The Dissociation of Hypersensitivity and Immunity in the Spectrum of Leprosy

TO THE EDITOR:

Having recently visited Brazil and Cuba, I gained an impression that leprosy in these countries, viewed by comparison with leprosy in some other endemic areas, raises a question regarding the relationship between immunity and hypersensitivity in the spectrum of leprosy. I write this comment with some reluctance in view of my limited experience of leprosy in these countries, but it will serve a purpose if it provokes verification or dissent. For simplicity I shall use the term "Brazilian" to embrace also my experience of leprosy in Cuba, but I have no knowledge of its applicability to other parts of Latin America.

Whatever system of classification is used one finds that there are two main groups, tuberculoid and lepromatous. In the Madrid classification there is also a borderline group (apart from indeterminate which is outside the spectrum). Problems may arise partly because these three groups do not constitute the whole spectrum, partly because their positions within the spectrum may not be identical in all endemic areas. Nevertheless, on the Ridley-Jopling scale the common groups everywhere are BT, BL and LL (usually LLs), and this was true also of Brazilian leprosy.

What was most striking about the biopsies I saw in Brazil and Cuba was the preponderance of cases with a high content of lymphocytes in the lesions. This applies to all parts of the spectrum except LL. Thus near the middle of the spectrum BL, a lymphocytic group, appeared to be relatively common; whereas I saw no case of BB, a non-lymphocytic group, in about 60 biopsies. The BT group can be characterized either by lymphocytes, giant cells or both. In the Brazilian form BT cases were common, and in all or most of them lymphocytes were plentiful and giant cells sparse. BT probably converted to BL and vice versa, without passing through the BB position.

On the clinical side I saw fewer cases, but in both countries a number of problem cases were drawn to my attention. In each case the patient was in the borderline region of the spectrum, and the problem was one of recurrent reactions which never completely resolved. When several biopsies were available one might see a modest upgrading in the second biopsy but sometimes this was not sustained. Even in post-reaction BT biopsies it was usually possible to find acid-fast bacilli, which ought to have been eliminated during the reaction. After returning home, I searched through my own collection of material from other parts of the world and found only two cases of reaction in borderline patients that were not associated with significant upgrading or downgrading ([6]). In Brazil this seemed to be the norm.

In none of the skin biopsies was nerve damage as conspicuous as might have been expected in BT patients with a predisposition to react, and I enquired, therefore, whether nerve damage was a serious problem clinically. In both countries I was told more than once that it was not a serious problem.

Whether the picture of a form of leprosy as given here is typical of leprosy in any part of Latin America is not really the point at issue. But, although confirmation is needed, it seems that such a form exists, and that it may be more common in some places than others. It contrasts with a form better known to many people for the histological signs and destructive consequences associated with delayed type hypersensitivity in mycobacterial disease, and it lends support to the view that over a large part of the spectrum of leprosy there may be a dichotomy between immunity and hypersensitivity.

The evidence for the existence of such dichotomy is partly clinical. In the common form, severe reactions in the borderline region lead to severe nerve damage in many cases but often terminate with effective upgrading, possibly to TT ([5,6]), and elimination of bacilli. By contrast, the Brazilian reactions rumble on without causing severe nerve damage and stop, only to recur because the bacilli are not finally eliminated.

The histological evidence of dichotomy correlates with the clinical outcome. In the first group, reactions terminate with the formation of large giant cells but fewer lymphocytes ([6]). The giant cells and the severe nerve damage, which is another feature, both correlate with strong elevation of the lymphocyte transformation test (LTT), which was an expression of delayed hypersensitivity ([3,4]) but not of patient resistance ([1]). On the other hand, the presence of many lymphocytes in lesions, as seen in the Brazilian form, does not correlate with high LTT values ([3]) and is often most conspicuous in lesions with few histological signs suggestive of delayed hypersensitivity. Yet lymphocytes are almost the only histological feature of early indeterminate lesions, some of which are self-healing. Lymphocytes presumably denote the cell-mediated form of immunity without the destructive aspects of hypersensitivity. There is immunological support for the view that these two forms of response may be dissociated ([2,7,8]).

Although many leprosy patients do, of course, display a fairly mixed response, it is possible to identify histologically cases with a strong preponderance of one or the other type. This applies to the TT ([5]) and BT groups. In the middle of the spectrum BB and BL occupy slightly different positions, but more important than this difference is the almost complete differentiation of epithelioid cells without lymphocytes in the one and macrophages with lymphocytes in the other. It may be that each denotes either a hypersensitive or an immune response at a fairly low level. Only in the anergic LL group is dissociation always absent. However, there are plenty of instances of patients with a lymphocytic type of response acquiring effective hypersensitivity, and only in the Brazilian form of the disease does this seem to be an unusual event. It is this form, if I have not misconstrued it, which suggests that the histological dissociation of the spectrum may be clinically important.

—D. S. Ridley, M.D., F.R.C.Path.

Hospital for Tropical Diseases
St. Pancras Way
London NW1 0PE
England

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