CHAPTER 1

INTRODUCTION
Leprosy is a disease which predominantly affects the skin and nerves in man (Stoner, 1979). The preferred targets for Mycobacterium leprae, the causative agent of leprosy, are the phagocytic cells of the monocytic lineage and the Schwann cells of the peripheral nerve (Bjune, et al. 1983). The latter feature of M. leprae is responsible for the unique property of this organism to cause peripheral nerve damage (Antia, 1982). Nerve damage is seen throughout the spectrum of the disease (Pandya, 1974; Pearson and Weddell, 1975).

Lepromatous form of leprosy (LL), is characterised by little immunological response, unrestrained multiplication of bacilli and slow but diffuse peripheral nerve destruction. In tuberculoid leprosy (TT), on the other hand, the bacilli provoke a vigorous host cellular immune response which results in near complete destruction of the nerve tissue. The tuberculoid lesions consist essentially of well demarcated granuloma containing lymphocytes. In borderline leprosy (BL, BB, BT), the picture is dimorphous, one may see elements of both of the above types. Nerve damage is also seen in early leprosy and in LL, BL patients where the nerve is not infiltrated with mononuclear cells (Antia, 1982).

Nerve damage so far has been measured by estimating the degree of loss of sensory function or recording electrical activities. Studies conducted in nerve tissue culture models reveal that the pathology may be initiated immediately after invasion of the Schwann cells by M. leprae and changes in the
neurons occur as a subsequent effect (Mukherjee et al., 1980a & b, Mukherjee and Antia, 1986). *M. leprae* primarily bind to Schwann cells in a specific manner (Mukherjee and Antia, 1986; Itty et al., 1986) and once internalized the organisms are metabolically active (Mistry et al., 1989) and multiply (Mukherjee and Antia, 1986) simultaneously causing inhibition of proliferation and migration of host Schwann cells (Mukherjee et al., 1980b). *M. leprae* infected Schwann cells are recognized by immune cells (Mehta et al., 1988). Schwann cells are capable of expressing MHC class I and class II molecules (Samuel et al., 1987) and present *M. leprae* antigen to T-cells (Wekerle et al., 1987). These experimental evidences suggest that invasion of peripheral nerves by *M. leprae* triggers an immune response not only to its constituents but also possibly to constituents of the peripheral nerves. These findings call for a detailed investigation into autoimmune responses directed to the peripheral nervous system in leprosy. In this thesis the existence and the role, if any, of antineural antibodies have been investigated in depth by first developing a sensitive immunoassay to quantitate the antineural antibodies, then the reactive antigenic determinants have been identified using immunoblot and immunofluorescence techniques, and the pathogenic role of these antineural antibodies have been explored. Attempts were also made to develop a diagnostic test for monitoring nerve damage in leprosy based on nerve antigen which at the moment looks promising.