REPLY: THE USE OF HISTOPATHOLOGY IN LEPROSY DIAGNOSIS AND RESEARCH

Sir,

The intention of our editorial (*Lepr Rev*, 1989; **60:** 257–62) was to reassess the role of histology in leprosy in relation to recent developments, which are mainly technological. Early diagnosis, with which Dr Porichha's letter is concerned, is an outstanding problem for which, we had to conclude, newer methods have not produced a solution. A patient must not be diagnosed without near proof, yet early treatment is needed if the risk of irreparable nerve damage is to be avoided. We suggest that new thinking is needed.

The primary lesion of leprosy becomes clinically apparent at a very early stage, partly due to depigmentation. Histology reflects well the immunological response, but at this stage there is no response at the site: the scanty bacilli are in immunologically protected positions, mainly nerves. Not surprisingly, such inflammation as is present is non-specific. Unless bacilli happen to be detected, an uncommon event in lesions of less than 6 months' duration, a biopsy is likely to be inconclusive. Later, especially after one year, the finding of bacilli is more probable and the histology perhaps more specific. Many studies of early leprosy, and most 'comparability studies' between histologists, have been on lesions under one year, which of course is when a diagnosis is wanted; but it is difficult to see how at this stage histology alone is ever going to be decisive. Reliance on finding bacilli is hampered by the time needed to search serial sections, and the possibility that those found could be contaminants.

It has to be remembered that all skin inflammation is perivascular *ab initio*, and nerves accompany vessels. Identification of the point at which inflammation constitutes specific involvement of the nerve component of a neurovascular bundle is one of the main points of contention between histologists, not all of whom have regular experience of skin diseases other than leprosy. It would be of great educational benefit if a reference biopsy collection of early skin diseases could be compiled, and an atlas published. But it is to be feared that the outcome of greater familiarity with other diseases might be even more noncommital reports on early leprosy. A reference collection of early cases that proved on follow-up to be leprosy, if it were feasible, would be similarly useful. Without these two reference points comparability studies highlight the problem without contributing to its solution. We fully support Dr Porichha's plea for an improvement of laboratory services and standards in endemic countries. In our experience, outside leprosy centres, dermatopathology is the least well served of the histological subspecialties. But this is not the whole answer.

It is interesting that cell mediated and antibody responses to leprosy are already detectable at the contact stage. Presumably the bacilli (at non-protected sites) that induce these responses are destroyed in the process. It would seem logical therefore to use immunological tests as the basis for diagnosis, but the results are disappointing. Either the antigens are insufficiently specific or they fail to differentiate healthy contacts from early infections. Diagnostic immunocytochemistry tends to fail in complex diseases.[1]

There is an admirable tradition that a histological report stands on its own evidence and is complete in itself. It should, and for the classification of leprosy it can be so. For diagnosis, more progress might be made, we suggest, if it were the rule to take histological reports in conjunction with other available evidence. A tuberculoid granuloma in skin points to leprosy if it is associated with loss of sensation; but is against it if the lepromin test is negative. Lymphocytes in a nerve are stronger evidence of leprosy if supported by independent immunological evidence. Yet any one of these criteria alone may be insufficient.

More studies are needed, with full evaluation and follow-up of cases, both for early diagnosis and prediction of the outcome. A probability scale that incorporated data from diverse sources ought to be compiled, on the lines of the histopathology scale already in use.[2] One wonders if a comprehensive prospective study carried out by a multidisciplinary working group might not offer the best, perhaps the only, way forward.

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References

[1] Gatter K C. Diagnostic immunocytochemistry: achievements and challenges. *J Pathol*, 1989; **159:** 183–90.
[2] Fine PEM, Job CK, McDougall AC, Meyers WM, Ponnighaus JM. Comparability among histopathologists in the diagnosis and classification of lesions suspected of leprosy in Malawi. *Int J Lepr*, 1986; **54:** 614–25.