Immunology of Leprosy

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Clinical forms of leprosy are extremely variant, both with regard to their signs, symptoms, as well as their prognosis. Consequently, leprologists have classified the disease into several types. These clinical types are so distinctly divergent as to make one suspect that they are different diseases all-together. However, it has been proved beyond doubt that it is the same disease process produced by the same etiological agent, Mycobacterium leprae, but manifesting as widely varient clinical forms. Basically, there are two "polar" types, Tuberculoid (T) and Lepromatous (L). The tuberculoid type is a localized, resistant form of the disease with very few bacilli in the lesions and is generally non-infectious. Its prognosis is good. The lepromatous type on the other hand is a generalized, poorly resistant form of the disease, containing a large number of bacilli in the lesions and is infectious. The prognosis of this type is poor. Between these two polar types, there is a middle group called the "Borderline type" (B) including a gradation of features from the tuberculoid to the lepromatous variety. This group, therefore, forms a wide spectrum including those cases towards the tuberculoid end (BT), those towards lepromatous end (BL) and a pure middle group (BB). It is easily understood that any such subgroupings can only be artificial and one could conceive of several stages forming a slow gradation from one end to the other.

The types of leprosy described above are shown schematically in Figure 1. It is obvious that this scheme is based on the resistance of the host against parasite. There is a gradual fall of host resistance from the tuberculoid towards lepromatous end. The host-parasite relationship in leprosy, as in any other infectious disease, depends upon the specific immunological response of the body. The immunopathology of leprosy is therefore a fundamentally important subject because it is the immunity that decides the type of the disease and its prognosis, and on these factors depend the treatment and management of the condition.

Before describing the immunology of leprosy, a few facts on the present day knowledge of immunity may be briefly mentioned.[5,7] The immunological response of the body against invading organisms is essentially two-fold : (1) the production of certain special serum proteins which are of the nature of immunoglobulins, and (2) the propagation of specifically sensitized lymphocytes. The former process is termed as "humoral antibody production" whereas the latter is referred to as "cell mediated immune response." The effect of either of these responses is to deal suitably with the antigen by setting up a chain of events resulting in an inflammatory process, aimed ultimately at eliminating the offending agent.

The humoral antibodies may react directly with the antigen and are therefore anti-toxic or anti-bacterial. They may also facilitate phagocytosis of the invading organisms by the appropriate cells thus helping to destroy and remove these organisms. Humoral antibody production is seen mainly in bacterial or viral infections, and such antibodies can be detected in the blood. By using suitable in vitro techniques, it is possible to abtain an estimate of the actual levels of such circulating antibodies.

The cell mediated immune response manifests as a specific reactivity against the antigen resulting in a process termed as "Delayed Hypersensitivity Reaction." This process depends as mentioned already, not on the presence of any circulating antibody but on the propagatian of certain specific cells, primarily lymphocytes which have the property of inter-acting with the antigen to produce a specific type of inflammatory reaction. Examples of such reactions are seen in allergic conditions, rejection of homograft, certain bacterial and viral infections, auto-immune diseases, and in immunity against cancer.

Both types of immune responses are initiated by the so called "immunologically competent cells" which

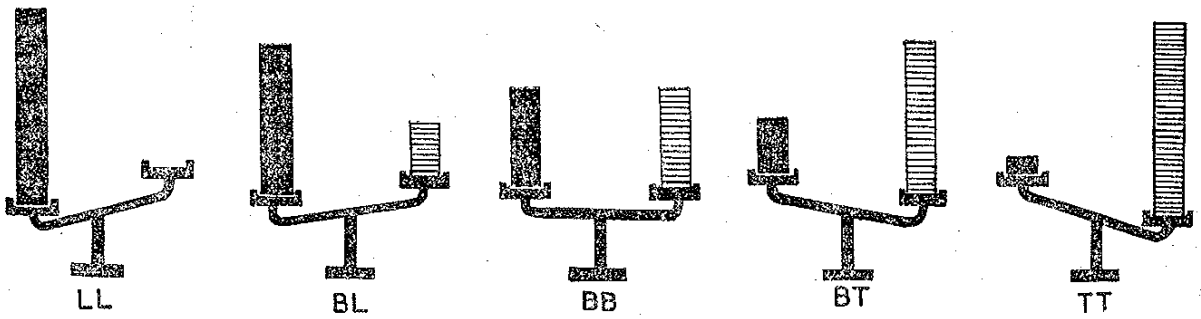

Figure 1.

are specialized small lymphocytes. They are inducted to perform their special function by the influence of the Bursa of Fabricicius (a lymphoid organ in birds) or the thymus. The "Bursa-dependent cells" or the B lymphocytes, are lodged in the germinal centres of the lymphnodes, and the red pulp of the spleen. When stimulated by appropriate antigens, these cells proliferate to form plasmablasts and plasma cells, which initiate humoral antibody production. Based on immuno-electrophoretic analysis, these antibodies which are immunoglobulins, are classified into several types designated as IgG, IgA, IgD, IgM, etc. The commonest type of immunoglobulin associated with the inflammatory conditions is IgG. Mammals do not possess the Bursa of Fabricicius. The B lymphocytes of man and other mammals are supposed to be influenced by the lymphoid system in the gut—the Payer's patches. These B lymphocytes behave in a manner similar to those in chickens and other birds. The "thymus-dependent cells" or T cells, are lodged in the para-cortical areas of the lymph nodes, or peri-arteriolar areas of the spleen. When stimulated by the corresponding antigen they proliferate, and by a process of cell mediated immunity, they take part in the lesions seen in delayed hypersensitivity.

The cell mediated immunity as well as humoral immunity play an important part in pathogenesis of leprosy. In lepromatous leprosy, there is a suppression of the cell mediated immunity, whereas in the tuberculoid type of the disease, there is an enhancement of this type of immune response. Between these two "polar" types of the disease are the divergent varieties of the intermediate forms grouped variously as 'Dimorphous' or 'Borderline' leprosy. There is, therefore, a wide spectrum of immunological patterns in leprosy.

The possibilities of such immunological variation in leprosy were recognized several years ago by the employment of the "Lepromin Test."[2] In this procedure the "antigen" prepared from leprosy bacilli obtained from human tissues is injected intradermally. A delayed hypersensitivity type of reaction seen at the end of 48 to 72 hours and observed as a wheal, suggests the existence of cell mediated immunity. This is followed by the development of a nodule at the site of injection in about 3 to 4 weeks, with the nodule presenting a structure that is compatible with the structure of a delayed hypersensitivity reaction. This type of reaction is seen typically in tuberculoid on leprosy. In lepromatous leprosy, on the other hand, skin reaction is evident either at the early or late stage suggesting the absence of cell-mediated immunity against M. leprae. In the intermediate forms the reactions are variable, ranging from a negative response in some cases, through doubtful to moderately positive responses. The skin test in the intermediate forms also varies in the same patient at different times suggesting that the immunological status in these patients is variable. These forms of leprosy are therefore regarded as 'unstable' forms since the immunological response seems to fluctuate between the two extremes, depending upon changes in the antigen load or the level of cell mediated immunity. On the contrary the two 'polar' forms—lepromatous and tuberculoid—are true to type as they remain stable.

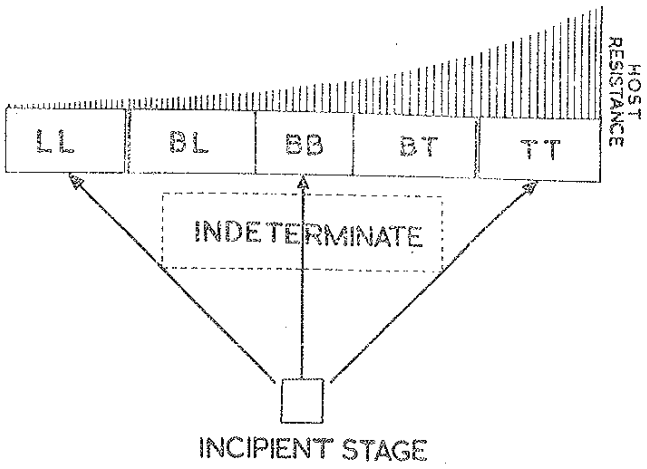

Figure 2.

The instability of the Borderline type of leprosy is diagramatically represented in Figure 2. There is a delicate balance between the specific immunity and antigen load. If the leavel of Cell Mediated Immunity (CMI) falls in an individual due to intercurrent infections or due to any other cause, or if there is an increase in bacillary load due to neglect or failure to get treated, the case would shift towards the lepromatous type. This is described as "down-grading reaction" and is commonly seen in leprosy. If on the other hand, the bacillary load falls due to treatment, there is a possibility of the balance tilting in the other direction, and the case progressing towards the tuberculoid type. This feature has also seen to occur occasionally in leprosy and is called "reversal reaction." A borderline type of leprosy can therefore be in a state of constant flux and hence, should be carefully managed.

Assignment of an individual case to a particular level in the scale of immunity is possible by clinical findings, but more accurately by histological examination of skin lesions. In addition, certain in vitro methods are also available to assess the level of CMI. Transformation of lymphocytes to lymphoblasts by the addition of Phytohaemagglutinin (PHA) is an indication of CMI. Lymphocytes cultured from a case of lepromatous leprosy, show a depression of lymphoblast transformation.[3] While normal lymphocytes show a blast transformation of 80% of the cells, lymphocytes from a case of lepromatous leprosy show a transformation of only 10% of the cells. Secondly, the study of the function of macrophages provides another method of assessment of CMI. It has been found that the macrophages from a case of lepromatous

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