IM4 - SOME OBSERVATIONS ON THE SUSCEPTIBILITY OF CEBUS APPELLA (PRIMATES: CEBIDAE) TO THE EXPERIMENTAL INFECTION BY LEISHMANIA (L.) CHAGASI.

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Introduction: The monkey Cebus apella has a very large geographical distribution in South America, and in north Brazil this species has been associated with the silvatic cycle of Leishmania (V.) shawi, a dermotropic parasite causing cutaneous leishmaniasis of man (Lainson et al., 1988). This monkey has been successfully used as a model for studying cutaneous leishmaniasis (Lainson & Shaw, 1977; Silveira et. al., 1989, 1990, 1997) and, for this reason, we are at present investigating its susceptibility to experimental infection with Leishmania (L.) chagasi. Objectives: To determine the susceptibility of Cebus apella to experimental infection with Leishmania (L.) chagasi and the animal’s usefullness as a model for Americans visceral leishmaniasis. Materials & Methods: 10 specimens of Cebus apella were used - 4 males and 6 females 8 week adults and 2 juveniles. All were born and raised in captivity. Protocol: 6 monkeys (3 that had previously been used to study the animal’s susceptibility to L. (V.) shaw, and 3 that had no previous contact with Leishmania) were inoculated intradermally into the base of the tail with 2 x 10³ promastigotes from stationary cultures in Difco B45 culture medium. Four others, all having had no previous contact with Leishmania, were inoculated with 3 x 10⁴ amastigotes from infected hamsters by two routes: two by intravenous injection and two by intraperitoneal inoculation. Evaluation of infections; clinical examination, IgG humeral response (IFAT) and a search for amastigotes in Giemsa-stained bone-marrow smears were made monthly. Results: In animals inoculated with promastigotes we have till now found no signs or symptoms of clinical infection 16 month post inoculation: neither have we been able to detect parasites in the bone-marrow or demonstrate IgG antibody against L. (L.) chagasi. Among the animals injected with amastigotes, the monkeys inoculated by the intravenous route showed parasites in bone-marrow smears one month later. The two inoculated by the intraperitoneal route have till now shown no parasites in the bone-marrow at one month p.i.. Other indications of infection have not been observed till now, doubtless due to the short period of incubation. Conclusion: It is as yet too early to say if Cebus apella can serve as a satisfactory model for American visceral leishmaniasis, but the present results are considered encouraging.

IM5 - OUTCOME OF LEISHMANIA (V.) BRAZILIENSIS INFECTION IN THE EAR DERMS OF MICE

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Extensive work with Leishmania major has revealed that Th1 T cells and associated cytokines IFN-γ and TNF-α mediate healing while Th2 cells and associated cytokine IL-4 mediate susceptibility. However, little work has been done in L. (V) braziliensis, probably due to the fact that an experimental model is not readily available. Recent reports have shown that parasite inoculation in the ear dermis closely resembles the natural infection, leading to important findings concerning the pathogenesis of disease. We investigated the course of infection with L. (V) braziliensis (MMOM/BR/01/BA/788) by injection of 10³ parasites in the ear dermis of BALB/c mice. Parasite burden was assessed weekly and by day 35 post infection, parasites achieved a 1000-fold expansion. Thereafter, parasites were gradually destroyed so that beyond day 63 they could not be detected at the inoculation site. Histopathological evaluation revealed an intense inflammatory infiltrate at the peak of lesion development (day 35 post infection) composed mainly by infected macrophages and granulocytes and scarce lymphocytes. Accordingly, RT-PCR failed to detect IFN-γ at the inoculation site. On the other hand, TNF-α expression was detected at days 14, 35 and 49 post infection. Concerning the draining lymph nodes, parasites were detected from day 14 to day 125 post infection, although at lower levels. In terms of cytokine production, RT-PCR showed the presence of IFN-γ and TNF-α throughout the infection period. Regarding chemokine expression, we observed, by RT-PCR, the presence of MCP-1, MIP 1α, MIP 1b and RANTES in the draining lymph nodes. Presently, we are evaluating the chemokine expression at the inoculation site by immunohistochemistry. Similar to recently published data, inoculation of Leishmania parasites in the ear dermis resembles the natural infection. Our results confirm that BALB/c mice cure an infection with L. (v) braziliensis due to the development of a parasite-specific Th1 response. To our knowledge, this is the first report showing that the activation of the Th1 pathway also occurs after inoculation of L. (v) braziliensis in the ear dermis.

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IM6 - SERA FROM CHRONIC CHAGASIC PATIENTS WITH MUSCARINIC ACTIVITY PROLONGBS QT INTERVAL IN ISOLATED RABBIT HEARTS.


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Introduction: Chronic chagasic patients (CChP) with cardiac disease present several arrhythmias that could evolve in sudden death. QT interval parameters are potential prognostic markers of arrhythmogenicity risk, cardiovascular mortality and have been evaluated in chagasic patients (Circulation. 2003, 108(3): 305-12). We previously showed that sera from CChP induced alterations in cardiac electrogensis and impair atrioventricular conduction in isolated hearts (Circ 1997, 96(6): 2031-7). These effects could be explained by β-adrenergic and muscarinic receptor activation. The aim of our study was analyze the acute effect of CChP sera, previously characterized as having muscarinic activity, on QT interval in isolated rabbit hearts.

Methods and Results: Rabbits (both gender) were killed by cervical dislocation and hearts were immediately cannulated through the aorta, and perfused by modified Langendorff technique with Tyrode solution (in mmol/L: NaCl 137, glucose 9, NaHCO₃ 18, KCl 2.7, NaH₂PO₄ 1.8, MgCl₂ 0.5, CaCl₂ 2.7, bubbled with carbogenic mixture 95%CO₂ 95% O₂). The experimental protocol consisted of three 20 minutes perfusion period (control, serum and washout). In the second period serum from CChP (n=16) and normal blood donors (NBD, n=10) was diluted 1:100 (vol.:vol.) in control solution. The QT interval was measured in all periods (10 representative beats from each period. The QT interval measured in presence of CChP serum (255 ± 6.2; mean ± SEM) was significantly different of control (241.2 ± 6.2; p<0.01) and washout periods (233.8 ± 6.5; p<0.001). NBD sera had not effect on QT interval; control (271.1±12.1), serum (280±13.3), and washout (277±13.1).

Conclusion: Our result suggest that sera from CChP with muscarinic like activity were able to prolong QT interval. This effect can contribute for the genesis of some arrhythmias present in CChP.

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