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Letters to the Editor

INTRACEREBRAL *MYCOBACTERIUM LEPRAE* DO NOT ENHANCE SUBSEQUENT FOOTPAD INFECTIONS IN MICE

Sir,

Dr Stoner has elegantly proposed[1] an hypothesis to explain the selective cell mediated immune (CMI) anergy of lepromatous leprosy patients. In this hypothesis, Dr Stoner proposes that lepromatous leprosy may result, not from a genetic defect, but from active suppression of a genetically normal response capability. Effective CMI to *Mycobacterium leprae* follows the presentation of bacillary antigens by the intradermal route to regional lymph nodes, i.e. the peripheral lymphon compartment. If bacillary antigens are first presented intravenously to the spleen, thymus and bone marrow, i.e. the central lymphon compartment, then a humoral immune response occurs accompanied by a suppressed CMI response. A primary infection of peripheral nerves with *M. leprae* results in the bacilli being isolated from peripheral lymphatic channels but having direct access to the central lymphon compartment. Thus, it is reasoned, continuous leakage of bacilli directly into the circulation, with their concomitant exclusion from draining lymph nodes, preferentially stimulates the central compartment producing a humoral immune response and suppression of CMI.

We reasoned that an experimental approach to testing this hypothesis might be the intracerebral inoculation of viable *M. leprae* into mice followed by standard footpad challenge[2] with viable bacilli. To the extent that the central nervous system is isolated from the peripheral lymphon compartment, to the extent that *M. leprae* antigens might leak from the central nervous system into the central lymphon compartment and to the extent that the mouse footpad infection is analogous to the human infection, this experimental approach seems appropriate.

BALB/c mice, 2–3 weeks of age, of either sex were divided into 3 groups. One group

Table. The effect of intracerebral *M. leprae* on subsequent mouse footpad infection with *M. leprae*

Inoculation		Footpad harvests of *M. leprae* [Mean ± S.D. (N) × 10^6 AFB/Footpad] at days after footpad inoculation:		
Intracerebral	Footpad*	237	270	365
1.0×10^6 *M. leprae*	5.0×10^3 *M. leprae*	0.30 ± 0.31(6)	1.17 ± 0.22(3)	0.16 ± 0.18(3)
Normal saline	5.0×10^3 *M. leprae*	0.93 ± 0.11(6)	3.26 ± 0.33(3)	0.93 ± 0.68(3)
1.0×10^6 *M. leprae*	Normal saline	Not done	Not done	$< 0.016^{\dagger}$(3)

*Footpad inoculation 43 days after intracerebral inoculation.

†Less than 1.6×10^4 AFB/footpad, the lower limit of detectability in this system.

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was injected with 1.0×10^6 *M. leprae* in a volume of 5.0 µl suspended in Hanks's Balanced Salt Solution with 1% bovine serum intracerebrally using a 27 gauge needle, 2.5 mm in length. Forty-three days later the animals were challenged with 5.0×10^5 viable *M. leprae* of human origin in a volume of 30 µl, using standard methodology.[2,3] A second group received sterile normal saline intracerebrally and 5.0×10^3 *M. leprae* of human origin in the footpad 43 days later. A third group received the identical intracerebral inoculation as the first group but received normal saline in the footpad 43 days later (to control for dissemination from the intracerebral site).

Results are given in the Table. At all 3 time-intervals mice inoculated intracerebrally with *M. leprae* had fewer bacilli in their footpads than the control animals. As with any negative experiment, these findings by no means invalidate the hypothesis being tested. On the other hand, the data do not support the hypothesis that intracerebral inoculation of viable *M. leprae* enhances subsequent footpad infections in mice and, thus, the data do not support Dr Stoner's hypothesis regarding the pathogenesis of human leprosy.

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