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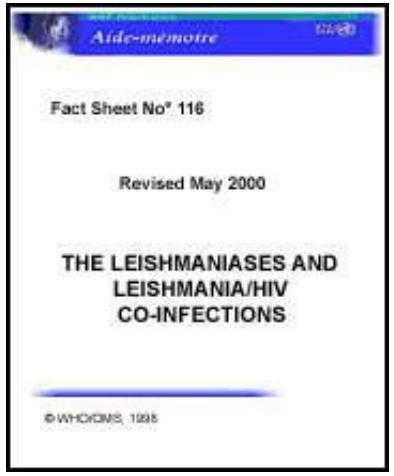

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- *(introduction...)*
- Increased Prevalence
- Geographic Distribution
- Leishmania/HIV Co-infection
- Areas of Co-infection
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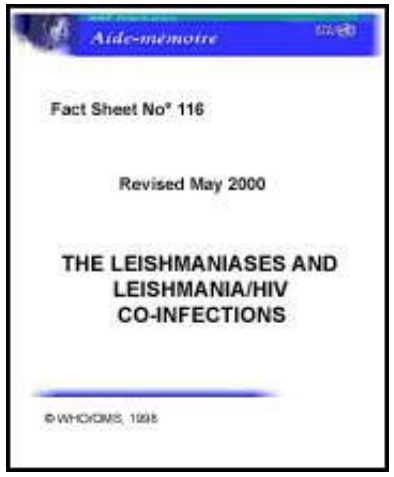

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Revised May 2000

Transmitted by the bite of the infected female phlebotomine sandfly, the leishmaniases are a globally widespread group of parasitic diseases. The sandfly vector is usually infected with one species of flagellate protozoa belonging to the genus *Leishmania*.

About 30 species of sandflies can become infected when taking a blood meal from a reservoir host. Hosts are infected humans, wild animals, such as rodents, and domestic animals, such as dogs. Most leishmaniases are zoonotic (transmitted to humans from animals), and humans become infected only when accidentally exposed to the natural transmission cycle. However, in the anthroponotic forms (those transmitted from human to human through the sandfly vector), humans are the sole reservoir host.

Leishmaniasis presents itself in humans in four different forms with a broad range of clinical manifestations. All forms can have devastating consequences.

Visceral leishmaniasis (VL), also known as *kala azar*, is the most severe form of the disease, which, if untreated, has a mortality rate of almost 100%. It is characterized by irregular bouts of fever, substantial weight loss, swelling of the spleen and liver, and anaemia.

Mucocutaneous leishmaniasis (MCL), or *espundia*, produces lesions which can lead to extensive and disfiguring destruction of mucous membranes of the nose, mouth

and throat cavities.

Cutaneous leishmaniasis (CL) can produce large numbers of skin ulcers - as many as 200 in some cases - on the exposed parts of the body, such as the face, arms and legs, causing serious disability and leaving the patient permanently scarred. Diffuse cutaneous leishmaniasis (DCL) never heals spontaneously and tends to relapse after treatment. The cutaneous forms of leishmaniasis are the most common and represent 50-75% of all new cases.

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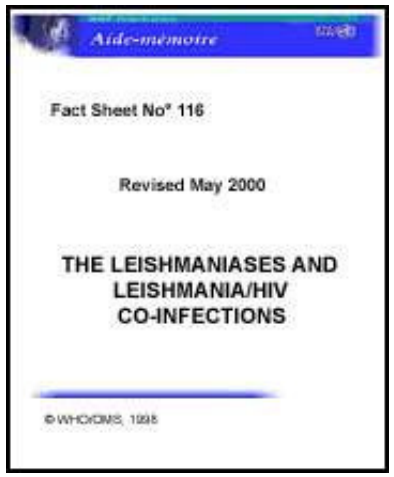

Increased Prevalence

- **Since 1993, regions that are *Leishmania*-endemic have expanded significantly, accompanied by a sharp increase in the number of recorded cases of the disease.**

- **The geographic spread is due to factors related mostly to development. These include massive rural-urban migration and agro-industrial projects that bring non-immune urban dwellers into endemic rural areas. Man-made projects with environmental impact, like dams, irrigation systems and wells, as well as deforestation, also contribute to the spread of leishmaniasis.**

- **AIDS and other immunosuppressive conditions increase the risk of *Leishmania*-infected people developing visceral illness. In certain areas of the world the risk of co-infection with HIV is rising due to epidemiological changes.**

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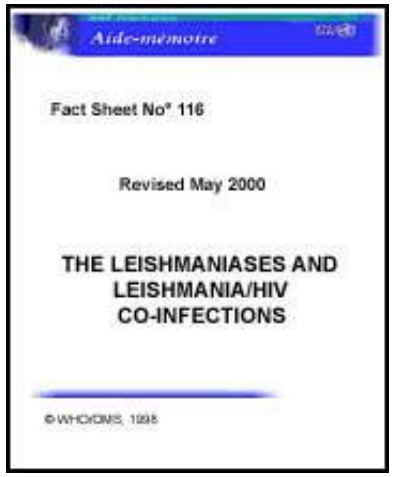

Geographic Distribution

- The leishmaniases are now endemic in 88 countries on five continents - Africa, Asia, Europe, North America and South America - with a total of 350 million people at risk.

- It is believed that worldwide 12 million people are affected by leishmaniasis; this figure includes cases with overt disease and those with no apparent symptoms. Of the 1.5-2 million new cases of leishmaniasis estimated to occur annually, only 600 000 are officially declared.

- Of the 500 000 new cases of VL which occur annually, 90% are in five countries: Bangladesh, Brazil, India, Nepal and Sudan.

- 90% of all cases of MCL occur in Bolivia, Brazil and Peru.

- 90% of all cases of CL occur in Afghanistan, Brazil, Iran, Peru, Saudi Arabia and Syria, with 1-1.5 million new cases reported annually

worldwide.

- **The geographical distribution of leishmaniasis is limited by the distribution of the sandfly, its susceptibility to cold climates, its tendency to take blood from humans or animals only and its capacity to support the internal development of specific species of *Leishmania.***

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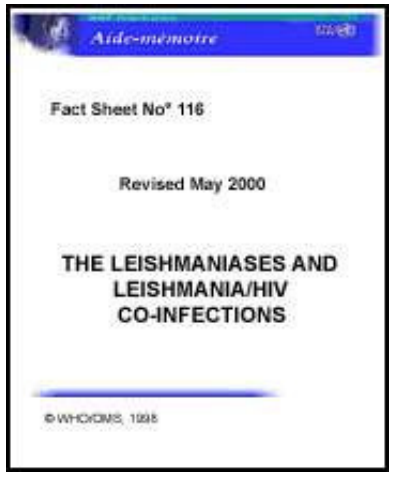


Leishmania/HIV Co-infection

***Leishmania*/HIV co-infection is emerging as an extremely serious, new disease and it is increasingly frequent. There are important clinical, diagnostic,**

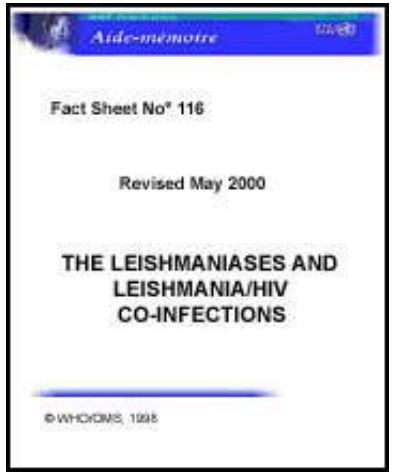
chemotherapeutic, epidemiological and economic implications of this trend.

- **Although people are often bitten by sandflies infected with *Leishmania* protozoa, most do not develop the disease. However, among persons who are immunosuppressed (e.g. as a result of advanced HIV infections, immunosuppressive treatment for organ transplants, haematological malignancy, auto-immune diseases), cases quickly evolve to a full clinical presentation of severe leishmaniasis.**

- **AIDS and VL are locked in a vicious circle of mutual reinforcement. On the one hand, VL quickly accelerates the onset of AIDS (with opportunistic diseases such as tuberculosis or pneumonia) and shortens the life expectancy of HIV-infected people. On the other hand, HIV spurs the spread of VL. AIDS increases the risk of VL by 100-1000 times in endemic areas.**

- **This duo of diseases produces cumulative deficiency of the immune response since *Leishmania* parasites and HIV destroy the same cells, exponentially increasing disease severity and consequences. VL is considered a major contributor to a fatal outcome in co-infected patients. Lately, however, use of tritherapy, where it is available, has improved the prognosis for *Leishmania*/HIV cases.**

- **Leishmaniasis can be transmitted directly person to person through the sharing of needles, as is often the case among intravenous drug users. This group is the main population at risk for co-infection.**



Areas of Co-infection

Cases of *Leishmania*/HIV co-infections are being reported more frequently in various parts of the world. It is anticipated that the number of *Leishmania*/HIV co-infections will continue to rise in the coming years and there are indications that cases are no longer restricted to endemic areas.

The overlapping geographical distribution of VL and AIDS is increasing due to two main factors: the spread of the AIDS pandemic in suburban and rural areas of the world, and the simultaneous spread of VL from rural to suburban areas.

- ***Leishmania*/HIV co-infections are considered a real threat, especially in south-western Europe. Of the first 1 700 cases of co-infection which have**

been reported to the World Health Organization (WHO) from 33 countries worldwide up to 1998, 1 440 cases were from the region: Spain (835); Italy (229); France (259); and Portugal (117). Of 965 cases retrospectively analyzed, 83.2% were males, 85.7% were young adults (20-40 years old) and 71.1% were intravenous drug users.

- **Most co-infections in the Americas are reported in Brazil, where the incidence of AIDS has risen from 0.8 cases per 100 000 inhabitants in 1986 to 10.5 cases per 100 000 inhabitants in 1997. As HIV transmission has spread into rural areas, VL has simultaneously become more urbanized - especially in north-eastern Brazil - increasing the risk of overlapping infection.**

- **The number of cases of *Leishmania*/HIV co-infection is expected to rise in Africa owing to the simultaneous spread of the two infectious diseases and their increasingly overlapping geographical distribution, complicated by mass migration, displacement, civil unrest, and war.**

- **In general, the reported cases of *Leishmania*/HIV co-infection in Africa are a very modest estimation and would substantially increase if active surveillance were implemented throughout the continent. Ethiopia has a well-organized system of detection, management and reporting of co-infection. Kenya and Sudan began surveillance in 1998 and Morocco has also established a surveillance centre.**

- **In East Africa, cases of *Leishmania*/HIV co-infections have been reported in Djibouti (10), Ethiopia (74), Kenya (15), Malawi (1) and Sudan (3). West**

Africa has no official surveillance system yet, but several cases have been reported: Cameroon (1), Guinea Bissau (1), Mali (4) and Senegal (2). In North Africa, cases have been reported in Algeria (20) and Morocco (4).*

***Figures from countries without surveillance systems are based upon random reports only. To properly assess the scale of the problem, there is an urgent need for more accurate information based on specific studies**

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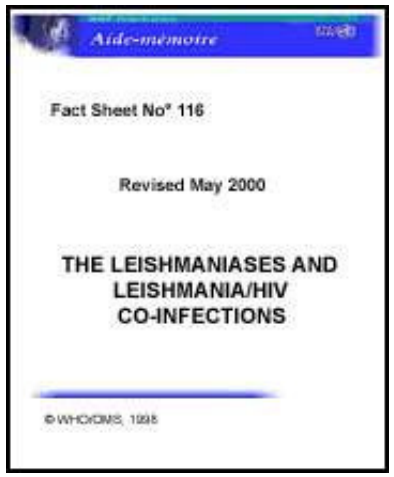

Specific Problems

• *Leishmania*/HIV co-infections impose specific difficulties in terms of diagnosis and treatment. The usual clinical features (fever, weight loss, liver and spleen enlargement, inflammation of the lymph nodes) are not always present. The clinical diagnosis can also be made difficult by associated diseases such as cryptosporidium, disseminated cryptococcosis, cytomegalovirus infection or mycobacterial infection.

• The serological diagnosis is falsely negative in 42.6% of co-infected patients. HIV-positive patients have difficulty in producing antibodies against new infectious agents, especially at a late stage or during relapses. Consequently, there is a need to use two or more serological tests and antigens freshly prepared in the laboratory to increase sensitivity.

• Although multiple localizations are frequent (blood, skin, digestive tract, lungs, central nervous system), parasitological diagnosis can be difficult and has to be repeated to orient the treatment. Bone marrow aspirate (BMA) remains the safest and most sensitive technique, but spleen aspirate and liver biopsy are also used. When BMA cannot be performed, the search for *Leishmania* can be conducted in peripheral blood samples.

• Treatment for co-infected patients is aimed at clinical and parasitological cures and prevention of relapses. Unfortunately, in such patients treatment failure, relapses due to drug resistance and drug toxicity are very common. In south-western Europe, follow-up studies using pentavalent antimonials, the same first-line drug used to treat classic leishmaniasis, show a positive response in 83% of cases. However, 52% of patients relapse within a period of one month to three years, with the number of relapses ranging

from one to four.

The main alternative drugs include pentamidine, amphotericin B and amphotericin B encapsulated in liposomes. This encapsulation reduces the occurrence of side-effects, but relapses still occur and the drug remains extremely expensive.

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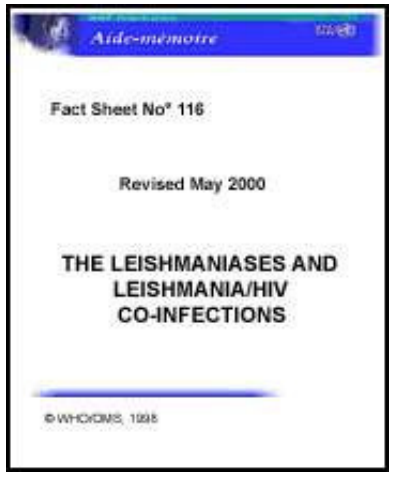

Epidemiological Changes

- ***Leishmania*/HIV co-infections can lead to epidemiological changes which modify the traditional patterns of zoonotic VL. Co-infected patients harbour**

a high number of *Leishmania* in their blood so there is also a risk of them becoming reservoirs of the disease (that is, infective for the sandfly vector) as in anthroponotic foci in Bangladesh, India, Nepal and East Africa. Consequently, there is an increased risk of future epidemics.

- **Experimentally, sandflies can be infected through a blood meal containing a very small quantity of blood from co-infected patients. The quantity may be less than the content of a needle. As 71.1% of co-infected patients in south-western Europe are intravenous drug users, transmission of *Leishmania* has occurred through the sharing of syringes in this population group.**

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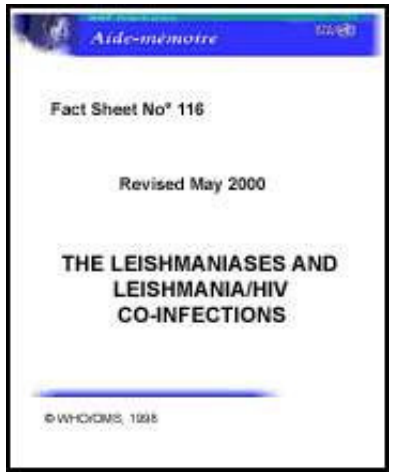

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The World Health Organization Response

Because of the anticipated substantial increase in *Leishmania*/HIV co-infections, they are among the priorities for WHO's Department of Communicable Disease Surveillance and Response (CSR).

- **In 1996, WHO established an initial surveillance system, comprised of 14 institutions in 10 countries. A standardized Case Report Form was elaborated and endorsed by the members of the network, and a Central International Registry was set up within WHO to centralize, process and disseminate information on co-infections.**

- **In 1998, a new WHO/Joint United Nations Programme on HIV/AIDS (UNAIDS) initiative was launched which helped strengthen the surveillance network; it has been expanded to include 28 institutions, especially in East Africa and the Indian subcontinent (India, Nepal). All member institutions of the network report to WHO on an annual basis. A computerized Geographic Information System (GIS) is used to map and monitor co-infections in a way that permits easy visualization and analysis of epidemiological data.**

The evolution of *Leishmania*/HIV co-infection is being closely monitored by extending the geographic coverage of the surveillance network and by improving case reporting. WHO encourages active medical surveillance, especially in south-western Europe, of intravenous drug users, the main population at risk. Finally, because case notification of leishmaniasis is compulsory in only 40 of the 88

endemic countries, WHO strongly suggests the remaining 48 endemic countries follow suit.

For further information, please contact the Office of the Press Spokesperson, WHO, Geneva, Tel.: +41 22 791 2599; Fax +41 22 791 4858; E-mail: inf@who.int or Dr Philippe Desjeux, Tel.: +41 22 791 3870/3186; Fax: +41 22 791 4878; E-mail: Desjeuxp@who.int **All WHO press releases, fact sheets and features are available on Internet on the WHO home page: http://www.who.int**