

ABSTRACT

Leishmaniasis is a disease circulating in endemic areas between sand flies (Diptera: Phlebotominae) and reservoir hosts, which - in the case of *Leishmania major* - are principally rodents (Rodentia). Unlike in human patients, leishmaniasis is often asymptomatic in animal hosts. For transmission and maintenance of the parasite in nature, infectiousness of hosts for sand flies is essential; and the only method to directly test the infectiousness is xenodiagnosis. The main objective of this thesis is to establish a laboratory model for studying xenodiagnosis with *L. major* on inbred BALB/c mice and then to apply this model to potential reservoir rodents from the genus *Mastomys*.

BALB/c mice were infected by intradermal inoculation of infective stages of *L. major* (isolated from sand fly guts) together with salivary gland homogenates from *Phlebotomus duboscqi*; infected mice were then exposed to *P. duboscqi* females for a period of ten weeks. Two inbred lines of BALB/c mice differed significantly in both the manifestation of the disease and infectiousness for sandflies. In BALB/c OlaHsd mice, great lesions were formed (up to 10 mm), mice were able to infect sand flies from the 2nd week after infection and their infectiousness reached up to 20.1% during the experiment. In BALB/c AnNCrl mice, only small lesions were formed (up to 2 mm) which closed into nodules in an average of six weeks after infection. Mice became infectious for the vectors only after the fourth week after infection and the infectiousness did not exceed 4%. Change in the body weight was not a good indicator of a disease progress in any of the lines, because it did not differ between experimental and control groups. While antibodies were a good indicator of acute diseases progress, because they positively correlated with number of parasites in the body of mice. The xenodiagnosis mouse model showed also a significant effect of repeated feeding of sand flies on the disease development and host infectiousness. In BALB/c OlaHsd mice, lesions were formed in average one week earlier and they developed to a larger size at the end of the experiment than in mice unexposed to sand flies. In BALB/c AnNCrl mice, lesions or nodules were formed only in groups exposed to xenodiagnosis. Feeding of *P. duboscqi* led also to increased dissemination of the parasites in the body of mice and higher infectiousness for the vectors.

The experimental infection and xenodiagnosis method was subsequently applied to the rodent species *Mastomys natalensis*, a potential reservoir host of leishmaniasis in subSaharan Africa. *Mastomys natalensis* females showed no signs of disease over thirty-five weeks after

infection, although the parasites were detected by PCR in four types of their tissues. None of the 638 tested sand flies was infected by feeding on the inoculated ear. In parallel experiments, sand flies feeding on animals previously exposed to feeding of infected sand flies remained uninfected. Based on these results, the role of *M. natalensis* as a reservoir host of *Leishmania major* cannot be confirmed.

Keywords: xenodiagnosis, leishmaniasis, reservoir host, *Mastomys natalensis*, BALB/c mice, *Phlebotomus*