Editorial

TO SMEAR OR NOT TO SMEAR?

None of the older leprologists, 40 or 50 years ago, attempted to work without the aid of slit-skin smears. When I joined Dr R. J. W. Rees’s laboratory in 1959, he immediately taught me the techniques of staining and scoring of smears, using the as then unpublished logarithmic scale of Ridley. A month later, on my arrival at Sungei Buloh Leprosarium (SBL), to head the Leprosy Research Unit (LRU), the departing Dr J. M. McFadzean demonstrated ‘best practice’ methods for the taking and fixing of smears, and the care of microscopes in the tropics. The then recently appointed senior laboratory technician, Mr (Haji) Mohd Bakri, was also carefully trained in the laboratory handling of smears, the making-up, storage and shelf-life of the reagents used, and the care of microscope lenses; for over 20 years, he stained and scored smears meticulously—subsequently, external audit confirmed his consistent accuracy—and he trained the small number of assistant laboratory technicians who came to the LRU. Most became very reliable; the one or two who did not soon applied for a transfer to ‘more interesting work, where they could better develop their potential’. But the research programme made the skin smear results of great interest and their scoring very satisfying.

One of the first assignments that Rees gave the LRU was to study the alteration in the morphology of Mycobacterium leprae in serial smears from new LL and BL patients receiving dapsone therapy, from which was developed the Morphological Index (MI), although we did not introduce that name ourselves. This entailed my personally taking and reading hundreds of sets of smears, and Bakri also quickly mastered the scoring of the MI. Throughout, all LRU smears were taken and fixed (usually with a small spirit lamp) by doctors; they were always taken from both ear lobes, but there were no other standard sites. In addition, in previously untreated LL and BL patients, four (initially six) other active skin sites were smeared, and in TT, BT and BB patients one to four active skin sites, and these same sites were used for serial smears. The face was only smeared in exceptional circumstances, so as not to embarrass unduly the patient.

In these ways, the quality and usefulness of each smear taken were assured, and the accuracy of the scoring maintained, supported by the informed and skilled interest of the medical and technical staff. This situation is essential for any successful smear laboratory. Lack of skill and/or lack of interest by senior staff lowers the morale of technical staff, especially if the latter are expected to examine large numbers of ill-chosen and ill-taken smears, and there is nothing more boring and hard on the eyes than having to examine large numbers of negative smears.

Smears were considered essential to confirm the diagnosis of multibacillary leprosy, especially in early LL, to study the effect of chemotherapy in LL and BL patients (they
revealed immediately the extremely rapid killing caused by rifampicin when the LRU first tested the drug in 1967, confirmed in the mouse footpad many months later5), to detect relapses, particularly at the beginning of the dapsone resistant epidemic in the early 1960s, and in chemotherapy trials, to indicate if a new patient had indeed active, untreated leprosy; it was not unusual for 'new' patients to deny previous treatment, even if they had received 3–6 months of dapsone, especially if their leprosy did not appear clinically very active. They were also essential in the differential diagnosis of leprosy, combined with careful clinical examination.

SBL had in 1959 around 2400 'inmates', typical of the old style leprosaria. The routine smears were performed in the general laboratory, which was mostly staffed by one 'healthy' and several 'ex-patient' technicians. There was little staff turnover, and all understood the importance of the smear test. The laboratory had originally been set up by Dr G. Ryrie, and after the end of the Second World War, recreated by Dr B. Molesworth. Smears were taken from all patients on admission, and once a year throughout their stay, perhaps 5 years in BT and TT, and over 10 years (often for social reasons for life) in LL leprosy. They were taken from both ear lobes and from one active skin site, and were scored as negative, +, +, 2+, and 3+, on a simple descriptive scale1 which was easy to understand, and the three results were not averaged into a Bacterial Index (BI). These results were recorded in the laboratory smear book, and on each patient’s 'papan', a piece of wood, perhaps 20 by 15 cm, to which was glued one or more sheets of paper, on which were recorded the personal details, hospital number, date of admission, initial classification, whether N, N7L, or L1, 2 or 3, and past and current dapsone treatment. These data, by then already considered 'old fashioned', were accurate enough to enable one to classify several hundred old patients who started on sulphone therapy in 1948–1951, and whose dapsone treatment was stopped abruptly (they had all been smear negative for at least 5 years) in July, 1970. From these patients were identified 361 who had had lepromatous (LL and BL) leprosy; they were followed up for 9 years, to assess the rate of relapse after completion of 20 years of supervised therapy.4 The SBL routine laboratory, therefore, with stable if largely ex-patient personnel, good supplies of reagents, adequate microscopes, and the strong support of the Medical Superintendent, was able to maintain accurate skin smear tests and basic, essential records for many years.

Working in this environment, it was only gradually that one learnt of the difficulties experienced in many routine smear laboratories. Poor, often monocular, microscopes, unprotected from fungus, bored smear technicians, taking smears themselves from 'standard sites', many of which were unhelpful and unnecessary, staining with poor quality reagents, and gaining little support and encouragement from doctors unskilled and uninterested in laboratory work, all led to a low standard throughout many leprosy control programmes (LCPs). This was commented on by the WHO 5th Expert Committee on Leprosy, which met in 1976, and which drew attention to 'the extremely low standard of the bacteriological examination techniques used in many LCPs, and stressed the need to improve them'.5

After the introduction of MDT, the very unsatisfactory situation was discussed in depth by Georgiev and MacDougal in 1988.6 They noted the often inadequate training and frequent lack of support given to smear technicians, many of whom had to work in the periphery in isolation and boredom, with inadequate facilities, shortage of reagents and glassware, and with no means of maintaining their microscopes in good condition. They recommended the diagnosis and classification of paucibacillary leprosy (PBL) on clinical grounds, fixed duration (of 2 years) treatment of multibacillary leprosy (MBL), and that 'all cases requiring smears would have them taken, processed and reported at the referral centre laboratory,
preferably by the same technician, or, in certain circumstances, by trained referral centre staff using a mobile unit'. They also commented that the advent of HIV strengthened their conviction that 'such work should be undertaken by highly trained, centralized, and supervised personnel and not by small, unsupervised, peripheral units'.

In the endeavour to achieve the elimination goal by the year 2000, and in view of the unreliability of most smear laboratories, simple clinical methods of diagnosis and of classification into PBL and MBL were introduced. Smears were no longer considered mandatory, and as Porsche has recently commented in his 'plea to revive skin smear examination', in the rush for early elimination, 'the practice of skin smear examination—the only affordable laboratory test to detect M. leprae—has gradually been made optional in programmes. When a difficult procedure is made optional, it amounts to near deletion'. He noted that the New Case Detection Rate (NCDR) after MDT had been static or slightly increasing. Despite well organized MDT programmes for a long time in the states of Tamil Nadu, Andhra Pradesh and Maharastra, the detection of a large number of cases with a high MBL rate, high child rate and low disability rate in these states during the Modified Leprosy Elimination Campaigns 'makes one uneasy in terms of NCDR . . . the possibility of a reservoir of infection and continuing transmission failed to draw due attention'. He recommended a revival of smear laboratories to check the presence of the causative agent, M. leprae. He did, however, suggest certain simplifications. These included the limiting of smear sites to three, and that repeat smears could be taken from the highest initial site. He considered that the grading should be simplified, suggesting that negative and positive should be sufficient. I fully support his first point; SBL showed that three sites are indeed sufficient, but would prefer some simple grading such as that used so successfully by Molesworth.3

After all, some grading is required to choose the single follow-up site. It is agreed that there is no need to average the three sites to produce a BI. He also suggested that as TT and indeterminate lesions are almost always smear negative, if the clinical diagnosis is dependable, these cases do not require smear examination. This also appears wise, although as Indeterminate is so notoriously difficult to diagnose, one wonders how often it is being diagnosed, and with what degree of certainty and accuracy. Finally, Porichha recommended that smear laboratory technicians should not be attached to general health service laboratories, 'to which they rapidly transfer to escape the monotony of smear reporting', but be placed in surveillance units, and given good working conditions, quality reagents and binocular microscopes. His plea for good working conditions is fully supported, although a possible site of work could also be in a tuberculosis laboratory.

But do we need a skin smear service today? The proportion of MBL patients (nowadays defined as having more than five skin lesions!) has fallen, even in those Indian States that have only recently introduced full scale MDT.3 Surely, they are indeed needed, at least in referral centres. First, they are useful for the diagnosis of difficult cases. It is likely that the leprosy epidemic is being largely maintained by undetected, early cases of lepromatous leprosy, which are not easy to diagnose clinically, who may have little skin infiltration, scarcely detectable skin lesions, and no clinical nerve enlargement, but may be suspected, perhaps on contact tracing or on reporting to the health service with vague symptoms. Second, they rapidly help to rule out, or confirm, lepromatous leprosy in the differential diagnosis of such conditions as secondary syphilis, lymphoma with skin involvement, and mycosis fungoides, to name but a few, and help in various neurological conditions, perhaps the commonest in South East Asia being motor neurone disease. Third, in the diagnosis of relapse after stopping MDT; this usually does not develop in less than 5 years, and judging
from experience with dapsone, and from the Malta experiment, may occur as late as 15–20 years. Here smears are virtually essential, especially as relapse, if detected early, may present with very few, asymmetrical skin lesions, which can prove very puzzling to the inexperienced. And fourth, smears will be very useful in research, at least in better equipped LCPs, into the incidence of post-MDT relapse. There are significant data to suggest that LL patients with a high bacterial load (BI > 4.0) are at greater risk of relapse. There is also the need to carry out long-term follow up, for at least 10, ideally for 20 years, of MBL patients treated with the various new experimental chemotherapy regimens. Therefore, in such LCPs, perhaps all overt cases of LL leprosy should be smeared, and their basic records, in many ways similar to those preserved at SBL from 1948 to 1980, held at the central referral centre. If this is done, very valuable data may be available by the year 2020 AD. But this would have to be planned now. There is no time to lose. The International Leprosy Association’s Technical Forum, of February, 2002, has reported that in more and more programmes, the patients are removed from the register as soon as they have completed MDT, and very often essential records, such as identity, address, initial BI and history of treatment, are lost, making it difficult to retrieve patients for follow up and analysis. The leprosy world of 2002 must set up the central referral centres, and store the minimal but essential details of all patients. As Porichha has so rightly commented, ‘The problem with a disease under control is that once there is relaxation in the intervention efforts, there often is a risk of the disease returning with added complications’. We have seen this happen with malaria and tuberculosis. Can we afford to neglect the lessons of the past, and not plan ahead for leprosy?

References


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