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MULTIPLICATION OF MYCOBACTERIUM LEPRAE FROM LARGE INOCULA IN NEONATALLY THYMECTOMIZED LEWIS RATS

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There is a well recognized need for an experimental animal more susceptible to M. leprae to be used during the course of leprosy chemotherapy to detect small numbers of surviving M. leprae in the presence of large numbers of killed M. leprae. Such an animal must have minimal immunological responsiveness so that the large numbers of dead M. leprae will not act as an immunogen, preventing subsequent multiplication of the few viable organisms. The neonatally thymectomized Lewis rat (NTLR) appears to be such a host.

We reported earlier that as few as 25 viable M. leprae added to 10^7 heat-killed M. leprae are capable of multiplying in the foot pad of the NTLR. This experiment has since been repeated and the observations confirmed. In addition, we have carried out simultaneous titration of M. leprae in the foot pads of intact BALB/c mice and NTLR. The end point in both groups of animals was the same; no more than 5 M. leprae were required for infection. The basic difference between the two groups was that multiplication continued in the NTLR to a ceiling of around 10^8, about 100 times that in BALB/c mice.

Because NTLR do not develop wasting disease, immunosuppression is probably not complete. Further studies were carried out to determine if NTLR could mount an immune response against a small number of viable M. leprae after immunization with a large number of viable M. leprae. When intact rats were inoculated in the left hind foot pad with 10^7 viable M. leprae, there was complete protection against 5×10^3 M. leprae inoculated in the opposite foot pad. Further, only about 10^6 organisms were recovered from foot pads inoculated 6 months earlier with 10^7 acid-fast bacilli (AFB) indicating that multiplication of the large inoculum was also inhibited. No such inhibition occurred in the NTLR. Multiplication not only occurred in the foot pads inoculated with 10^7 AFB, but also proceeded at a normal rate in the opposite foot pad inoculated with 5×10^3 M. leprae. The former averaged 3.04×10^7 AFB per foot pad and the latter averaged 1.18×10^6 six months after inoculation. It thus appears that the NTLR is severely immunosuppressed.

This information has now been put to practical use. The NTLR is being utilized for the detection of small proportions of surviving M. leprae in patients during the course of chemotherapy. Thus far only one patient is of interest. A biopsy specimen yielded sufficient AFB to inoculate 3 rats with 1.77×10^5 AFB/foot pad as well as a group of mice with the standard 5×10^3 AFB/foot pad inoculum. No multiplication was noted in the foot pads of the latter up to 419 days after inoculation. Multiplication did occur in the foot pads of the rats as determined 368 and 528 days after inoculation.

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