Antileprosy Vaccine; an Apprehension

TO THE EDITOR:

Leprosy or Hansen's disease is a chronic disease resulting from infection with *Mycobacterium leprae.* Variation in host immune responses to *M. leprae* results in a spectrum of clinical manifestations ([7]). At one end of the spectrum is tuberculoid leprosy in which lesions are paucibacillary and cell-mediated immunity is essentially normal. At the opposite end is the lepromatous form of the disease in which monocytes/macrophages are packed with viable *M. leprae* and cellular immunity to *M. leprae* is poor. Since leprosy is a great health problem for tropical and subtropical countries, the development of vaccine(s) for control of this disease has been one of the favorite choices and has attracted a great deal of attention for many years. Although several candidate vaccines have been claimed ([1, 2]) no approved vaccine is available to date for immunoprophylactic use in the population. The trial studies for some of the vaccines have demonstrated varying levels of protection against leprosy. In the present communication, I have discussed a possible apprehension about the protective efficacy of an antileprosy vaccine.

Generally, most individuals who are infected with *M. leprae* develop protective immunity and do not show clinical symptoms. However, individuals who contract the disease have either the lepromatous or the tuberculoid type. The reasons for these varied forms of the disease are not know so far. Nonetheless, it is now well understood that protective immunity against *M. leprae* is provided by cell-mediated immunity (CMI) ([5, 9]) in which T cells play a major role. For induction of CMI, the T cells require that the antigen is processed and presented by antigen-presenting cells ([11]). This involves the internalization of the antigens into an acidic compartment, proteolytic degradation of the antigen, and binding of the resulting antigenic peptide fragments to the MHC molecules. *M. leprae* is known to parasitize macrophages (the main antigen-presenting cells), principally in lepromatous leprosy ([6, 8]). Studies on the interaction between *M. leprae* and macrophages have shown that following *M. leprae* infection macrophages fail in inducing the *M. leprae* degrading mechanisms ([4, 10]), a prerequisite for antigen processing and presentation. The molecular biology of these defects is as yet obscure. In addition to this, Hirschberg ([3]) has reported that patients with lepromatous leprosy are unable to exert a cell-mediated immune response due to the failure of their macrophages to present *M. leprae* antigens in an immunogenic form. Thus, all of the foregoing information raises intriguing questions as to the success of an antileprosy vaccine.

An ideal vaccine elicits protective immunity and memory so that subsequent exposure to the respective pathogen will result in an immune response of a protective nature. For stimulation of memory, T cells (generated after vaccination) and bacterial antigens need to be processed and presented by antigen-presenting cells. Using candidate vaccines against leprosy it may be feasible to generate the memory cells to provide protection against *M. leprae* infection. However, I wish to suggest that perhaps lepromatous leprosy-prone individuals, whose antigen-presenting cells are not capable of killing *M. leprae* and presenting *M. leprae* antigen(s), might present no/insufficient antigen(s) after *M. leprae* infection to stimulate the memory T cells. If this is so, then it is worth arguing that probably for such persons an antileprosy vaccine may not be successful in providing protective immunity. Contrary to this, tuberculoid leprosy-prone individuals, whose antigen-presenting cells are capable of killing *M. leprae* and presenting the *M. leprae* antigen(s), could be made immune against *M. leprae* infection.

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REFERENCES

1. ANTIA, N. H. and BIRDI, T. J. Leprosy vaccine; a reappraisal. Int. J. Lepr. **56** (1988) 310–313.
2. DESIKAN, K. V. Vaccines against leprosy. Natl. Med. J. India 7 (1994) 153–156.

3. HIRSCHBERG, H. The role of macrophages in the lympho-proliferative response to *Mycobacterium leprae in vitro.* Clin. Exp. Immunol. **34** (1978) 46–51.
4. HOLZER, T. J., NELSON, K. E., SCHAUF, V., CRISPEN, R. G. and ANDERSEN, B. R. *Mycobacterium leprae* fails to stimulate phagocytic cell superoxide anion generation. Infect. Immun. **51** (1986) 514–520.
5. KAPLAN, G. and COHEN, Z. A. The immunobiology of leprosy. Int. Rev. Exp. Pathol. **28** (1986) 45–78.
6. RIDLEY, D. S. Histological classification and immunological spectrum of leprosy. Bull. WHO **51** (1974) 451–465.
7. RIDLEY, D. S. and JOPLING, W. H. Classification of leprosy according to immunity; a five-group system. Int. J. Lepr. **34** (1966) 255–267.
8. RIDLEY, M. J. The mononuclear cell series in leprosy; an ultrastructure report. Lepr. Rev. **52** (1981) 35–50.
9. SENGUPTA, U. Cell-mediated immunity in leprosy; an update. Int. J. Lepr. **61** (1993) 439–454.
10. SIBLEY, L. D., FRANZBLAU, S. G. and KRAHENBUHL, J. L. Intracellular fate of *Mycobacterium leprae* in normal and activated macrophages. Infect. Immun. **55** (1987) 680–685.
11. UNANUE, E. R. Antigen presenting function of macrophages. Ann. Rev. Immunol. **2** (1984) 395–428.

Differences in *M. leprae*-Induced Nerve Damage in Swiss White and C57BL/6 Mice

TO THE EDITOR:

Based on our earlier observations that Schwann cells ([2]) and macrophages ([1, 4]) of Swiss white and C57BL/6 mice respond differently to *Mycobacterium leprae* infection, the present study was undertaken to determine if this difference was reflected in the pattern of nerve damage induced by *M. leprae* in these two strains.

The mice were inoculated with 10^4 *M. leprae* in each hind foot pad. At regular time intervals, the mice were anesthetized with pentobarbitone and the sciatic nerve biopsies were obtained. The biopsies were fixed in 2.5% glutaraldehyde, post-fixed in osmium tetroxide, and embedded in araldite. Semithin sections 1-μm thick stained with toluidine blue were used for light microscopy, and subsequent ultrathin sections stained with uranyl acetate and lead citrate were observed under the electron microscope. After the nerve biopsies were collected the mice were killed and the foot pad harvests done according to the method of Rees ([5]).

M. leprae growth in the mouse foot pad was comparable in the two strains up to the 20th post-inoculation month.

The pathology observed in the sciatic nerves of *M. leprae*-inoculated Swiss white mice was similar to the early changes seen in leprosy patients ([6, 7]): at 6–8 months post-inoculation there was an involvement of predominantly unmyelinated fibers which progressed to extensive demyelination by the 20th post-inoculation month (Fig. 1). In the C57BL/6 strain, however, while the unmyelinated fiber involvement at 8th month post-inoculation was comparable to the Swiss white mice, it did not progress further to demyelination even though the acid-fast bacilli count at the 20th month was similar in both strains (Fig. 2).

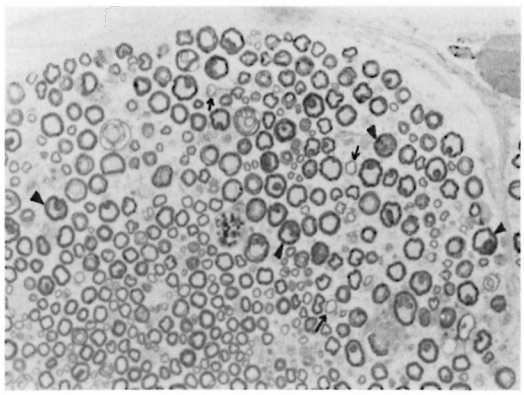

FIG. 1. Part of the sciatic nerve from a Swiss white mouse inoculated in the foot pad with *M. leprae* 20 months prior to biopsy. Increased interfiber space seen, suggestive of loss of myelinated fibers. Also present are small thinly myelinated fibers (arrows) and several large myelinated fibers with highly irregular myelin (arrow heads), indicating remyelination and atrophic changes respectively (araldite-embedded tissue, 1-μm thick section stained with toluidine blue ×200).