the burrows is remarkably stable (although variable at different points within the burrows), enabling sandflies to live and breed there all the year round. With such an intimate relation between the vertebrate and invertebrate hosts of the parasite it is not surprising that the infection rate in some colonies may reach 100%, and that of the sandflies in the region of 65%. Neither is it surprising that the incidence of cutaneous leishmaniasis is high in nearby human settlements.

It has been noted that there are natural fluctuations both in the number of sandflies inhabiting the burrows of different colonies and the infection rate among the gerbils. This is attributed to alterations in the microclimate, largely because of variations in the water content of the soil: if this drops too low, conditions are unsuitable for the sandflies, and if it is in excess, the gerbils will move their colony for long distances away from the area in question.

From these and other observations, it has been possible to reduce the incidence of cutaneous leishmaniasis due to *L.* (*L.*) *major* by making marked changes in the natural landscape. Poisoning of gerbils and insecticide application in the burrows is followed by deep ploughing, to disrupt the colony and, as *Rhombomys* shows a remarkable ability to reinvade a cleared area, a wide belt of continuously cultivated land is maintained around the affected human settlement. This, and the use of wide irrigation canals, is usually sufficient to avoid re-colonization.

*Meriones libycus* usually shows a much lower infection rate than that of *Rhombomys*. It may approximate 20%, however, and as this rodent appears to prefer newly cultivated ground, near towns and villages, the above-mentioned control measures may actually favour enzootics in this animal.

Control of rodents by eliminating their preferred, natural food, may be achieved by environmental changes involving the flora. This must be done with care, however: in North Africa, species of the plant *Atriplex* are the specific food of *Psammomys obesus*, and cultivation of these plants on a large scale for sheep-fodder has resulted in population explosions of this rodent (Anon. 1984), a potentially hazardous situation as *P. obesus* is a known reservoir-host of *L.* (*L.*) *major*.

### (*b*) *Urban cutaneous leishmaniasis due to L.* (*L.*) *tropica*

Classical 'oriental sore' is predominantly associated with towns and ancient settlements of Central and Southeast Asia and the Indian subcontinent. Modern methods of parasite identification are beginning to cast doubt on records of its existence in North Africa, where much cutaneous leishmaniasis attributed to *L.* (*L.*) *tropica* was almost certainly due to *L.* (*L.*) *major*, and in the western Mediterranean region where it seems that past confusion may have been made with certain enzyme variants of *L.* (*L.*) *infantum* Nicolle 1908, which produce skin lesions rather than a visceral disease (§ 3*c*(i)).

Claims to have found both dogs and domestic rats infected with *L.* (*L.*) *tropica* have been




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made, but other workers maintain that transmission is directly from man to man. It has been suggested, for example, that the common Middle Eastern and Asian habit of sleeping on flat roofs of houses in hot weather may contribute substantially to intra-familial transmission by the suspected vector, *P. sergenti*, which is closely associated with man's dwelling places (Peters 1979).

The peridomestic transmission of oriental sore has enabled excellent results in control programmes, combining the treatment of infected persons with the application of insecticides in and around houses. Soviet workers go so far as to claim that the disease is, for this reason, now only of historical interest in their country. Unfortunately, it still seems to be common elsewhere, notably in Afghanistan and Iraq.

### (*c*) *Visceral leishmaniasis of the Old World*

Lysenko (1971) suggested that disease due to parasites of the *L.* (*L.*) *donovani* complex originated from a rural enzootic in wild canids, such as foxes, jackals and wolves, in Central Asia. Later, dogs became involved and, accompanying the migrations of man, were a major factor in the spread of infection from Transcaucasia to Southwest Asia, Africa and the Mediterranean basin in one direction, and to China in the other.

Attractively simple as this hypothesis is, there remain some epidemiological peculiarities that do not fit into it very well. As discussed below, in parts of Africa and in India, it is still not clear if there is any effective reservoir other than man himself, and the dog is certainly of little, or no, epidemiological importance.

#### (i) *Mediterranean and middle-Asian visceral leishmaniasis due to L.* (*L.*) *infantum*

This important disease of dogs and man extends throughout the Mediterranean littoral and the Balkan countries; West Asia, from the U.S.S.R. in the north into the Arabian peninsula; East China, and some of the northern, northeastern and northwestern provinces of that country (for review and bibliography, see Ashford & Bettini (1987)).

It is a sad fact that the dog has become the major reservoir of infection for man; sadder still that the canine disease is almost always lethal, and seemingly incurable. Infection rates may be extraordinarily high: thus, in Italy, figures of 90 %, 24 % and 37 % have been given for dogs in Calabria, Tuscany and the island of Ustica, respectively.

In the epidemiology of the Mediterranean disease, dogs are best regarded as 'amplification' hosts which, at the acute phase of the infection, provide the sandfly vector with a rich source of parasites located in their skin and blood. Add to this the high infection rate and the great attraction the dog has for the vector, and it is easy to understand why human visceral leishmaniasis due to *L.* (*L.*) *infantum* is frequently at epidemic level.

The lethal nature of the canine infection suggests that the dog is a relatively recent and ill-adjusted host, and the records of chronic, inapparent infection in wild canids indicates these to be the original, primitive source of the parasite (see also §4*a*). Isolations have been made from the red fox, *Vulpes vulpes*, in France, Italy, Spain, Portugal and the Caspian area of Iran. Infected jackals, *Canis aureus*, have been found in Iran and in Tadjikistan, Turkmenia and Kazakhstan S.S.R. Finally, a natural infection has been reported in the 'raccoon dog', *Nyctereutes procyonoides* (Canidae) in Miyun, China.

Foxes may travel long distances and, together with stray dogs, have a frequent if discreet




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association with man, often scavaging in search of food at rubbish tips and even in residential areas. For these reasons they may serve to introduce the parasite into new areas.

Naturally infected black rats (*Rattus rattus*) have been recorded in Yugoslavia and Italy, and it has been shown that *P. perniciosus* – considered an important vector in the Mediterranean region – can be infected by feeding them on experimentally infected rats. Natural infections in *R. rattus* are inapparent.

The cosmopolitan nature of rats, and their frequent migration – either purposefully, following floods, lack of food, etc., or involuntarily by way of ships and other means of transport – are possible factors in the spread of *L.* (*L.*) *infantum* that require further study.

Reasons for the sudden appearance, or abrupt cessation, of epidemics of Mediterranean visceral leishmaniasis are still inadequately explained. Extensive increase of the canine and non-immune human population, after the establishment of new settlements in areas of hitherto low endemicity, are clearly of very great importance. Both *P. perniciosus* and *P. ariasi* (the vector in the Cévennes area of France) have very catholic tastes and will readily turn their attention from wild animals, or scarce farm animals, to a new and more abundant source of blood from man and dogs. Primarily silvatic, they both show a capacity to adapt to, and breed in, the peridomestic situation. With the build-up of the dog, sandfly and human populations to a high level, in the presence of the parasite – either already there, or newly introduced via a dog, marauding fox or migratory sandfly – all the ingredients are present for an impending epidemic. The first build-up of infection will take place in the dogs, as the sandflies attack these animals with greater avidity than they do man. Once the number of dogs in the acute phase of infection reaches a high level, human infections will begin to appear and, if control measures are not introduced, an epidemic may result.

Although zoonotic visceral leishmaniasis can be controlled by the destruction of infected dogs, insecticide spraying and the treatment of human cases, it is unlikely ever to be eliminated because of the silvatic cycle of transmission.

(ii) *Kenyan and Sudanese visceral leishmaniasis*

On the African continent, Le Blancq & Peters (1986) considered isolates from man, dog, a rodent (*Arvicanthis*) and a sandfly (*Phlebotomus martini*) as indistinguishable from *L.* (*L.*) *infantum* on isoenzyme profiles, using 13 different enzymes. The parasites studied were from Kenya, Sudan and Ethiopia.

In northern Africa the epidemiology of the disease is characteristically that of *L.* (*L.*) *infantum* (§3*c*(i)), and this possibly extends down through the countries of the Atlantic coast, for dogs are commonly found infected in Senegal (although the human disease has not been recorded). In East Africa, however, the epidemiology is not typical of *L.* (*L.*) *infantum* and neither are the clinical features. In addition, Jackson *et al.* (1982) found that 'Sudanese, Ethiopian ... and Kenyan *L. donovani* isolates ... had different kDNA fragment patterns ...'. For these reasons, Lainson & Shaw (1987) preferred to regard the causative agents of Kenyan and Sudanese visceral leishmaniasis provisionally as 'other possible species within the *donovani* complex'.

*Kenya*. Here, it seems that an anthroponosis has become superimposed on what was basically a zoonosis. Thus outbreaks of visceral leishmaniasis have been recorded in troops operating in normally uninhabited regions, strongly suggesting the existence of a feral reservoir. There is also, however, much evidence indicating a man–man cycle, occurring in the villages and

associated with the emergence of large numbers of the suspected vector, *P. martini*, from eroded termite hills, in the rainy season. One epidemiological investigation, for example, showed that 70% (111 of 161) of the houses near such termitaries had cases of visceral leishmaniasis, compared with only 20% (32 out of 148) in others that were situated well away from abandoned nests (Southgate 1977). Moreover, the incidence of infection was found to be much higher among males than among females, presumably because it is the men who suffer most sandfly bites, as they sit outdoors chatting in the evening. The women, on the other hand, are relatively well protected in the smoky interior of the houses as they prepare the evening meal, etc.

Man–man transmission would certainly help to explain new epidemics that have occurred after the mass evacuation of human populations from one area to another (Ashford & Bettini 1987), and the fact that spread of Kenyan visceral leishmaniasis seems to have largely been along the major routes of communication.

The disease in Kenya differs from that of the Mediterranean region in both the frequency of dermal manifestations and involvement of the lymphatic glands in the apparent absence of visceral disease, and the high rate of spontaneous recovery, which is said to sometimes be as high as 80%. Epidemiologically, it differs in the extreme rarity of canine infection.

*Sudan*. Sudanese visceral leishmaniasis is notorious for its explosive outbreaks, highly lethal nature and poor response to drugs. It is the only focus of the African disease where a definite zoonosis has been demonstrated, involving local wild mammals (in the Palioch–Malakal area).

The most important of these appears to be the rodent *Arvicanthis niloticus*, with three isolates of the parasite made from 188 animals examined (1.2%). The authors (Hoogstraal & Hyneman 1969) felt, however, that many infections had been missed because of inadequate isolation technique, and that the infection rate was much higher. Single specimens of two other rodents, *Acomys albigens* and *Rattus rattus*, were also found infected, whereas two carnivores, *Felis serval* and *Genetta genetta*, were thought to have acquired their infections after eating rodents.

The ecology of the rodents has not been studied extensively, but it was noted that in the dry season *Arvicanthis* was mostly found in large cracks in the ground that had become filled with dead leaves and other débris. Moreover, they were most abundant in those areas regularly flooded in the rainy season. Where they migrate to at this time is uncertain, but this ecological feature quite probably has some influence on the seasonality of visceral leishmaniasis, assuming that the rodents are an effective source of infection for the sandfly vector, *Phlebotomus orientalis*.

*P. orientalis* is most abundant in the denser parts of the *Acacia–Balanites* forest, where as many as 600 flies have been captured, during 1 h, from a single man acting as bait. The relation between the wild rodents and the vector has yet to be established.

Finally, Fuller *et al.* (1979) emphasized the influence of soil type on the distribution of visceral leishmaniasis in the Kenyan–Sudanese–Ethiopian focus, and demonstrated a close relationship between leishmanin skin-test positivity in the human population and certain types of clay soil. Most probably this is linked with the ecology of the vector (breeding sites?); in this respect, it is interesting to note that foci of cutaneous leishmaniasis in Italy have been associated with soils of high clay content, and it has been suggested that their marked water retention is favourable for the development of sandfly larvae (Pozio *et al.* 1980).




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(iii) *Indian visceral leishmaniasis: 'kala-azar'*

Periodic and devastating epidemics of this disease have been recorded in India for over a century, the first documented outbreak being in 1824, in the Jessore district, where it was supposedly responsible for the loss of about 75000 lives (Sen Gupta 1944). How long the disease has been in India, and where it came from, remains uncertain.

Between the 1930s and the mid-1950s, a combination of improved treatment and house-to-house antimalarial DDT spraying contributed to a steady decline in the disease, to almost zero, but the virtual cessation of the spraying led to a serious outbreak of kala-azar, in Bihar, as recently as 1977, and extending into the 1980s. At the moment the incidence seems to be declining, although infection has spread to new areas.

Very many dogs have been examined during these epidemics, but not one canine infection has been recorded. Indian kala-azar is considered by most, therefore, to be solely anthroponotic, a view supported by the common presence of parasites in the peripheral blood of patients and the peridomestic habits of the sandfly vector, *Phlebotomus argentipes*.

The epidemics of kala-azar appear to occur in cycles of approximately 10–15 years, and it has remained difficult to explain the source of the organism that periodically sparks off an outbreak of the disease. A small percentage of treated and apparently cured patients, however, subsequently develop chronic, nodular skin lesions containing amastigotes, and it has been suggested that these cases of 'post kala-azar dermal leishmaniasis' (PKDL) are the reservoir from which new outbreaks arise, after a build-up of the *P. argentipes* population. On the other hand, it would seem that PKDL only develops in antimony-treated cases, which rather precludes them as a source of infection during those epidemics that occurred before antimony compounds became the routine form of treatment, in the 1920s. This, and the occurrence of isolated, sporadic cases in some parts of India other than Bihar during the recent resurgence of kala-azar, has led once more to suspicions that either an animal reservoir does exist, or that some persons act as chronic, symptomless carriers for long periods of their lives.

As in Kenya, it is suggested that movements of the human population have '... played a pivotal role in the spread of the disease ...' (Chowdhury 1983). Finally, although there is as yet no evidence incriminating domestic animals as reservoirs of *L.* (*L.*) *donovani*, the intimate rural contact of man with cows, pigs and other livestock – frequently all under the same roof – encourages a high density of *P. argentipes* and *P. papatasi* (a suspected secondary vector).

## 4. Leishmaniasis of the New World

Modern man's ecological impact on the Latin American continent, following his devastation of forests and other natural landscapes, is very considerable, unlike that of the indigenous Amerindians, who had wisely learned to exploit the riches of the forests without destroying them.

The variety of leishmanial parasites at present being disclosed in the mammalian fauna of relatively undisturbed Amazonian forests suggests that all the neotropical *Leishmania* species known to infect man were probably once limited to silvatic enzootics. Why then, is the disease so rarely seen among the Indians, who spend most of their lives in the forest?

The most logical explanation is that their intimate contact with these enzootics has led, over the centuries, to an acquired immunity, probably gained at a very early age. The few lesions




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one sees among Indians are usually inconspicuous, self-healing, and mostly in children or women: virtually 100% of the adult males of a given tribe, however, may have a positive leishmanin skin-test, indicative of past infection, and their immunity will presumably be kept at high level by the periodic bites of infected sandflies.

The neotropical *Leishmania* species known to infect man do not cross-immunize, and the Indian's immunity is largely restricted, therefore, to the parasite(s) circulating in his particular tribal region. Thus in Brazil, a severe outbreak of cutaneous leishmaniasis in the Waurá tribe followed when they were driven out of their own territory by enemy tribes and took refuge in an ecologically very different forest along the banks of the Xingu river (Carneri *et al.* 1963). Non-indigenous settlers, members of labour-forces temporarily engaged in deforestation, and occasional visitors such as topographers, geologists, naturalists and hunters, will not have the Indian's acquired immunity and, where optimal conditions for transmission occur, acquisition of leishmaniasis is not only almost inevitable but usually leads to a much more serious disease.

At first sight it would seem that destruction of primary forest should lead to the elimination of zoonotic leishmaniasis, but this is often far from the case. It is true that some *Leishmania* species infecting man, or potentially capable of doing so, may be eliminated by drastic ecological unheavals, especially when their sandfly and mammalian hosts have very specialized habits. As discussed below, however, there are instances when environmental changes may actually increase the endemicity of leishmaniasis due to a given *Leishmania* species, or result in the appearance of another form of the disease due to a totally different parasite, which is now thrown into closer contact with man. Finally, certain sandfly species are much more resistant to ecological change than are others, and some may actually invade human dwelling places and animal shelters in considerable numbers. When such sandflies have catholic and anthropophilic feeding habits, an extrasilvatic transmission to domestic animals (e.g. the dog) and man may be established, leading to a much higher incidence of human leishmaniasis than existed before the natural biotope was destroyed or modified.

### (*a*) *American visceral leishmaniasis*

This disease has been recorded in Argentina, Bolivia, Brazil, Colombia, Ecuador, El Salvador, Guadeloupe, Honduras, Mexico, Paraguay, Surinam and Venezuela; for reviews of the literature on the history and epidemiology, see Lainson & Shaw (1979) and Lainson (1983*a*, 1988).

The origin of the causative agent, variously referred to as *L. donovani chagasi*, *L.* (*L.*) *infantum chagasi* or *L.* (*L.*) *chagasi*, has been the subject of some debate and speculation. Briefly, one opinion is that the organism is *L.* (*L.*) *infantum* which was introduced by immigrants from the Iberian peninsula in post-Columbian times, most probably by way of infected dogs. Points in favour of this hypothesis are the close similarity of the isoenzyme profiles (for those studied) of the two parasites, and the role of the dog as the amplification host in their epidemiology. Another view is that the history of the parasite is likely to go back much further, possibly to that of early neotropical canids, present in South America in the Pleistocene era, some 2–3 Ma BP. Arguments in support include the high percentage of inapparent infections in foxes (*Cerdocyon thous*) in relatively remote areas of Amazonian Brazil; the wide distribution of both foxes and *L.* (*L.*) *chagasi* throughout South and Central America; restriction of the parasite to a single vector, *Lutzomyia longipalpis*; a relatively strict limitation of *L.* (*L.*) *infantum*




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to a few sandfly species within the subgenus *Larroussius*; and differences in both the kinetoplast DNA fragment patterns and the radio-respirometry profiles of *L.* (*L.*) *infantum* and *L.* (*L.*) *chagasi*.

I have suggested elsewhere (Lainson 1988) that '... the present-day enzootology and epidemiology of *L.* (*L.*) *chagasi* ... as seen in the more remote parts of South America such as the Amazon region, probably represents a recapitulation of what transpired when early settlers first commenced their slow but relentless ecological upheavals in many parts of the Latin American continent'; this has probably followed a similar pattern to that discussed in §§ 3*c* and 3*c* (i) for *L.* (*L.*) *infantum* in the Old World.

Transmission of *L.* (*L.*) *chagasi* among foxes is presumably by silvatic sandflies, and the species involved is probably *L. longipalpis*, although its silvatic association with foxes still remains to be indicated, and it is quite possible that another sandfly is implicated. There is no doubt, however, regarding the role of *L. longipalpis* as the peridomestic vector to dogs and man, because of its remarkable capacity to invade this new habitat after deforestation and the establishment of human settlements. When these are of the 'shanty-town' type, with poor hygiene, overcrowding and an abundance of domestic animals such as dogs, chickens and pigs, very large number of *L. longipalpis* may concentrate in houses and animal shelters.

Two highly preferred blood-sources of this insect are chickens and dogs, which has an important bearing on the epidemiology of American visceral leishmaniasis. Firstly, it is unusual for chicken-houses to be sprayed during antimalarial DDT programmes and, although houses may be freed of sandflies, the *L. longipalpis* population in chicken-roosts may build up to a very high level. Under such circumstances the introduction of *L.* (*L.*) *chagasi* into a rural community with many dogs will result in a rapid spread of the canine disease.

How the parasite is first introduced remains to be investigated, but it is reasonable to suppose that when foxes are scavenging for food in villages they may be fed on by peridomestic *L. longipalpis*; alternatively, infected sandflies may be attracted from the silvatic habitat by the lights of nearby houses. Once a single dog becomes infected, the scene is set for a focus of the human disease. As the number of infected dogs increases, so does the sandfly infection rate and, although *L. longipalpis* is more highly attracted to dogs than to man, human infections will inevitably begin to appear. At this stage, foxes will no longer be necessary to maintain the endemic, because although most dogs eventually succumb to the disease, they survive long enough, and are sufficiently numerous, to provide a prolonged reservoir of infection for the sandflies.

Destruction of forest results in more and more open land, with interspersed patches of woodland. This may diminish the incidence of silvatic cutaneous leishmaniasis (see, however, §§ 4*b* (ii) and 4*b* (iv) but increase that of visceral leishmaniasis. The new habitat is ideal for foxes, and the opening of roads through forested areas offers long distances of roadside habitation suitable for invasion by *L. longipalpis*; in this manner there may arise new and widely dispersed foci of visceral leishmaniasis.

Superimposed on this epidemiological landscape is the spread of infection by migrants, with their infected dogs, coming from more highly endemic areas to the less heavily populated regions. In Brazil, the inhabitants of the northeastern State of Ceará are famous for their nomadic tendencies (largely because of long-lasting droughts in their part of the country), and it is precisely there that visceral leishmaniasis is at its highest epidemicity.




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### (*b*) *Cutaneous and mucocutaneous leishmaniasis*

#### (i) *Central American 'chiclero's ulcer' due to L. (L.) mexicana Biagi*, 1953 *emend. Garnham*, 1962

Once very common among forest workers collecting chewing-gum latex ('chiclé') and extracting mahogany, in the Yucatan peninsula, Belize and Guatemala, this disease is now much less common since a decline in these professions due to the present-day usage of artificial 'gums', and decimation of the mahogany trees after many years of inadequately controlled felling.

The reservoir-hosts of the parasite are small rodents, and the sandfly vector is *Lutzomyia olmeca olmeca*. This insect is only moderately anthropophilic, and largely noctural: the high incidence of infection among the chicleros was the outcome of a prolonged sojourn in the forest, for periods of up to 6 months at a time.

Although fluctuations in the rodent population have not been directly related to the incidence of chiclero's ulcer, Lainson & Strangways-Dixon (1964) noted a striking increase in the number of rodents coming to their trap-lines in Belize after severe damage to the forest by hurricane 'Hattie', in 1961. It seems that the tangled mass of fallen trees and dense secondary undergrowth formed a highly suitable and protective habitat, leading to a marked increase in the small mammal population.

Recently another *Leishmania*, of the *braziliensis* complex, has been found in Belize, causing cutaneous lesions among British soldiers undergoing jungle training. Earlier failure to encounter this parasite was probably because of the very different epidemiological circumstances associated with military manoeuvres, compared with the activities of the chicleros.

#### (ii) *South American cutaneous and diffuse cutaneous leishmaniasis due to L. (L.) amazonensis Lainson & Shaw*, 1972

This close relative of *L. (L.) mexicana* is widely distributed throughout the Amazon basin, where it infects a wide range of terrestrial rodents and, less frequently, marsupials. The vector, *Lutzomyia flaviscutellata*, is of the *olmeca* group, not very anthropophilic, and feeds only at night. Transmission to man is consequently uncommon compared with that of parasites of the *braziliensis* complex, the vectors of which are usually highly attracted to man and frequently feed during the night and the day (§§4*b*(iii, iv)).

The importance of *L. (L.) amazonensis* lies in the organism's frequent production of an incurable, disseminated form of dermal leishmaniasis in patients with a deficient cell-mediated immunity, and the capacity of both the vector and the reservoir-hosts to thrive in all types of woodland: from high primary forest, to secondary and degraded forests resulting from deforestation.

Dense undergrowth associated with the latter is particularly favourable for both rodents (see also §2*b*(i)) and *L. flaviscutellata*, and man is constantly producing new ecological niches for this enzootic, by his destruction of primary forest. In north Pará State, for example, vast areas have been totally destroyed and planted with exotic trees such as pine and gmelina, for the production of paper pulp: *L. (L.) amazonensis* is now firmly established in these new 'forests' after the invasion of the plantations by small mammals and *L. flaviscutellata*.

Humid riverine forest ('varzea' and 'igapó') is another favoured biotope of rodents and *L. flaviscutellata*, and the recent construction of a series of hydroelectric dams in the Amazon




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region will vastly increase this type of forest–water interface, following the creation of huge lakes. It remains to be seen if the incidence of leishmaniasis due to *L.* (*L.*) *amazonensis* increases as new swamp-forest becomes established around the reservoir edges.

(iii) *Cutaneous leishmaniasis produced by L.* (*V.*) *panamensis Lainson & Shaw*, 1972 *and L.* (*V.*) *guyanensis Floch*, 1954

The former parasite is the most common cause of dermal leishmaniasis in Panama and neighbouring parts of Colombia and Costa Rica; the latter is responsible for most of the disease north of the Amazon river, in the Guyanas and across Brazil to at least as far as Manaus in Amazonas State.

The major reservoir-host of *L.* (*V.*) *panamensis* is the sloth, *Choloepus hoffmanni*, and the principal vector *Lutzomyia trapidoi*. The most important hosts of *L.* (*V.*) *guyanensis* are again sloths (*Choloepus didactylus*), and anteaters (*Tamandua tetradactyla*); the principal vector is *L. umbratilis*. Transmission of both *L.* (*V.*) *panamensis* and *L.* (*V.*) *guyanensis* among the natural hosts is largely at night, and in the forest canopy.

Oviposition site(s) of both vectors are most likely to be on the forest floor, and at certain times, notably in the cooler, more humid hours of early morning, the female flies concentrate on the bases of the larger trees, from where they may attack nearby persons when disturbed. As human activities in the forest are largely diurnal (e.g. clearing forest), human infection is mostly acquired in the daytime.

In addition to this daytime activity on the part of the vector, a combination of other factors maintains a high infection rate among persons entering primary forests harbouring these two parasites. Two-toed sloths are common, have few predators, and are very frequently infected. They often stay for prolonged periods in the same trees and there tends to be, therefore, a build-up of infected sandflies on the tree-trunks in the territory of an infected sloth. This is reflected in the frequency of multiple lesions in the human disease due to *L.* (*V.*) *guyanensis*.

Prolonged observations on the effects of deforestation on the ecology of *L.* (*V.*) *guyanensis* in north Pará, Brazil, indicated that the enzootic is incapable of adapting to the pine and gmelina plantations, unlike the essentially terrestrial enzootic of *L.* (*L.*) *amazonensis* in the same region. Failure to do so is most likely due to the unsuitable microhabitat for *L. umbratilis* on the slender trunks of the non-indigenous trees, and a new environment that is totally foreign to the sloth. Apart from a physical difficulty in supporting its body mass in such small trees, this animal is unable to find its natural diet in the plantation. For similar reasons it may be concluded that neither *L. umbratilis* nor *C. didactylus* is likely to thrive in secondary forests.

Although peridomestic transmission of *L.* (*V.*) *guyanensis* has been recorded, this has been associated with houses situated in the forest itself, or on its fringes. No evidence has yet been found of *L. umbratilis* colonizing human habitations, and peridomestic transmission clearly depends on infected sandflies that are attracted to villages from the neighbouring forest, presumably by the lights of the houses. Clearing the forest to a distance of about 400 m around such villages has been found to eliminate the problem entirely (Esterre *et al.* 1986).

(iv) *Cutaneous and mucocutaneous leishmaniasis due to L.* (*V.*) *braziliensis and related parasites*

Vianna (1911) gave the name *L. braziliensis* to an organism causing disseminated skin lesions in a man from Alem Paraíba, on the borders of Rio de Janeiro and Minas Gerais States in southeast Brazil, and Splendore (1912) found *Leishmania* in the nasal mucosae of cases of mucocutaneous leishmaniasis in south Brazil. It was assumed that these infections were due to




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the same parasite but, in the light of our improved epidemiological knowledge and methods of parasite identification, it is quite likely they were not. Similar organisms have since been described as '*L. braziliensis*' or *L. b. braziliensis* sensu lato' from widely separated geographic areas: not only in Brazil (States of Pará, Bahia, Rio de Janeiro, São Paulo, Ceará and Espirito Santo), but also in Venezuela, Colombia, and as far north as Belize and Honduras in Central America.

Because of the considerable differences in the fauna of most of these regions, it is difficult to believe that these parasites are identical unless we assume a variety of mammalian and sandfly hosts to be involved in the life cycle of the same *Leishmania*, a suggestion I cannot view with conviction. It remains likely that continuing elaboration of modern methods will eventually enable a clearer distinction between these organisms. For this reason, caution is needed when comparing the epidemiological features of the disease(s) they cause; in the meantime, however, studies on leishmaniasis in some of these localities do indicate a spectrum of epidemiological changes that have taken place after the destruction of primary forest, culminating in a relatively large-scale invasion of the peridomestic habitat on the part of some sandfly vectors.

At one end of this spectrum, infection with *L.* (*V.*) *braziliensis* sensu lato, in the Serra dos Carajás region of the State of Pará, Amazonian Brazil, is acquired only in the primary forest on the hills above an altitude of about 300 m. The vector, *Psychodopygus wellcomei*, is the most common man-biting sandfly during the rainy season (December–May), but disappears in the dry season, when it enters into diapause; this, and the tendency of the fly to attack man during the night and the day, leads to acquisition of human infection principally by day, and almost exclusively during the months of December–May. The reservoir-host(s) remain undetected, but are probably terrestrial animals, as indicated by the low flight range of the vector. As far as is known, *P. wellcomei* displays no tendency to invade human habitations situated near primary forest.

Along the Brazilian Atlantic coast, approximately from Natal in the north to Porto Alegre in the south, there once existed a vast tract of luxuriant forest that extended inland to cover most of Minas Gerais and São Paulo States, and nowhere in South America is devastation by man more apparent. The areas that now form these States, for example, supported Brazilian agriculture for some 400 years, during which time the great forests were virtually destroyed for the production of charcoal and timber, and the pathetically small remnants of the Atlantic forest that remain are fast dwindling.

In spite of these drastic environmental changes, however, cutaneous leishmaniasis is still a problem in this area of Brazil and, although infection is probably still acquired in those wooded parts that are left (and where *L.* (*V.*) *braziliensis* sensu lato has been isolated from both rodents and sandflies), the presence of considerable numbers of some sandfly species in the peridomestic habitat suggests that there may now exist a secondary, extra-silvatic transmission to man, dogs and equines.

*Lutzomyia intermedia*, for example, is the predominant sandfly around rural houses in Rio de Janeiro State, where it is suspected to be involved in peridomestic transmission. In the States of Espirito Santo and São Paulo, the majority of sandflies captured in villages and nearby banana plantations were *L. intermedia*, with smaller numbers of *L. fischeri*, *L. migonei* and *L. whitmani*. Promastigotes, which were possibly those of *L.* (*V.*) *braziliensis sensu lato*, have been recorded in the last two species in São Paulo.

*Lutzomyia whitmani* is another silvatic sandfly that has invaded the peridomestic situation, at




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least in some areas of its distribution. In Amazonian Brazil it is a relatively infrequent tree-trunk dwelling species, which shows little inclination to bite man and no tendency to invade his dwelling places. Large populations of what appears to be the same fly show various degrees of 'domestication' in parts of northeast, southeast and south Brazil, however, where this insect is considered an important vector of *L.* (*V.*) *braziliensis* sensu lato, in the silvatic habitat and in and around houses. Moreover, the simultaneous infection of man, dogs and equines has led to the suggestion that these hosts are serving as a source of infection for the peridomestic sandfly population.

To substantiate such a hypothesis, however, several questions need to be answered. Thus although infected *L. whitmani* have been found in or close to houses, it is not clear where they came from or what the source of their parasites was. Does the peridomestic sandfly population simply represent an accumulation of insects attracted from nearby woodlands, or are the sandflies breeding in the new environment?

If the former, then the focus of leishmaniasis remains essentially a silvatic zoonosis, with man and domestic animals merely 'victim' hosts, following transmission either in the woodlands or in and around houses.

If the latter, the case for transmission among man and domestic animals becomes stronger, but by no means proven. Investigations on breeding sites, movements of sandflies, and the efficiency of man and domestic animals as sources of infection for sandflies remain vital.

## Conclusions

Natural or man-made ecological changes may profoundly affect the epidemiology of the leishmaniases, after fluctuations in the human, sandfly and animal reservoir populations. Newly created environments may diminish or eliminate one form of the disease, but encourage another.

In south Brazil, destruction of primary forest has, contrary to expectation, not diminished the problem, largely because of the invasion of the peridomestic habitat by some sandfly species in rural settlements, and the possible role of domestic animals, or man himself, in an extrasilvatic transmission cycle.

It is likely that a similar process may take place in the Amazon region. The incidence of visceral leishmaniasis there has certainly increased greatly in recent years, after ever-escalating deforestation, the establishment of new settlements, and the creation of peridomestic environments that are highly attractive to the vector.

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## *Discussion*

R. Killick-Kendrick (*Imperial College at Silwood Park, Ascot, U.K.*). Professor Lainson has highlighted a point concerning control which is often overlooked. He illustrates how major changes in the environment may result in the disappearance of one set of parasite–vector–reservoir, only to be replaced by another. Radical changes may not therefore necessarily result in the disappearance of leishmaniasis. In fact, one mild form may be replaced by another form of greater severity.

We have heard how *Lutzomyia whitmani*, a suspect vector in southern Brazil, may inhabit habitats varying from the forest to settlements. Is there any evidence that this species is a complex of siblings?




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R. Lainson. There is no information yet on this subject. We are proposing to establish colonies of both the Amazonian and southern *L. whitmani* in the hope of doing cross-fertilization experiments and comparative isoenzyme-profile studies, to answer this question.

Similar studies are also needed for *L. umbratilis*, which is the major vector of *Leishmania* (*V.*) *guyanensis* north of the Amazon, but seemingly not in the forests south of the river. Different behavioural patterns have been observed for the northern and southern populations.

Ana Flisser (*National University, Mexico City, Mexico*). Have the mammalian reservoirs of *Leishmania* been studied so as to understand why they do not get the disease in presence of parasites, compared with human immunobiological characteristics which favour the disease?

R. Lainson. The usual answer to this question as to why some hosts suffer disease after infection with a given parasite, whereas others do not, is that the latter represent 'well-adjusted' hosts in which there has developed a well-balanced relationship, over a long time. Killing off the host is clearly not in the interest of the parasite if it is to maintain itself successfully in the wild, and animals suffering disease from *Leishmania* (such as man, dogs and equines) are commonly referred to, therefore, as 'victim hosts'. Although they are sometimes of importance in the epidemiology of the human disease (as, for example, dogs in Mediterranean and American visceral leishmaniasis), they are not essential for the maintenance of the parasite in the wild.

The actual mechanism by which a 'good' host–parasite relationship is developed is experimentally difficult to study, as presumably it is only achieved after a relatively ancient host–parasite association. Immunologists doubtless have explanations of a more intrinsic nature!




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