# Intralesional Variation in Histology

TO THE EDITOR:

The clinical note by Job, *et al.* (IJL 1991: 59:116–119) describing the histological picture from tuberculoid through what appears to be borderline tuberculoid (BT) to lepromatous pathology from the deeper to the superficial layers of the dermis, with a thin subepidermal clear zone, co-existing in the same lesion along with a hypopigmented lesion elsewhere in the body of a 10-year-old boy only goes to show that we are rediscovering things that have been known before. Job, *et al.*'s note may be the first clear-cut documentation of this occurring, but the appreciation of this phenomenon of co-existing lesions of varied histology at different sites of the same patient, or in the same lesion, has been known even before the Ridley-Jopling (R-J) outline of classification was described. I shall cite here relevant passages from three observers to substantiate this.

In his concluding remarks at the Ciba Foundation study group meeting on the "Pathogenesis of Leprosy" held in London in January 1963 to honor the late Prof. Khanolkar, James Doull observed: "The pathologist gets a single biopsy from a selected portion of a patient's body. . . . Of course, what the pathologist should do is to take specimens from many parts of the body. He might be astonished to find, if that were done, that in many cases the picture might vary quite a bit. . . . we think that cases of what one might call dimorphous leprosy are very much more common than was formerly thought. If you take biopsies from several parts of the body, you will sometimes find not only lepromatous structure but also structure indicating the tuberculoid type."

In an International Seminar on Leprosy at Agra in 1967, organized jointly by the Ministry of Health, the Indian Association of Leprologists, and the HKNS to coincide with the inauguration of the JALMA laboratory, Stanley Browne, initiating the discussion of the session on borderline leprosy, observed: "In the individual patient, the histological appearance may vary with time, with treatment, with the lesion, and at different sites and different depths of the same lesion" (Proceedings of the Workshop, Ministry of Health, January 31 to February 2, 1967, p. 55).

Years later, in correspondence to this JOURNAL (IJL 1981:47:64–65), Kundu of the School of Tropical Medicine, Calcutta, commenting on the R-J classification, observed: "To be more explicit borderline lesions of the same patient often present pleomorphic lesions which both clinically and histologically vary from BT, BB, BL type of clinical as well as histopathologic lesions. Even the larger single borderline lesion at times presents a BB lesion at one end and

a BT lesion at the (histopathologically) opposite end of the same individual" (meaning lesion, of course, the same lesion—BRC).

The purpose of my pointing these facts out through this Letter to the Editor is to draw the attention of the planners of leprosy chemotherapy to the fact that almost all cases of leprosy encountered are borderline. The moment a single tuberculoid lesion starts increasing in size, develops satellite lesions or has a multiplicity of lesions, the patient starts slipping and downgrading. A TT lesion that Ridley calls TTp (primary tuberculoid) manifests cell-mediated protection (protective cell-mediated immunity) and lesions from TTs (Ridley calls secondary, but there is no harm in calling it subpolar TT also—BRC) on down to LLs are all borderline, unstable, reaction-prone, and damaging to both skin and nerves. Taking note of such discordant reports suggesting difficulty with universal applicability of the R-J classification, Ridley and Ridley explained Srinivasan, *et al.*'s report (Indian J. Lepr. 1982:54:275–282) as due to an autonomy in immunological responsiveness between dermal and neural lesions (Ridley and Ridley, IJL 1986:54:595–605). In view of Job, *et al.*'s report and the other reports I have cited, it is quite obvious that this autonomy applies to different regions of the skin and different planes of the same lesion also.

The relevance of these findings in the context of leprosy treatment is profound. I have never felt very comfortable with the rather arbitrary grouping of leprosy patients into paucibacillary (PB) and multibacillary (MB) for multidrug therapy (MDT) eligibility. Ridley, in the paper cited above, stated: "The results emphasize a point that was apparent before, that paucibacillary patients may harbour multibacillary loads in their nerves. It is now clear that this load is unpredictable." If for a moment we look back at Job, *et al.*'s report and reverse the ordering of the skin histology so that the lepromatous picture lies in the deeper layers and the tuberculoid histology superficially as the presenting clinical sign, we will never know of this boy's 3+ to 5+ bacillary load in his skin even if we did a skin smear examination (because the slit made to take the smear does not usually go that deep), and we will use paucibacillary MDT for the patient. This differential dermal bacteriological load apart, as Ridley observed, the nerves usually display a more multibacillary picture.

In this context, I am impelled to recall the fairly free and frank deliberations of the participants at a meeting of the Indian and THELEP scientists held at Karigiri in March of 1988. The participants were quite exercised over paucibacillary leprosy, the length of MDT to be given these cases, etc., particularly after Chacko showed the bacteriological picture in the nerves of these cases. The proceedings of the meeting, excellently put together by Cariappa and Pannikar of the Karigiri Institute, were reviewed by me in the Indian Journal of Leprosy (1989:61: 249–257). One remark made by Prof. Grosset should be very relevant in this context: He wondered if someday we will end up treating paucibacillary cases for longer durations. He did not elaborate; even if he did, it is not to be found in the proceedings. I only hope he will have said that we should use the same kind of regimen for all cases of leprosy, only taking care of the type 1 reaction and nerve-damaging potential of the so-called PB cases. As argued in Ridley and Ridley's paper cited here, the bacilli seek the refuge of the immunologically protected nerves to avoid the "heat" of the immune response of the skin in PB leprosy, which is not there in MB leprosy and, hence, we see more bacilli in the skin than in the nerves in MB leprosy. But bacilli are there in all types of cases of leprosy and the cut-off point between PB and MB leprosy of a $10^6$ bacillary load would appear to be unrealistic and arbitrary. While there is little doubt that bacteriologically speaking PB and MB leprosy may be overlapping, the real division is the immune responsiveness, with a delayed-type-hypersensitivity-mediated downgrading potential in TTs-BT leprosy and a cell-mediated-immune upgrading potential in LLs-BL leprosy. Ganapati's remark at that Karigiri meeting could not be more appropriate from this point of view: We cannot have a bacteriological solution to what is basically an immunological problem.

I think it is still not too late to think things over afresh in light of what has been discussed here, and to plan treatment strategies

that take into consideration the immunological dimensions of the disease and tread a therapeutic path that ensures the least encounter with immunological phenomena that downgrades the disease or prolongs the treatment.

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