Lepr. Rev. (1977) **48**, 283–286

The Treatment of Leprosy Today and Tomorrow: The LEPRA Consultation on Chemotherapy

S. G. BROWNE
The Leprosy Study Centre, 57a Wimpole Street, London W1M 7DF, U.K.

Several disturbing factors have recently appeared in the world of leprosy—so disturbing are they, in fact, that the whole strategy of leprosy treatment and leprosy control must be critically reviewed and revised as a matter of urgency. Any one of these factors would distort predictions ostensibly based on accumulated experience or on data fed into an epidemiometric model programmed for situations fast becoming out of date. Together, they pose such problems for governments and voluntary agencies that the sooner the nature and dimensions of the crisis are realized, and steps taken to meet it, the better for all concerned. To repeat the obvious, these factors are: the emergence of dapsone-resistant leprosy bacilli wherever they have been looked for, the persistence of viable organisms, dapsone-sensitive, despite ordinarily adequate treatment, reduced patient compliance, as evidenced by serious irregularity in following prescribed treatment; in short, a leprosy problem whose size and gravity have not apparently been significantly changed by the vast expenditure and the vast efforts of the past few decades.

These considerations were uppermost in the minds of an international and heterogeneous group of leprosy workers invited by LEPRA to thrash out the implications of these factors and make practical recommendations to guide field workers in the treatment of leprosy sufferers and fund raisers as they orientate themselves and their constituencies to the changing outlook. The Medical Commission of ILEP, for long conscious of the need to help guide the thinking of organizers who are raising annually about 15 millions of US dollars for "leprosy", was well represented, with Belgian, German, Dutch, French and British members from diverse voluntary organizations, and others came from the Medical Advisory Board of LEPRA, the World Health Organization, and The Leprosy Mission. Three of the participants had been members of the 5th Expert Committee on Leprosy of the WHO, whose report had emphasized the seriousness of the present situation. The group met in London on 16 August.

As the vigorous discussions proceeded, under the able chairmanship of Dr R. J. W. Rees, Chairman of LEPRA's Medical Advisory Board, a consensus began to emerge, which may be taken to indicate the distillation of informed medical opinion viewing the whole problem objectively and dispassionately.

The basic facts are, generally, known and admitted. The implications of dapsone-resistance will in the future undoubtedly pose novel problems similar to

those encountered before the arrival of the sulphones on the therapeutic scene. While the extent of the problem may not at present appear to be equally grave in all countries, and may indeed continue to be minimal in those few areas of low lepromatous/tuberculoid ratio and satisfactory whole population detection and treatment coverage, the global outlook is far from reassuring.

So far, secondary dapsone-resistant bacilli have been demonstrated only in lepromatous and near-lepromatous leprosy, and in view of the relatively small numbers of bacilli present in tuberculoid leprosy—and also apparently adequate degrees of cell-mediated immunity—there would seem to be a negligible risk of resistance appearing in patients suffering from this form of leprosy. Since among the dark-skinned African, about nine-tenths of those with diagnosable leprosy are suffering from non-lepromatous forms of the disease, the problem of dapsone-resistance should be seen in its proper global perspective. The situation is, of course, potentially more serious in Asia and South America.

When the group got down to the real business of its meeting, which was "to prepare guidelines for the application of therapeutic regimens and individual drugs to be used in large scale field programmes", it became abundantly evident that, by whatever route this central problem was approached, the way seemed to be blocked by barriers of ignorance or finance or prejudice.

Some of the barriers of ignorance could—and should—be removed quite speedily. For example, the practicability and long-term effectiveness of a single dose of say, 1200 mg, of rifampicin at the beginning of treatment, to be followed by dapsone; or a definite pronouncement on the "reactogenic propensity" of high doses of dapsone in patients with borderline leprosy who are liable to suffer down-grading neuropathies; or the short-term efficacy of the combination thiacetazone-dapsone, and its acceptability in different countries. The answers to these, and similar, questions are to be sought in centres where good clinical and laboratory standards are maintained and accurate records kept. Certain other investigations were considered to be urgently necessary, such as the true extent and worldwide prevalence of dapsone-resistant disease, and its correlation with various treatment regimens.

The financial barriers were mostly an expression of the greater expenditure required in all parts of a serious leprosy treatment/control programme: for alternative and additional drugs, like rifampicin and clofazimine and such anti-inflammatory agents as the corticosteroids (and perhaps thalidomide); for better laboratory cover in field work and institutions (and this would include microscopes and stains, and better-trained laboratory technicians); for upgrading of auxiliary and supervisory staff, and in-service training of all grades, with special emphasis on the recognition and management of patients whose relapse—or whose primary disease—is probably due to dapsone-resistant organisms. In addition to the few existing centres where mouse foot-pad inoculation facilities are available for the confirmation of clinically suspected drug resistance, or the detection of primary resistance in newly-diagnosed patients, the group considered that the dimensions of the problem of drug resistance were such as to justify a recommendation that more centres for experimental monitoring of suspected instances should be created in selected countries faced with the actual or potential risk on a large scale.

The social barriers may be less easily appreciated by armchair scientists, and less easily quantifiable or categorized, but in the long run they may prove to be just as important as the mouse foot-pad or the armadillo. The group had to admit

that patient compliance, in the sense of continuing regular treatment for a long time in the case of multibacillary leprosy, was dangerously—even abysmally—low in many leprosy programmes. Not only would this predispose to the emergence of dapsone resistance on an unmanageable scale, but it would also tend to nullify any attempt to introduce multi-drug regimens. Another very practical socially-orientated (as well as medically important) problem concerns the prescription of an additional (and, of course, more expensive) drug to standard dapsone: should this regimen be advised for all patients with multibacillary disease, newly diagnosed, or should it rather be given to those patients who have already been receiving monotherapy for some years, some of whom may be in the incubating stage of dapsone-resistance? In either case, the social repercussions may be serious, and the long-term medical consequences unforeseeably grave.

If these social barriers appear formidable when seen by workers in the field, those faced by fund-raisers and publicists in the voluntary agencies are likely to prove just as insurmountable, but in different ways. The new situation arising (because particularly of drug resistance) must entail a re-examination of conventional appeals. The group considered that voluntary bodies and governments should take advantage of the growing interest in leprosy to upgrade the training of all field staff, to finance postgraduate study of research workers, to train laboratory technologists (particularly in accurate assessment of bacteriological and morphological indices, and in mouse footpad procedures), to encourage the strengthening of health services generally, from which the leprosy programmes should benefit.

Coming down to the practical problems of therapy in the light of the implications of the 5th Expert Committee Report, the group emphasized the following points:

(1) A good therapeutic regimen for the individual is also good in the long term for the community. Thus, dapsone with the addition of either rifampicin or clofazimine, given to patients with multibacillary leprosy, will lead to clinical and bacteriological improvement, and postpone indefinitely the risk of the emergence of dapsone-resistant bacilli—which would be bad for the patient and bad for the community.

(2) While in theory, combined regimens should henceforth be advocated for patients suffering from any kind of leprosy—since in tomorrow's world many of those with non-lepromatous disease will necessarily be infected with dapsone-resistant organisms—in practice this counsel of perfection is probably unnecessary, and would be financially and socially unacceptable.

(3) For the time being, it would be advisable in most situations to proceed with extreme caution with new plans for the integration of leprosy programmes into the general health services. Leprosy requires rather specialized knowledge not readily available to or assimilable by the average multipurpose health auxiliary. Notwithstanding the continuing danger of the perpetuation of stigma if the leprosy programme is kept separate from the other parts of the general health services, the group considered that the clinical recognition of drug-resistant relapse, as well as the diagnosis and management of leprosy, required an intensification rather than a dilution of leprosy control programmes.

The only practicable departure the group would admit from this general pronouncement would be that the combination of leprosy control and

tuberculosis control in a joint programme may be explored in certain situations.

(4) Although dapsone enjoys a well-deserved reputation for relative freedom from undesirable side-effects, the group recommended that clinicians should maintain good and standardized records of all side-effects they encounter, with particular attention to allergic phenomena, skin rashes, anaemia, hypermanic activity (including insomnia and suicidal tendencies), nephrotoxicity, etc. Since rifampicin and clofazimine will probably be used on a much larger scale than heretofore, clinicians and auxiliaries should be on the look-out for signs of toxicity caused by these drugs, and keep notes. In particular, auxiliaries should be taught what to watch for, how to recognize these side-effects, and how to treat them.

(5) Clofazimine would probably be the commonest drug to be used, after dapsone. At a dose of one 100 mg capsule every other day, the incidence of unacceptable degrees of skin darkening is much reduced, and intestinal disturbances are unknown. The disadvantages inherent in a treatment to be taken at less frequent intervals than daily suggest that a 50 mg capsule would be highly desirable.

(6) Since there exists a very widespread experience that dapsone given daily in doses of 100 mg may apparently precipitate serious reversal reaction in a small but important proportion of patients with borderline leprosy (the proportion possibly varying from country to country), any implementation of this regimen should ensure that facilities for immediate recognition and adequate treatment of this eventuality are readily available to all patients at risk.

(7) While in some quarters "voluntary and temporary admission to hospital" is being advocated for certain categories of newly-diagnosed patients (for full assessment, stabilization on drugs, administration under medical supervision of an expensive drug like rifampicin), the group did not agree that more hospital beds would be required for the more intensive therapy advised for patients with multibacillary disease. Just as with tuberculosis, outpatient treatment with admittedly more toxic drugs than dapsone, has a considerable history and a reasonably small risk of untoward drug-related complications.

The group considered that many of its deliberations had perhaps emphasized the obvious, but that knowledge of the obvious had not yet filtered down to many workers in clinical charge of leprosy control programmes. While some of the recent research findings and deductions might seem far removed from the individual leprosy patient in some remote village in a distant land, yet he should be the first to benefit from the new knowledge: the treatment he receives should not only arrest his disease but should save him from the risk of relapse.