The Lymphocyte and Resistance to Leprosy

Immunosuppression in bacterial disease as a determining factor in the pathogenesis of different types of leprosy has been the subject in recent months of an increasing number of published scientific reports. It may be noted in passing that the related phenomenon of rejection of grafted tissue has also attained wide popular understanding through the television and public press coverage of recent attempts at human organ transplantation.

The now apparent role of immunologic suppression in leprosy and the part it plays in lepromatous disease were set forth in detail by Shepard[1] in a recent editorial in THE JOURNAL. Referring to experiments by Rees and his associates, by Gaugas, and by himself and his colleagues, Shepard called attention first to a marked trend in recent research toward attempts by immunosuppressive measures to produce a more severe and extensive experimental leprosy than the usual infectious process induced by *M. leprae* in the mouse foot pad, and, second, to efforts in exploration of the role of immunosuppression in the lepromin reaction and in the phenomena of allergy and anergy in leprosy in man.

Shepard's editorial noted that these two fields of research were discussed at a workshop on The Immunology of Leprosy, in October 1967, sponsored by the U.S.—Japan Cooperative Medical Science Program. In the interval since that editorial was written the discussions at that workshop have been printed in abstract.[2] Among the papers presented were several that bore on what seems to be a basic factor in immunosuppression, viz., interference with the protec-

[1] SHEPARD, C. C. Immunologic suppression in leprosy and its relation to lepromatous disease. Internat. J. Leprosy **36** (1968) 87-90. *(Editorial)*

[2] Abstracts from workshop in immunology of leprosy. Experimental Hematology, No. 15, 1968, 139-157. (Published by the Biology Division, Oak Ridge National Laboratory)

tive role the lymphocyte plays against bacterial infection.

The now well known studies of Rees and his associates, and Shepard and his colleagues, on the depression of lymphocyte transformation by thymectomy, irradiation and other means, were extended at the workshop by new reports by these investigators on the artificial production of lepromatous-type disease in mice.

Other studies previously in course in the general field[3, 4] were supplemented at the workshop by their original participants also through new reports. Bullock[5] has recently published in more detail data on which his expressed views were based, i.e., that leprosy is associated with a generalized depression of the delayed allergic inflammatory response, which was found to be much greater among patients with lepromatous leprosy than among patients with tuberculoid disease. This has led to additional editorial discussion.[6] That the two phenomena of anergy to lepromin and low resistance to leprosy are related in some way no one doubts, and indeed they have their counterpart in the case of other microbic diseases. Tuberculosis, which has so many analogies with leprosy,[7] is a notable example. Laboratory animals and man, after infection with tubercle bacilli, generally become highly sensitive to the antigenic component of the tubercle bacillus in tuberculin. But that sensitivity can be depressed or abolished by a variety of processes, including intercurrent disease. Measles, for example, greatly depresses a previously disease-acquired sensitivity to tuberculin, and at the same time apparently reduces resistance to the disease, as evidenced by not infrequent exacerbation of the illness following the measles infection. To be sure the difference in manifestations between the lepromatous and tuberculoid types of leprosy is far greater than that between progressive tuberculosis and its acute exacerbation after resistance-depressing intercurrent infection, but a related principle may be involved. Also, in tuberculosis, there appears to be no clearly defined hereditary predisposing anergic state, as there may be in lepromatous leprosy, although some of Lurie's[8] results with inbred rabbit families suggest that such might be the case.

The relation of the lymphocyte to the two related but still independent phenomena of hypersensitivity to tuberculin and resistance to disease was recognized years ago. M. W. Chase[9] noted as far back as 1945 that hypersensitivity to tuberculin could be passed from a tuberculin-positive guinea-pig, sensitized by injection of dead tubercle bacilli, to a normal guinea-pig by the transfer of leucocytes or washed lymph node or spleen cells from the former. The observation was confirmed in detailed experiments by Kirchheimer and Weiser,[10] and has since been repeated many times. But there has been relatively little tendency until recently to relate it to the pathogenesis of the disease characterized by the hypersensitive state. Not much attention has been paid in texts and other comprehensive treatises on leprosy to the basic importance of the lymphocyte and its transformation to the larger cells of blast type concerned with immunologic reactions. A number of papers in which the

[3] Bullock, W. E. Depression of the delayed-type allergic response in leprosy. Clin. Res. **14** (1966) 337.

[4] Waldorf, D. S., Sheagren, J. N., Trautman, J. R. and Block, J. B. Impaired delayed hypersensitivity in patients with lepromatous leprosy. Lancet **2** (1966) 773-775.

[5] Bullock, W. E., Jr., Studies of immune mechanisms in leprosy. 1. Depression of delayed allergic response to skin test antigens. New England J. Med. **278** (1968) 298-304.

[6] IJL Current Literature, this issue, page 367-368.

[7] Long, E. R. Leprosy and tuberculosis. Internat. J. Leprosy **36** (1968) 90-93. (*Editorial*)

[8] Lurie, M. B. Resistance to Tuberculosis: Experimental Studies in Native and Acquired Defensive Mechanisms. Cambridge, Mass., Harvard University Press, 1964, pp. 152-153.

[9] Chase, M. W. The cellular transfer of cutaneous hypersensitivity to tuberculin. Proc. Soc. Exper. Biol. & Med. **59** (1945) 134-135.

[10] Kirchheimer, W. F. and Weiser, R. S. The tuberculin reaction. 1. Passive transfer of tuberculin sensitivity with cells of tuberculous guinea pigs. Proc. Soc. Exper. Biol. & Med. **66** (1947) 166-170.

subject is approached through special technics are appearing currently, however.[11]

It may well be that this new appreciation of differences in intrinsic cellular mechanisms in the body's defenses against leprosy will prove to be one of the most important approaches in recent years, opening a new field in understanding its polar types, and the phenomena of susceptibility to leprosy in general.[12]

—E.R.L.

[11] See for example: Morgenfeld, M. C., Bonaparte, Y. de and Rodriguez Paradisi, E. Blasts in lepromatous leprosy. Lancet **1** (1968) 308-309. (*Letter to the Editor*) (Abstract, Internat. J. Leprosy **36** (1968) 244-245.) These authors have prepared an article for future publication entitled "Delayed cutaneous hypersensitivity in lepromatous patients. Response to leucocyte transfer factor."

[12] Editor's note. There was extensive discussion of this general subject, with numerous reports of progress, at the Ninth International Leprosy Congress, London, 16-21 September 1968.