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CORRESPONDENCE

This department is for the publication of informal communications that are of interest because they are informative and stimulating, and for the discussion of controversial matters. The mandate of this JOURNAL is to disseminate information relating to leprosy in particular and also other mycobacterial diseases. Dissident comment or interpretation on published research is of course valid, but personality attacks on individuals would seem unnecessary. Political comments, valid or not, also are unwelcome. They might result in interference with the distribution of the JOURNAL and thus interfere with its prime purpose.

Skin Smears and the Bacterial Index (BI) in Multiple Drug Therapy Leprosy Control Programs: An Unsatisfactory and Potentially Hazardous State of Affairs

TO THE EDITOR:

In 1977, the World Health Organization (WHO) Expert Committee on Leprosy drew attention to ". . . the extremely low standard of the bacteriological examination techniques used in many leprosy control projects and stressed the need to improve them . . ." ([9]). On countless occasions since that year, ministries of health, voluntary, and international agencies have reported that services for the examination of slit-skin smears in leprosy are deficient and of poor quality. In a recent communication to the *Indian Journal of Leprosy* ([1]) Dr. V. N. Bhatia, writing from the Division of Laboratories in a well known leprosy teaching center in India, commented on the unsatisfactory quality of skin smears in most of the control units, adding that the situation has not improved during the past decade. In the Report of Independent Evaluation of the Indian National Leprosy Eradication Programme in 1986 ([3]), the laboratory services were described as ". . . the weakest link of the programme all over the country . . ."—and a similar conclusion was reached by participants at a recent meeting in Calcutta on Laboratory Services for Fieldworkers ([4]).

But these deficiencies are by no means limited to India. We have visited a considerable number of countries in the main leprosy-endemic areas and find it difficult to list more than 10 centers, worldwide, where slit-skin smears in leprosy are taken, fixed, dispatched, stained, reported, and recorded accurately and systematically. Those we are able to list are, almost without exception, central or "referral" laboratories, with special facilities and trained staffs. By contrast, it would not be difficult to list hundreds of other units where the standard of work is deplorably low. This situation is manifestly unsatisfactory, but our main purpose in writing is to express the view that it is also misleading and potentially hazardous, notably in the context of multiple drug therapy (MDT) as recommended by the World Health Organization's "Chemotherapy of Leprosy for Control Programmes" ([8]). Present strategy relies heavily on the examination of slit-skin smears for the diagnosis and classification of this disease, assessment of progress, the duration of treatment in multibacillary leprosy, and the diagnosis of relapse. A considerable amount of this work, including the vital step of selecting and taking the smears, is carried out at the field or peripheral level. Different workers then stain and report the smears, and others interpret at the clinical level.

We question the safety and good sense of current policies with regard to slit-skin smear services in leprosy control programs in most parts of the world. Our main areas of concern include the following:

Diagnosis. Unless laboratory services achieve and maintain a certain level of accuracy and reliability, slit-skin smear results not only fail to contribute to correct diag-

nosis, but may be misleading. There is a tendency in some programs to rely almost completely on a laboratory report of smears, to the detriment of the development of clinical ability and skills, including observations made during the course of treatment and surveillance. Furthermore, it is often not appreciated that such reports may be meaningless (and misleading) if the sites have not been selected intelligently and the smears properly taken and fixed.

Classification. Current WHO advice on the treatment of all cases with multiple drugs ([8]) relies heavily on the taking of smears and the reporting of the bacterial index (BI) ([7]). The accuracy of this index is crucial to the allocation of patients to either the paucibacillary or multibacillary group which, in turn, dictates whether two drugs (dapsone or rifampin) or three drugs (dapsone, rifampin, and clofazimine) are to be used for 6 months only, or for a minimum of 2 years, respectively. The difference is crucial not only for the proper treatment and cure of leprosy in individual patients, but also for the reputation of WHO (or any other) regimens of MDT. "Over-classification" of paucibacillary patients as multibacillary, based on faulty smear reports, results in the unnecessary treatment of a patient for a minimum of 2 years with three drugs. The misgrouping as paucibacillary of a patient who is in reality multibacillary has even more serious consequences—dual therapy with dapsone and rifampin for 6 months only is inadequate in such cases. These patients will relapse, and this may be attributed to some inherent failure of the drug regimen used.

Period of treatment for multibacillary cases. The WHO recommendations ([8]) are that triple drug therapy should be continued for a minimum of 2 years in all cases, but wherever possible until slit-skin smears are negative. But, in fact, it requires considerable experience and confidence to report that smears from up to six different sites are all negative. Most qualified doctors or program managers in either leprosy or basic health care programs know little about the laboratory techniques and the factors which affect reliability. A totally negative report also a) assumes that adequate material has been obtained from each site smeared, and b) implies that use has been made in the laboratory of a known, positive, control slide to ensure that the staining technique is working properly. With regard to smears reported as positive in this context, low figures should never be accepted as the sole cause for continuing chemotherapy, unless confirmed by an experienced observer. It is, furthermore, doubtful if a BI reading should be accepted as the sole criterion for continuing triple drug therapy in multibacillary cases, after a period of 2 years' treatment, unless taken in conjunction with the clinical findings, regularity of attendance, and the evidence for compliance to unsupervised treatment.

Relapses. While acknowledging that the term is still in need of precise definition, notably in the context of MDT, we consider that apparent or real treatment failure can in fact be due to a number of factors, including wrong classification, basically ineffective drug regimens, reinfection, drug resistance, or inadequate compliance and/or regularity of attendance. The diagnosis of relapse is of such importance that it should never be made on the basis of doubtful bacteriological examinations carried out in the field; every suspect case should be thoroughly examined, clinically and bacteriologically, in a referral center for confirmation and elucidation of the reasons (Georgiev, G. D. and McDougall, A. C., unpublished data, 1987).

Isolation, boredom, and lack of supervision. Much has been written about the (undesirable) isolation of leprosy patients, but little about the professional isolation of peripheral unit laboratory workers, often over a period of many years. Their daily work in such circumstances is likely to be repetitive, monotonous, and boring. Supervision is often minimal or nonexistent, partly because few doctors and program managers in leprosy-endemic countries have adequate basic knowledge of the techniques involved.

Laboratory services and their cost-effectiveness. The current approach to slit-skin smear services, which has been followed for several decades, is that many dozens of laboratory "technicians" are employed in a given large area or zone. It has been considered reasonable to recruit and train such personnel, usually for a period of only 3–6 months, and then to establish them in peripheral units with laboratory space, re-

agents, a supply of electricity, and a microscope. In practice there are often appreciable difficulties, not only in the realm of supervision but also in the provision of reagents and basic laboratory glassware, slides, etc., and in the maintenance of a microscope in good condition. In many vertical programs, posts are often unfilled or intermittently vacant. The wisdom of employing and equipping personnel for this specialized task, in peripheral units, is open to serious doubt and requires investigation; it is almost certainly not cost-effective.

In considering the reasons for this unsatisfactory state of affairs it might fairly be asked if attention has been paid to teaching and training, including the publication and distribution of clear-cut practical instructions. But in fact the Ziehl-Neelsen technique was described in the last century; as a basic technique it is not particularly difficult, and clear instructions have been available to leprosy control programs for many decades. The World Health Organization published detailed instructions in 1980 ([11]) and excellent accounts, including detailed guidance on the selection of sites in patients of different classification, appear in the laboratory manuals by King ([5]) and Cheesbrough ([2]). Responding to a long felt need, Leiker and McDougall produced a short guide for slit-skin smears in leprosy in 1983 ([6]). Thousands of copies of this have been distributed in English and six other languages, including Spanish and French.

Despite these efforts, and a number of attempts through the decades to improve the quality of work by workshops and seminars, it is our conclusion that the situation is unacceptable by any standards and unlikely to change. We suggest that further delay is unrealistic and propose that the present approach should be radically revised, as a matter of urgency. This revision would entail a somewhat profound series of changes in operational methodology in leprosy control, starting with the closure of virtually all small (one-man) peripheral laboratories for slit-skin smears and the simultaneous development of a central "reference" laboratory, preferably in a referral center for leprosy patients. The best and most experienced staff could be selected on the understanding, from the outset, that their contribution is of crucial importance. Their interest and cooperation, coupled with a degree of respect from medically qualified staff, is basic to our recommendations. This change should be coupled with a fundamental reconsideration of the real value of slit-skin smears in diagnosis and classification, including the possibility of dealing with paucibacillary cases on purely clinical grounds, without the use of smears (except in certain problem cases), and agreement to treat multibacillary cases for a fixed period of time (essentially 2 years), without routine recourse to smears. Furthermore, after a period of transition, we envisage that all cases requiring smears would have them taken, processed, and reported at the referral center laboratory (preferably by the same technician or, in certain circumstances, by trained referral center staff using a mobile unit). The precautions to be observed by leprosy staff with regard to possible occupational risks from HIV infection ([10]) strengthen our conviction that such work should be undertaken by highly trained, centralized, and supervised personnel and not by small, unsupervised peripheral units.

These proposals will meet with opposition. They will not solve the problems overnight, and their implementation will require careful planning and preparation. We are in the process of writing a detailed description of the operational methodology and logistics of such a change, based on a population of approximately 400,000. We would be interested to hear from any of your readers who believe, as we do, that there is an urgent need to revise the present strategy.

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Treatment Regimens in Paucibacillary Leprosy

TO THE EDITOR:

I find it puzzling that Katoch, *et al.* ([2]) in their trial of three treatment regimens in paucibacillary (PB) leprosy found 32 patients (out of 207 tested) to be Mitsuda negative. We are not told how positive and negative cases are distributed in the three types of leprosy (indeterminate or I, borderline tuberculoid or BT, and polar tuberculoid or TT) included in the trial, so presumably some of the Mitsuda negatives were among the 29 indeterminate cases. But even so, an explanation is needed as to why some of the BT cases (surely not TT cases?) were negative. Two explanations come to mind: a) The authors break new ground by considering a papule of 5 mm in diameter the minimum size of a positive Mitsuda reaction. The generally accepted terminology is "negative" for absence of anything to see or feel at the test site, "doubtful" for a papule measuring 1 mm or 2 mm in diameter, and "positive" for one measuring 3 mm or more ([1]). We are entitled to ask how many reactions measuring 1–4 mm were recorded as "negative" in this report? Had they been labeled "doubtful," we would have known. b) Mitsuda lepromin supplied by the National Institute for Medical Research, London, carries the warning that the shelf life is 2 years. Had the lepromin used in this trial exceeded its shelf life?

In my 25 years of leprosy work in London, I tested many histologically proven BT patients with Mitsuda lepromin and never encountered a negative result, hence my surprise that so many "negatives" were recorded among PB patients in this trial. This letter is an attempt to find explanations for these bizarre findings, and to counter the impression that the lepromin test is of no help in designating patients as paucibacillary. The reverse is the truth, for a positive Mitsuda reaction will give reliable support for inclusion in the PB group; whereas a negative reaction makes a biopsy mandatory.

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