COMMITTEE 3: WORKSHOP ON IMMUNOLOGY OF LEPROSY

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IMMUNOCHEMISTRY AND LEPROSY

With greater quantities of *Mycobacterium leprae* made available from infected armadillo tissues during the past five years, there have been advances in the characterization of *M. leprae* antigens. There is now evidence that protein antigens specific for *M. leprae* exist.

Specific goals for the coming five year period should include studies to confirm this evidence and to characterize putative *M. leprae*-specific antigens with respect to:

a. The methodology for purification of these antigens.

b. Defining the physicochemical properties of these antigens that may help to increase their yields from bacilli and infected tissues.

c. Development of antigen-specific assay systems to allow quantitation either of antibody to these antigens or of antigens present in infected tissues.

d. Assessment of the role of these antigens in the stimulation of delayed-type hypersensitivity (DTH) and cell-mediated immunity (CMI) specific to *M. leprae*.

e. Assessment of the role of these antigens in ENL, reversal reactions and the Lucio phenomenon, with emphasis on the search for antigen within lesion sites and within circulating immune complexes.

f. Determining the significance of antibody to *M. leprae*-specific antigen(s) as an indicator of subclinical leprosy in contacts of lepromatous patients who have positive or negative lepromin skin tests as compared to contacts of tuberculoid patients.

EXPERIMENTAL STUDIES OF IMMUNOREGULATORY MECHANISMS IN LEPROSY

A significant advance in immunology during the past five years has been the identification of functionally specific subpopulations of lymphocytes that modulate the immune response in the mouse. The availability of markers for specific immunoregulatory cell function provides a powerful tool for more precise study of the complex cell-to-cell interactions that result in net help or suppression of the cell-mediated immune defense mechanisms in chronic infectious disease models.

Future studies should first be directed to resolving the nature of the immunoregulatory disturbances evoked by chronic infection of the mouse with *Mycobacterium lepraemurium*.

Much needed are detailed immunologic studies of the normal and *M. leprae*-infected armadillo with special efforts directed to the identification of specific markers for immunoregulatory cell subpopulations in this genus.

Knowledge gained from these models will have direct application to studies of the immunoregulatory disturbances in human leprosy. Critical will be the development of technics for recognizing specific markers on human regulatory cell subpopulations. As these technics are perfected, they will yield information of great value in permitting clinical investigators to assess the impact of both chemotherapy and immunotherapy upon the immune functions of leprosy patients; these studies in turn can be expected to aid in the design of

therapeutic approaches that will provide maximum long-term benefit.

THE IMMUNOLOGY OF HUMAN LEPROSY

A complex series of immunologic perturbations has been delineated in leprosy patients during the past five years. In general, the DTH and CMI responses to contact sensitizing agents and a variety of "recall" antigens, including *M. leprae*, are not impaired substantially in patients with tuberculoid forms of disease. Conversely, in borderline and especially in lepromatous forms of infection, significant impairment of the immune response is observed frequently. Both nonspecific generalized impairment of cellular immune function occurs as well as a highly specific impairment of *M. leprae*-specific immunity. These abnormalities are frequently associated with disturbances in the ratio of T and B lymphocytes in the peripheral blood of lepromatous patients. The nonspecific abnormalities of CMI appear to be reversible by chemotherapy of at least several months' duration, whereas impairment of the responses to *M. leprae* antigens is long-lasting.

Additional advances in the immunology of human leprosy include:

a. The finding that antibodies that appear to be *M. leprae*-specific are detectable in a large percentage of tuberculoid patients as well as in lepromatous patients.

b. The finding that circulating immune complexes may be present in patients with leprosy, more commonly in those with lepromatous disease.

c. Evidence that patients with reversal reactions demonstrate increased lymphocyte transformation responses to *M. leprae*.

Goals of high priority during the next five years include:

a. Definition of immunoregulatory subpopulations in man and the assessment of abnormalities within these subpopulations in patients with leprosy.

b. Extensive studies of macrophage function in leprosy, with emphasis upon the mechanisms of the processing of *M. leprae* antigen.

c. Longitudinal studies of circulating immune complexes in leprosy patients, and immunopathologic studies of tissue reactions evoked by these complexes.

d. Further exploration of the possibility of a genetic predisposition to leprosy by studying the distribution of HLA antigens in the population of leprosy patients and their families.

e. Development of a vaccine against leprosy. The availability of *M. leprae*-specific antigens and of quantitative assays for these antigens, and antibody responses to these antigens, will aid in this pursuit.

f. Exploration of the thesis that peripheral nerves may serve as "protected sites" for multiplication of *M. leprae*.