LEISHMANIOSIS IN BRAZIL: CLINICAL AND IMMUNOPATHOGENETICS ASPECTS OF THE HUMAM AND EXPERIMENTAL DISEASE

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The american cutaneous leishmaniasis (ACL) presents a large spectrum of manifestation, varying from asymptomatic and/or subclinical in resistant individuals to different forms in susceptible individuals, such as localized cutaneous leishmaniasis (LCL), borderline disseminated cutaneous leishmaniasis (BDCL), mucocutaneous leishmaniasis (MCL), mucosal leishmaniasis (ML) and anergic diffuse cutaneous leishmaniasis (ADCL), depending on the species and host immunoresponse (TCD4+ Th1/Th2).

In spite of the advances in the knowledge about the classic form of the disease, there are still many gaps regarding the parasite, *L. (L.) chagasi*, and the human immunogenetic system. The clinical spectrum of the human infection still needs more precise definition to improve the clinical diagnosis of infected, symptomatic and asymptomatic individuals, as well as suitable treatments for the different forms.

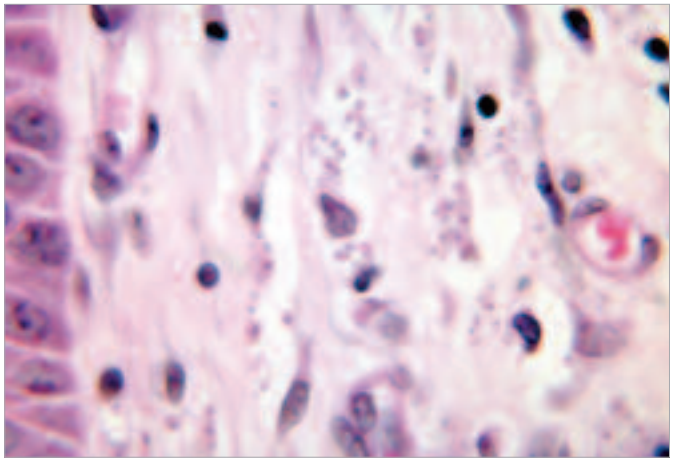
Longitudinal field studies are needed for identification of only infected, symptomatic and asymptomatic individuals. Long-term follow up for identification of the clinical immunological patterns of the human infection by *L. (L.) chagasi* is also needed.

The human immune response to infection by *L. (L.) chagasi* has received more attention in the classical form than in the symptomatic and/or subclinical forms of the disease, which have been neglected to some extent so far.

Experimental models for american visceral leishmaniasis (AVL) are usually made in hamsters and mice. However, data obtained from such models cannot be fully converted to figures comparable to those data that would expectedly be obtained in humans due to the philogenetic distances between the species, which makes a suitable experimental model closer to man highly desirable.

The *Cebus apella* has been shown as a potentially viable model for *in vitro* immune response studies using experimental infection in peritoneal macrophages for AVL and ACL species of *Leishmania* in Brazil.

The models of non-human primates, *in vivo* and *in vitro*, may be useful for immunopathogenical studies either for AVL or ACL.



Histopathology of leishmaniasis of skin due to Leishmania brasiliensis

The project aims at characterizing the role of the Langerhans cells in the CD4/CD8 immune response in the different clinical forms of the Brazilian ACL and different species in the immunopathogenesis modulation. An additional goal is the characterization of the clinical and immunological spectra of human infection by *Leishmania (L.) chagasi* in the Brazilian Amazon region, along with the humoral and cellular immune responses of the infected individuals.

Also proposed is the evaluation of the susceptibility of *Cebus apella* as an experimental model for experimental visceral leishmaniasis , *Leishmania (L.) chagasi*, and cutaneous leishmaniasis by *Leishmania (V.) braziliensis* and *L. (L.) amazonensis*.

In relation to the murine experimental model we proposed the kinetic analyses of the interaction between the Langerhans cells with the CD4+/CD8+ immune response in BALB/C e C57BL/6 mice elicited by *L. (V.) braziliensis* and *L. (L.) amazonensis* from different clinical isolates of ACL.

Mechanisms of resistance and susceptibility associated to the innate immune response of peritoneal macrophages from infected neotropical primates with *Leishmaia (V.) braziliensis*, *L. (L.) amazonensis* and *L. (L.) chagasi* will also be studied.

SUMMARY OF RESULTS TO DATE AND PERSPECTIVES

A cross-sectional study on the clinical and immunological spectrum of human *Leishmania (L.) infantum chagasi* infection in the Brazilian Amazon region.

The objectives of this study were i) to identify individuals with symptomatic and/or asymptomatic infection due to *Leishmania (L.) infantum chagasi*; ii) to study the two types of infection, both clinically and immunologically, and iii) to determine the prevalence rate of infection at the beginning of the study. This was a cross-sectional study with a cohort of 946 individuals, of both sexes, from the age of one year on, living in an endemic area of american visceral leishmaniasis (AVL), municipality of Barcarena, Pará State, Brazil. For the diagnosis of infection, the delayed hypersensitivity skin reaction (LST) and the indirect fluorescent antibody test (IFAT) were used. One hundred and twenty cases of infection were diagnosed, with a prevalence rate of 12.6%; eight cases showed high seroreactivity (1.280 to 10.240, IgG) in IFAT and no reaction in LST; four cases being of typical AVL and another four cases of subclinical oligosymptomatic infection. The two immunological methods used simultaneously with the clinical examination enabled us to identify five clinical-immunological profiles: Asymptomatic Infection (AI) 73.4%; Subclinical Resistant Infection (SRI) 15%; Subclinical Oligosymptomatic Infection (SOI) 3%; Symptomatic Infection (= AVL) 3% and, Indeterminate Initial Infection (III) 5%.

MAIN PUBLICATIONS

Crescente JAB, Silveira FT, Lainson R, Gomes CMC, Laurenti MD, Corbett CEP. 2008. A cross-sectional study on the clinical and immunological spectrum of human *Leishmania (L.) infantum chagasi* infection in the Brazilian Amazon region. *Trans. Roy. Soc. Trop. Med. Hyg*, in press.

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