News

Leishmaniasis in Brazil

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In the past few years, leishmaniasis has become an increasingly important public health problem in Brazil. The increase in the incidence of the disease, associated with higher morbidity rates and the spread of some of the forms of leishmaniasis to new geographic areas, is causing much concern among public health authorities. The most worrying problems are the urbanization of American cutaneous leishmaniasis (ACL) in such places as Manaus, Amazonas State and Belo Horizonte, Minas Gerais State, and of American visceral leishmaniasis (AVL) in São Luis, Maranhão State, Teresina, Piauí State and Natal, Rio Grande de Norte State. A national workshop was therefore held that focused on research and control of leishmaniasis in Brazil.

The workshop was organized into sessions devoted to regional eco-epidemiology, advances in biology and taxonomy of New World *Leishmania*, improvements in specific diagnostic methods, applied molecular biology, treatment, vector control, advances in the understanding of the immune response in the leishmaniases, vaccines and the role of the Ministry of Health's control programme that is presently elaborated and performed by its National Health Foundation (Fundação Nacional da Saúde, FNS). Some priorities were specifically identified in areas where integrated research projects would be beneficial in identifying ways to interrupt the transmission cycle among both reservoirs and humans.

Points Worth Pursuing

After general discussions on the presentation it was evident that there was a general consensus of the participants that the following points were considered to be particularly important:

(1) To achieve a better understanding of the eco-epidemiology in the regional or state endemic areas, especially the zoonotic cycle, distribution, dispersion and incrimination of vectors and reservoirs, as well as comparisons of the effect of the socio-economic activities on the risk of infection in different regions.

(2) To make use of the more detailed eco-epidemiological information that is available for the different parasites of Amazonia as base lines for comparisons in other regions.

(3) To identify the vertebrate source of ACL infections in sylvatic foci in both recent and established areas of colonization. To evaluate more critically the present control measures for visceral leishmaniasis, such as the elimination of sick dogs associated with or without insecticide application against the vector.

(4) To determine the impact of insecticidal spraying programmes in endemic ACL areas that were colonized many years ago and in urban AVL foci (regions where the vectors are *Lutzomyia intermedia* and *Lu. whitmani*, for ACL, and *Lu. longipalpis* for AVL).

(5) To encourage the participation of the community in combating the different forms of leishmaniasis. In many areas, the mechanism of transmission is not understood by the local population, especially in AVL endemic areas, and the elimination of infected dogs is not readily accepted. It was recommended that the National Health Foundation (FNS) should produce films and radio programmes that would be aired by local TV and radio stations in endemic areas to explain to the general public why the control programmes are necessary and how they are executed.

(6) To inform veterinary surgeons in endemic AVL areas of the importance of the dog as a reservoir of the disease, and to enlist their help in combating the disease by the use of specific diagnostic methods and the elimination of sick dogs.

(7) To begin to incorporate new molecular biological diagnostic methods, such as the polymerase chain reaction (PCR) and DNA diagnostic probes, as complementary diagnostic tests in specific situations.

(8) To develop new, fast and reliable diagnostic methods that are simple to perform and can be used under field conditions. For example, in the present Ministry of Health's control programme of AVL, there is generally a long interval between the collection of the dog's blood and receiving the result. In the case of a positive result, it means that the dog has served as a source of infection for a longer period than would have been necessary if a rapid diagnosis had been made, and the risk of transmission to other dogs and people becomes greater.

(9) To obtain more information on the hosts' immune response; mechanisms of cellular immunity and the role of cytokines will help to understand the different pathologies.

(10) To investigate further immunotherapy using a vaccine developed in Brazil (VDB), shown to cure up to 70% of the cases of cutaneous leishmaniasis in Minas Gerais. The use of a semi-purified fraction of *L. (Viannia) braziliensis* in patients from Pernambuco was considered to be efficient in curing 74% of the cases. The use of VDB was discussed at length, but at the present there was no evidence that it would give protection against the different parasites known to occur in different endemic areas. A new protocol for the preparation of VDB from a strain of *L. (Leishmania) amazonensis* is presently in Phase I of clinical trials. It was particularly recommended that vaccination trials should be focused on protecting dogs against visceral leishmaniasis.

The Development of a Leishmaniasis Network

An announcement was made about the International Leishmaniasis Network (ILN), which was established as a result of a meeting sponsored by International and Governmental agencies in Campinas, São Paulo State, in February 1992. ILN is still very much in an embryonic stage: opinions as to what databases should be included are needed, as are volunteers to manage them.

A preliminary list of the various fields that will be covered are as follows: standard strains, cryobanks, country by country who's who lists of people interested in leishmaniasis (including areas of interest and contact address), projects, monoclonal antibodies, sequences of specific DNA regions and primers, epidemiology, parasite/vector catalogues, immunology reactions related

to infection (experimental and natural), treatment, diagnosis, drug resistance, host resistance, and control (methods, countries and responsible governmental agencies). As part of the ILN, a bulletin board* has been established which can be accessed by anybody who uses INTERNET or BITNET for their e-mail and the Network databases that can be accessed by a GOPHER server.

Participants were keen to join, but many had no e-mail facilities, especially the public health workers. This emphasizes, once again, the communication gap that unfortunately exists between research workers and the public health workers who have to deal with the day-to-day problems associated with leishmaniasis.

At the end of the four-day workshop it was unanimously decided that future meetings should be intra-institutional and held in endemic areas. It was suggested that the next one be held in Rio de Janeiro in September 1994.

Acknowledgements
The National Workshop on Strategic Research on Leishmaniasis, attended by 34 research and public health officers involved in the Brazilian Ministry of Health's National Leishmaniasis Control Programme, was held in Recife, Pernambuco, Brazil, 13–17 September, 1993. It was generously supported by funds from the Pan-American Health Organization, the Brazilian Research Council (Conselho Nacional de Desenvolvimento Científico, CNPq), the National Health Foundation (FNS) and the Oswaldo Cruz Foundation (Fundação Oswaldo Cruz, FIOCRUZ). The meeting was organized by the Centro de Pesquisas Aggeu Magalhães, FIOCRUZ and the participants expressed their congratulations to the organizers for hosting such an interesting and well-organized event.

Papers presented at the meeting will be published as a special issue of the *Memórias do Instituto Oswaldo Cruz*.

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* To subscribe to the *Leishmania* bulletin board (Leish-L) the following e-mail message should be sent:
Address: listserv@bdt.ftpt.br
Subject: (leave blank)
Message: subscribe Leish-L <your full name> (without brackets).

BSP Malaria Meeting

D.J. Roberts

Oxford, UK
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Many of the latest advances in malaria research provided the focus for this meeting.

Cytokines

The role of cytokines in malarial infection is undoubtedly complex and includes not only effects on parasite growth and clearance, but also direct and indirect contributions to host pathophysiology. Many studies have shown levels of tumour necrosis factor α (TNF-α) are elevated in severe malaria. It is now clear that the spectrum of cytokine release is extensive. Cytokines are stimulated by as yet poorly characterized soluble factors from both adherent and non-adherent parasite lines *in vitro*, and include the interleukins IL-6, IL-8 and IL-10, tumour growth factor β (TGF-β) and the IL-1 receptor antagonist (M. Wahlgren, Karolinska Institute, Stockholm, Sweden). While these findings suggest a cascade of monokines and lymphokines are released during acute infections, the raised serum cytokine levels from patients with malaria should be interpreted cautiously. In a rodent model of malaria, the concentration of immunoreactive TNF-α is increased during the primary wave of infection. However, the levels of soluble TNF-α receptors are also increased and bioactive TNF-α is not detectable (C. Hermsen, University of Nijmegen, The Netherlands). So it appears that, here, TNF-α may produce significant local effects, even though the concentration of circulating bioactive TNF-α is not raised. Furthermore, in this model, monoclonal antibodies against TNF-α do not alter the outcome of infection.

The complex roles of cytokines and downstream inflammatory mediators in malaria have been illustrated by recent observations of nitric oxide (NO) during malaria infections in rodents. TNF-α can stimulate the release of NO, and reactive nitrogen intermediates are toxic to parasites during the primary wave of infection in murine models of malaria[1]. However, NO may also contribute to the pathophysiology of severe disease. It was suggested that NO could cause vasodilatation and disturbed neurotransmission in humans (I.A. Clarke, Australian National University, Canberra, Australia).

Adhesion

The adhesion of mature trophozoite-infected erythrocytes to host endothelium and to uninfected cells is a virulence factor in falciparum malaria. Cerebral malaria is associated with the sequestration of parasites in the blood vessels of the brain. Thus, investigation of the interaction of parasite-induced receptors and host ligands on endothelium or uninfected red blood cells has attracted considerable attention.

Several studies have underlined the molecular and functional diversity of these adherence phenomena. Thrombospondin, CD36, ICAM-1, VCAM-1 and E-selectin have been established as ligands in static cytoadherence assays, but only limited data are available on their behaviour under flow. In contrast to the adhesion of neutrophils, ICAM-1 mediated a rolling type of interaction on HUVEC, whereas CD36 caused direct immobilization of parasitized erythrocytes (B.M. Cooke, University of Birmingham, UK). When adhesion of parasitized cells to human dermal vascular endothelium was studied, both CD36 and ICAM-1 mediated binding of infected erythrocytes and these two ligands acted synergistically [C.J. McCormick, Institute of Molecular Medicine (IMM), Oxford, UK]. In addition, both studies suggested that parasitized cells used other unidentified molecule(s) to bind to umbilical vein and dermal endothelial cells.