

II National Meeting on Strategic Research in Leishmaniases

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Human Moment

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EPIDEMIOLOGY

Over 200 participants gathered for five days to discuss strategic research in leishmaniases. The meeting was designed to offer an opportunity for interaction between those working in control and research of the diseases. The meeting was held against a background of a worsening epidemiological situation regarding the diseases in Brazil. This was highlighted by the reports from many participants. Figures from the National Health Foundation (Fundação Nacional de Saúde - FNS) showed that in 1994 over 3000 cases of visceral leishmaniasis (VL) and over 30000 cases of cutaneous leishmaniasis (CL) were reported in Brazil. In addition, evidence was reported of considerable subnotification of cases. These figures reflect both: an increase in the number of cases reported in recent years and an extension of the endemic areas.

Equally worrying is the increase in the urbanization of the diseases. Besides the recrudescence of epidemics of VL in cities such as São Luis (Maranhão, MA), Fortaleza (Ceará, CE) and Teresina (Piauí, PI) outbreaks have occurred in cities where this disease was previously unknown such as Belo Horizonte (Minas Gerais, MG). Outbreaks of CL were reported in all states of Brazil except Rio Grande do Sul (RS) and Santa Catarina (SC). These outbreaks occurred not only in the usual areas of forest and recent colonization but mainly in areas of ancient colonization and increasingly in urban areas. The focal and extensive nature of these cases were reported by several participants. The significance of this urbanization was discussed. One factor was the uncontrolled growth of urban areas in recent decades due principally to rural migration. This has led to the formation of districts (normally on the periphery of the cities) where the population lives in conditions of extreme poverty and which favour the spread of endemic diseases. Where detailed investigations had been made many of the cases were related to special ecological conditions in the urban areas, such as proximity to parks, rural surroundings or vacant plots, presence of trees or abundant vegetation, or absence of sanitation. Peri-urban or semi-urban may be a better description for many of these foci.

DOGS

The role of dogs and their control was a recurrent theme during presentations and discussions. The current policy of the FNS is for the elimination of serologically or clinically positive dogs in areas of visceral leishmaniasis. This strategy has often met with resistance from the owners of affected pets and with its growing implementation in urban areas due to the recent epidemics this opposition has increased. This position was made clear by the presence of a representative of a dog breeders association at the meeting. Pedigree dogs are more susceptible to infection than mongrels. In one case all the females of a colony were found to be serologically positive dooming the colony to extinction and the owners to economic distress. The technical basis for this strategy were discussed and although it was felt that no immediate changes in current policy should be made. It was proposed that the strategy should be re-examined with the use of controlled trials and the study of alternative methods of control (see below).

The role of a canine reservoir for cutaneous leishmaniasis caused by *Leishmania braziliensis* has also been an object of controversy. In a case control study in the area of Baturité (CE), a strong correlation was found between human cases and the presence of infected dogs in the household. Furthermore the age distribution of the human cases and the feeding behaviour of the sand flies indicated intra-domiciliary transmission. Similar results were found in the area of Viana, Espírito Santo (ES). In addition studies on feeding preferences of the most frequent sand fly species found in the intra- and peri-domestic habitat showed that they were attracted to dogs and humans and not to wild animals. In the discussion it was noted that although these two foci are widely separated and may be representative of the former Atlantic forest areas where *L. braziliensis* circulates, there exists other epidemiological situations where the importance of dogs has not yet been demonstrated. The issue of the primary reservoir host in the silvatic habitat was also discussed and it was felt that with the new *in situ* molecular hybridization and amplification techniques, the answer to this riddle would soon be found.

CONTROL

Vector control was another important theme of the meeting. There was some discussion on the importance of the repellent as opposed to the insecticidal activity of the chemicals used in household spraying. The use of ultra low volume (ULV) spraying using organophosphates as an alternative to canine control was suggested. There exists anecdotal reports of the interruption of VL transmission after ULV spraying for the control of dengue in some cities in the northeast of Brazil. Older reports relate a similar interruption of transmission when spraying organochlorides against anophelines for the control of malaria was carried out. It was felt that a controlled trial was needed to test the efficacy of ULV, perhaps together with the use of insecticide dips for dogs, as an alternative to the elimination of dogs in leishmaniasis control.

There was not much news in the area of chemotherapy. Concern was expressed at the near monopoly situation in the supply of pentavalent antimony and the lot to lot variation of the active ingredients. Experimental information is urgently required on the effect of temperature, light and other factors on antimonial drugs and on the change in concentration of pentavalent and trivalent ions during storage. It was felt that many studies aimed at identifying optimum drug doses were not comparable because of these factors which could also be responsible for some reports of increasing drug resistance.

Difficulties in the treatment of certain patients were also pointed out, in particular, those who are resistant to antimonials and do not respond to amphotericin as well as those who suffer from diffuse cutaneous leishmaniasis. The necessity of further research was emphasized to develop safer and better drugs to treat not only humans but also to cure canine leishmaniasis. Reports of trials with immunotherapy were also presented. The results although limited indicated some utility as an alternative to chemotherapy in treatment of pregnant women or when combined with antimonials to lower the dosage and thus reduce toxicity. Further controlled trials are however required.

VACCINATION

Vaccination was another prominent theme of the meeting. Canine vaccination studies though starting later than human studies appear to be making greater progress. Three vaccines were presented by

groups from Pernambuco, Minas Gerais and Rio de Janeiro. All showed promise in early studies. The vaccine from MG is currently undergoing a double blinded controlled phase III trial in a VL endemic area in Montes Claros (MG). The codes are expected to be broken in December of this year. The Pernambuco vaccine is also expected to undergo a phase III trial shortly. The results of these trials are eagerly awaited to see whether canine vaccination can become an effective control tool. The long history of human vaccination studies in Brazil including the results of the different trials was reviewed at the meeting. Currently the vaccine produced by the group from MG has been reformulated and is now based on a single strain of *L. amazonensis*. This vaccine has completed its phase I trials and will shortly start phase II. The large number of skin-test positives found in volunteers from an apparent non-endemic area promoted a discussion on the Montenegro test and the sensitivity to the timerosal used in its preparation.

Difficulties with diagnostic tests was another topic of discussion. Current serological tests have a low sensibility especially in patients with localized cutaneous lesions, who are the most frequent cases. The need for more sensitive antigens was emphasized as well as the hope expressed that molecular biological techniques would assist in a rapid and precise diagnosis. A need for a rapid simple diagnostic test for field use with dogs was also brought up. A number of candidates exist and the FNS is planning multi-centred field trials to test these kits.

A number of more didactic presentations were also made on aspects of the immunology, molecular biology, characterization, clinical signs and epidemiology of the diseases for the benefit of the large number of technical personnel involved in control that were present. The interaction between people involved in administration, control and research in these diseases was one of the aspects that contributed to the success of the meeting. The full proceedings of the II National Meeting on Strategic Research on Leishmaniasis will be published shortly as a supplement to the *Revista da Sociedade Brasileira de Medicina Tropical*. It was decided to hold the next national meeting in Fortaleza (CE) in 1997.

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