COMMITTEE 3: WORKSHOP ON IMMUNOLOGY OF LEPROSY

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Major advances made in the past five years in the understanding of immune responses in leprosy were discussed. Although universal agreement on mechanisms underlying the unresponsiveness in lepromatous leprosy (LL) was lacking, interesting *in vitro* studies indicated that several suppressive mechanisms were operative. One study showed that *Mycobacterium leprae* and phenolic glycolipid-induced, OKT8(+) T cells, capable of suppressing mitogen responsiveness, were present in lepromatous individuals. Their activity was reversed by chemotherapy and immunotherapy with BCG + killed *M. leprae.* Other studies reported diverse, membrane-associated alterations in blood-borne macrophages of lepromatous patients and 75% of their familial contacts. These changes were specific for *M. leprae* in the patient group. Fc, HLA-DR, and Con A receptors were found to be diminished, and macrophage lysates inhibited lymphocyte responses. Moreover, LL monocytes inhibited antigen-induced lymphoproliferation through the release of soluble factor(s). The inhibitory factors were heat stable, indomethacin resistant, and were greater than 25,000 molecular weight. Macrophage lysates, monocytes, and monocyte-released soluble factors from LL patients inhibited antigen-induced lymphoproliferation. Production of gamma interferon, a macrophage activating factor, was found to be reduced in lepromatous patients. However, LL monocytes were capable of responding to it in microbiocidal assays. Interleukin (IL) 1 (lymphocyte activating factor) production in response to *M. leprae* was found to be normal, but interleukin 2 (T cell growth factor) was not detectable in lepromatous leprosy. Interestingly, antigen-responsive lymphocytes were also observed in some lepromatous patients. The addition of exogenous IL2 along with *M. leprae* restored proliferative responses and reversed the gamma interferon defect. Similar data were obtained in C57BL mice infected i.v. and subcutaneously with *M. lepraemurium.* Moreover, murine T cell clones induced by *M. leprae* were shown to produce IL2, macrophage activating factor, gamma interferon, proliferative responses, induce delayed hypersensitivity reactions, bactericidal and tumorcidal activity. The T cell clone technology in analyzing immune mechanisms in leprosy was further emphasized. The alteration of T cell subsets as well as the characterization of immune complexes in erythema nodosum leprosum (ENL) and reversal reactions were reported. Moreover, *M. leprae* antigens were recognized in the immune complexes, and a possible defect in their handling in reactional patients was postulated.

An important advance has been the detection and characterization of *M. leprae*

antigens in several laboratories. A unique phenolic glycolipid present in *M. leprae* and not in other related mycobacteria has been characterized and partly synthesized. Leprosy patients have been shown to have mainly IgM and IgG antibodies to this antigen. Chemotherapy reduced antibody titers, but immunotherapy with BCG + heat-killed *M. leprae* had no effect. Healthy individuals and tuberculosis patients did not show antibodies to the phenolic glycolipid. In addition, protein and glycoprotein of 12,000 Dalton antigens specific for *M. leprae* were described. A skin test antigen which measures 24-hour-delayed hypersensitivity is also being characterized. Specific monoclonal antibodies against the glycolipid and protein antigens have been developed. Possible tests for the early diagnosis of leprosy and for immuno-epidemiological studies were discussed. ELISA, radioimmunoassay, and indirect immunofluorescence against several *M. leprae* antigens are being tested in the field. Concomitant skin tests and tests for the presence of antibodies may help in the identification of high-risk groups in the community. Such tests would be of value not only in understanding the disease, but in screening for future vaccine trials.

The feasibility of developing immunoprophylaxis and immunotherapy for leprosy was indicated in three studies. *M. leprae,* BCG, ICRC, and *Mycobacterium "w."* and acetoacetylated *M. leprae* are being investigated in Venezuela and in India; 50–75% of lepromatous patients showed conversion from negative lepromin reactivity to positivity status and developed reversal reactions. Skin biopsies revealed upgrading of tissue reaction, and bacillary clearance of significance was seen together with the conversion of 90% of lepromin-negative healthy individuals to lepromin positivity with all of the above preparations.

In order to generate alternate sources of production of *M. leprae* antigens, libraries of *M. leprae* DNA cloned in *Escherichia coli* have been made in the U.S.A. and in India. Recent studies on the relationship of *M. leprae* Schwann cells and axons in nerve damage associated with leprosy were presented. One study also showed a deficiency of zinc and alterations in Langerhans' cells in LL patients. An association between HLA DR2 and tuberculoid leprosy has been confirmed. Furthermore, one study has shown HLA MT1 to be associated with lepromatous leprosy. A general improvement of cellular immunity and immunoregulatory T cell function by a synthetic thymic factor was reported in experimental models and in human disease.

The understanding of the inverse relationship between the genetically controlled natural resistance to primary attack by live mycobacteria and the ensuing disease and cell-mediated immunity in mice was discussed. Preliminary data found in human leprosy seem to indicate analogous mechanisms. Several of the above studies suggest that the lepromatous population is heterogeneous in its restoration of responsiveness *in vitro,* as well as after specific immunotherapy. Such differences in the population as well as genetic and environmental factors need to be precisely defined for the future strategy for control of the disease.