Implementing Multiple Drug Therapy For Leprosy

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PREFACE

This booklet was originally written mainly to accompany a pack of teaching/learning materials on leprosy distributed by Oxfam between 1983 and 1988. The 'question and answer' format was used as an aid to the interpretation of the WHO publication *Chemotherapy of Leprosy for Control Programmes: Technical Report Series 675*, WHO, Geneva, 1982. Several hundred copies of the booklet were included in the teaching packs, but several thousand were also sold as individual copies. The level of interest in various parts of the world was quite surprising and it was necessary to revise and reprint in 1985 and 1987 to meet demand. The present fourth edition includes an account of progress in the implementation of multiple drug therapy for leprosy, together with up to date information from the *13th International Leprosy Congress in the Hague* (September 1988) and the deliberations of the WHO Expert Committee on Leprosy, published by WHO in 1988 (*Expert Technical Report Series 768, WHO Expert Committee on Leprosy*, WHO, Geneva, 1988). Consideration is also given to the possible effect of AIDS on the control of mycobacterial diseases, including leprosy.

It should be noted that the teaching/learning pack referred to above has now been discontinued, since demand fell in mid-1988 and we had the impression that most teaching centres, control programmes and other interested people had received a pack. The TALMILEP section of the *International Federation of Anti-Leprosy Associations* (ILEP) has now produced an extremely valuable *English Language Booklist* which gives details of a wide range of teaching and learning materials. Further details are given in Appendix 1.

Many leprosy control programmes in various parts of the world have already implemented MDT and it has been found that a number of problems and questions of a practical nature have arisen, some of them rapidly and unexpectedly.

This Guide attempts to answer some of these questions and to propose, if only tentatively, solutions or methods of procedure for others. It is absolutely essential that it should be read in conjunction with the above WHO document on MDT; in fact the WHO publication should be studied in detail first.

The text of this Guide is not suitable for and will not be understandable by the novice. It is aimed essentially at those in senior positions who may be concerned with teaching, programme planning and implementation. The hope is that it will encourage people to write their own national guide or memorandum on the implementation of MDT. The intended readership is as follows:

Medically qualified doctors
Medical students
Leprosy control programme managers
Leprosy control supervisors
Tutors in medical and para-medical training schools
Training directors in leprosy training centres
Programme planners in Ministries of Health, especially those concerned with leprosy or combined leprosy-tuberculosis control
Senior staff in pharmacies and drug distribution.

Level of knowledge of leprosy
This is not a basic guide to clinical leprosy or control work and we are assuming a reasonable knowledge of the disease, preferably coupled with some experience in the examination and treatment of patients. Without this basic knowledge, much of the terminology and discussion of such matters as adverse immunological reactions will not be readily understood by the reader.

Level of English language
We are assuming a good knowledge of spoken and written English, equivalent to grades which are required for entry into para-medical training schools, or above.
The following pages give very considerable emphasis to the use of drugs in leprosy, and to various aspects of a practical nature which may arise during the process of implementing multiple drug regimens in the field.

Whilst these operational aspects of drug treatment are of tremendous importance, it must be remembered that many other factors, some of them equally or even more important, are concerned in the treatment of patients with leprosy. Our attention to the down to earth, practical aspects of leprosy control should not divert attention from what – for want of a better phrase – is usually called ‘the human element’. It is of paramount importance to recognise the social and psychological factors in leprosy in dealing with patients, medical staff, administrators and politicians. Furthermore, the distribution of drugs, even if it is safely and effectively carried out by trained staff, will not – at least for many years – remove the problems of disability, deformity and blindness, which so often call for expert care, including physiotherapy, surgery and rehabilitation.

The use of multiple drug treatment in many leprosy-endemic countries has already produced some impressive changes. Prevalence rates (essentially the total numbers of registered, known patients) have come down, in some cases dramatically, partly due to the release from control of large numbers of patients who, on careful reassessment, were not in fact in need of drug treatment; and partly due to the successful use of WHO regimens of relatively short duration. This has already emphasised the need to reconsider staffing levels in vertical programmes and to study, as a matter of urgency, the factors which are currently impeding the change from vertical (specialised) to horizontal (integrated) leprosy control – an important and now virtually unavoidable step which should lead to the detection and treatment of larger numbers of cases.
THE BASIC WHO RECOMMENDATIONS ON MULTIPLE DRUG THERAPY FOR LEPROSY (Technical Report Series 675, 1982), USING ADULT DOSES, ARE AS FOLLOWS:

Multi-bacillary leprosy

Duration a minimum of 2 years (or 24 monthly doses within a 36-month period) in all cases, but wherever possible until slit-skin smears are negative

Number of drugs used three: Rifampicin, Dapsone and Clofazimine*

Dosage: Rifampicin 600mg once-monthly, supervised
Dapsone 100mg daily, self-administered
Clofazimine 300mg once-monthly, supervised and 50mg daily, self-administered

Surveillance minimum of 5 years after stopping treatment, with clinical and bacteriological examination at least every 12 months

* Ethionamide/prothionamide, in a daily self-administered dose of 250-375mg, may be used if the skin pigmentation or other side effects of clofazimine render this drug totally unacceptable.

However, clofazimine should be used as the standard drug in this combination whenever possible.

Pauci-bacillary leprosy

Duration 6 months (or 6 monthly doses within a 9-month period)

Number of drugs used two: Rifampicin and Dapsone

Dosage: Rifampicin 600mg once-monthly, supervised
Dapsone 100mg daily, self-administered

Surveillance minimum of 2 years after stopping treatment with clinical examination at least every 12 months

NOTE These are adult doses. For children’s dosage, see pages 19-20

Diagrams/charts of the above regimens for both pauci- and multi-bacillary patients are shown in Appendix 8.
IMPLEMENTING MULTIPLE DRUG THERAPY FOR LEPROSY

To the reader:

It is the aim of this Guide that it should indeed be practical.

In the three previous editions we have included many valuable suggestions submitted by readers from different parts of the world. Ideas from people who are actually working in leprosy control programmes have been particularly valuable.

If you have comments, criticisms, proposals or new ideas, please contact Oxfam or the author so that appropriate changes can be made in future editions.
1. WHAT IS MDT?

MDT means Multiple Drug Therapy and refers to the use of *more than one drug* for the treatment of leprosy. For many years – in fact since the 1940s – the bacterial infection in leprosy has been treated with one drug (dapsone) i.e. by mono-therapy. Although this arrested or cured the disease in tens of thousands of patients with leprosy (provided it was given in adequate dosage and for long enough) it was, in retrospect, an unwise policy. It is now only too clear that the use of a single drug has given rise to alarming numbers of patients with dapsone resistance in various parts of the world.

It is mainly for this reason that WHO have recommended the use of *more than one drug* in all cases of leprosy, in regimens of relatively short duration. The present document is based on the assumption that Multiple Drug Therapy (MDT) will be used in all leprosy-endemic areas from now on – provided that the quality of health service is adequate for the safe and effective implementation of such therapy.

2. ARE THERE ANY OTHER SYSTEMS OF MDT, APART FROM THOSE ADVISED BY WHO?

Yes, several. For a number of years before the publication of the WHO recommendations in 1982, multiple drug regimens were used mostly for the treatment of multi-bacillary cases. One of the best known of these, pioneered by a group of doctors and scientists in Germany, used a combination of isoniazid, prothionamide and dapsone in one tablet, often associated in the first phase with rifampicin (the latter administered separately, in capsules).

Multiple drug regimens have also been used for a number of years by LEPRA in Malawi, by the Ministry of Health in Tanzania and in various French-speaking African countries.

These initiatives have involved differing regimens, usually of long duration, and they have not routinely included pauci-bacillary cases. For these and other reasons, there is a very strong case for the acceptance, more or less universally, of the regimens recommended by WHO for both pauci- and multi-bacillary leprosy patients.

Neither WHO nor anyone else would claim that the recommendations are final, or that they necessarily exclude the possibility of other, similar regimens being used. There is, however, a consensus of opinion that every effort should be made to persuade those responsible for leprosy control to adopt the WHO recommendations, *preferably without modification*. There are at least two good reasons for this view:

i. The WHO Study Group recommendations were made by a carefully chosen group of experts from various parts of the world, and they were based on a detailed consideration of the present state of knowledge with regard to leprosy and the drugs available for its treatment.

ii. Variation, modification and the use of countless alternative regimens is
more than likely to lead to confusion and extreme difficulty in assessment of the effects of MDT.

There is in our view a very strong case for accepting the WHO recommendations as they stand, if only in the ordering of drugs, training of staff, records and assessment.

3. SHOULD MDT BE INTRODUCED IN ALL LEPROSY CONTROL PROGRAMMES NOW, REGARDLESS OF THE NUMBERS AND QUALITY OF PERSONNEL IN THE MEDICAL SERVICE?

Most definitely not. Although it is the hope of WHO and other agencies dealing with leprosy that multiple drugs (as opposed to single drug treatment: mono-therapy with dapsone) should be introduced into all control programmes as soon as possible, it would be disastrous to do this unless the necessary work, at all levels, can be carried out safely and effectively, with adequate numbers and quality of staff. The definitions of ‘safety’, ‘effectiveness’, ‘adequate numbers of staff’ and ‘quality’ are extremely difficult in this context but, if there is any doubt, it may be advisable to seek expert consultancy from WHO\(^1\), the International Federation of Anti-Leprosy Associations (ILEP)\(^2\) or similar agencies which have vast experience in assessing the quality of control programmes. For programme managers and planners, there is an article\(^3\) in *International Journal of Leprosy*, Volume 50, Number 3, September 1982 entitled ‘Factors influencing the quality of service to leprosy patients’, which may be of value in making such an important decision. An editorial entitled ‘Managerial implications of Multiple Drug Therapy’ by Dr Felton Ross, in *Leprosy Review* 56, 1985, pp.89-97 is essential reading for anyone contemplating the introduction of MDT. In Appendix 2 the flowchart may also indicate the basic steps to be taken and give some idea of how then to proceed.

If MDT is to be applied at all, should it be at national, regional or district level? In other words, having decided to do it, should the first attempts be local or country-wide? The answer to this will depend on staff, money and facilities, in that a well-favoured control programme may in some cases be able to institute a country-wide MDT programme from the outset. But in most instances this will be beyond the available resources. In such cases, there is now a widespread agreement amongst leprologists that MDT should be started on a modest scale in one area, and then systematically spread to other areas one by one, building on the experience gained in this process.

Although it may be unpalatable for some countries or Ministries of Health to decide that the quality of their service, whether specialised/vertical or general/horizontal, is simply not good enough for the implementation of MDT, such a courageous decision may be necessary. It cannot be too strongly emphasised that the mere purchase and issue of drugs, without a reasonably competent and reliable health infrastructure, will be disastrous both for the individual patient and also for the prospects of leprosy control in the country concerned.

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1 Leprosy Unit, Division of Communicable Diseases. The World Health Organisation. 1211 Geneva 27, Switzerland
2 The International Federation of Anti-Leprosy Associations (ILEP). 234 Blythe Road. London W14 0HJ. United Kingdom
3 Available on request from The Health Unit, OXFAM, 274 Banbury Road. Oxford OX2 7DZ. United Kingdom
4. **DO ALL PATIENTS WITH LEPROSY NEED MDT? IF SOME PATIENTS DO NOT NEED MDT, WHAT CRITERIA ARE TO BE APPLIED IN MAKING THIS DECISION AND IN RELEASING THEM FROM CONTROL?**

The brief answer to the first question is – no. In view of the potentially considerable expense of treating patients with MDT, especially in the case of those with multi-bacillary disease, it must be emphasised that there are indeed certain categories of patients who do not need to be considered for MDT at all. These can be further described under two main headings:

i. **Pauci-bacillary leprosy: release from control of cases who do not require MDT**

The *WHO Study Group Report* (page 26) gave an order of priority for short-course chemotherapy in pauci-bacillary patients but did not specifically say which patients need not be offered MDT at all. Since their group refers to the need to give MDT to patients “...who have not yet completed two years of treatment”, it could be concluded that patients who have indeed completed two years or more of treatment are not eligible for MDT. In our view a period of only two years for this category of patient, in the context of releasing pauci-bacillary patients from control and not offering them MDT, is rather short. We prefer to advise that *pauci-bacillary patients should have had at least three years of dapsone mono-therapy and that they should show no clinical or bacteriological evidence of activity, before being released from control.* Depending upon the quality of leprosy control work in previous years and the records, it may be necessary to modify this policy in some leprosy-endemic countries in favour of even longer periods of treatment for pauci-bacillary cases, before release from control is considered.

ii. **Multi-bacillary leprosy: release from chemotherapy of cases who do not require MDT**

Here the position is decidedly less clear. The *WHO Study Group Report* may well be interpreted as advising (page 22) that *all categories of multi-bacillary patient should have MDT, including those who have responded satisfactorily to previous dapsone mono-therapy.*

Such a statement would, however, mean that in many countries a large number of patients with multi-bacillary leprosy would be included and treated for a minimum of two years. The inclusion of absolutely all patients with lepromatous leprosy would inevitably include a large number who had already been treated with dapsone mono-therapy for long periods of time and who are clinically and bacteriologically inactive; that is to say, they show no clinical signs of activity in the skin, nerves, or other body systems and have negative slit-skin smears from all sites examined. The definition of a long period of adequate treatment is difficult, but in Ethiopia, where this problem has called for careful consideration, it has been decided (*Manual on Multiple Drug Therapy (MDT) for Ethiopia*, National Leprosy Control Programme,
Addis Ababa, 1983) to define this as the collection of dapsone for 400 weeks or more during a 10 year period. Provided very careful attention is given to a) the history and record of drug intake, b) clinical findings and c) the slit-skin smear results, we advise that such a policy may be pursued and that patients in this category may therefore be released from control and not offered MDT.

If this discussion seems somewhat lengthy, this is at least partly because of the serious implications for both patient and staff of putting a multi-bacillary patient on to MDT for a minimum of two years, together with the cost of the drugs concerned (see Section 15). It is no exaggeration to say that the difference between treating absolutely all multi-bacillary patients and eliminating those in the above category may have a profound effect on the practical implementation and cost of MDT in many parts of the world.

In the case of multi-bacillary patients who have already (i.e. previously) been released from chemotherapy, and who are also perhaps totally released from any form of care or follow-up, there is really no clear indication that such patients should be recalled and given MDT. (Having treated all other patients, it is just conceivable that some well-staffed control projects, with adequate facilities, might consider this group for MDT, but the priority is low.)

**Multi-bacillary patients who had already received various regimens of MDT for varying periods of time before the publication of the WHO recommendations in 1982.**

In some parts of the world (for instance Malawi, East Africa, South America and Malta) patients with multi-bacillary leprosy had already been treated with various regimens of MDT for varying periods of time before the *WHO Report* was published. The drugs used included dapsone, rifampicin, clofazimine, prothionamide, isoniazid, thiambutosine and thiacetazone. In many cases, the doses used and the duration of therapy were different from those in the *WHO Report*. Such cases present a problem when it comes to the general application of the present WHO regimens in a control scheme, and it is difficult to lay down hard and fast rules. Perhaps the most useful thing to say is that if multi-bacillary patients have in fact already received MDT of a type closely resembling the WHO regimen for two years or more, there is absolutely no point in treating them all over again with the WHO regimen. On the other hand, patients who have received only a few weeks or months of some other regimen might well qualify for a change to the regimens advised by WHO. Where facilities and staff are available, some care should be taken to follow up and assess those cases who received various regimens before the WHO recommendations were published, and to compare results with patients treated with standard WHO regimens. (If significant differences are revealed, they should be reported to WHO and other agencies without delay.)
5. WILL THE ‘MDT DRUGS’ GIVE RISE TO SERIOUS TOXIC OR SIDE EFFECTS?

It is first of all important to establish that we are using the term ‘toxic’ or ‘side effects’ in the usually accepted sense of directly damaging effects on body systems such as those which include the bone marrow, liver, kidney, etc. They should be clearly distinguished from adverse immunological reactions of the type described in Section 13 of this Guide, which may precede, accompany, or follow the use of drugs.

It is then important to consider if there is any evidence that the combinations such as dapsone and rifampicin (for the treatment of pauci-bacillary leprosy), or dapsone, rifampicin and clofazimine (for the treatment of multi-bacillary leprosy) are more toxic than dapsone mono-therapy, or combinations which have been previously used such as dapsone, isoniazid and thiacetazone. The brief answer is that there is no evidence for any unusual or unexpected toxicity from such combinations. Indeed, both from the use of ‘Isoprodian’ (dapsone, isoniazid and prothionamide in one tablet) in the years before the WHO Report of 1982, and also from the considerable experience which has already accumulated on the use of MDT as recommended by WHO, from various parts of the world, the evidence indicates that the regimens are well accepted and safe. It is nevertheless extremely important to be aware of the possible side effects of the anti-leprosy drugs in common use and, for those who are not familiar with them, there is no better account than that published by Jopling in Leprosy Review, 54, 1983, p. 270, on precisely this subject.

With regard to the thioamides (ethionamide and prothionamide), the situation is far from reassuring. They are potentially hepato-toxic and there is a possibility that this might be enhanced if they are used with rifampicin (or isoniazid, although this is not a recommended drug for MDT in the WHO Report), or if the patient is alcoholic. It should also be noted that the exact daily or twice daily dosage has yet to be established with confidence for use in leprosy. For these and other reasons (see Section 2), it is strongly recommended that clofazimine should be used as the third drug in the treatment of multi-bacillary cases, not the thioamides.

Hepatitis and jaundice

Jaundice – or any other evidence of hepatitis, whatever its origin – must be taken seriously in a patient on MDT. It is beyond the scope of this Guide to go into the clinical and laboratory procedures which must be followed, but the essential point is that all patients with jaundice or other evidence of hepatitis must be referred for specialist investigation in a centre with appropriate laboratory facilities. The cause of the trouble must be established. Anti-leprosy drug treatment must be adjusted accordingly, bearing in mind that rifampicin and the thioamides (either ethionamide or prothionamide) are potentially hazardous in this context.
6. IS MDT SAFE DURING PREGNANCY AND LACTATION?

In the case of dapsone, many thousands of women have taken this drug during pregnancy and lactation with an extremely low incidence of toxic effects, either to themselves, the foetus or the breast-fed infant. In the case of clofazimine, the manufacturers point out that the drug does indeed cross the placental barrier and that the active drug also passes into breast milk; they therefore advise caution in its use during pregnancy and lactation. But the fact of the matter is that virtually no instances of toxicity have been recorded. For rifampicin there are some risks, and the pros and cons of its use in pregnancy have been admirably summarised by Alison Summers in a letter to *Leprosy Review*, 57, 1986:

"Current consensus is that rifampicin is probably not teratogenic and that any increased risk to the foetus must be small compared to risks from other sources. Is its use justified under all circumstances? It is important to assess the possible risks in the context of leprosy. My own view, in the light of current evidence, is that I would not be happy to expose an unborn child of my own to even small possible risks if it were merely for the sake of beginning chemotherapy for non-lepromatous leprosy a few months earlier. With *lepromatous* leprosy however, the risks of transmitting the disease to others would seem to favour a decision to use rifampicin.

"However, in many leprosy-endemic areas and under field conditions, the decision is far from easy to make. For example, in some communities advice to avoid rifampicin in pregnancy might initiate unwarranted suspicion about leprosy treatment in general and, in some leprosy treatment programmes, additional complications in the treatment regimens may cause unacceptable difficulties for staff. For some patients, advice to delay starting treatment may mean they are, in fact, not seen again until the disease has caused severe and perhaps irremediable problems. However, it is in just these situations that an increased incidence of congenital malformations would easily go unnoticed.

"Administered in later pregnancy, rifampicin can, in an unknown proportion of cases, give rise to a haemorrhagic tendency in the newborn baby. This risk is easier to accept in situations where a baby with a bleeding problem is assured of appropriate treatment than it is in the circumstances of the majority of leprosy patients.

"Prescribing rifampicin during lactation is less worrying. There have been no reports of adverse effects on breast-feeding babies whose mothers were taking this drug. Such babies will ingest less than 1% of the normal therapeutic dose for infants and less than 0.1% of the dose taken by the mother. The recommendation that the breast-fed infant should be checked regularly for signs of toxicity may be impossible to follow and the suggestion of minimizing the infant's ingestion by giving rifampicin immediately after a feed and then not feeding again for several hours may be quite
inappropriate in developing countries. In most leprosy-endemic areas, the very real risks of artificial feeding must far outweigh any small theoretical risk from rifampicin in breast milk.”

7. WHAT IS THE MANAGEMENT OF PATIENTS WITH ACTIVE, CO-EXISTENT LEPROSY AND TUBERCULOSIS?

There is no straightforward answer to this question, so it is perhaps fortunate that the situation does not, in practice, arise as frequently as had been envisaged when MDT was first introduced. Each case has to be assessed individually, with regard to the relative severity of the two diseases and the drugs which are locally available and in current use. However, the following guidelines may help:

i. Leprosy is rarely a life-threatening condition, whereas the opposite is often true for TB, especially in its pulmonary form.

ii. It may therefore be necessary to give priority to the treatment of the patient’s TB, at least in the initial phase.

iii. Of the drugs which are advised for leprosy, dapsone and clofazimine have no practical application in the treatment of TB, but rifampicin and the thioamides are effective against both diseases. The thioamides were in fact used for the treatment of TB several years ago, but they were abandoned, mainly because of their side effects.

iv. In the case of a patient with pauci-bacillary leprosy on treatment with dapsone and rifampicin (for a period of six months), it is unlikely that the addition of drugs for the treatment of TB will cause any problem. The initial phase of treatment with anti-tuberculosis drugs may in any case include rifampicin. The ingestion of daily dapsone (for the treatment of leprosy) is very unlikely to interfere with any anti-tuberculosis drugs prescribed.

v. In the case of a patient with multi-bacillary leprosy taking dapsone, clofazimine and rifampicin (for a minimum of two years), the same comments hold true for dapsone and rifampicin. With regard to clofazimine, it is unlikely that the monthly supervised dose of 300mg will create any difficulty, but the ingestion of 50mg daily – as recommended by WHO – must be assessed in relation to the number of anti-tuberculosis drugs prescribed and the possibility of gastro-intestinal intolerance.

vi. The most important point to make in the treatment of patients with co-existent leprosy and TB centres on the matter of liver damage. It should be clearly understood that rifampicin, the thioamides (either ethionamide or prothionamide), pyrazinamide and isoniazid are all potentially hepato-toxic, especially if given in combination. Malnutrition and alcoholism may accentuate the risks.

vii. It is difficult to avoid the conclusion that all patients with co-existent leprosy and TB should be in close touch with a medically qualified specialist in these diseases or a general physician (internist).
8. HOW IMPORTANT IS THE EXAMINATION OF SLIT-SKIN SMEARS IN IMPLEMENTING MDT?

It is certainly extremely important, provided the smears are properly selected, taken, fixed, despatched, stained and interpreted. There is now abundant evidence that poor quality technical and laboratory work in this context is not only useless, but likely to be misleading. If the technical aspects of this procedure have not been properly set up and are unreliable, it is probably better, in most circumstances, to rely on clinical observations for diagnosis and classification. Having said this, it is, however, necessary to record that WHO base their crucial division of cases into pauci- and multi-bacillary groups (page 3) partly on the use of slit-skin smears. Furthermore, their Expert Committee on Leprosy proposed, in 1988, an important change in this context:

"Pauci-bacillary leprosy will include only smear-negative indeterminate (I), polar tuberculoid (TT) and borderline tuberculoid (BT) cases in the Ridley-Jopling classification or indeterminate (I) and tuberculoid (T) cases in the Madrid classification. Any case belonging to these types but showing smear positivity will be classified as multi-bacillary for purposes of multi-drug therapy programmes."

To return to the point above about acceptable standards for laboratory work; it may be helpful to concentrate on the establishment in a country or region of one, absolutely reliable, centre of excellence, with properly trained staff and good facilities, rather than attempting to cover the area with numerous smaller units where supervision is impossible and standards of work unreliable. The despatch of fixed slides to a central unit from various parts of the area is in fact much easier than the handling of sputum slides in tuberculosis, and in practice, has not been found an insuperable difficulty under field conditions.

For those who need information on slit-skin smear techniques, the following publications are available:

i. Manual of Basic Techniques for a Health Laboratory, WHO, 1211 Geneva 27, Switzerland, 1980. This is an extremely comprehensive manual of nearly 500 pages, with information on a wide range of laboratory procedures, including the staining of smears for leprosy (and tuberculosis). The cost is approximately US$13.00.

ii. A Medical Laboratory for Developing Countries, Maurice King, Oxford University Press, Walton Street, Oxford, UK, 1973. This is a rather similar manual, again of considerable length, covering all important procedures, including the examination of smears in leprosy and tuberculosis. Cost approximately US$5.00.

iii. Medical Laboratory Manual for Tropical Countries, Monica Cheesbrough, Tropical Health Technology, 14 Bevills Close, Doddington, Cambridgeshire, PE15 0TT, UK, 1984. An extremely valuable publication avail-
able at remarkably low cost, covering all aspects of bacteriological examination in leprosy and tuberculosis. Cost approximately US$12.50.

iv. Technical Guide for Smear Examination for Leprosy by Direct Microscopy, Leiker and McDougall, 1983. This is a booklet of only 35 pages, in a light-weight, inexpensive format suitable for more or less mass distribution to central and peripheral laboratories working with leprosy patients. English, French, Spanish, Portuguese and Arabic versions are available. (See Appendix 1.)

Appendix 4 is a diagram or chart giving details of the vitally important Bacteriological Index (BI).

Appendices 5 and 6 show outline diagrams and a grid system which may be of considerable practical value in accurately recording the site from which slit-skin smears or biopsies have been taken. This is particularly important in relapse lesions, which may be small and localised and which not infrequently have a much higher bacillary content than is found at other sites smeared. (The diagrams and grids are also valuable for the routine drawing of skin lesions and this can be particularly useful in distinguishing relapse from reaction; see Section 13.)

9. SHOULD MDT BE OFFERED ON AN OUT-PATIENT OR IN-PATIENT BASIS?

There is no doubt that the WHO recommendations are based on an outpatient approach and indeed this principle has been accepted in most leprosy control programmes, especially where large numbers of patients are concerned and financial resources limited. However, as in the case of chemotherapy for tuberculosis, there are some exceptions, and in certain circumstances a period of in-patient treatment and supervision may be considered. In-patient care is often essential for leprosy patients suffering from adverse immunological reactions, including neuritis.

A distinction has to be made between the admission – it sometimes amounts to banishment – of a patient to a traditional leprosarium, which may be isolated, poorly staffed and lacking in expert supervision, as against admission to a hospital or special unit, where conditions may be vastly superior. In quite a number of areas (e.g. East Africa, Nepal) the availability of beds and the difficulties of supervising multiple drugs in out-patients have led to the policy of admitting leprosy patients for a period of weeks or a few months. Although by no means universally accepted by patients, even where such policy is standard, it appears that many will accept an initial period of hospitalisation. This has been found to be beneficial, not only in order to ensure a definite period of fully supervised MDT, but also to make sure that the patient has a good diet and ample opportunity for instruction about drugs and the personal care of anaesthetic limbs and of eyes. The importance of regular drug intake and attendance after discharge from hospital can also be established during such a period.
It must be kept in mind that in-patient treatment, even if simple and basic, costs a great deal more than out-patient treatment and in some circumstances it may divert attention and resources away from case-finding, diagnosis, classification and treatment of much larger numbers of patients, some of whom may be infectious or contagious. In general, the drug regimens discussed in this Guide refer to out-patients, as do all the attendant problems of supervision, etc.

10. WHAT IS THE DEFINITION OF A SUPERVISOR FOR ‘SUPERVISED’ CHEMOTHERAPY?

Particularly in view of the expense, but also because of the medical need to see patients on rifampicin and clofazimine at regular intervals, the element of supervision in these regimens is crucial. The exact definition of a ‘supervisor’ in this context is not easy, but the general view in leprosy circles is that a supervisor should be a responsible member of the medical service. It must, however, be admitted that in some parts of the world (for instance Brazil, Nepal, Sudan) geographic and logistic problems make it virtually impossible to arrange for a member of the medical service to supervise the monthly doses of rifampicin and clofazimine. In such circumstances, rather than totally deny the patient the benefit of MDT, it may be necessary to consider supervision by a local ‘chief’, schoolmaster or other responsible person. Such deputies should themselves be supervised by a member of the health staff as frequently as conditions allow.

11. ON COMPLETION OF MDT SHOULD PATIENTS BE FOLLOWED UP AND, IF SO, FOR HOW LONG?

Ideally patients – whether pauci- or multi-bacillary – should certainly be followed up, but it has to be recognised that by no means all leprosy control programmes have the staff, time, money and transport to make this possible. The priority in MDT should be the detection, classification and drug treatment of as many patients with leprosy as possible, and it would be wrong to give the impression that follow-up should take priority over these basic activities.

Having said this, every effort should be made to ensure that facilities are available to follow up at least a certain number of those who have been treated with the MDT regimens recommended by WHO. As we shall indicate below, it may be possible to concentrate time and effort on selected groups of patients who are particularly important in this respect, rather than attempting to follow up all patients treated. Before going into these details, it is worth repeating here that the term ‘released from chemotherapy’ does not necessarily correspond to ‘released from care’. It is in fact confidently expected that a considerable number of patients, for various reasons, will remain under care, in some cases for long periods, after stopping MDT. All patients should be encouraged to report back and to contact the leprosy or general health service at any time, particularly if they have new symptoms, complications or
signs of relapse. Many patients who remain under care will therefore be seen regularly enough to be included in attempts at follow-up or assessment, in some cases for several years. Appendix 7 outlines the main steps between starting MDT and completing the period of surveillance.

Follow-up of pauci-bacillary patients

After stopping treatment, WHO recommends that pauci-bacillary patients should be kept under surveillance for a minimum of two years, with clinical examination at least every 12 months (Epidemiology of Leprosy in Relation to Control, Report of a WHO Study Group, Technical Report Series 716, WHO, Geneva, 1985). This should certainly be attempted wherever possible; but it has to be admitted that not all programmes will be able to maintain such standards and some managers have decided that, for instance, they will not actively follow up pauci-bacillary patients who were inactive at the outset. On the other hand, if the work load is not excessive and adequate numbers of trained staff are available, valuable information will be obtained, notably about relapse and reaction, if patients can be examined as advised by WHO above, or even more frequently.

Follow-up of multi-bacillary patients

After stopping treatment, WHO recommends that multi-bacillary patients should be kept under surveillance for a mimimum of five years, with clinical and bacteriological examination at least every 12 months (see reference above). This is certainly ideal, but here again it has to be acknowledged that lepromatous patients who have been under treatment for many years before MDT was introduced are unlikely to attend for long periods of surveillance, especially if they are symptom-free and not deformed. The decision on a period of surveillance depends heavily on local conditions, workload, number of staff available, etc, but one point has to be emphasised: in the case of multi-bacillary patients who stop treatment at two years but who are still positive on slit-skin smears, it is extremely important to follow them up, preferably as advised above by WHO.

12. IF PATIENTS INTERRUPT OR STOP TREATMENT OF THEIR OWN ACCORD, WHAT SHOULD BE DONE?

With both pauci- and multi-bacillary patients there has always been a problem with poor attendance or non-attendance, and although the overall shorter periods of treatment currently advised by WHO may well encourage patients to 'stay the course', there will undoubtedly be many who fail in this respect. It has already become clear that some patients attend for a few weeks or months then drop out, sometimes to reappear after a variable period, sometimes not. It must also be remembered that interruption of treatment may be for some extremely valid reason, such as pregnancy, serious illness, floods, harvesting, or the prolonged failure of transport. Such deserving cases obviously require special consideration; but persistent defaulters and those who stop their treatment of their own accord for no good reason, should be interviewed with
care. Unless they are psychologically abnormal, it is not infrequent to find
that there is in fact some quite good reason for their apparent lack of
cooperation, which can be remedied. The time devoted to such investigative
work is likely to be fully justified, since it will contribute to the group feeling
in both patients and staff that a very high standard of regular attendance and
ingestion of prescribed medication is not only expected by the medical ser-
vice, but vital for a successful outcome in the individual patient.

**Pauci-bacillary leprosy**

If treatment is interrupted (stopped by the patient), the regimen should be
recommenced where it left off to complete the full course. As this may occur
on more than one occasion, it has already become clear that some limit must
be placed on the total period of time during which MDT can be attempted for
this category of patient. The Medical Commission of the International Fed-
eration of Anti-Leprosy Associations (ILEP) has proposed the following:
“...In irregular pauci-bacillary patients...the maximum period of treatment
should be 12 months, at the end of which chemotherapy is stopped...”

**Multi-bacillary leprosy**

Patients with active, smear-positive, multi-bacillary leprosy are obviously of
extreme importance from the public health point of view, and virtually no
excuse should be accepted for serious irregularity, or for the patient stopping
treatment of his/her own accord. Despite the work involved, very consider-
able efforts should be made to trace irregular patients in this category and to
ensure that they continue regular treatment with three drugs. In the case of
multi-bacillary patients who are negative at the time of starting MDT, ILEP
has advised that the standard, minimum treatment period of two years should
not be allowed, in practice, to extend over more than 36 months.

It must be stressed that these recommendations are a) provisional and poss-
ibly not universally acceptable; and b) distinctly ‘second best’ as far as oper-
ational technique is concerned. They are certainly not to be encouraged or
allowed except in special cases.

13. **AFTER PATIENTS HAVE STOPPED TREATMENT, HOW DOES
ONE RECOGNISE RELAPSE? HOW CAN RELAPSE BE
DISTINGUISHED FROM THE VARIOUS FORMS OF
IMMUNOLOGICAL REACTION?**

The definition of relapse in leprosy has given rise to argument and is still far
from clear. Both in practical field work and also in the literature, there has
been confusion between a) simple relapse in the sense of a return of the
disease; b) ‘acute exacerbation’; and c) various forms of ‘reaction’ which are
based on immunological responses in the patient and which are in themselves
often damaging.

In relation to MDT, it is now more important than ever to try to establish
some distinction between relapse or recurrence of the disease which is due to
insufficient or inadequate drug intake on the one hand; and an adverse or
damaging immunological response on the other. The accurate recognition of
relapses which occur in patients who have a) taken their prescribed medica-
tion with great care and regularity; or b) failed to take medication as pre-
scribed, is now of the greatest importance, as is also the precise timing of such
events. In both pauci- and multi-bacillary groups, we need much more in-
formation from various parts of the world and in different ethnic groups, on
the incidence of immunological reactions before, during and after MDT.

An operational definition of 'relapse'

Although the word 'relapse' in leprosy could cover a number of different
situations, we believe that the most useful definition for operational purposes
is: "A return of active disease in a patient who has apparently completed a
prescribed course of treatment, and whose treatment has therefore been
stopped by an authorised member of the health services". We would prefer
(and advise) that this definition does not include patients with the various
types of adverse immunological reaction which will be described below.

Such a return of active disease may occur for any of the following reasons:

i. The patient has simply not taken (ingested) the prescribed medication,
and is thus inadequately treated.

ii. The prescribed medication has been taken, but the patient has leprosy
bacilli which are resistant to one or more of the drugs used.

iii. The prescribed medication has been taken and, although it was effective
against the patient's original leprosy infection, a second or re-infection has
been acquired.

Failure to take prescribed medication is common and worldwide, and is
probably the most frequent cause of relapse at the present time. Dapsone
resistance may occur, but it is precisely to combat this that WHO has placed
such great emphasis on the need to treat all leprosy patients with more than
one drug, and it is hoped and expected that the 1982 regimens will prevent
this possibility occurring. Re-infection is probably unusual and has so far been
suspected and discussed as a possibility rather than proven, but it should be
kept in mind.

The patterns of relapse in pauci-bacillary leprosy

Not a great deal is known about these since accurate observations have not
yet been made on a large number of patients. Using the symbol I for
indeterminate, and the Ridley-Jopling system for the determined forms of
leprosy (TT = tuberculoid; BT = borderline-tuberculoid; BB = mid-border-
line; BL = borderline-lepromatous and LL = lepromatous), the following are
the main possibilities in patients originally grouped as pauci-bacillary:

i. Relapse may occur with skin and nerve features of the original classifica-
tion.
ii. The manifestations of relapse may be clinically and immunologically 'worse' than the original classification, i.e. a patient originally classified as BT may relapse with BB or BL features. (In both instances, the main grouping would of course then change to multi-bacillary.)

iii. The manifestations of relapse may, in the above sense, be 'better', i.e. a patient originally BT (this being the 'maximum' for pauci-bacillary cases) could relapse with TT features. (A relapse with indeterminate features is theoretically possible but would be extremely difficult to prove, even with the histopathological examination of a biopsy.)

Apart from these possibilities, some of which still need confirmation in a large series of patients, there are no 'peculiar' or characteristic features of relapse in pauci-bacillary patients, either in skin or nerves, though it is possible that they exist but have not yet been clearly documented. Establishing the diagnosis of relapse in pauci-bacillary leprosy calls for examination by an experienced observer. Slit-skin smear examination is virtually essential and in some cases, especially for research purposes, the histopathological examination of a biopsy is indicated.

The patterns of relapse in multi-bacillary leprosy

Using similar terminology and symbols, the possibilities are as follows:

i. Relapse may occur with features of the original classification.

ii. The manifestation, in the sense described above, may be 'worse', i.e. a patient originally BB or BL may relapse with LL features.

iii. The manifestations, again in the sense above, may be 'better', i.e. a patient originally LL may relapse with a borderline form of leprosy, such as BL, BB or even BT. This happens not infrequently and has been well described in the literature.

iv. Curious lesions of a type called 'histoid' may occur and, in a considerable number of cases, these are peculiar to relapse caused by drug resistance (essentially to dapsone). A full description is available in any textbook, but briefly, these are small localised lesions of 'button mushroom' type which tend to occur in unusual situations, such as mid-line of chin, antecubital fossa, surface of the eye, etc. They contain vast numbers of bacilli and a biopsy is often diagnostic. As with pauci-bacillary leprosy, confirmation of relapse in multi-bacillary leprosy calls for expert help.

Immunological reactions in pauci- and multi-bacillary leprosy

A full description of this complex subject is beyond the intention of this Guide and standard textbooks should be consulted. It is necessary here only to point out:

i. The terminology of reactions in leprosy is somewhat confusing, partly because of the use of a number of synonyms. Essentially there are two main types. Reactions in non-lepromatous leprosy are based on cell-mediated
immune mechanisms and the most important and best-defined of them is called a reversal reaction, the synonyms for which are ‘upgrading’ and ‘Type 1’. (These three terms thus refer to the same phenomenon.) Reactions in lepromatous leprosy are either based on, or associated with, immune-complex disturbances involving antigen, antibody and complement and, although often referred to simply as ‘ENL’ reactions (since erythema nodosum lepromatum on the skin is a prominent clinical feature), this is an inadequate term and ‘lepromatous reaction’ or ‘immune-complex reaction’ are far better. This type is also called ‘Type 2’. All these terms – ENL, lepromatous reaction, immune-complex reaction and Type 2 – thus refer to the same phenomenon.

ii. This division of reactions – between non-lepromatous and lepromatous cases – is fairly accurate and works well in practice, but like all divisions in medicine, it is by no means invariable. There are some mixed reactions which can be difficult to interpret and, if there is any doubt about the clinical findings, such patients should always be referred to an experienced observer.

iii. The timing of the reversal (upgrading, Type 1) reactions which occur in borderline-tuberculoid (BT), mid-borderline (BB) and borderline-lepromatous (BL) cases is of considerable interest and importance. There is evidence from some parts of the world that reactions in BL cases may occur much later, following the initiation of drug treatment, than in BT and BB cases. In view of the difficulties of distinguishing relapse from reaction, this aspect of leprosy calls rather urgently for further observation and field research.

**How can relapse be distinguished from reaction?**

This is perhaps the most difficult question raised in this Guide. Some of the answers are known, and have been set out in the accompanying table; but many are unknown, and call for a great deal more clinical observation and analysis. It is no exaggeration to say that this is the aspect of MDT implementation which most urgently calls for operational research from those who are actually implementing the regimens in the field, and who have the opportunity to keep good records and report results. Information is required on the incidence of various reactions before, during and after MDT in both pauci- and multi-bacillary groups. Where possible, it would also be of the greatest help to have some idea of the incidence of reactions with MDT as compared with previous dapsone mono-therapy.
Table 1 lists and compares some of the main features of relapse and reaction. It is more than likely that it will require modification and revision in the light of experience, which is currently being obtained by those who are already treating pauci-bacillary leprosy with MDT on a large scale.

**TABLE 1. LEPROMATOUS ('ENL' OR IMMUNE-COMPLEX) REACTION VERSUS RELAPSE WITH 'HISTOID' LESIONS; ESSENTIAL POINTS OF DIFFERENCE**

<table>
<thead>
<tr>
<th>Clinical findings</th>
<th>Lepromatous reaction</th>
<th>Relapse with 'histoid' features</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fever, general systemic disturbance</td>
<td>Common</td>
<td>No</td>
</tr>
<tr>
<td>Neuritis – tender nerves, loss of function</td>
<td>Common</td>
<td>Unusual</td>
</tr>
<tr>
<td>Nodules tender</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Nodules transient (come and go)</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Nodules in chronic cases confluent</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Nodules always circumscribed and shiny</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>Oedema present</td>
<td>Common</td>
<td>No</td>
</tr>
<tr>
<td>Hyperpigmentation present in areas where nodules have disappeared</td>
<td>Common</td>
<td>No</td>
</tr>
<tr>
<td>Nodules in areas previously involved</td>
<td>Yes</td>
<td>Unusual</td>
</tr>
<tr>
<td>Skin smears</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lepromatous reaction</td>
<td>Routine sites have a Bacteriological Index (BI) of 1 to 4+ with Morphological Index (MI) = 0</td>
<td>Routine sites have a BI of 0 or only 1 to 2+, whereas new (relapse) lesions have a BI of 4 to 6+, with a high MI (up to 50%)</td>
</tr>
</tbody>
</table>

Relapse lesions with histoid features may occur on unusual sites – backs of calves, thighs, buttocks, lumbar region, around the umbilicus, ante-cubital fossa, palate and surface of the eye.

[With grateful acknowledgements to Dr Harold Wheate, London.]
Table 2 deals with reversal (upgrading) reactions, based on cell-mediated immune processes. In some cases it must, however, be remembered that there may also be difficulty in distinguishing lepromatous (ENL, immune-complex) reaction from the lesions which occur in the histoid form of leprosy described on page 14, Section iv.

### TABLE 2. REVERSAL REACTION (UPGRADING REACTION) VERSUS RELAPSE; ESSENTIAL POINTS OF DIFFERENCE

<table>
<thead>
<tr>
<th>Classification of patient affected</th>
<th>Reversal (upgrading) reaction</th>
<th>Relapse</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bacillotology</td>
<td>Compared with previous findings bacillary numbers in skin smears or biopsies are reduced</td>
<td>Bacillary numbers are increased</td>
</tr>
<tr>
<td>Site of lesions</td>
<td>Reactions occur mainly if not exclusively at the site of skin and/or nerve lesions which were present at the outset. Some apparently new lesions may in fact be ‘revealed’ (made more obviously visible) by the reactional process</td>
<td>Either in the original lesions or at new sites, or both. In contrast to rection, the original lesion or lesions in relapse may increase in size (extent or surface area)</td>
</tr>
<tr>
<td>Timing</td>
<td>Mainly within a few weeks or months of starting treatment, although reactions also occur before treatment in some cases. Reactions may occur up to 1 year, less commonly up to 2 years after starting treatment; this may also apply for pauci-bacillary patients who receive a period of only 6 months’ treatment</td>
<td>Relapse due to drug resistance may occur during treatment or at any point after stopping treatment. Relapse due to the growth of persisting organisms, after a long course of treatment, may take some years to appear</td>
</tr>
<tr>
<td>Pain and/or tenderness in skin and/or nerve lesions</td>
<td>Frequent; characteristic; nerve pain and tenderness may be extremely severe</td>
<td>Does not occur</td>
</tr>
<tr>
<td>General condition</td>
<td>Frequently affected; there may be malaise, fever, oedema of the hands and feet (not necessarily related to lesions in those parts of the body) etc</td>
<td>Not affected</td>
</tr>
<tr>
<td></td>
<td>Reversal (upgrading) reaction</td>
<td>Relapse</td>
</tr>
<tr>
<td>-------------------------</td>
<td>------------------------------</td>
<td>------------------------------</td>
</tr>
<tr>
<td><strong>Speed of onset</strong></td>
<td>Usually rapid; may be extremely rapid, i.e. within a few hours, overnight</td>
<td>Slow, gradual</td>
</tr>
<tr>
<td><strong>Frequency of occurrence</strong></td>
<td>Frequent, common; probably occurs in about 25% of all borderline (dimorphous) patients under treatment</td>
<td>Not uncommon in poor quality control schemes, especially if low-dose, irregular dapsone has been used extensively. Should be uncommon, hopefully very rare, if multiple drugs are implemented regularly and for long enough</td>
</tr>
<tr>
<td><strong>Cause (aetiology)</strong></td>
<td>Immunological reaction of delayed hypersensitivity type, accompanied by a rapid increase in cell-mediated immune responses; exact precipitating factors unknown</td>
<td>Either a) prescribed drugs have not been taken as directed, regularly and for long enough, so that the patient is inadequately treated, or b) drug resistance</td>
</tr>
<tr>
<td><strong>Possible relation to malaria, TB, other infections, trauma, abortion, pregnancy, intake of other drugs, etc</strong></td>
<td>Apparently frequent, but by no means invariable</td>
<td>Unclear, but conditions causing debility or reduction in normal immunological responses (i.e. malnutrition) might predispose to relapse in general, though not to relapse due to drug resistance</td>
</tr>
</tbody>
</table>
14. WHAT DOES OF DRUGS ARE SUITABLE FOR MDT IN CHILDREN?

As with other drugs, such as those used in tuberculosis, it is possible to arrive at appropriate doses for children based on body surface, weight or age. (It might be possible to use height, if data were available for a given country or community, accurately relating height to weight and/or age, but this has rarely been done.)

In practice, accurate scales are seldom available, especially under field conditions, so that weight may be difficult to assess. However, experienced staff who know their own people well acquire considerable skill in estimating weight. If common sense is combined with clinical observation and any information which may be forthcoming from the parents on the date of birth, it is also possible to use age with a fair degree of accuracy as a basis for drug dosage in leprosy. The relevant anti-leprosy drugs are dapsone, rifampicin and clofazimine, and suitable dosages for children based on age or weight are as follows:

**DOSAGES BASED ON AGE**

*Pauci-bacillary Leprosy (2 drugs – Dapsone and Rifampicin)*

<table>
<thead>
<tr>
<th>Age groups</th>
<th>Dapsone: daily dose, unsupervised</th>
<th>Rifampicin: monthly dose supervised</th>
</tr>
</thead>
<tbody>
<tr>
<td>Up to 5 years</td>
<td>25mg</td>
<td>150-300mg</td>
</tr>
<tr>
<td>6-14 years</td>
<td>50-100mg</td>
<td>300-450mg</td>
</tr>
<tr>
<td>15 years and above*</td>
<td>100mg</td>
<td>600mg</td>
</tr>
</tbody>
</table>
* i.e. use adult doses

*Multi-bacillary Leprosy (3 drugs – Dapsone, Rifampicin and Clofazimine)*

<table>
<thead>
<tr>
<th>Age groups</th>
<th>Dapsone: daily dose, unsupervised</th>
<th>Rifampicin: monthly dose supervised</th>
<th>Clofazimine: Unsupervised dose</th>
<th>Monthly dose supervised</th>
</tr>
</thead>
<tbody>
<tr>
<td>Up to 5 years</td>
<td>25mg</td>
<td>150-300mg</td>
<td>100mg once weekly</td>
<td>100mg</td>
</tr>
<tr>
<td>6-14 years</td>
<td>50-100mg</td>
<td>300-450mg</td>
<td>150mg once weekly</td>
<td>150-200mg</td>
</tr>
<tr>
<td>15 years and above*</td>
<td>100mg</td>
<td>600mg</td>
<td>50mg daily</td>
<td>300mg</td>
</tr>
</tbody>
</table>
* i.e. use adult doses
DOSAGES BASED ON WEIGHT

**Pauci-bacillary Leprosy (2 drugs – Dapsone and Rifampicin)**

<table>
<thead>
<tr>
<th>Weight</th>
<th>Dapsone: daily dose, unsupervised</th>
<th>Rifampicin: monthly dose supervised</th>
</tr>
</thead>
<tbody>
<tr>
<td>Up to 20kg</td>
<td>25mg</td>
<td>150mg</td>
</tr>
<tr>
<td>21-30kg</td>
<td>25-50mg</td>
<td>300mg</td>
</tr>
<tr>
<td>31-50kg</td>
<td>50-75mg</td>
<td>450mg</td>
</tr>
</tbody>
</table>

**Multi-bacillary Leprosy (3 drugs – Dapsone, Rifampicin and Clofazimine)**

<table>
<thead>
<tr>
<th>Weight</th>
<th>Dapsone: daily dose, unsupervised</th>
<th>Rifampicin: monthly dose supervised</th>
<th>Clofazimine: Unsupervised monthly dose</th>
<th>Monthly dose supervised</th>
</tr>
</thead>
<tbody>
<tr>
<td>Up to 20kg</td>
<td>25mg</td>
<td>150mg</td>
<td>100mg once weekly</td>
<td>100mg</td>
</tr>
<tr>
<td>21-30kg</td>
<td>25-50mg</td>
<td>300mg</td>
<td>150mg once weekly</td>
<td>150-200mg</td>
</tr>
<tr>
<td>31-50kg</td>
<td>50-75mg</td>
<td>450mg</td>
<td>50mg daily</td>
<td>200-300mg</td>
</tr>
</tbody>
</table>

In the above tables, it should be noted that whilst dosages in children for dapsone and rifampicin are reasonably well established, those for clofazimine are not. In giving a figure for the unsupervised dose and the monthly supervised dose, it is possible that we are erring on the side of caution. This drug may, however, be cumulative in the tissues and we hesitate to suggest dosages for children which may be excessive. Even with the doses recorded in the above table, the effects of clofazimine on children up to five years, and from 6-14 years of age (and of corresponding weights) should be monitored with some care.
15. HOW EXPENSIVE IS MDT?

At the risk of stating the obvious, it is clearly more expensive to treat leprosy with two or three drugs than to treat it with one. Furthermore the standard drug, dapsone, used as mono-therapy in the past, is remarkably cheap. Leaving aside the possible use of the thioamides (ethionamide or prothionamide; see page 24 of the WHO Study Group Report, 1982), the two other drugs to be used in the advised regimens, namely rifampicin and clofazimine, are both expensive.

With regard to the cost of treating the two main groups of patients, the facts are as follows:

**Pauci-bacillary leprosy**

The cost of dapsone and rifampicin for the entire period of six months is approximately US$3, depending on the quantity purchased.

**Multi-bacillary leprosy**

The cost of the minimum period of two years' treatment with three drugs – dapsone, rifampicin and clofazimine – is approximately US$50. Each additional year after that costs approximately US$25. (Remember that treatment should ideally continue until slit-skin smears are negative. For an untreated lepromatous (LL) case with a high bacteriological index (BI) at the outset, this could take at least five years.)

It will thus be apparent that the first few years (the initial phase) of MDT are going to be expensive, and in some leprosy-endemic countries the outset expenditure on drugs has already been found to be almost prohibitive. It must, however, be pointed out that approximately 80% of all the leprosy patients in the world are pauci-bacillary. After their period of six months' dual therapy (at a very reasonable cost), many will be released from control without further need to report back. Some will of course remain under care (see Appendix 7), but many of these will in turn eventually be released. For pauci-bacillary cases, the workload on the leprosy control service is therefore likely to drop, in some cases very markedly indeed, quite soon after the introduction of MDT. Furthermore, in the case of multi-bacillary patients, many will be negative on smears after only two years of treatment, and can therefore stop treatment altogether.
16. WILL THE IMPLEMENTATION OF MDT LEAD TO THE CONTROL, AND PERHAPS EVEN TO THE ERADICATION, OF LEPROSY?

It is certainly too early to say if this will happen. What can be stated with considerable confidence, however, is that IF a large number of those in charge of leprosy control programmes decide to implement MDT along the lines recommended by WHO, remarkable improvements will be seen within the next few years. The decision to implement MDT (or not) involves factors which are by no means only medical. Political factors, using the phrase in its broadest sense, will also be of paramount importance. Furthermore, as already indicated in this Guide, there is very much more to the conquest of leprosy than the mere availability of the necessary drugs, or the money to purchase them. Social and psychological factors need constant attention and any attempt to control this disease will fail unless these are constantly kept in mind.

These reservations apart, it can be said that MDT, as recommended by WHO or along very similar lines, is more than likely to have beneficial effects on the world leprosy situation, the most important of which may be summarised as follows:

i. The problems of dapsone resistance and bacillary persistence (see pages 9-16 of the *WHO Study Group Report of 1982*) are being addressed.

ii. For both pauci- and multi-bacillary leprosy patients, it is likely that the recommended regimens of MDT will prove highly beneficial to the individual.

iii. There is a strong possibility that the application of MDT will greatly reduce the infectious/contagious pool of leprosy cases in the community, thus breaking the chain of transmission.

iv. There is already encouraging evidence from various sources that the early use of MDT will actually reduce, and perhaps eventually prevent, the development of disability and deformity due to nerve damage. It is certainly beyond doubt that the best way to prevent neuritis is by early detection and treatment, together with good clinical observation to 'spot' the threat of potential nerve damage at the earliest possible moment.

v. The whole concept of 'new' regimens, with relatively short periods of treatment, has given a new impetus and drive to the treatment of leprosy which was lacking in the previous era of dapsone mono-therapy.

vi. Finally, the challenge of MDT has already stimulated programme managers and leprologists in many parts of the world fundamentally to assess their case-load of registered patients with regard to activity, inactivity and the possibility of release from chemotherapy (or from control) of vast numbers of people. This factor alone, amongst all the other benefits which are likely to come from the implementation of MDT, may be predicted as having an astounding effect in clarifying the real situation and the size of the 'leprosy problem' in many leprosy-endemic areas.
17. WHAT CAN BE DONE TO ENSURE THE PROPER USE OF THE DRUGS RECOMMENDED FOR THE TREATMENT OF LEPROSY?

A great deal can be done! Within the subject of MDT for leprosy, it is probably true to say that the area which most urgently calls for study and improvement centres on the proper use of the available drugs by patients. Neither money, nor the availability of the drugs, nor the expert advice given by WHO will control leprosy if we ignore the patient and his/her attitude to medication.

To ensure the proper use of drugs, five important areas have been identified in a Report on an Informal Working Group on Educational Material for Patients, convened by the WHO Action Programme on Essential Drugs, New Delhi, October 1985, (DAP/85.10). They are:

i. accurate diagnosis,
ii. rational prescription,
iii. correct dispensing,
iv. suitable packaging, and
v. adequate, clear instructions to the patient.

In leprosy, some progress has been made in the first three areas but less attention has been paid to packaging and labelling. The handing out of drugs screwed up in a newspaper – or even loose in the hand – is commonplace, although it is almost certainly counter-productive. Attempts should be made to develop some form of 'respectable' container from locally available materials (card, plastic, glass, etc) and to ensure that it is properly labelled. A high percentage of leprosy patients or their close family members can understand simple instructions and diagrams about drugs and how often to take them. There is therefore little excuse for not providing appropriate written instructions, in the local language, for patients on MDT for pauci- or multi-bacillary leprosy.

Blister-calendar packs for multiple drug therapy

Blister-calendar packs for MDT are now commercially available from two different companies i) Ciba-Geigy, CH-4002, Basle, Switzerland and ii) Pharmanova, PO Box 10, Industrieparken, DK-2750 Ballerup, Copenhagen, Denmark. Both produce packs suitable for the treatment of patients with either pauci- or multi-bacillary leprosy. In Appendices 9 and 10 we print diagrams of the kind of pack which may be useful in this context, illustrating the way in which the calendar format may aid compliance. Such packs, understandably, are more expensive than loose drugs, but in view of the crucial importance of getting patients to actually ingest (take, swallow) their drugs regularly and in the correct dosage, for an adequate period of time, they may well prove cost-effective. They are already extensively used in leprosy (and tuberculosis) programmes in India, the Philippines and Thailand.
18. AIDS – WILL THE IMMUNE DEFICIENCY SYNDROME HAVE AN EFFECT ON PATIENT CARE AND LEPROSY CONTROL?

Fortunately there is, so far, no definite evidence that the pandemic of AIDS is having a detrimental effect on either patient care or leprosy control programmes. However, in the case of tuberculosis, in which disease the organisms divide much faster and the development of clinical disease is also faster, there is already evidence that the suppression of the immune system in AIDS may render more patients susceptible and produce problems for the control of the disease in the community. In the case of leprosy, it is too early to say if the continuing spread of AIDS will either cause deterioration of the disease in patients already affected, or impair their response to treatment, or will impede attempts to limit the spread of infection. Furthermore, amongst the 5-10 million people who are estimated by WHO to be HIV-positive already, we do not know how many of them may be rendered unusually susceptible to leprosy. Finally, in some countries, notably Africa and South America, there is a sinister possibility that the numbers of cases of AIDS and AIDS-related diseases may be so great and the consequent burden on national finances and health services may become so heavy that other diseases, including leprosy, are neglected.

With regard to possible risks to health staff handling patients with AIDS, detailed instructions have been issued by WHO – Guidelines for personnel involved in the collection of skin smears in leprosy control programmes for the prevention and control of possible infection with HIV (WHO/CDS/87.1) This paper should be studied carefully by those responsible for control programmes. Somewhat similar precautions should be taken with regard to minimising the risk of spread of infection with hepatitis B virus under both field and laboratory conditions.

Perhaps the most important message with regard to AIDS for those working in leprosy (and tuberculosis) control is that the implementation of MDT, under appropriate conditions, should be pursued without delay. Time is not on our side.

19. IS THE IMPLEMENTATION OF MDT IN LEPROSY PROCEEDING FAST ENOUGH AND COVERING ADEQUATE NUMBERS OF PATIENTS?

The brief answer has to be – no. The WHO recommendations on MDT were clearly published and widely distributed in 1982 and although many leprosy-endemic countries have implemented MDT to some extent, the world picture of coverage to date (late 1988) is far from satisfactory. Of the 10-12 million people estimated by WHO to have leprosy, about half have been officially registered as leprosy patients and of these only about a quarter are receiving regular treatment. By mid-1988 just over 2 million patients had been put on MDT and of those a quarter had completed treatment and were no longer considered to have active leprosy. Generally speaking the percentages of patients on MDT, or already treated, are disconcertingly low, although the
figures are improving. The speed of implementation and the numbers of patients covered leaves much to be desired and there is now an increasing acceptance in leprosy circles that this can only be improved by changing from a vertical (specialised) approach to a horizontal (general) service, including the primary health care approach. This, if properly planned, should increase case-finding, increase the number of patients treated with MDT and decrease the social and psychological stigma associated with the disease. The challenge to health planners, programme managers, national and international agencies in bringing about the change from vertical to horizontal is enormous and it will have to begin with a literally vast programme of training and orientation of nearly all members of the general health staff in most countries. But without this, it is doubtful if MDT can be implemented to full advantage.
ACKNOWLEDGEMENTS

Many ideas and proposals in this Guide stem directly from correspondence or discussions with colleagues in various parts of the world and we gratefully acknowledge their valuable contribution. Our thanks go to:

Dr Ad de Rijk, Department of Leprology, Wibautstraat 135, 1097 DN Amsterdam, The Netherlands.

Dr Marijke Becx-Bleumink, ALERT Leprosy Control Programme, PO Box 165, Addis Ababa, Ethiopia.

Dr Tadele Tedla, National Leprosy Control Programme, PO Box 5033, Addis Ababa, Ethiopia.

Dr Gjalt Boerrigter, LEPRA-MALAWI, PO Box 148, Lilongwe, Malawi.

Dr Michael Waters, Hospital for Tropical Diseases, 4 St Pancras Way, London NW1 0PE.

Dr Harold Wheate, 50 Avenue Road, Belmont, Surrey SM2 6JB.

Dr Ruth Pfau, Leprosy Research Cell, National Institute for Health, Islamabad, Pakistan.

We are particularly grateful to members of the staff of the All Africa Leprosy and Rehabilitation Training Centre (ALERT), Addis Ababa, and the National Leprosy Control Programme in Ethiopia, who supplied ideas and a wealth of valuable information during discussions on the occasion of the visit of the Medical Advisory Committee of ALERT in September 1983.

ILEP (The International Federation of Anti-Leprosy Associations, 234 Blythe Road, London W14 0HJ) have produced a valuable booklet, The Introduction of Multiple Drug Therapy for Leprosy (1983) in English and French versions, and excellent manuals on MDT have also been produced from India and Ethiopia:

Multidrug Therapy; Working Guide; The Leprosy Mission; E S Thangaraj; The Leprosy Mission (Southern Asia Office), 4th Floor, Sheetla House, 73-74 Nehru Place, New Delhi 110019, India.

Manual for Multiple Drug Therapy in Ethiopia, National Leprosy Control Programme, Ethiopia, PO Box 5033, Addis Ababa, Ethiopia.
APPENDIX 1

TEACHING-LEARNING MATERIALS FOR LEPROSY

The Oxfam-Lepra pack of teaching-learning materials for leprosy, distributed from Oxfam between 1983 and mid-1988 has now been discontinued, due to falling demand and the likelihood that most interested individuals and agencies had received a copy. (It may, however, be revived at some future date, perhaps for the teaching of medical students and paramedical staff in Africa, and the possibility of producing a similar pack for tuberculosis is under discussion.)

The availability and supply of teaching-learning materials for leprosy is now highly organised. A sub-section of the International Federation of Anti-Leprosy Associations (ILEP) has been dealing with this subject specifically for some years and, under the title of TALMILEP (Teaching and Learning Materials for Leprosy) has now produced a comprehensive English Language Booklist (1988). This is a list of 28 items which are available, some free, some at cost. The UK contact for further enquiries is:

Teaching and Learning Materials
The Leprosy Mission International
80 Windmill Road
Brentford, Middlesex TW8 0QH

In addition:

i) TALC, Teaching Aids at Low Cost, PO Box 49, St Albans AL1 4AX, UK, produces the following colour transparency teaching sets, each with full text:

a) Lp; Leprosy; a description of the disease with particular reference to childhood,

b) Lp Cn; the classification of leprosy; new understanding that improved immunology leads to improved classification,

c) Lp D; leprosy lesions in skins of different colours.

ii) The Wellcome Tropical Institute, 200 Euston Road, London NW1 2BQ, UK, has produced (1988) a limited edition of full-colour posters on leprosy, of extremely high quality, together with a 64-page handbook. There are 10 separate posters, covering all basic aspects of the disease. Cost UK£50, including packing and postage.
APPENDIX 2

BASIC STEPS FOR CONSIDERATION IN THE IMPLEMENTATION OF MDT

DECIDE: ARE YOUR HEALTH INFRASTRUCTURE AND LABORATORY FACILITIES ADEQUATE IN QUALITY AND NUMBERS OF PERSONNEL TO IMPLEMENT MDT SAFELY AND EFFECTIVELY

YES

Decide if implementation is to be at national, regional or district level.

Issue clear-cut instructions on MDT and implement as soon as possible in the area chosen.

NO

Maintain the status quo of your leprosy control programme – even if this means continuing dapsone monotherapy for the time being.

TRAIN and RE-TRAIN your staff until they are capable of implementing MDT safely and effectively.

Issue clear-cut instructions on MDT and implement in a limited area only.

Assess your registered cases with regard to:–
– activity/inactivity
– duration of treatment already received
– results of slit-skin smears.

Release from control all those cases who meet suitable criteria.

Give MDT to all the others.

Follow up, analyse and report results.

Intensify case-finding, especially of multi-bacillary cases, and treat them with MDT.

As already noted in the opening pages, a particularly important and valuable paper for this purpose is Dr Felton Ross, ‘Managerial implications of Multiple Drug Therapy’, Leprosy Review, 56, 1985, pp. 89-97 – essential reading for anyone, particularly with limited experience, embarking on the implementation of MDT.
APPENDIX 3

LEPROSY CONTROL PROGRAMME – QUALITY CONTROL OF SLIT-SKIN SMEARS

1. Selection of slides
   a) The six slides submitted in each batch should be chosen by a supervisor from the total examined by the technician during the previous 2-3 months.
   b) They should be selected by reference to the technician’s register (not by an examination of his collection of slides), taking some from the early, middle and late part of the 2-3 months’ period.
   c) The batch should consist of three which have been found positive and three negative.
   d) The slides in any one batch should have all been examined by one technician; i.e. submit separate batches and forms for each technician.

2. Indices: BI and MI
   a) The BI should be recorded at the local laboratory for the three positive cases.
   b) The MI may also be recorded at the local laboratory, if this is in accordance with programme policy, available expertise, the quality of microscopic equipment and lighting, etc.
   c) The reference laboratory, virtually by definition, should routinely record both the BI and the MI on all positive slides.

3. The number of forms
   a) The technician at the local laboratory fills in the form in duplicate. He keeps one copy and sends the other with the slides to the reference laboratory.
   b) The supervisor at the reference laboratory gives a number to the batch of slides and then enters the six patient identification numbers on another (third) form.
   c) He passes this third form, with the slides, to his technician.
   d) After the slides have been examined and reported by the technician, the results are checked by the supervisor and compared with those from the local laboratory.
   e) The supervisor then: i) enters the local laboratory results and all other details on his own form, which is kept in the reference laboratory and ii) enters the reference laboratory results on the form originally sent in from the local laboratory.
# APPENDIX 3 (CONT.)

**LEPROSY CONTROL PROGRAMME — QUALITY CONTROL OF SLIT-SKIN SMEARS**

<table>
<thead>
<tr>
<th>Name of local laboratory submitting slides</th>
<th>Address of local laboratory</th>
<th>Name of technician submitting slides</th>
<th>Date slides submitted</th>
</tr>
</thead>
</table>

Number of slides examined at the local laboratory by the above technician:

(a) In the last month........

(b) This year so far........

<table>
<thead>
<tr>
<th>Patient's identification number</th>
<th>Smear</th>
<th>Reading at the local laboratory</th>
<th>Quality control reading at the reference laboratory</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Positive or negative Indices</td>
<td>Quality of smearing</td>
</tr>
<tr>
<td></td>
<td></td>
<td>BI MI</td>
<td>Good Fair Bad</td>
</tr>
</tbody>
</table>

| Comments or explanation from the reference laboratory | |

- Date received at the reference laboratory: 
- Batch number: Date reported: 

* This form provides for the examination of 4 smears from each patient but can easily be modified if 6 smears are regularly taken.
APPENDIX 3 (CONT.)

f) This is sent back to the local laboratory as soon as possible. Whenever possible, the original slides should also be sent back to the local laboratory.

4. Analysis; assessment; quality control

a) At the local laboratory – The results on the form sent back from the reference laboratory should be examined as soon as possible by the local technician and supervisor, jointly. Good, accurate work should be acknowledged. Minor defects or imperfections should be corrected locally. Major defects, or outright errors, especially if repeated, point to a need for re-training of the technician, possibly at the reference laboratory.

b) At the reference laboratory – The results from local laboratories should be filed systematically and analysed at regular intervals with the leprologist or programme manager.

c) At Ministry of Health, communicable disease control or leprologist level – Preferably in close association with those working in tuberculosis (who rely heavily on sputum examination, using closely related techniques), the overall quality of slit-skin smear work in the country or region should be reviewed at 2-3 monthly intervals. The trend in standards (up, down, unchanging) should be monitored in relation to the possible need for the training or re-training of laboratory staff or supervisors.

With grateful acknowledgements to Dr Ad de Rijk (Amsterdam), Dr Daan Mulder (London) and Mr Eric Edwards (Nairobi).

Postscript, October 1988

Dr Ad de Rijk and colleagues have published further experiences on the quality control of slit-skin smears in *Leprosy Review*, 56, 1985, pp.177-191.

Two publications in 1987 and 1988 may be of value with regard to the establishment of procedures in the field, and laboratory standards which ensure that slit-skin smears, if taken and examined are reliably reported. They are:


APPENDIX 4

LEPROSY SMEARS: BACTERIOLOGICAL INDEX – B1 (ZIEHL-NEELSEN STAIN)

**B1 = 0**
No bacilli in 100 oil immersion fields

Examine 100 oil immersion fields

**B1 = 1**
1-10 bacilli, on average, in 100 oil immersion fields

Examine 100 oil immersion fields

**B1 = 4**
10-100 bacilli in an average oil immersion field

Examine 25 oil immersion fields

**B1 = 5**
100-1000 bacilli in an average oil immersion field

Examine 25 oil immersion fields
APPENDIX 4 (CONT.)

**B1 = 2**
1-10 bacilli, on average, in 10 oil immersion fields

Examine 100 oil immersion fields

**B1 = 3**
1-10 bacilli in an average oil immersion field

Examine 25 oil immersion fields

**B1 = 6**
1000 or more bacilli in an average oil immersion field

Examine 25 oil immersion fields


Details of taking, fixing, staining and reading smears, including the B1, are given in Leiker, DL and McDougall, AC, *Technical Guide for Smear Examination for Leprosy by Direct Microscopy*. Available in English, French, Spanish, Portuguese, Turkish, Arabic, Bengali and Thai. Obtainable from TALMILEP, The Leprosy Mission International, 80 Windmill Road, Brentford, Middlesex, TW8 0QJ, UK.
APPENDIX 5

BODY DIAGRAMS FOR LESIONS, SLIT-SKIN SMEARS OR BIOPSIES
APPENDIX 6

GRID SYSTEM/DIAGRAM FOR THE CHARTING OF LESIONS, SLIT-SKIN SMEARS OR BIOPSIES

APPENDIX 7

‘START OF MDT’ TO ‘COMPLETION OF SURVEILLANCE’ AND ‘CONTINUING CARE’

START OF MDT

COMPLETION OF MDT

START OF SURVEILLANCE

COMPLETION OF SURVEILLANCE

CONTINUING CARE

CONTINUING CARE

6 months for pauci-bacillary cases

24 months minimum for multi-bacillary cases

2 years minimum for pauci-bacillary cases

5 years minimum for multi-bacillary cases

a) All patients should be encouraged to keep in touch with the medical services at any time, if they so wish.

b) CARE starts, in fact, at the outset of MDT and continues throughout the years, but after completion of surveillance it is important to realise that it may continue indefinitely in the case of patients with anaesthesia, paralysis or eye problems.

For operational purposes, all cases of leprosy may be regarded as falling into one of the following four categories:

i) Those requiring, or actually receiving, chemotherapy.

ii) Those who have completed a satisfactory course of chemotherapy and are under surveillance.

iii) Those who have completed surveillance but are in need of continuing care because of disability.

iv) Those who have completed both chemotherapy and a period of surveillance and who are not in need of any form of continuing care. They may be released from surveillance and there is no need to maintain them on any register or list.

APPENDIX 8

DIAGRAMS OF THE DRUGS RECOMMENDED BY WHO FOR PAUCI- AND MULTI-BACILLARY LEPROSY

Because of the crucial importance of the WHO regimens, including the need to understand fully the doses and periods of follow-up after stopping treatment, we use the following pages to reproduce charts or diagrams of a size which can easily be photocopied for reference, teaching and the instruction of patients.

Note that the doses are for adults. Children’s doses are given on pages 19-20.
Drugs for Pauci-

WHO recommended regimen: “Chemotherapy of leprosy for control programmes”,

Rifampicin

300mg ➔ 600mg Monthly
300mg ➔

Supervised

Duration of treatment:
6 months (or 6 monthly doses within a 9 month period); then stop and keep patient under surveillance.

(Produced by Richard L. Jones & A. Colin McDougall, The Department of Dermatology, The Slade Hospital, Oxford OX3 7JH, England)
bacillary Leprosy


Dapsone

28 tablets of Dapsone (100mg) for the treatment of leprosy

Unsupervised

Duration of surveillance:
Minimum of 2 years after stopping treatment, with clinical examination at least every 12 months.
Drugs for Multi-

WHO recommended regimen: “Chemotherapy of leprosy for control programmes”,

<table>
<thead>
<tr>
<th>Rifampicin</th>
<th>Dapsone</th>
</tr>
</thead>
<tbody>
<tr>
<td>300mg</td>
<td>100mg</td>
</tr>
<tr>
<td>300mg</td>
<td></td>
</tr>
<tr>
<td>600mg Monthly Supervised</td>
<td>100mg Daily Unsupervised</td>
</tr>
</tbody>
</table>

Duration of treatment:
Minimum of 2 years (or 24 monthly doses within a 36 month period). However, wherever possible, continue treatment until slit skin smears are negative. Then stop, and keep the patient under surveillance.
bacillary Leprosy


Clofazimine

100mg
100mg
100mg
300mg
50mg
Monthly
Daily
Supervised
Unsupervised

Duration of surveillance:
Minimum of 5 years after stopping treatment, with clinical and bacteriological examination at least every 12 months.

(Produced by Richard L. Jones & A. Colin McDougall, The Department of Dermatology, The Slade Hospital, Oxford OX3 7JH, England)
The diagram shows the design (flat side) of a blister-calendar pack, similar to those actually in use in the Philippines, India and Thailand, for the administration of monthly, supervised rifampicin and clofazimine capsules, together with a tablet of dapsone for that day, and daily unsupervised clofazimine capsules and dapsone tablets. All medication is contained (sealed) in ‘blisters’ which can be easily pressed out by the patient.
APPENDIX 10

DIAGRAM OF A BLISTER-CALENDAR PACK FOR MULTIPLE DRUG THERAPY IN PAUCI-BACILLARY LEPROSY

The diagram shows the design (flat side) of a blister-calendar pack, similar to those actually in use in the Philippines, India and Thailand, for the administration of monthly, supervised rifampicin capsules (together with the tablet of dapsone for that day) and daily, unsupervised dapsone tablets. All medication is contained (sealed) in 'blisters' which are easily pressed out by the patient.

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SELECTIVE FEEDING PROGRAMMES
Price £2.95
ISBN 0 85598 097 4
Originally produced to accompany the Oxfam Feeding Kit, at the time of the large-scale famine in Ethiopia in the 70s, this book has been expanded into a comprehensive manual for use in treating different degrees of malnutrition in emergency situations. The first part of the book describes the assessment and monitoring of the nutritional needs of the population at risk; Part Two gives detailed directions for the setting up and administration of selective and therapeutic feeding programmes. There are several useful appendices – checklists, tables, recipes, etc. This book provides all the basic, essential information for those working in the fields of health and nutrition faced with emergency relief situations.

Oxford Practical Health Guide No. 1

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Oxfam Practical Health Guide No. 2

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Tuberculosis is likely to remain a major health problem in developing countries as long as communities face poor housing, overcrowding and poor nutrition. Many countries have national tuberculosis control programmes, but these are seldom as effective as they could be because of difficulties in implementation at village level. This book combines the most recent developments in the scientific understanding of tuberculosis with the realities of working at the level of a primary health centre and suggests ways of improving the efficiency of tuberculosis control programmes by an increased under-
standing of the importance of the sputum-positive patient as the source of transmission and therefore the target of control. It looks at the problems of diagnosing and poor drug compliance, and emphasises the importance of monitoring and evaluation of tuberculosis programmes. It will be a valuable practical handbook for those working in health care projects in developing countries.

Oxfam Practical Health Guide No. 4

CITIES OF HUNGER
Urban Malnutrition in Developing Countries
ISBN 0 85598 085 0 Hardback £19.95
ISBN 0 85598 084 2 Paperback £4.95

By the end of the century, half the world’s population will live in cities, so the need to improve the conditions of live of the urban poor is becoming increasingly urgent. A specific problem for poor city-dwellers, which to date has been under-researched, is that of providing sufficient food for themselves and their children. Cities of Hunger, an important contribution to nutrition studies, focuses on the causes of urban malnutrition and adopts an innovative way of analysing these in terms of the social level – individual, family, community, national/international – at which they operate.

The second part of the book provides a detailed examination of three projects in contrasting urban settings and describes how their ways of working evolved dynamically. It relates these changes and the successes and failures of the projects to the analysis developed in the first part of the book.

Cities of Hunger will be of interest both to those working in the field of health and nutrition in particular, and those with a more general interest in development.
EVALUATION

Despite revision and up-dating, we are only too conscious of the fact that MDT is a complicated and fast-moving subject; perhaps you have some important questions which you would like to see answered? Perhaps you disagree with some of the answers?

This page is for your criticisms and suggestions. Please write your proposals in the space below (continuing over the page if necessary) and post to: Oxfam Health Unit, 274 Banbury Road, Oxford OX2 7DZ, UK.

Name

Address

Position held
notes
notes
notes
notes
notes