Editorial

THE MORPHOLOGICAL INDEX

The morphological index (MI), or percentage of solid-staining *Mycobacterium leprae* in a smear stained by an acid-fast technique, is an index with a well-substantiated theoretical basis. The solid-staining state has been correlated with the viability of the organism as assessed by its ultrastructure (McFadzean and Valentine, 1960; Rees and Valentine, 1962) and with viability as assessed by mouse footpad inoculation (Shepard and McRae, 1965). In theory, the MI is a fairly accurate indication of the proportion of viable organisms on one or more lesions, and it has been widely and readily accepted as a good index of the activity of an infection. There have, however, been a few criticisms. Bechelli and Guinto (1970) have given a timely reminder that there is no final proof of a relationship between the MI and contagiousness. This is a measure of present-day dependence on this index. An MI of zero indicates only that no solid-staining bacilli were seen among the bacilli actually examined, often 100, sometimes more. It could not be taken as evidence that no bacterial activity at all was taking place, bearing in mind the vast number of organisms in the body, even if the MI gave a true indication of the viability of all the bacilli examined. In fact, it is not claimed that it can do so. There is evidence that a small proportion of dead bacilli remain solid, at least temporarily (Shepard and McRae, 1965). A more serious difficulty is the uncertainty surrounding very short bacillary rods, which could be no more than fragments of whole organisms and which are therefore regarded as non-solid, though Chang and Andersen (1969) have demonstrated that some very short rods of *Myco lepraemurium* are capable of elongation and multiplication; some of their other criticisms of the morphology-viability concept appear to be less well founded.

The MI remains a tenable concept, therefore, within limits. In practice, its reliability is marred to some extent by inadequate standardization, not so much in definition as in technique, and the results obtained depend on a number of factors. A simple estimate of the percentage of solids in a smear does not give quite the same result as a count of the "solid ratio" as defined by Shepard and McRae (1965). On the other hand, it is probable that some workers who are now using the latter criteria retain the older term "morphological index" which has been in use since the early 1960's by Browne (1966, 1968), Goodwin (1963), and others. It would avoid confusion if there were only one index with an agreed definition. For a technician to be able to obtain reproducible MI's requires both skill and training, and these are not quickly acquired. To ensure that 2 workers regularly obtain the same answers is still more difficult. Technique affects the result at every stage. A smear contaminated with blood is difficult to stain, and is likely to provide misleading results. The MI is also affected by the method of fixation and by almost every part of the staining procedure, subjects that are dealt with in a separate paper in this issue (Ridley and Ridley, 1971, see p. 88).

Finally, the result will be influenced by the choice and number of sites examined, depending on whether there is selection of 1 or 2 active lesions, or whether a site on the ears alone or multiple sites are used to estimate the index. There can be at least a 10-fold difference from one site to another (Levy and Murray, 1969). These questions require further thought and study. Another problem is that when 2 or 3 smears are taken simultaneously from one site for the purpose of comparative study, it has been found that the 2nd and 3rd smears often give an MI different from that from the first smear; this may be either because of contamination with blood, or because the amount of material obtained is too sparse or it dries on the scalpel. If multiple smears are needed for study, they should be impression smears made from a biopsy.

Standardization could be improved, but it seems unlikely that it will ever be perfected. This does not invalidate the primary use of the MI, but it does call for a reconsideration of its use and its limitations. As an index of the bacterial response to chemotherapy in the early stages of treatment (Waters and Rees, 1962) there is no substitute for the MI, which is of particular value in comparing the rates of response to two or more drugs or combination of drugs. In this connection, nothing that has been said above is of any consequence provided the same conditions are maintained throughout the period of the trial. On the other hand, to stipulate that for acceptance to a drug trial a patient must have an MI of 25 or 10 or only 4 (U.S. Leprosy Panal Protocol, 1967) could be seriously misleading without a very high level of skill and critical perception on the part of the technician and observer. As a supplementary method of assessing activity, biopsies of 1 or 2 of the more active-looking lesions have advantages that are not sufficiently appreciated. The cytology of the granuloma and the indications of infiltration or expansile spread are useful pointers to be considered in conjunction with the morphology of the bacilli. Furthermore, even a small proportion of solid organisms is significant if they are situated in groups. It is doubtful if the bacilli located in nerve bundles, which tend to be solid staining, are at all frequently extracted in the preparation of smears. But here again one assumes a good measure of skill on the part of the histologist and also of the clinician who selects the lesions.

Finally, there is the question of the routine management of patients. The MI is, of course, quite valid provided the conditions remain constant, but there is something to be said for using the SFG index (Ridley, 1971; see p. 96) as an alternative. In spite of its apparent complexity, a technician can be trained to get reproducible results with this index more quickly and easily than he can with the MI. Equally important, it can with practice be estimated almost at a glance. There is, therefore, no difficulty in estimating the SFG index on smears from all sites, which allows a better chance of detecting a relapse in its early stages than does an MI based on only 1 or 2 lesions.

The above considerations may not only serve as a background to the interesting observations of Leiker appearing in this issue (see p. 121), but should stimulate more precise investigation of this aspect of leprosy that has most important clinical, therapeutic, and microbiological repercussions.

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