A Guide to Leprosy Control

Second edition

World Health Organization
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1988
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Preface

Leprosy continues to be a serious cause of morbidity and disability in the developing countries, and the social stigma associated with the disease further compounds the problem. While it has not been possible to bring about any significant reduction in the prevalence of the disease worldwide, in recent years there has been a considerable increase in leprosy control activities and in the application of improved methods of control. The recommendations made by the WHO Study Group on Chemotherapy of Leprosy for Control Programmes and the WHO Study Group on Epidemiology of Leprosy in Relation to Control have had a major impact in that regard.

As a result of these developments, it became obvious, and necessary, that the Guide to leprosy control, published in 1980, should be thoroughly revised. The guide has proved to be a valuable document for both field workers and programme managers alike, and it is hoped that the revised version will meet all the current needs from the technical and managerial points of view. Earlier publications by WHO, such as the Fifth Report of the WHO Expert Committee on Leprosy and the reports of the two WHO Study Groups referred to above, as well as the recent sixth report of the WHO Expert Committee on Leprosy, have provided much of the material for this version.

The guide is not intended to be a comprehensive textbook on leprosy. Rather, it aims to provide all the background information necessary for planning and operating a successful control programme, in all its aspects. If it succeeds in this, and in making the lives of leprosy patients easier, it will have attained its objective.

The revised version of the guide has been prepared by Dr M. Christian, Chief, Epidemiology and Control, Schleifelins Leprosy Training and Research Centre, Karigiri, India, and members of the Leprosy unit at WHO Headquarters in Geneva. Acknowledgement is made to the various WHO publications and documents on leprosy and to reports of the International Leprosy Congress.

Chapter 1

Magnitude of the problem and geographical distribution

The problem of leprosy

Leprosy continues to be a serious public health problem in the developing countries—the populations at risk of contracting the disease are very large, and more than one-third of all leprosy patients face the threat of permanent and progressive physical and social disability. It should be emphasized that the problem is far more serious than is indicated by the number of cases alone; the human suffering involved, resulting from the physical deformities and related social problems, is intense.

Estimated number of leprosy patients

It is difficult to estimate the number of cases of leprosy in the world. Case diagnosis and definition are not always clear or consistent. Further, the enumeration of cases in many regions of the world is incomplete or irregular. Information is often available only from limited areas and for registered cases, on the basis of which estimates of prevalence are made after applying certain arbitrary correction factors. Occasionally, estimates are based on reliable sample surveys, but even then there are problems in discriminating between active and inactive cases, and in ensuring adequate coverage for examination. Factors such as inadequate examination of individuals also play a role. Some of these factors lead to overestimation of prevalence, while others lead to underesti-
mation and there is no way of knowing the extent of under- or overestimation in these surveys. Despite all these difficulties, estimates are extrapolated from available data from time to time. The WHO estimates for 1966 and 1976 were 10.8 and 10.6 million cases respectively. Prevalence is currently estimated at 10–12 million cases, and this is believed to be a reasonable reflection of the true situation.

Population at risk

Approximately 1.6 billion people live in areas where leprosy is an important problem (i.e., where the estimated prevalence is over one case per 1000 persons), and thus may be considered at significant risk of contracting the disease.

Registered cases

Information on leprosy cases registered for treatment is much more reliable than information on estimated cases, as it is based on actual records. There has been a steady increase in the number of registered cases over the past 20 years: 2,831,775 in 1966, 3,599,949 in 1976, and 5,368,202 in 1985. The last figure represents an increase of 49.1% over 1976, and 89.6% over 1966. The prevalence of registered cases has correspondingly increased from 0.84 cases per 1000 population in 1966 to 0.88 in 1976, and 1.2 in 1985. The total number of registered cases in 1987 was 5,069,283; their geographical distribution is shown in Fig. 1.

Although information on registered cases appears to be fairly reliable, there are several problems in evaluating it for the purpose of leprosy control. Firstly, not all registered cases are necessarily under regular treatment (whatever the drug regimen). The regularity of treatment varies widely from programme to programme, often by as much as 50%. Even among patients who collect their drugs from clinics, a certain proportion do not con-
sume them as expected, a fact revealed by more than one study involving urine checks for dapsone. Information on registered cases is often not kept up to date. Inactive cases often remain on the registers, either because patients have been lost to follow-up or because of inability to assess the patients’ clinical and bacteriological condition periodically. In addition, there are also problems of duplicate registration of patients in more than one clinic. However, the situation appears to have improved in recent years, partly as a result of the introduction of multidrug therapy, which has made it necessary for workers responsible for leprosy control to review their records and to classify patients according to their bacteriological status. In spite of the problems, the information on registered cases is very valuable for planning, monitoring and evaluating leprosy control activities.

The distribution of registered cases, the prevalence rates, and the proportion of cases by WHO Region in 1987 (or for the most recent year for which information is available) are shown in Table 1. Although only a proportion of estimated cases ever register for treatment, the information on registered cases reflects to a large extent the leprosy situation in any given region and its relative importance, compared with other regions.

Disabilities

The most important cause for concern in leprosy is the occurrence of deformities in a proportion of patients. In more than one-third of untreated patients, and particularly in advanced cases, leprosy results in disabilities which increase with time and are permanent. These disabilities affect the extremities and the face, including the eyes, often resulting in severe impairment of working capacity and seriously limiting the social life of patients. They are also largely responsible for the
high level of ostracism and the intense social prejudice against the disease.

**Trends in the geographical distribution of leprosy**

Leprosy is remarkably cosmopolitan in its distribution. Although the estimated 10–12 million patients are at present concentrated mainly in developing countries in the tropical and subtropical belt, the disease was endemic as far north as the Arctic Circle until the nineteenth century. The distribution is not uniform and both distribution and prevalence have varied markedly over the years.

At the subcontinental level, on the basis of geographical distribution and long-term trends, several zones can be recognized.

1) **Tropical and subtropical belt of Africa and southern Asia.** This is considered to be the ancestral home of leprosy, where the disease can be traced back more than 2500 years. It continues to persist in these areas at a high level of endemicity. In Africa, leprosy is mainly distributed in the western, eastern and

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**Table 1. Distribution of registered leprosy cases by WHO Region, 1985**

<table>
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<tr>
<th>WHO Region</th>
<th>Population (thousands)</th>
<th>No.</th>
<th>Prevalence per 1000 population</th>
<th>Percentage of all cases</th>
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<td>443,238</td>
<td>624,266</td>
<td>1.41</td>
<td>12.3</td>
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<td>Americas</td>
<td>666,006</td>
<td>355,232</td>
<td>0.50</td>
<td>6.6</td>
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<td>Eastern Mediterranean</td>
<td>323,525</td>
<td>79,452</td>
<td>0.25</td>
<td>1.6</td>
</tr>
<tr>
<td>Europe</td>
<td>814,052</td>
<td>12,242</td>
<td>0.02</td>
<td>0.2</td>
</tr>
<tr>
<td>South-East Asia</td>
<td>1,159,735</td>
<td>378,2532</td>
<td>3.26</td>
<td>74.6</td>
</tr>
<tr>
<td>Western Pacific</td>
<td>1,365,527</td>
<td>235,559</td>
<td>0.17</td>
<td>4.6</td>
</tr>
</tbody>
</table>

4,772,083 | 5,009,283 | 1.06 | 100.0

* Or for the most recent year for which data are available

central parts, while prevalence is low in northern and southern Africa. India has an estimated four million cases.

2) The Mediterranean basin. Leprosy has probably been present in this region for 2000 years. However, its prevalence now is low, focal and declining.

3) Northern Europe. Leprosy was widespread in this area 1000 years ago, reaching as far north as the Arctic Circle. It increased in prevalence until the thirteenth century, after which it progressively declined to extinction. The disappearance of leprosy from northern Europe remains one of the major puzzles of its epidemiology and has been variously attributed to:
- improved socioeconomic conditions and better living standards;
- improved nutrition;
- effective isolation of infectious cases;
- genetic selection of the population;
- competitive inhibition with other mycobacteria, notably Mycobacterium tuberculosis;
- selective mortality of leprosy patients during plague epidemics.

4) Northern Asia. Leprosy is present in some parts of the USSR at a low level of endemicity. China has a case load of 100,000 patients, mainly in the western provinces.

5) South and Central America. Leprosy was introduced into this region by African, French, Portuguese, and Spanish immigrants at the beginning of the sixteenth century. It has remained endemic at a low level of prevalence ever since. Only Chile has remained free of endemic transmission, and the incidence is now declining in Venezuela.

6) Northern United States of America and eastern Canada. Leprosy was introduced into these areas in the eighteenth and nineteenth centuries, mainly by French, German, and Norwegian immigrants. It persisted in several clearly defined foci and within certain family groups for several decades and then disappeared.

7) Pacific Islands and Australia. Leprosy has been introduced into a number of islands during the last 200 years and, in some instances, this has led to epidemics lasting several decades, e.g., in Nauru. Leprosy is reported to have been introduced on to the Australian mainland in the middle of the nineteenth century, and it still persists among the aborigines in the Northern Territory.
Epidemiology

Natural history of the disease

The agent

Hansen’s discovery of *Mycobacterium leprae* in Norway in 1873 represented one of the first identifications of a microbial pathogen of man. Despite its early discovery and repeated claims to the contrary, the organism has not yet been cultured in *vitro*. Quantitative bacteriological studies of *M. leprae* became possible after 1960, when Shepard established that the organism would grow in the mouse footpad (1, 2). The more recent recognition that the organism grows in the nine-banded armadillo (*Dasypus novemcinctus*) has provided larger amounts of antigen and allowed a more precise characterization of the bacilli. *M. leprae* is an obligatory intracellular parasite with a special affinity for Schwann cells and cells of the reticuloendothelial system.

Source of infection

The existing epidemiological evidence suggests that human infections are the most important, if not the only, source of infection to man. Observations made from incidence studies among contacts of leprosy patients have clearly established that multibacillary patients in the mid-borderline (BB)-lepromatous (LL) spectrum are of the highest epidemiological importance in disease transmission. Such data have consistently shown that household contacts of paucibacillary leprosy patients are twice as likely to contract the disease as individuals with no known household contact, whereas similar contacts of multibacillary leprosy
patients have a 4–10-fold increase in risk. Paucibacillary leprosy patients are usually negative in bacteriological tests on skin and nasal smear specimens, and are therefore substantially less infectious than positive multibacillary patients with a high bacterial load.

It must, however, be appreciated that exposure to known cases cannot be established in a high proportion of leprosy infections. This is partly because of the long incubation period of the disease and the social stigma, which often results in patients denying a history of intrafamilial contact. "Inapparent" lepromatous cases with minimal, inapparent lesions may also account for a certain proportion of untraceable infections.

Self-healing in paucibacillary leprosy has been reported extensively in the literature. However, at the time of diagnosis it is not possible to identify the patients whose lesions will resolve favourably and those whose lesions will progress. It is therefore necessary to treat all paucibacillary patients.

**Modes of transmission**

**Portals of exit**
Lesions in the skin and nasal mucosa of leprosy patients have long been recognized as sources of *M. lepra*. The present evidence is consistent with the hypothesis that the upper respiratory tract of multibacillary patients is the most important source of *M. lepra* in the environment. The organism can also be discharged from the skin surface of multibacillary patients, especially when there is a breach in its continuity, e.g., leprous ulcers.

**Portals of entry**
The skin and the respiratory tract have traditionally been considered as the most likely routes of entry of *M. lepra* into the body. Recently there has been increased emphasis on the respiratory tract as the principal portal of entry.

**Host factors**
Immunological studies have now established that *M. lepra* infection is far more common than is suggested by the number of cases of overt disease. In other words, leprosy is a disease of high infectivity but low pathogenicity. The occurrence or non-occurrence of disease is closely interlinked with the cell-mediated immune response of the host to the challenge by *M. lepra*, although the immunological mechanisms underlying this are not clear.

**The main epidemiological features**

**Age**
Leprosy can occur at all ages. It is, however, rare among infants. Incidence rates generally rise to a peak between 10–20 years of age and then decline. This has been observed in Burma, Southern India, Norway, and the Philippines. Incidence rates for lepromatous forms tend to rise at a higher age and to be lower than those for tuberculoid disease; in part this may be a reflection of the possibly longer incubation period of lepromatous leprosy. The age distribution of paucibacillary leprosy shows a distinct bimodal pattern. There is an early peak at approximately 15 years of age followed by a trough at 20 years. It has been suggested that the early peak is attributable to self-healing lesions following infections contracted early in life, particularly among child contacts of leprosy patients within their homes, but this has not been confirmed.

**Sex**
Both the incidence and the prevalence of leprosy are higher in males than in females in most regions of the world, with the
exception of certain areas of Africa where higher rates have been reported among females. This sex differential is greater in adults than in children. It is also more obvious in lepromatous leprosy than in tuberculoid leprosy.

**Clustering**

Leprosy is neither uniform nor random in its distribution. It has a distinct tendency to clustering, which is most obvious in areas of low prevalence. In the middle of the nineteenth century, Danielsen & Boeck made the astute epidemiological observation that "leprosy tends to cling to families" (3). This evidence has often encouraged the view that genetics may play an important role in determining susceptibility. The question of the extent to which clustering is due to shared environment, shared genes, or shared contact with infectious cases has still not been fully resolved. Whatever the reason, clustering has important implications, particularly for the design and interpretation of sample surveys, and this must always be borne in mind.

**Time trends in the prevalence of leprosy**

Leprosy appears to be maintained at a relatively constant level of prevalence in most endemic areas, with a steady occurrence of new cases every year. However, there is evidence that important changes in the prevalence of leprosy have occurred in some areas of the world during the last century. Several temporal patterns have now become apparent.

**Natural decline in the incidence of leprosy**

In northern Europe, Hawaii, Japan, continental United States of America, and Venezuela, there have been well documented, progressive declines in the incidence of leprosy, which in some instances have gradually led to the virtual disappearance of the disease among the indigenous population. Careful analyses of these trends have revealed several features similar to those observed during the decline of tuberculosis in the same populations, e.g., a shift in the peak age-specific incidence to older groups.
Limitations of the classical control strategy based on dapsone monotherapy

Introduction

Until recently, treatment of leprosy was largely based on long-term chemotherapy of patients with dapsone alone. However, the emergence of drug resistance in *M. leprae* and the need for early detection of cases to minimize transmission have presented problems for programmes using this classical control strategy, particularly in developing countries.

This chapter outlines some of the reasons why a control strategy based on dapsone monotherapy is no longer recommended. Details of the currently recommended drug regimens for therapy of leprosy are given in Chapter 6.

Elements of the classical strategy

The modern era in the chemotherapy of leprosy commenced in 1941, when Faget and his coworkers (4) at the National Hansen’s Disease Center in Carville, L.A., USA, studied the efficacy of a series of sulfone compounds, commencing with glucosulfone. By the early fifties, the remarkable efficacy of dapsone and its widespread use revolutionized the whole concept of chemotherapy in leprosy and the approach to its control. Isolation was no longer considered necessary, and even infectious patients could be treated on a domiciliary, ambulatory basis. Outpatient clinics and mobile treatment circuits began to assume
the primary role in leprosy control projects.

The thrust of this strategy was based on the secondary prevention approach. It was widely believed that early detection of patients and regular treatment with dapsone monotherapy would reduce the reservoir of infection and hence interrupt the chain of transmission of the disease in the community. The objectives of leprosy control therefore became:

1) to interrupt transmission of infection, thereby reducing the incidence of disease so that it no longer constituted a public health problem;
2) to treat patients in order to achieve their cure and, where possible, complete rehabilitation;
3) to prevent the development of associated deformities.

Dapsone proved to be effective, safe, comparatively nontoxic in the doses used, easily administered and inexpensive. The dapsone-based strategy has therefore been adopted by virtually all countries where leprosy is endemic during the last 30 years.

Since a specific vaccine was not available, it was suggested that BCG might have a protective effect against leprosy. Accordingly, BCG was tested against leprosy in large-scale, prospective field trials, but the results were widely varying and it was not possible to recommend BCG specifically as an important prophylactic measure for the prevention of leprosy.

The other method of primary prevention attempted was chemoprophylaxis. However, the WHO Expert Committee on Leprosy, in its fifth report in 1977 (5), did not recommend the use of dapsone as a prophylactic in large-scale control programmes.

Constraints
In many countries, it soon became obvious that it was difficult to mount and sustain field operations, involving the two main elements of early detection and prolonged chemotherapy, on a sufficiently wide scale to make a significant impact on the problem. The reasons for this were manifold and were related to operational, organizational and technical factors.

Operational factors
a) Patient compliance was poor, drug intake was frequently irregular, and high drop-out rates were common. All these factors were directly related to the length of the treatment. The need for regimens of shorter duration therefore became increasingly obvious.

b) Case-detection rates were low and case-holding was inadequate. A strategy based on secondary prevention is not likely to succeed unless all hidden sources of infection in the community are identified and given effective chemotherapy.

c) The main thrust of the approach was to provide treatment to as many patients as possible. This emphasis on quantitative rather than qualitative care led to poor case management which negatively affected patient compliance.

Organizational factors
a) It gradually became obvious that the organization of regular chemotherapy for 3–5 years in paucibacillary patients, and often for life in multibacillary patients, was very difficult to sustain in most developing countries.

b) The restrictive vertical approach of the programmes in many countries led to limited coverage of both rural and urban populations.

Technical factors
Dapsone resistance
Resistance to dapsone per se was first proved in the mouse footpad by Pettit & Rees in 1964 (6), though it had been
suspected on clinical grounds even earlier, during the late fifties.

Dapsone resistance develops as the result of a process of selection of resistant mutants already pre-existing in wild strains. The resistance occurs in a "stepwise" fashion. The selection and mutation theory implies that resistant bacteria are singled out through the elimination of the susceptible majority. In leprosy, at the commencement of treatment with dapsone monotherapy, the number of drug-sensitive organisms diminishes over a period of 1–3 years, while the pre-existing resistant mutants remain unaffected. Gradually, the composition of the reduced bacterial population changes as the resistant mutants gain the upper hand. The resistant bacilli, gaining the biological advantage, rapidly outgrow and finally completely replace the drug-sensitive organisms. This is reflected in the initial clinical improvement observed in patients during the first 2–3 years, as the drug-sensitive organisms rapidly diminish, the total bacterial load is reduced, and the bacterial index (BI) declines. However, when the resistant organisms gain the upper hand and start multiplying, clinical deterioration occurs (reactivation/recrudescence), and the BI shows a rising trend.

Monotherapy is the most frequent cause of the development of drug resistance. There are two types of drug resistance—secondary or acquired resistance as a result of inadequate chemotherapy, and primary resistance, which occurs in patients who have not received any chemotherapy. The latter results from infection with drug-resistant organisms that originated from a patient who had relapsed with secondary resistance.

Secondary dapsone resistance
A major problem in leprosy control in recent years has been the widespread and increasing occurrence of secondary dapsone resistance. During the past 15 years it has been reported with increasing frequency among multibacillary patients treated with dapsone monotherapy. A large number of countries have now reported dapsone resistance, and the prevalence is steadily increasing. Wherever it has been sought among treated and relapsed patients with lepromatous or borderline lepromatous leprosy, it has been found. It is now clear that secondary dapsone resistance is a worldwide phenomenon.

Primary dapsone resistance
When lepromatous and borderline-lepromatous patients relapse with secondary dapsone resistance, they can infect their contacts with dapsone-resistant strains of *M. leprae*. Those who subsequently develop clinical leprosy will suffer from primary dapsone resistance. It follows that primary dapsone resistance can occur in any type of leprosy. Moreover, among paucibacillary patients it is impossible to differentiate either clinically or by the mouse-footpad system, since too few organisms can be recovered from skin-biopsy specimens. Primary dapsone resistance in paucibacillary leprosy patients can only be recognized when treatment with the drug does not result in the expected clinical improvement.

Since the prevalence of secondary dapsone resistance is steadily increasing, and because the incubation period of tuberculoid leprosy is believed to be several years shorter than that of lepromatous leprosy, it is possible that primary dapsone resistance is currently occurring in a high proportion of new tuberculoid leprosy patients.

Microbial persistence.
Bacterial persistence is a phenomenon of special pathogenic and therapeutic importance. Bactericidal drugs kill organisms only when they are in the metabolically-active multiplication phase. Bacilli that are in a state of low metabolic activity, i.e., when bacterial growth has almost come to a standstill, and the organisms are "dormant", are not killed by bactericidal drugs.
Such organisms are referred to as “persisters”. Though they may survive in the presence of drugs, behaving as if they are drug-resistant, they are in fact susceptible to the same drugs. Thus if, for some reason, these organisms regain their ability to multiply freely, they will then be killed by the very drugs that had not harmed them previously. These persisters may die of inanition, but sometimes they may suddenly start to multiply again. If this occurs during effective chemotherapy they are killed, but if chemotherapy has been discontinued they will cause relapse.

Experience in the treatment of tuberculosis indicates the importance of using drugs with a specific sterilizing action on “persisters” if the time required for cure is to be significantly shortened. Unfortunately, so far, no drug alone or in combination with others appears to be capable of eliminating persisting M. leprae.
Case-finding

The role of case-finding in leprosy control

Case-finding, i.e., an organized and systematic search for patients in the community, will continue to be an integral component of the strategy for leprosy control. However, case-finding per se has little relevance unless it is followed by effective chemotherapy. Case-finding activities often outstrip the treatment capacity of a leprosy service because of lack of personnel or drugs, or of organizational difficulties. Intensification of case-finding is therefore justifiable only if it can be ensured that every new patient identified will be provided with adequate and effective treatment.

Case-finding methods

There are two major approaches to case-finding: active and passive.

Passive case-finding

This includes: voluntary reporting; and referral and notification.

Voluntary reporting

There are two distinct factors directly related to voluntary reporting:

1) increased community awareness regarding the disease; and
2) an efficient and reliable diagnostic and treatment service.

Symptoms of leprosy are very often absent or minimal, particularly during the early stages of the illness, hence patients do not voluntarily seek relief through the
health care system. This situation is further aggravated by the intense social prejudice against the disease. Increased awareness regarding the early signs and symptoms of the disease and dissemination of information regarding the facilities available for its treatment can be facilitated by intensive health education in the community, utilizing all available resources, including the mass media.

The other important factor in promoting voluntary reporting is an efficient and reliable diagnostic and treatment service. Convenient clinic timings, efficient professional performance, good working morale, and the identification of the health workers with the community they serve, are all positive motivating factors that can encourage reluctant patients to come forward voluntarily for treatment. It must also be appreciated that the most convincing motivating factor is the demonstration that leprosy can be cured, and that the treatment of patients is successful.

Several operational studies have clearly revealed that patients reporting voluntarily are more likely to undergo treatment regularly than those detected by other methods. This criterion alone is sufficient to justify the promotion of self-reporting.

**Referral and notification**

Referral from other medical institutions within the area, including the school health services, can be promoted by wide dissemination of information regarding the salient features of the leprosy control programme.

Reporting the disease to the health department is a legal requirement in some countries. However, its importance as a means of case detection is negligible in endemic countries.

**Active case-finding**

The aim of active screening is to find cases of unreported disease in the population. Screening implies clinical examination that does not arise from a patient's request for treatment of specific complaints.

In the planning and operational phases of a leprosy control programme the types of survey generally undertaken are: sample surveys; total population surveys; focal surveys; selective surveys; and contact surveillance.

**Sample surveys**

In countries where no information exists on the extent of the leprosy problem, it is very useful to conduct a sample survey to obtain a precise and rapid assessment. While this information is necessary for planning purposes, it has little relevance to case-finding. Another important use of sample surveys is to monitor the progress and impact of a control programme in operation.

Sample surveys have a degree of limitation when the endemicity is very low, as the sample size would have to be quite large in order to obtain the required degree of precision in estimating prevalence. While a high degree of precision is desirable on scientific grounds, it may often prove unduly expensive and may not always be required for planning purposes. Sample surveys are subject to sampling errors, which can be controlled by the sample design, as well as non-sampling errors such as incomplete coverage of the sample population and errors in diagnosis. It should be emphasized that no sample survey should be planned without obtaining appropriate statistical advice.

The first prerequisite of a sample survey is the preparation of a sampling frame, e.g., a list of villages with the population in each. The nature of the frame is relevant to the choice of the most appropriate technique to be used, such as simple random sampling, stratified sampling, cluster sampling, multistage sampling, etc.

It is necessary to emphasize that the sample must be adequate, unbiased and
truly representative of the population from which it is drawn.

The following general considerations regarding sample surveys also deserve emphasis. Once the sample has been selected it is imperative that efforts should be made to achieve as high a coverage as possible. Leprosy is often more common among adults than children, but coverage of children is easier to obtain. An apparently good total coverage may therefore consist of an exceedingly high coverage of children combined with a poor coverage of adults. The sampling may therefore need to be stratified for children and adults.

Total population survey (mass survey)

Total population surveys are a useful method of case detection in areas of high endemicity, particularly during the initial phases of a leprosy control campaign. However, they are time-consuming, expensive to perform, and involve the use of a considerable amount of trained manpower and can, therefore, only be justified on the basis of cost-effectiveness. Before commencing a survey, careful and systematic planning is necessary. It must be emphasized that screening for leprosy or any other communicable disease that is not followed by health action aimed at effective treatment or prevention should never be undertaken in any country.

The success of a mass survey will depend upon the cooperation and involvement of the public. This cannot be achieved without effective and appropriate health education.

A spot map of each village should be prepared in advance, with easily distinguishable landmarks for identification, and the latest available census information should be obtained in as much detail as possible, including the age and sex composition of the population.

The criteria for the diagnosis of leprosy in the field must be standardized. The diagnostic procedures are mainly clinical and to some extent bacteriological. The clinical examination should include inspection of skin surface, palpation of nerve trunks and testing for sensory loss, both for light touch and pain. Skin smear examinations should be carried out on all individuals identified as having definite or suspect leprosy. Those undertaking the survey should have had adequate training and reasonable experience in these methods. It may be useful for an independent, reliable senior examiner to carry out periodic checks of individuals identified as cases, suspect cases or normal.

Group surveys using a team of workers are often more reliable. The survey should be carried out at times of the day convenient to the population and when a good coverage can be obtained.

Two approaches may be adopted for the examination of the population:

a) A systematic house-to-house visit covering the entire village. This is undertaken by teams of workers fanning out in different directions and then converging at a central point. Each household is given a number and a separate card is completed for every family in the household, i.e., those who habitually sleep and reside together and share the same kitchen. The family members are all listed on the card, together with information regarding their age and sex, relationship to the head of the household, and the date and result of the clinical examination.

b) The gathering approach. This is possible in more disciplined societies where the population has already been registered by the administration. The people are requested to report at one or more central points in the village at the scheduled time for the examination. The survey team makes prior arrangements at these predetermined locations for the reception, registration and examination of persons reporting to them. It will be necessary to ensure the privacy and
confidentiality of the examination in such situations.

Focal surveys
These are also known as gathering, chase, or rapid surveys; there may be slight variations in the methodology and approach. The main purpose of such surveys is to screen the population in as short a time as possible. Their success depends on a considerable extent on the publicity given to them and the cooperation of the community.

The people are informed about the date and time of the survey by an advance publicity campaign. The survey team makes prior arrangements at predetermined locations for the reception, registration and examination of persons reporting to them. Cultural shows and screening of films can serve the dual purpose of attracting people to attend and providing a forum for imparting health education. Such surveys, especially when combined with general health examinations, can sometimes achieve an excellent coverage of the population. After all the people have been examined, visits are made to the houses nearby to examine those who could not attend.

Selective surveys
Selective surveys are mass health examinations directed towards a specific subgroup of the population that is relatively easy to examine, for example, schoolchildren, factory workers, police recruits, etc.

School surveys provide a simple method of case detection and are productive when prevalence among children is high. The staff should, however, ensure that the confidentiality of the diagnosis is maintained. It will also be necessary to examine, in their homes, the other family members of children diagnosed as suffering from leprosy.

Selective surveys are particularly useful for case detection in areas of low and moderate endemicity.

Contact surveillance
Whereas a survey is an examination at a particular point in time, surveillance requires repeated examinations.

Contacts of leprosy patients are at a high risk of developing both infection and disease. However, though contact surveillance with annual examinations fulfils the objective of early detection in a high-risk group and is obviously important, it nevertheless identifies only a small proportion of the total of new cases occurring in a community.

While every effort should be made to examine all household contacts annually, priority should be accorded to contacts of multibacillary patients and household contacts under 15 years of age. Further, with the introduction of multidrug therapy, it is now considered that:

a) Contact surveillance of households with a multibacillary case should be maintained for a minimum period of 5 years after the patient completes treatment.  
b) Contact surveillance of households with a paucibacillary case should be maintained for a minimum period of 2 years after completion of therapy. If this is not possible contacts should be examined at least once during this period.  
Apart from household contacts, other contacts are also subject to varying degrees of risk of both infection and disease. If such contacts can be defined and identified they too should be kept under surveillance for similar periods.

Organization of case-finding activities
In organizing case-finding activities in a country, the most important aim should be to conform to the sociological and cultural expectations and traditions of the community in an acceptable way. The methodology adopted should also be cost-
effective both in terms of financial and manpower resources.

The choice of the method to be adopted will depend on:
- the prevalence of the disease;
- the population density;
- the terrain;
- the communication network, e.g., roads, rivers, etc.;
- the distribution of the population (rural and urban); and
- the structure of the health care system.
Chapter 5

Diagnosis and classification

Diagnosis

Diagnostic tools
The tools available for the diagnosis of leprosy are very limited and diagnosis still has to be based mainly on clinical grounds. It must, however, be confirmed by bacteriological examination, which is positive only in multibacillary patients. The lepromin test\(^1\) has no relevance to the diagnosis of leprosy. In certain special situations, when the diagnosis is in doubt and facilities are available, a biopsy may be necessary for histopathological examination. However, the interpretation of histopathological investigations can present difficulties.

Although considerable inter- and intra-observer variation has been noted among both medical and paramedical workers, the sensitivity and specificity of diagnosis can be considerably enhanced when it is undertaken by well trained and experienced staff using standard criteria and standardized methods of examination.

Signs of leprosy
The diagnosis of leprosy is based on the demonstration of at least two of the first three cardinal signs enumerated below or the last one independently.

1) *Characteristic skin lesions*. The essential characteristic of lesions of tuberculoid and indeterminate leprosy in a dark skin is hypopigmentation, whether the lesions are macular or infiltrated, with

\(^1\) This test is described on page 29
sensory loss. In light skins the lesions are copper coloured or erythematous. The lesions of lepromatous leprosy show one or more of its characteristic features such as diffuse infiltration, macules, papules and nodules.

2) Sensory loss. This may be of individual skin lesions or of an area of the skin supplied by a peripheral nerve.

3) Thickened nerves at the sites of predilection, e.g., the ulnar nerve immediately above the ulnar groove; the posterior tibial nerve behind the medial malleolus; the lateral popliteal nerve as it winds round the neck of the fibula; the radial cutaneous nerve at the wrist; the facial and greater auricular nerves; and the median nerve proximal to the flexor retinaculum. In addition, cutaneous branches associated with a lesion may be enlarged.

4) The presence of acid-fast bacilli in slit-skin smears. The appearance of skin lesions is very often characteristic and alone is sometimes sufficient to suggest the diagnosis. A long history of disease, a slow and insidious onset combined with absence of irritation and itching, are highly suggestive of leprosy but not diagnostic unless they are supported by at least one of the other signs, i.e., sensory loss, thickened nerves, or acid-fast bacilli in the skin smears.

The diagnosis should be established after a detailed clinical examination, and only when the signs and symptoms are clear and unequivocal. If there is even the slightest doubt, the patient should be kept under observation until further evidence confirms the diagnosis.

Clinical examination for leprosy

History
A history should be taken eliciting the timing, site, and nature of the first lesions noticed. The timing, order of development, and nature of subsequent lesions both of the skin and the nerves should also be noted. Details regarding past treatment should be carefully elicited and the family history, including information regarding the possible source of infection, should be ascertained. The general history should include information regarding significant past diseases and intercurrent illnesses.

Examination for leprosy
The examination should be performed in good, preferably oblique, light. The patient should be disrobed and the whole skin should be examined, care being taken to respect the patient’s privacy. Special attention should be given to areas where lesions commonly occur, i.e., the face, ears, buttocks, lateral aspect of extremities, back, etc. The examiner should look for skin lesions, e.g., infiltration, macules, papules and nodules, and should also note any muscular wasting, weakness, paralysis, deformities, or trophic ulcers. The number and type of skin lesions, whether macules, plaques, annular lesions, nodules or infiltration, should be recorded and may be mapped on outline body charts.

The activity of the skin lesions should be noted, including the presence or absence of erythema, the degree and extent of infiltration, and the presence or absence of reaction, including oedema and scaling of lesions and oedema of hands and feet. The periphery of each skin lesion, especially the proximal edge, should be carefully palpated for the presence of enlarged cutaneous sensory nerves.

The main peripheral nerve trunks involved in leprosy should then be examined and their size (whether normal or slightly, moderately or markedly enlarged) and their consistency (whether normal, firm or hard) should be recorded. Tenderness should also be noted. Each nerve on one side should be carefully compared with the corresponding nerve on the opposite side.
The nerves to be palpated include:

1) the ulnar nerve — palpation immediately above the ulnar groove;
2) cutaneous branch of the radial nerve — palpation at the lateral border of the radius proximal to the wrist joint;
3) median nerve — deep palpation above or below the antecubital fossa, medial to the brachial artery and/or in front of the wrist between the tendons of the palmaris longus and the flexor carpi radialis;
4) radial nerve — deep palpation of the radial groove on the humerus posterior to the deltoid insertion;
5) lateral popliteal nerve — palpation around the knee to feel the nerve in the popliteal fossa just medial to the biceps femoris tendon, and as it passes around the neck of the fibula;
6) posterior tibial nerve — palpation of the nerve posterior and inferior to the medial malleolus;
7) anterior tibial nerve — palpation of the nerve as it emerges from under the flexor retinaculum lateral to the tendon of the extensor hallucis longus;
8) great auricular nerve — palpation after turning the head to one side thus stretching the nerve across the sternomastoid; and
9) supraorbital nerve — palpation by running the index finger across the forehead from the midline laterally.

Of the above, the examinations of the ulnar and lateral popliteal nerves are the most important.

The loss of cutaneous sensation may be to light touch, pain or heat and cold. Testing is usually carried out for both light touch and pain sensation. Sensitivity to heat and cold may also be tested. Loss of sensation is more marked in the centre of a lesion than at its margin. Loss of sensation is not a characteristic feature in early leprous ulcers; however, in advanced cases it may be extensive, for example, bilateral anaesthesia of the glove-and-stocking type.

Tactile sensitivity is examined by light touch using a piece of thin paper, a light feather, a wisp of cotton wool, or graded nylon bristles. Loss of sensation is called anaesthesia, its impairment is hypoesthesia.

The loss of pain sensation is called analgesia and its impairment is hypoalgesia. In leprosy only superficial pain sensation is lost while sensitivity to deep pain and pressure remains intact. Superficial pain sensation is tested by pin prick.

All sensory tests should be performed with the patient blindfolded or with a barrier so that the stimuli cannot be seen. The test must, however, first be demonstrated with the eyes open and using a normally sensitive skin area so that the patient can see and understand what is required.

Sensory loss could be due to:

a) nerve trunk damage, e.g., ulnar area of forearm and hand;
b) widespread damage to dermal nerves, e.g., glove-and-stocking type of anaesthesia; or
c) localized damage to dermal nerves, e.g., at the site of tuberculoid or borderline lesions.

Areas of sensory loss should be recorded, if possible, on a body outline chart.

In some situations it may be necessary to test for thermal sensation. This can be done using two test-tubes, one half-filled with cold water at 20°C (70°F), and the other with hot water at 40°C (104°F). Normal parts are first touched alternately with the two test-tubes to ascertain whether the patient can differentiate between the hot and cold tubes. After this the affected part and the corresponding normal part on the other side of the body are similarly tested.

Nerve motor function should also be assessed, especially that of the ulnar, median, facial, lateral popliteal, and posterior tibial nerves using the abbreviated
voluntary muscle test (VMT), which is outlined in Annex 1.

The presence and degree of severity of deformities should be carefully recorded, e.g., lagophthalmos, claw-hand, foot drop, claw toes, etc. A scheme of classification of disabilities was recommended by the WHO Expert Committee on Leprosy in its sixth report in 1988 (8). It provides a baseline from which a disability grading can be made to indicate treatment needs, and also permits assessment of progress under treatment. The recommended grading system has three grades, each related to the severity of the disability and the possible action that can be taken by the field staff. The details of the WHO disability grading are given in Annex 2. The presence of trophic lesions and evidence of healed trophic ulcers should also be noted.

The eyes should be carefully examined including the eyebrows, eyelashes, lids, conjunctiva, lens and pupil. The nose and nasopharynx should also be inspected and any abnormalities recorded.

**General physical examination**

This is necessary in all patients in whom the diagnosis of leprosy is confirmed. It is a prerequisite for the commencement of multidrug therapy, the objective being to determine contraindications or intercurrent ailments that may preclude the use of drugs recommended in the combined chemotherapeutic regimens.

**Routine laboratory investigations**

**Bacteriological examination**

This is an essential aid to the clinical examination and a prerequisite for the commencement of multidrug therapy. It is an essential screening procedure for all patients in whom the diagnosis of leprosy is made after a detailed clinical examination. It assists in:

1) the diagnosis of leprosy;
2) classification before commencement of multidrug therapy;
3) monitoring the response to treatment in multibacillary patients;
4) defining the end-point of treatment in multibacillary patients;
5) assessing the prognosis of patients; and
6) estimating the epidemiological importance of patients and assigning priorities for treatment, contact examination, etc.

In the past, when dapsone monotherapy was the sheet anchor in leprosy treatment while diagnosis was critical, classification was relatively less important, as the treatment was then similar for all types of the disease and only its duration varied. Now, with the introduction of multidrug therapy with different regimens for paucibacillary and multibacillary leprosy and the implementation of the revised strategy, the issue has become much more important. Hence smear examination has now become critical for the choice of drug regimens and the success of chemotherapy.

Unfortunately, despite its importance and its relevance to control, smear microscopy is probably the weakest link in most leprosy control programmes in endemic countries. In peripheral health units, laboratory technicians are often unwilling to take and process smears from leprosy patients. Even when they are, the preparation, staining and examination of smears are not usually done under optimum conditions. The common practice is therefore to rely on clinical examination alone for the diagnosis of leprosy, neglecting bacteriological examination or ignoring its result. For the purpose of diagnosis and classification and for the choice of drug regimens, the correct technical performance of smear examinations is most important, and a standardized technique must be used. Such examinations also permit the clear
identification of patients who, if untreated, would have the most unfavourable prognosis and would be the most dangerous source of infection in the community.

It is therefore essential to organize an efficient service for the collection of skin smears and their processing in order to ensure the uniformity and reliability of smear microscopy. This will involve the provision of equipment and supplies, the training and retraining of staff and their continuous monitoring and supervision.

Skin smears should be taken from a minimum of three sites, including one earlobe and two representative, active skin lesions. In paucibacillary patients, if there is only a single skin lesion, then two smears may be taken from its active edge at sites diametrically opposite to each other. Smears can also be made from nasal secretions obtained by swab, by washing the nose, or by getting the patient to blow his or her nose. Details of the methodology for taking, fixing, processing and reading smears, including care of the microscope, are given in Annex 3.

Detection of acid-fast bacilli and assessment of their numbers and morphological appearance require a carefully standardized acid-fast stain and skilful use of a good microscope. The bacillary count is generally measured by Ridley's logarithmic scale and the bacterial index (BI) calculated.

The results of smear examinations are sensitive and specific when properly performed by adequately trained laboratory technicians. False positive results may occur owing to:

1) precipitate stains—freshly prepared stains should always be used to avoid this;
2) saprophytic acid-fast bacilli;
3) fibres, pollen, etc.;
4) scratches on the slide;
5) contamination through transfer of bacilli from one smear to another—slides should therefore never be used more than once.

False negative results may occur owing to:

1) inadequate preparation of smears—the smear is too thin or too thick; overheating during fixation; or insufficient fixation.
2) improper staining—staining with carbol fuchsin is too short or overdone by boiling; counter-staining is too intensive so that the acid-fast bacilli are obscured.
3) inadequate examination of the smear—scanning is done erratically or too briefly so that few fields are examined.

Administrative errors that may arise are:

1) mistakes in labelling, code numbers or identification of patients;
2) false reporting.

Quality control and continuous supervision and monitoring are therefore necessary to ensure that performance standards are maintained at a high level of operational efficiency and do not deteriorate in scope and function. Observer errors and reader variation can be avoided if laboratory technicians are properly trained and adequately supervised.

Other laboratory investigations

Other facilities for routine investigations should also be available, e.g., sputum for acid-fast bacilli, haemogram, urine, etc. The need for such investigations may arise to determine contraindications or intercurrent ailments that may preclude the use of drugs recommended in the combined chemotherapeutic regimens. The resources of the district public health laboratories and the peripheral laboratory service must be made available for leprosy patients to the same extent as for other types of patients, if the need arises.
Histopathological examination

A diagnosis of leprosy can usually be made on the basis of a detailed clinical examination and a careful bacteriological examination. In a small number of cases, when the diagnosis is still in doubt, a histopathological examination may be of some assistance. Histopathology is useful in confirming a diagnosis of leprosy, particularly in children, when sensory testing cannot be carried out easily, and in early lesions, e.g., indeterminate leprosy.

Two aseptic techniques are used for performing skin biopsies, the incision method and the punch method, using a 5- or 6-mm punch. While biopsies can be taken in field situations using aseptic techniques, histopathological examination can only be done in the laboratory by a trained pathologist. It is possible to send biopsy specimens to a central laboratory for this purpose either within the country or abroad. The procedures for taking biopsies and for their storage and shipment are given in Annex 4.

In macular lesions, the appearance of non-specific round-cell infiltration is not characteristic of leprosy. Only the presence of acid-fast bacilli in one of several characteristic sites—a nerve bundle, the subepidermal zone or an arrector pili muscle—is diagnostic of leprosy. This usually involves meticulous searching of a number of serial sections.

Operational definition of a case of leprosy

At present, leprosy patients who need or are receiving treatment, those who have completed multidrug therapy (see Chapter 6) and require, or are under, surveillance, as well as those with deformities and disabilities resulting from leprosy in the past and in need of care, are grouped together as "cases of leprosy". The failure to distinguish between these categories continues to be a source of error in computing and comparing prevalence and other statistics necessary for planning and organizing leprosy control programmes.

A case of leprosy is a person having clinical signs of leprosy, with or without bacteriological confirmation of the diagnosis, and requiring chemotherapy. It is recommended that this definition be adopted by all countries so that information on prevalence can be meaningfully interpreted. It is also recommended that separate lists be maintained for the other two categories (patients who have completed treatment and require, or are under, surveillance, and those with deformities and disabilities due to past leprosy).

Thus, for operational purposes, those who have or have had leprosy will fall into one of the following three categories:

- those requiring or under chemotherapy;
- those who have completed chemotherapy and require to be, or are under, surveillance; and
- those released from surveillance but in need of care or assistance because of disabilities.

There will be also a fourth category of individuals who need not be maintained in any register or list, i.e., those released from surveillance and not in need of any further attention.

Prevalence of leprosy should be computed on the basis of the first category of patients only.

Classification

A system of classification is of value in many diseases; it has increased importance in a chronic disease such as leprosy, which has wide variations in its clinical manifestations associated with marked differences
in immunology, histology, evolution and epidemiology.

The main relevance of classification to the revised strategy for leprosy control relates to:

1) the choice of appropriate chemotherapeutic regimens required for treatment;
2) the identification of infectious patients who are of the highest epidemiological importance and should therefore be the principal target of chemotherapy; and
3) the identification of patients who are most likely to develop deformities.

The primary basis of the classification should be clinical, concerning the morphology of skin lesions and the neurological manifestations; bacteriological examination of smears from skin lesions is an indispensable adjunct. Classification should also be broadly structured in relation to the immunological and histological background.

**International classification**

In 1953 in Madrid, the Sixth International Congress of Leprosy (9) recommended that leprosy should be classified as follows.

**Lepromatous form (L)**

A malign form, especially stable, strongly positive on bacteriological examination, presenting more or less infiltrated skin lesions, and negative to lepromin. The peripheral nerve trunks become manifestly involved as the disease progresses, habitually in symmetrical fashion, and often with neural sequelae in advanced stages.

**Tuberculoid form (T)**

Usually benign, stable; generally negative on bacteriological examination; presenting in most cases erythematosus skin lesions which are elevated marginally or more extensively; positive to lepromin.

Sequelae of peripheral nerve trunk involvement may develop in a certain proportion of cases and this may give rise to serious and disabling deformity. This frequently appears to occur as a result of extension from, or through, cutaneous nerve branches, rather than of systemic dissemination, and consequently it is often asymmetric and unilateral.

**Indeterminate group (I)**

A benign form, relatively unstable, seldom bacteriologically positive, presenting flat skin lesions which may be hypopigmented or erythematous; the reaction to lepromin may be negative or positive. The indeterminate group consists essentially of the "simple macular" cases. These cases may evolve towards the lepromatous form or the tuberculoid form or may remain unchanged indefinitely. Neuritic manifestations, more or less extensive, may develop in cases that have persisted for long periods.

**Borderline (dimorphous) group (B)**

A malign form, very unstable; almost always strongly positive on bacteriological examination; the lepromin reaction generally negative. Such cases may arise from the tuberculoid form as a result of repeated reactions, and sometimes they evolve to the lepromatous form. The nasal mucosa often remains bacteriologically negative even when the skin lesions are strongly positive. The skin lesions are usually seen as plaques, bands, nodules, etc., with a regional distribution similar to that of lepromatous leprosy except for conspicuous asymmetry. The ear-lobes are likely to present the appearance of lepromatous infiltration. The lesions frequently have a soft or succulent appearance, and peripherally they slope away from the centre and do not present the clear-cut, well-defined margins seen in the tuberculoid form; they are therefore liable to be mistaken for lepromas. The surface of the lesions is

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1 The word "stable" implies stability as regards the form, not as regards the severity of the disease.

2 The lepromin test is described on page 28.
generally smooth with a shiny appearance and a violaceous hue, sometimes (in light skins) with a brownish (sepia) background.

In 1977, the WHO Expert Committee on Leprosy (5) considered that the Madrid classification was precise and simple enough to be used by auxiliary health workers, and recommended that the classification should continue to be used in leprosy control programmes.

The Indian classification, as revised in 1980 (10), is now more in line with the Madrid classification. Maculoanaesthetic lesions (well-defined flat patches with loss of sensation) are now included with the tuberculoid type of leprosy. The only difference between the two classifications is the retention in the Indian classification of purely neural cases without recognizable skin lesions as a separate class, designated “pure neuritic”.

The Ridley & Jopling classification

The classification proposed by Ridley & Jopling in 1962 (11) was originally intended for research purposes. In 1966, it was developed into a five-group system (12) which expressed the immunity of the patient, since it is the immune response that determines both the disease spectrum and the prognosis.

Some modifications have been made in the groups originally proposed, and those now recommended by Ridley are (13, 14): 1) indeterminate (I) first stage and second stage; 2) tuberculoid (TT); 3) borderline tuberculoid (BT); 4) mid-borderline (BB); 5) borderline lepromatous (BL); and 6) lepromatous (LL).

Indeterminate (I)

First-stage indeterminate lesions

Infection with a small number of leprosy bacilli will produce no obvious response in the patient and no immediate disease. If the patient’s immune response is good enough to detect and destroy the bacilli before multiplication occurs, the patient will develop immunity and will never have the disease. If the immune response is slightly less good, a clump of bacilli will become established and multiply to the point at which they become detected. A lesion will develop, but because the bacilli are few and hypersensitivity has not yet developed the response will be mild, nonspecific and, from the viewpoint of classification, indeterminate. The lesion will also probably be self-healing. If the patient’s immune system is still less good, the bacilli will multiply further before they are detected immunologically and the disease will not be self-healing. If the immunity is very low, the bacilli will become disseminated before they are detected.

The lepromin test usually gives a weak response and is of little help. Multiple lesions always indicate low immunity.

Second-stage indeterminate lesions

When the disease becomes slightly more advanced, its character becomes apparent clinically from the size and distribution of the lesions, the nature of their edge, the degree of erythema, and subtle sensory changes. These characteristics are largely due to vascularity and nonspecific infiltration, neither of which is of much value for histological classification, which is dependent mainly on the finding of a granuloma. At the earliest stage, therefore, histological classification is dependent on good selection of the biopsy site and quite possibly on the cutting of serial sections to find a clump of granuloma cells; even then the biopsy may be histologically indeterminate, even though the patient is clinically classifiable. At this stage the lepromin test usually supports the clinical classification.

Tuberculoid (TT)

This form corresponds essentially to the stable tuberculoid form of the Madrid classification. Histologically, it is an epithelioid granuloma with a significant number
of lymphocytes containing giant cells of any sort but no clear subepidermal free zone. There is deep and fairly extensive erosion of the epidermis, central caseation of a nerve bundle in the dermis, or massive enlargement of a nerve bundle. The bacterial index on histological examination for acid-fast bacilli (AFB) in the granuloma is 0–1. This form is stable immunologically and lepromin-positive: 3+.

**Borderline tuberculoid (BT)**

In this form there are relatively few skin lesions; they closely resemble TT lesions but tend to be more symmetrical. The nerves are commonly involved and nerve damage may occur silently or during a reaction. The bacterial index on histological examination is 0–2½ (AFB in granuloma). Lepromin (Mitsuda) reaction: 2+ or 1+.

**Mid-borderline (BB)**

The skin lesions are more numerous and are raised and plaque-like, even dome-shaped, with punched-out areas. There is relatively little involvement of nerves. Histologically the appearance is one of an epithelioid granuloma without giant cells and with a clear subepidermal zone. The bacterial index on histological examination is 3–4½. Lepromin (Mitsuda) reaction: negative or mildly positive.

**Borderline lepromatous (BL)**

In this form the skin lesions are innumerable and present a variety of forms, tending to be shiny with rather indefinite edges. The nerve trunks are often asymmetrical and enlarged. Histologically the appearance is one of a macrophage granuloma with some foamy change; the subepidermal zone is clear. Smears are markedly positive in lesions, but may be negative elsewhere. The bacterial index on histological examination is 4–5½. Lepromin (Mitsuda) reaction: negative.

**Lepromatous (LL)**

This form corresponds essentially to the lepromatous form in the Madrid classification. Histologically there is a macrophage granuloma with no epithelioid cells; there may or may not be foamy change; there is a subepidermal free zone. The nerves may show slight enlargement or be fairly normal. Cases are strongly positive on bacteriological examination and immunologically stable, i.e., lepromin-negative.

Because of the important public health significance of the multibacillary forms, more specific descriptions are given of the polar lepromatous (LLp) and subpolar lepromatous forms (LLs) of leprosy.

Classical polar lepromatous leprosy (LLp) is well recognized wherever leprosy occurs; the lesions show marked bilateral symmetry. The skin lesions are numerous with smooth, shiny erythematous surfaces and are neither anaesthetic nor anhidrotic. Early cases may have numerous small hypopigmented macules and papules with indefinite edges; the nerves may be only slightly thickened at this stage, although significant involvement of the nasal mucosa is frequently detected. With time, plaques and nodules develop and the skin thickens progressively as lepromatous infiltration increases. The ear lobes enlarge and the lines of the face coarsen and deepen to produce the characteristic "leonine facies". The lips often swell and the eyebrows and eyelashes become scanty. Iritis and keratitis are common. Nasal blockage occurs and saddle-nose deformity may develop. The lymph nodes frequently enlarge and the testes are infiltrated and may later become atrophic. Dermal nerve damage leads to progressive anaesthesia resembling glove-and-stocking anaesthesia, so that light touch, pain and temperature sensation are eventually lost over most of the body except the hairy scalp and the flexures. Numerous bacilli are present in the skin lesions and nasal mucosa as well as at a number of other sites.
Classical LLp leprosy appears to arise de novo. However, in some lepromatous patients, probably in all races but most commonly in those of South-East Asia, there is evidence that the disease originated as borderline leprosy and, in the absence of treatment, evolved to the lepromatous form. Such patients are now classified as subpolar lepromatous (LLs).

The majority of LLs patients present an appearance closely resembling that of polar lepromatous cases. However, many state that months or years before they began to develop papules and thickening of the skin, they had noticed a numb patch or an annular lesion. On careful inspection, others may be found and their likeness to the various forms of borderline lesions is evidence of their less extreme position in the spectrum. As in LLp leprosy, most of the nerves of predilection are slightly enlarged symmetrically, but one or even two nerves may be markedly enlarged and the damage may be severe enough to result in claw-hand or foot drop.

The lepromin (Mitsuda) reaction is absent, i.e., negative, in LLp and LLs.

Classification for control programmes

The new approach to leprosy control, involving the use of multidrug therapy, has inevitably resulted in some changes in terminology. It must, however, be stressed that this is not an attempt to formulate another system of classification but only a systematic method of grouping patients according to chemotherapy, which is, in effect, antibacterial treatment directed specifically against *M. leprae*.

In this context, the disease is now classified as either multibacillary or paucibacillary leprosy. The descriptive terminology used is essentially a working definition meant to serve as a basis for action. Therefore, it must be judged by its practical applicability and not by the degree of its completeness.

**Paucibacillary leprosy**

Paucibacillary leprosy will include only smear-negative indeterminate (I), tuberculoid (TT) and borderline tuberculoid (BT) cases on the Ridley-Jopling scale or indeterminate (I) and tuberculoid (T) cases in the Madrid classification. Any case belonging to these types but showing smear positivity should be classified as multibacillary for purposes of multidrug therapy programmes.

**Multibacillary leprosy**

Multibacillary leprosy includes all mid-borderline (BB), borderline lepromatous (BL) and lepromatous (LL) cases in the Ridley-Jopling scale or borderline (B) and lepromatous (L) cases in the Madrid classification, as well as any other types when smear-positive.

For purposes of multidrug therapy (see Chapter 6), patients who have already been treated should be classified as follows:

- **a)** those who would have been in the multibacillary group at the time of diagnosis of their disease should still be classified as such, irrespective of their current bacterial index;
- **b)** those who would have initially been in the paucibacillary group should be classified according to their current clinical and bacteriological status.

**Important clinical features related to classification**

The importance of a proper classification in leprosy is clearly of more than academic interest, since it forms the basis for appropriate chemotherapy. Tables 2 and 3 briefly describe the main characteristics of multibacillary and paucibacillary leprosy. In field conditions they permit an accurate differentiation of these two distinct types of leprosy.
Table 2. Clinical characteristics of multibacillary leprosy

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Lepromatous (LL)</th>
<th>Borderline lepromatous (BL)</th>
<th>Mid-borderline (BB)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lesions type</td>
<td>macules, diffuse infiltration, papules, nodules</td>
<td>macules, plaques, papules, infiltration</td>
<td>plaques, bands, and dome-shaped punched-out lesions</td>
</tr>
<tr>
<td>number</td>
<td>numerous, widely distributed, practically no normal skin areas</td>
<td>many, but normal skin areas present</td>
<td>several, normal skin present</td>
</tr>
<tr>
<td>distribution</td>
<td>symmetrical</td>
<td>tends to be symmetrical</td>
<td>conspicuous asymmetry</td>
</tr>
<tr>
<td>surface</td>
<td>smooth and shiny</td>
<td>smooth and shiny</td>
<td>slightly shiny, some lesions may be dry</td>
</tr>
<tr>
<td>definition</td>
<td>vague, merge imperceptibly with the surrounding areas</td>
<td>vague, sloping outwards</td>
<td>vague, sloping outwards</td>
</tr>
<tr>
<td>sensation</td>
<td>not affected</td>
<td>slightly diminished</td>
<td>moderately diminished</td>
</tr>
<tr>
<td>Acid-fast bacilli in skin lesions</td>
<td>many (plus globi)</td>
<td>several</td>
<td>many</td>
</tr>
<tr>
<td>in nose blow</td>
<td>many (plus globi)</td>
<td>usually nil</td>
<td>nil</td>
</tr>
<tr>
<td>Lepromin test</td>
<td>negative</td>
<td>negative</td>
<td>usually negative, may be doubtful (±)</td>
</tr>
</tbody>
</table>

Table 3. Clinical characteristics of paucibacillary leprosy

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Tuberculous (TT)</th>
<th>Borderline tuberculous (BT)</th>
<th>Indeterminate (I)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lesions type</td>
<td>infiltrated patches</td>
<td>infiltrated patches</td>
<td>macules</td>
</tr>
<tr>
<td>number</td>
<td>single or few</td>
<td>single or few satellite lesions present</td>
<td>single or few</td>
</tr>
<tr>
<td>distribution</td>
<td>localized and asymmetrical</td>
<td>not wide, asymmetrical</td>
<td>variable</td>
</tr>
<tr>
<td>surface</td>
<td>dry and scaly</td>
<td>dry and scaly</td>
<td>may be smooth</td>
</tr>
<tr>
<td>definition</td>
<td>well-defined, clear-cut margins</td>
<td>well-defined, clear-cut margins</td>
<td>not always well defined</td>
</tr>
<tr>
<td>sensation</td>
<td>absent</td>
<td>absent</td>
<td>impaired</td>
</tr>
<tr>
<td>Acid-fast bacilli in skin smears</td>
<td>negative</td>
<td>negative or just 1+ at any site</td>
<td>usually negative</td>
</tr>
<tr>
<td>Lepromin test</td>
<td>strongly positive (3+) weakly positive (2+)</td>
<td>may be doubtful (1+)</td>
<td></td>
</tr>
</tbody>
</table>
The lepromin test

The lepromin test is not a diagnostic test for leprosy. It may, however, be useful in classifying a patient once a diagnosis has been made. First described by Mitsuda in 1919 (15), the test involves the intradermal injection of an autoclaved, emulsified preparation of lepromatous tissue, known as lepromin, standardized according to the content of killed *M. leprae*.

The usual number of acid-fast bacilli (AFB) in integral Mitsuda-type lepromin ranges between $4.0 \times 10^7$ and $1.6 \times 10^8$ AFB per ml. Lepromin can be prepared from either lepromatous skin lesions such as nodules of human patients (lepromin H) or from the tissues of experimentally-infected armadillos (lepromin A). Lepromin A tends to show slightly stronger reactivity than lepromin H. For studies in the field, lepromin A (40 million bacilli per ml) is recommended. It should be stored in a refrigerator at 4 °C.

To undertake the test, 0.1 ml of lepromin is injected intradermally into the flexor surface of the forearm using a 25-gauge hypodermic needle. A standard site should be used as a routine for operational purposes, e.g., 3 cm below the elbow crease on the flexor surface of the left forearm. This will prevent confusion when the result of the test is read after 4 weeks, particularly when the field worker reading the test is not the person who injected the lepromin.

The Fernandez reaction is read, like the reaction to tuberculin, after 48–72 hours. The late Mitsuda reaction is read after 4 weeks using a millimetre rule to measure the longest and perpendicular diameters of the induration, and the results are recorded. If ulceration is observed this is also recorded. The criteria for grouping the results are as follows:

- **0** = no reaction
- **±** = induration less than 3 mm
- **1+** = nodule of 3–5 mm
- **2+** = nodule of 6–10 mm
- **3+** = nodule >10 mm or with ulceration.

The letter U should be added to the size to indicate ulceration.

In general, the Mitsuda reaction is more reliable and should be preferred to the Fernandez reaction.

The test is positive in patients with tuberculoid and borderline tuberculoid leprosy, while it is negative in lepromatous and borderline lepromatous leprosy. In mid-borderline and indeterminate leprosy the results are variable, being usually negative or, rarely, weakly positive; the test may be of use in assessing the direction of immunological shift.
Treatment and patient care

Objectives

Treatment as an intervention strategy in the context of a public health programme implies an organized effort to provide efficient chemotherapy for all known cases of leprosy in the community. This involves administering the correct dosage and combination of drugs, and ensuring regularity of intake and adequate duration of chemotherapy. It is expected that, when all known sources of infection in the community are under effective treatment, transmission of the disease will be interrupted. Treatment therefore has wider implications than the cure of individual patients, though this remains an important aspect.

Recent advances in chemotherapy

As outlined in Chapter 3, in the early days of chemotherapy, it was considered that dapsone used as a single drug would be adequate to achieve the required objectives; however, in practice this was found not to be so. The situation was complicated by the difficulties in ensuring regularity of drug intake in the long term and the steadily increasing prevalence of dapsone resistance.

The problem of drug resistance can be overcome by using a combination of at least two fully potent drugs, as each drug prevents the growth of mutants that are resistant to the other. Mutants resistant to one drug are normally susceptible to the other and vice versa. The presence of mutants resistant to both drugs is extremely unlikely (about 1 in 10^{12}, for M. tuberculosis).
The recommendation by the WHO Expert Committee on Leprosy in its fifth report in 1977 (5), that all active cases of multibacillary leprosy should be treated with at least two effective antileprosy drugs, was not followed much in the field for several reasons, including financial considerations.

It was in this context that a WHO Study Group on Chemotherapy of Leprosy for Control Programmes met in Geneva in October 1981 to define drug regimens that would be both effective and applicable under field conditions (7).

Objectives of multidrug therapy

The objectives of combined chemotherapy are:

a) the effective killing of M. leprae in the shortest possible period; and
b) prevention of the emergence of resistant strains of M. leprae, in turn leading to the prevention of treatment failures and relapse.

Requirements of multidrug regimens

The drug regimen selected should be:
- therapeutically effective;
- operationally feasible for field use; and
- socially acceptable, with minimal adverse side-effects.

Implications for the treatment of multibacillary patients

It is expected that by analogy with the situation in tuberculosis, there is a direct quantitative or numerical relationship between the number of resistant organisms and the total bacillary load. The proportion of spontaneous mutants is believed to be between 1 in 10^3 and 1 in 10^6 in any bacterial load. Drug resistance is therefore more likely to occur in multibacillary patients who have a high bacterial load, i.e., about 10^11 viable organisms. The problem can be overcome in multibacillary patients by giving combined treatment with two fully potent drugs. Thus patients infected with drug-sensitive M. leprae can be effectively treated with a combination of dapsone and another potent drug, while those infected with dapsone-resistant organisms should be treated with a combination of two other drugs. However, in view of the rapidly increasing prevalence of both secondary and primary dapsone resistance throughout the world, and the virtual impossibility of diagnosing it under field conditions, every multibacillary patient must be considered as potentially suffering from dapsone-resistant leprosy. Hence the WHO Study Group on Chemotherapy of Leprosy for Control Programmes (7) recommended that all multibacillary patients should be treated with a combination of dapsone plus two other potent drugs, so that whatever the level of their dapsone resistance, they would receive fully effective chemotherapy.

Drugs suitable for multidrug regimens

The most important factors affecting the choice of drugs in combined regimens are their potency, acceptability and toxic side-effects. Considerations of cost can at best be only of secondary importance. It would be unrealistic to set up an efficient treatment service that delivers unsatisfactory chemotherapy.

A potent antileprosy drug may be defined as one that is able to prevent completely the multiplication of drug-sensitive M. leprae. If an antileprosy drug
has only bacteriostatic activity, the bacilli are able to resume multiplication as soon as the drug levels fall below the minimum inhibitory concentration, in which case regularity of drug intake becomes critical. When, however, drugs have a significant bactericidal or bacteriopausal activity, and are capable of either killing the bacilli or preventing regrowth for a significant period after the drug has been eliminated from the body, it is no longer essential to maintain continuous inhibitory levels in the body. Patient compliance then becomes less critical, and the possibility arises of devising effective regimens based on supervised intermittent dosage. Drugs with bactericidal activity against M. leprae are: dapsone, rifampicin, clofazimine, ethionamide and protonamide.

**Dapsone**

Dapsone is cheap, easily administered, and virtually without toxicity in the dosage used.

The drug is quickly and almost completely absorbed from the stomach, peak plasma levels being reached in 3-6 hours. It has excellent tissue penetration and is widely distributed in the body. About 75% of the drug is bound to plasma protein. It is an extremely active antileprosy drug with a minimum inhibitory concentration (MIC) of 0.003 mg/litre against M. leprae. It is excreted very slowly in the urine and has a long half-life of 27 hours. Serum concentrations of the drug remain higher than its MIC for 10 days. It can therefore inhibit the multiplication of fully sensitive M. leprae even if minor lapses occur in drug intake.

When given in a dose of 100 mg daily dapsone is weakly bactericidal against M. leprae both in mice and in human subjects. Such a dosage results in peak serum levels 500 times higher than the MIC of the drug against M. leprae. This large therapeutic margin is quite exceptional and is of great practical importance. Such high levels of the drug will inhibit the multiplication of mutants of M. leprae with low or even moderate resistance to dapsone.

Adverse side-effects are rare when dapsone is used in the recommended daily doses. They may include:

- anaemia (mild haemolysis is common but anaemia is rare);
- allergic rashes including exfoliative dermatitis;
- hypermelanosis or fixed drug eruption;
- hepatitis;
- psychosis.

In addition, peripheral neuropathy has been reported by dermatologists in a few cases, and agranulocytosis has been observed following use of the drug for malaria prophylaxis.

Dapsone treatment should not be commenced when haemoglobin levels are very low.

**Rifampicin**

*M. leprae* is extremely sensitive to this semisynthetic antibiotic.

Rifampicin is rapidly absorbed with a wide tissue distribution. The capacity of the drug to cross lipid membranes, while retaining its antimicrobial activity in an acid environment, finds one of its most useful applications in infections where bacteria survive within cells, e.g., tuberculosis and leprosy.

The MIC of rifampicin against *M. leprae* is 0.3 mg/litre. At a dosage of 600 mg the peak serum concentration is 30 times higher than the MIC. Its speed of bactericidal action is unique and its mode of action is through selective inhibition of DNA-dependent RNA polymerase.

Rifampicin is an expensive drug. The therapeutic dose recommended for daily administration is 4-8 mg/kg of body weight. In intermittent regimens, however, the dose should be increased to
12–15 mg/kg of body weight in both adults and children. It is relatively nontoxic when administered daily. When it is administered intermittently, however, toxic syndromes may be encountered, the toxicity depending both on dosage and the interval between doses. Toxic effects are more frequently seen when the drug is given at weekly intervals than at shorter intervals. No significant toxic effects have been reported in the case of monthly administration.

It has been shown that daily administration of 600 mg of rifampicin is no more effective than monthly administration of 600 mg on each of two consecutive days. Because of its expense and the risk of toxicity the administration of rifampicin should be fully supervised.

Rifampicin-resistant strains of M. leprae have been isolated from lepromatous leprosy patients who relapsed after approximately 4 years' treatment with rifampicin as monotherapy. It has no cross-resistance with other antileprosy drugs. The pattern of resistance is of the single-step type.

In tuberculosis, rifampicin is exceptional in killing resting or near-dormant bacilli, although the degree of activity is lower than against multiplying bacilli. Regimens containing rifampicin are therefore recommended as more efficient chemotherapy for the elimination of persistent bacilli. A similar action in leprosy has not been confirmed.

Adverse side-effects with rifampicin are rare. Reactions that may be observed with intermittent regimens are as follows:

- a cutaneous syndrome consisting of flushing and/or pruritus, with or without rash, involving particularly the face and scalp, often with redness and watering of the eyes;
- an abdominal syndrome consisting of pain and nausea sometimes accompanied by vomiting or, less frequently, diarrhoea;
- an "influenza" syndrome consisting of fever, chills, malaise, headache and bone pains;
- a respiratory syndrome consisting of shortness of breath rarely associated with shock and collapse—this is extremely uncommon;
- purpura and other rare reactions, such as haemolytic anaemia, shock and renal failure;
- elevated serum aminotransferase levels may occur with low risk of hepatitis; toxic jaundice is rare and often regresses spontaneously; systematic monitoring by liver function tests is therefore not necessary and has no predictive value for toxicity.

The first four syndromes typically begin 2–3 hours after the single morning dose. Many patients have more than one syndrome. The onset of the more common syndromes is as follows.

1) Cutaneous episodes usually start during the first month.
2) Gastrointestinal symptoms are usually spread out during the first 6 months.
3) The "influenza" syndrome usually occurs in months 3–5 of treatment.

The adverse reactions are generally self-limiting and do not require more than symptomatic treatment. Only rarely is it necessary to discontinue the drug, e.g., in the case of a hypersensitivity reaction. In patients with the respiratory syndrome or haemolytic anaemia caution is required, because shock, fall of blood pressure, and anaemia may occur. These patients will require immediate hospitalization.

In summary, adverse reactions to rifampicin when used at monthly intervals are rare and usually self-limiting. Definite withdrawal of the drug will only be required in exceptionally severe toxic reactions such as purpura, thrombocytopenia or anuria, which may occur only occasionally. The urine, sweat and tears may be coloured red; this should not cause alarm.

The effectiveness of steroids can be reduced if the patient is receiving daily rifampicin. Similarly, the effectiveness of oral contraceptives may also be impaired.
Clofazimine

Clofazimine is a substituted iminophenazine dye which has an antimicrobial effect against *M. leprae*.

The absorption of the drug varies appreciably among patients. When taken in the form of a microcrystalline suspension in an oil-wax base an absorption rate of about 70% is achieved.

The drug tends to be deposited predominantly in the fatty tissues and in the cells of the reticuloendothelial system. It is taken up by the macrophages throughout the body. The exact manner in which clofazimine is metabolized by the mammalian body is still not completely known. The drug tends to remain for a long time in the tissues and is eliminated very slowly from the body. Its half-life in human subjects following oral administration is at least 70 days. So far, three metabolites have been isolated from the urine of leprosy patients. Urinary excretion of clofazimine is negligible and accounts for only 0.1% of the dose in 24 hours, while faecal excretion varies considerably, amounting in some cases to as much as 35%. The presence of ingested drug in the faeces may be partly a result of excretion via the bile rather than failure of absorption from the gut. A small amount is eliminated in the sputum, sebum, and sweat.

It has been suggested that clofazimine interacts with mycobacterial DNA. Its precise mode of action, however, remains to be elucidated. It does not show cross-resistance with dapsone or rifampicin. It is not possible to determine the MIC of clofazimine against *M. leprae* in animals, since the drug is not homogeneously distributed in the tissues and there is marked tissue accumulation.

The antibacterial action of clofazimine is of approximately the same order as that of dapsone. However, while bacterial killing begins immediately after administration of dapsone it begins only after about 50 days in patients receiving 100–200 mg of clofazimine daily. The reason for this slower onset of action is obscure.

The drug has an anti-inflammatory effect when used in doses of 200–300 mg daily. This is valuable in controlling erythema nodosum leprosum (ENL) reactions, especially in women of child-bearing age. The anti-inflammatory action, however, has a slower onset than that of steroids or thalidomide.

The drug is weakly bactericidal against *M. leprae* both in the mouse and in human subjects. It is most active when administered daily or on alternate days. The dose should be adapted to the individual body weight. It can be administered at monthly intervals, thus permitting supervision of therapy. When administered in a dose of 600 mg on two consecutive days every month it exerts a measurable bactericidal effect. A dose of more than 100 mg daily should be given for as short a period as possible (less than 3 months) and only under supervision.

The drug is well tolerated and virtually nontoxic when administered in doses of not greater than 100 mg daily. The following adverse side-effects have been noted.

**Skin**

Reversible dose-related brownish black discoloration of skin lesions and darkening of areas of the skin exposed to sunlight have been reported. Symptoms may take some months to disappear after treatment is discontinued. Discoloration of sweat, urine and faeces may also occur. The skin discoloration is a troublesome side-effect and considerably reduces acceptability in light-skinned patients. General dryness of the skin (xeroderma), ichthyosis, pruritus, phototoxicity, acneiform eruptions and nonspecific skin rashes have also been described.

**Gastrointestinal tract**

Symptoms include nausea, vomiting, abdominal pain, intermittent loose stools, diarrhoea, anorexia and weight loss. There may be two separate entities:
a) an early syndrome—commencing within a few days of administration of the drug and due to a direct irritant effect; usually seen when the drug is given at a dose of 300 mg daily. Symptoms subside when the dosage is reduced;
b) a late syndrome—commencing after several months of continuous administration of the drug. Generally occurs in patients receiving high doses, 300 mg or more daily for several months. There is persistent diarrhoea, abdominal pain and loss of weight, sometimes ending in intestinal obstruction.

Eyes
Conjunctival pigmentation occurs but does not interfere with visual acuity.

In summary, the side-effects of clofazimine are mostly benign, reversible and dose-related. Skin discoloration can be minimized by reducing the dosage and duration of treatment and by protective measures such as using umbrellas and antisolar lotions. Clofazimine should not be given:

1) in the first trimester of pregnancy;
2) to patients with severe hepatic or renal dysfunction;
3) to patients subject to recurrent abdominal pain and diarrhoea.

Ethionamide and prothionamide
These thioamide derivatives are interchangeable and give cross-resistance to each other. Prothionamide, the propyl analogue of ethionamide, has largely replaced ethionamide in the treatment of tuberculosis, since its activity against *M. tuberculosis* is equal or slightly superior and it is better tolerated.

Against *M. leprae*, in the mouse footpad, both ethionamide and prothionamide are bacteriostatic when given in a dose of 0.1 g per kg of feed and bactericidal at 1 or 2 g per kg. The MIC of the drugs using the mouse footpad model is 0.05 mg/litre. Peak serum concentrations of either drug are about 3 mg/litre after a dose of 500 mg. At this dose, therefore, peak serum concentrations of the drugs exceed their MIC against *M. leprae* by a factor of approximately 60. The half-life of the drugs is about 2 hours.

The drugs kill *M. leprae* faster than full-dose dapsonc but more slowly than rifampicin. Experimental studies in mice suggest that the bactericidal activity of ethionamide and prothionamide would be severely compromised if the drugs were taken intermittently. However, these two drugs remain the only alternative to clofazimine in patients requiring combined chemotherapy who will not accept clofazimine.

The drugs are marketed in tablets of 125 mg and the dosage for leprosy treatment is approximately 5 mg/kg of body weight per day.

The principal adverse side-effects are gastrointestinal, e.g., anorexia, salivation, stomatitis, nausea, abdominal pain and diarrhoea. Gastric irritation can be reduced by putting an enteric coating on the pills. The most important side-effect reported is toxic hepatitis, particularly when the drug is used in combination with rifampicin.

Standard chemotherapeutic regimens

Multibacillary leprosy

Types of patient
The proposed multidrug regimens are designed for the treatment of all categories of multibacillary patients, including:

1) freshly diagnosed, previously untreated patients;
2) patients who have responded satisfactorily to previous treatment with dapsonc;
3) patients who have not responded satisfactorily to previous dapsone monotherapy;
4) dapsone-resistant patients;
5) patients who have relapsed while on dapsone monotherapy or after its cessation.

Since combined therapy can prevent or cure drug resistance in all patients, whether or not they are infected with dapsone-resistant *M. leprae*, there is no justification whatever for attempting to diagnose dapsone-resistant leprosy by means of a period of supervised dapsone monotherapy. Even in situations where mouse footpad testing can be accomplished, treatment with combined therapy should commence immediately after biopsy, without waiting for the results of the mouse-footpad inoculation.

**Doses for adults**

Rifampicin—600 mg once monthly, supervised.

Clofazimine—300 mg once monthly, supervised; and 50 mg daily, self-administered.

Dapsone—100 mg daily, self-administered.

The doses of rifampicin and dapsone should be adjusted for adults with low body weight. For those weighing less than 35 kg, rifampicin should be given at a dose of 450 mg; the dose of dapsone should be 50 mg daily (1–2 mg/kg of body weight per day). The dose of clofazimine will, however, remain unchanged.

**Doses for children (10–14 years)**

Rifampicin—450 mg once monthly, supervised.

Clofazimine—200 mg once monthly, supervised; and 50 mg on alternate days, self-administered.

Dapsone—50 mg daily, self-administered.

The dose should be adjusted for children with low body weight, as follows:

Rifampicin—12–15 mg/kg of body weight, monthly.

Dapsone—1–2 mg/kg of body weight per day.

Clofazimine—the optimum effective dose has not yet been established. The dose recommended above for children is half the adult dose, adjusted for operational suitability, since clofazimine is marketed in capsules of 100 mg and 50 mg.

**Alternative regimen**

Every effort should be made to persuade patients to agree to treatment with clofazimine since the acceptability of the only alternative drugs available, ethionamide and protonamide, has yet to be established.

When clofazimine is totally unacceptable owing to coloration of the skin lesions, especially in light-skinned patients, the following alternative regimen is recommended for adults:

Rifampicin—600 mg once monthly, supervised.

Dapsone—100 mg daily, self-administered.

Ethionamide or protonamide—250–375 mg daily, self-administered. The dose should be proportionately adapted for children and adults with low body weight, as mentioned earlier, on the basis of a dose of 5 mg/kg per day.

**Duration**

Treatment should be given for at least 2 years and, wherever possible, until smear negativity is achieved. Smear negativity means two consecutive negative skin smear examinations when undertaken at intervals of at least one month. The smears should be taken from a minimum of 3 sites (including active lesions, if any).

**Regularity**

A patient may be considered to have had regular treatment if he/she has received
combined therapy for at least two-thirds of the months in any interval of time. For example, regular treatment for 12 months implies that the patient has had at least 8 full months of therapy during that 12-month period.

Adequate treatment implies that the patient has received 24 monthly doses of combined therapy within 36 months.

**Precautions**

If a multibacillary leprosy patient also has active pulmonary tuberculosis, this regimen alone will not be sufficient, because of the risk of developing rifampicin-resistant *M. tuberculosis*. It is recommended that such patients should be given additional chemotheraphy appropriate for active pulmonary tuberculosis.

As far as possible, the administration of clofazimine should be avoided in the first three months of pregnancy.

**Contraindications**

Multidrug regimens should not be given to patients with severe hepatic or renal dysfunction. The use of clofazimine should also be avoided when there is recurrent abdominal pain and/or chronic diarrhoea.

In patients with severe anaemia the haemoglobin levels should be improved by appropriate treatment before therapy with dapsone is started.

**Reasons for discontinuing treatment**

The drugs will have to be temporarily discontinued when there is:

1) severe diarrhoea;
2) jaundice;
3) serious intermittent illness.

If jaundice occurs, the regimen can be recommenced only after the liver function tests revert to normal. The patient should preferably then be hospitalized for administration of a challenge dose of 600 mg of rifampicin before recommencing treatment. If the liver function tests performed after 48 hours are still normal or if there are no adverse reactions, e.g., nausea, vomiting, abdominal pain or recurrence of jaundice, the regimen can be restarted and the patient discharged. However, treatment should be continued with caution.

**Monitoring the progress of treatment**

1) At the periodic monthly contact for supervised administration of drugs the peripheral field worker should:
   - elicit information regarding side-effects of intercurrent ailments, e.g., diarrhoea;
   - monitor the occurrence of adverse reactions or intercurrent illnesses, e.g., hepatitis.
2) A detailed clinical examination must be undertaken every year by a medical officer or a senior auxiliary worker. This should include:
   a) a general physical examination;
   b) clinical examination for leprosy and assessment of progress; and
   c) bacteriological examination.

Bacteriological examination, if performed correctly, is a reliable and valuable guide in assessing the progress of the patient and the performance of the treatment services. However, it is not necessary to undertake this investigation too frequently, since changes in the bacterial index occur only gradually. Moreover, repeated examinations strain the resources of the laboratory, place unnecessary demands on the staff, and interfere with the accuracy of the results. A single examination performed reliably and accurately every year in any large-scale treatment programme is sufficient and adequate.

The importance of recording the results of these examinations on appropriately designed forms cannot be overemphasized. Documentation is essential to ensure a high quality of performance of the clinical services, including monitoring of the disease (see Annex 5).
These annual examinations should be continued until treatment is completed. Thereafter, the patient should be advised to come for examination at any time should symptoms recur or new lesions appear.

**Surveillance**

The success of chemotherapy is endangered mainly by two events: (1) in conventional long-term chemotherapy, the main concern is that drug resistance may develop; (2) in short-course chemotherapy, relapse may occur after cessation of treatment. Relapse can be prevented by short-course chemotherapy with sterilizing regimens, i.e., drugs that also kill persisters. The more quickly persisters can be killed, the shorter the duration of chemotherapy. In leprosy, however, no drug—either singly or in combination—has yet been shown to be effective against persisters.

Multibacillary patients must therefore be examined clinically and bacteriologically at least once every year for a minimum period of 5 years after completion of treatment in order to detect relapses early. Patients should be encouraged to report to the clinic whenever they suspect a relapse. There is no need for routine lifetime periodic recall for examination. Perpetuating follow-up of patients in this way diverts clinic personnel and resources away from those who really need them and contributes to the misconception that leprosy is a special disease.

A patient who has completed the required period of surveillance following the course of multidrug therapy, and shows no evidence of relapse, is considered to have completed surveillance.

**Paucibacillary leprosy**

**Types of patient**

The proposed regimen is designed for the treatment of all categories of paucibacillary patients including those with primary dapsone resistance.

A large number of paucibacillary patients with single lesions heal spontaneously. Nevertheless, all paucibacillary patients should be treated because it is not possible to distinguish those who will heal spontaneously from those in whom the disease will progress. Furthermore, unless properly treated, those who do not heal spontaneously will develop nerve lesions and some may even progress to multibacillary forms of the disease.

**Doses for adults**

Rifampicin—600 mg once monthly, supervised, for 6 months.

Dapsone—100 mg daily, self-administered, for 6 months.

The doses should be adapted for adults with low body weight. Rifampicin should be given at a dose of 450 mg for those weighing less than 35 kg; the dose of dapsone should be 50 mg daily (1–2 mg/kg of body weight per day).

**Doses for children**

The dose for children should be proportionately reduced according to body weight. For suggested doses for children see page 36.

**Duration**

Treatment should be continued until 6 monthly supervised doses of rifampicin have been administered. If treatment is interrupted the regimen should be recommenced where it was left off to complete the full course.

Treatment can then be terminated, provided that a clinical and bacteriological examination by a medical officer or a senior auxiliary worker shows that:

1) there is no extension of existing lesions or appearance of new lesions;
2) there is no new nerve involvement or paresis/paralysis;
3) the lesions show evidence of regression. The patient should be advised before discharge:

- that subsidence or disappearance of lesions will occur gradually;
- that it is not necessary to seek treatment elsewhere;
- that if at any time new lesions appear or symptoms recur, he/she should report for examination and advice immediately.

Clinical inactivity cannot be achieved with chemotherapy for 6 months. Since in paucibacillary leprosy the maximum bacterial load is about $10^6$ organisms, the objective of short-course chemotherapy is to render the patient free of viable bacilli. The problem of drug-resistant mutants arising as a result of treatment is insignificant. Any persisters remaining are likely to be contained by the adequate cell-mediated immunity this type of patient possesses. Resolution of skin and nerve lesions will occur gradually; however, some lesions are partially or totally irreversible and may persist. Lesions of a trophic or degenerative nature may occur much later but are rare and should not be considered as evidence of activity.

Occasionally, on completion of adequate treatment, the lesions may show no evidence of regression and, on the contrary, new lesions may appear. This is particularly likely to occur in patients in the borderline zone of the spectrum who are erroneously classified as paucibacillary. In such cases, the diagnosis must be carefully reviewed by a medical officer after detailed clinical and bacteriological examination. If the classification is correct, the treatment should be continued in the same dosage for a further period of 6 months. If the classification is erroneous, the treatment should be changed to the regimen recommended for multibacillary leprosy.

**Regularity**

For paucibacillary patients adequate treatment implies that the patient has received 6 monthly doses of combined therapy within 9 months.

A patient who has received adequate multidrug therapy and is taken off all drugs will be said to have "completed treatment".

**Precautions**

If a paucibacillary leprosy patient also has active pulmonary tuberculosis, this regimen alone will not be sufficient because of the risk of developing rifampicin-resistant *M. tuberculosis*. It is recommended that such patients be given additional chemotherapy appropriate for active pulmonary tuberculosis.

**Contraindications**

1) Rifampicin should not be given to patients with severe hepatic or renal dysfunction.

2) In patients with severe anaemia the haemoglobin level should be improved by appropriate treatment before therapy with dapsone is started.

**Reasons for discontinuing treatment**

Treatment should be discontinued in the event of adverse reactions to dapsone or rifampicin (see pages 32–33), or a serious intercurrent illness.

Treatment will have to be temporarily discontinued if jaundice occurs. The regimen should be recommenced only after the liver function tests revert to normal and remain so following a challenge dose of rifampicin (see page 37).

**Monitoring the progress of treatment**

1) At the periodic monthly contact for supervised administration of the drug the auxiliary field worker should:

- elicit information regarding side-effects or intercurrent ailments;
- monitor the occurrence of adverse reactions;
– take appropriate action, such as referral, if necessary.
2) A clinical and bacteriological examination must be undertaken by a medical officer or a senior auxiliary worker at the end of the month following the administration of the sixth supervised dose of rifampicin, before termination of treatment (see pages 38–39).

Surveillance
The risk inherent in short-course chemotherapy is the possibility of relapse. In order to detect this early, paucibacillary patients, after completing treatment, should be examined clinically once a year for a minimum period of 2 years and encouraged to report back to the clinic whenever they suspect a relapse.

A patient who has completed the required period of surveillance and shows no evidence of relapse is considered to have completed surveillance. The phrase “release from control” should not be applied in the context of multidrug therapy.

Deterioration and relapse

Deterioration
Deterioration is defined as clinical and/or bacteriological worsening while the patient is undergoing treatment. It is synonymous with recrudescence. Use of the term reactivation in the context of multidrug therapy is not recommended. An increase of more than 1 unit in the bacterial index on routine bacteriological examination is an indication that the response to treatment is not satisfactory. All such patients should be given a detailed clinical and bacteriological examination.

Clinically, deterioration may manifest as a worsening of existing lesions or the appearance of new lesions. Existing lesions may show increased erythema and induration or extension. In paucibacillary patients it may be difficult to distinguish deterioration from type 1 reactions, while in multibacillary patients there may be a close resemblance to type 2 reactions (see page 41).

The most common cause for deterioration while on treatment is noncompliance or irregularity in drug intake. Every effort must be made to ensure that the patient takes the self-administered component of the regimen regularly. This will require frequent home visits and intensive health education of the patient and his or her family members.

Relapse
A patient who successfully completes an adequate course of multidrug therapy, but who subsequently develops new signs and symptoms of the disease either during the surveillance period or thereafter, is considered to have “relapsed”.

Individuals with the highest risk of relapse are those who have had inadequate chemotherapy. It therefore seems rational to concentrate all efforts and resources on giving good treatment regularly for the prescribed duration, and then to re-treat the few patients that may relapse. Moreover, since the large majority of relapses occur with drug-sensitive organisms, the patients can be re-treated with the original regimen. In order to detect such patients early, periods of surveillance are recommended after treatment is discontinued.

Paucibacillary leprosy
In paucibacillary patients, relapse has to be distinguished from reversal reactions. It is often difficult to make this distinction, particularly under field conditions (see page 42). When relapse has been confirmed after detailed clinical and bacteriological examination, the classification must be
critically reviewed. If the classification remains unchanged the patient should be re-treated with the same regimen (dapsone and rifampicin) for a further period of 6 months. Close supervision must be maintained to ensure regularity of drug intake. If, however, the patient is reclassified as multibacillary, treatment should be given with three drugs in accordance with the prescribed regimen.

Multibacillary leprosy
Relapse may manifest as a clinical deterioration of existing lesions or the appearance of new lesions. It has to be considered seriously when more than the occasional organism appears in the smears. A bacteriological relapse can precede clinical relapse by 6–12 months. The new lesions that occur may take the form of erythematosus papulonodules and can be mistaken for erythema nodosum leprosum (ENL). ENL lesions are, however, evanescent and tend to disappear quickly. They are also usually painful and blanch on pressure.

If relapse is confirmed after a critical review, treatment should be recommenced immediately with dapsone, clofazimine and rifampicin according to the original dosage schedule. Close supervision is essential and every effort must be made to ensure regularity of drug intake. This will involve intensive health education of the patient and the family members and frequent home visits by the staff to promote compliance. If facilities are available, such patients may benefit from an initial period of admission to hospital for 4–8 weeks for supervised administration of drugs and intensive health education.

Reactive states in leprosy
Reactive episodes seen during leprosy control programmes are of two main types:

1) reversal reaction, otherwise known as type 1 lepra reaction;
2) erythema nodosum leprosum (ENL), otherwise known as type 2 lepra reaction.

Reversal reaction or type 1 lepra reaction

Clinical features
The reaction is classically seen in borderline tuberculoid (BT), mid-borderline (BB) and borderline lepromatous (BL) patients because of their immunological instability.

When the reaction is associated with a reduction in immunity it is called a “downgrading reaction”. In the absence of treatment there is a natural tendency for borderline leprosy to downgrade slowly towards the lepromatous pole. When the reaction is associated with a rapid increase in cell-mediated immunity, as in patients under treatment, it is called an “upgrading reaction”. In BT and BB patients, upgrading reactions usually occur during the first 6 months of treatment but longer intervals have been recorded, especially in BL patients.

Clinically, the most prominent feature is a rapidly developing change in some or all of the skin lesions. They become erythematous, more prominent and oedematous, shiny and warm to the touch. Sometimes necrosis supervenes with breakdown and ulceration. Often a crop of new lesions appears on the skin and systemic disturbances, though unusual, may occur with mild fever and malaise. The lesions desquamate as they subside.

Nerve involvement is common and is often a predominant feature of this episode. It takes the form of rapid swelling of one or more nerves with pain and tenderness usually where the nerve is most superficial. The cause of the pain is increased intraneural pressure from oedema and cellular reaction. More serious are motor disturbances in one or more of the
ulnar, lateral popliteal, and facial nerves with the patient at risk of developing claw hand, drop foot or facial paralysis, particularly when treatment is neglected or inadequate. However, the paralysis will disappear quickly with correct and prompt treatment.

**Differentiation from relapse in paucibacillary leprosy**

In paucibacillary patients it is often difficult to distinguish between relapse and reversal reaction. Nevertheless, it is essential that this distinction should be made correctly so that appropriate treatment can be instituted. The differences are summarized in Table 4.

**Management of reversal reactions**

In mild reactions, the antileprosy treatment should be continued unchanged. Analgesics should be given as required. If there is nerve tenderness, the affected limb(s) should be rested. The patient should be seen at least every 2 weeks and asked to return immediately if the reaction becomes more severe.

In severe reversal reactions, especially those with nerve pain and tenderness or loss of nerve function, the patient must be referred immediately to hospital. Analgesics should be given as required. Painful nerves should be rested and the affected limb supported in a splint if necessary. In hospital, antileprosy treatment should, in general, be continued unchanged; treatment with prednisolone should be started. The initial dosage is usually 10 mg 3 times a day, although individual patients will vary in their dose requirements. Provided that patients can be seen monthly by a doctor and respond well to therapy, they may be sent home at about the end of the second month. If necessary they should continue to take small doses of prednisolone until the reaction subsides.

The attention given to reactions in the field is usually not satisfactory. All field workers should be trained in the recog-

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**Table 4. Differences between reversal reaction and relapse**

<table>
<thead>
<tr>
<th>Feature</th>
<th>Reversal reaction</th>
<th>Relapse</th>
</tr>
</thead>
<tbody>
<tr>
<td>Time interval</td>
<td>generally occurs during chemotherapy or within 6 months of stopping treatment</td>
<td>usually occurs long after chemotherapy is discontinued, generally after an interval of 1 year</td>
</tr>
<tr>
<td>Onset</td>
<td>abrupt and sudden</td>
<td>slow and insidious</td>
</tr>
<tr>
<td>Systemic disturbances</td>
<td>may be accompanied by fever and malaise</td>
<td>never accompanied by fever and malaise</td>
</tr>
<tr>
<td>Old lesions</td>
<td>some or all become erythematous, shiny and considerably swollen, with infiltration</td>
<td>the margins of some may show erythema</td>
</tr>
<tr>
<td>New lesions</td>
<td>usually several</td>
<td>few</td>
</tr>
<tr>
<td>Ulceration</td>
<td>lesions often break down and ulcerate</td>
<td>ulceration is unusual</td>
</tr>
<tr>
<td>Subsidence</td>
<td>with desquamation</td>
<td>desquamation does not occur</td>
</tr>
<tr>
<td>Nerve involvement</td>
<td>many nerves may be involved, with pain, tenderness, and motor disturbances occurring rapidly</td>
<td>may occur only in a single nerve; motor disturbances develop very slowly</td>
</tr>
<tr>
<td>Response to steroids</td>
<td>excellent</td>
<td>not distinctive</td>
</tr>
</tbody>
</table>

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nition of reactions so that appropriate and early action is taken. Leprosy control services should include a system for the referral of cases to hospitals, particularly local district hospitals, so that acute cases receive early attention. Hospital medical staff should be appropriately trained to deal with these important complications.

**Erythema nodosum leprosum (ENL) or type 2 lepra reaction**

**Clinical features**
Erythema nodosum leprosum (ENL), also known as type 2 lepra reaction, is characterized by the appearance of tender erythematous nodules or plaques, commonly on the face, arms, and thighs. Fresh crops of lesions may appear and, when numerous, are accompanied by fever and malaise. Other features of the reaction that may or may not occur are nerve pain, bone and joint pain, iridocyclitis, dactylitis and orchitis. ENL is graded as severe if there is a high temperature and general malaise; if the skin lesions become pustular and/or ulcerate; if the nerves become painful or loss of nerve function develops; or if there is evidence of iridocyclitis, orchitis, or joint swelling. The patient should be referred immediately to hospital, analgesics being given as required for the journey.

Mild ENL should be treated in the field. If there is any nerve tenderness the affected limb(s) should be rested. Analgesics should be given as required, and the patient should be seen regularly by the health worker at least once every 2 weeks. In particular, the eyes should be checked at each visit to ensure that the patient is not developing iridocyclitis.

**Management of ENL reactions**
In general, treatment for leprosy should be continued unchanged. The drugs that are effective against such reactions are steroids, thalidomide and clofazimine. Prednisolone rapidly controls ENL but requires continuous and often increasing dosage; steroid toxicity and dependence have been seen frequently. Thalidomide has few toxic effects; the contraindication for its unsupervised use derives from its teratogenicity, and it should therefore not be given to women of child-bearing age. Clofazimine takes 4-6 weeks to exert its full effect. In very severe ENL, even at dosages of 300 mg daily (a dose level that should not usually be maintained for longer than about 3 months), clofazimine may not be as effective as steroids or thalidomide, and it may not be accepted by light-skinned patients.

**Treatment of eye, nerve, hand, and foot lesions**
Chemotherapy constitutes only a part of the treatment of leprosy, although a very important part. The treatment of different lesions affecting the eyes, nerves, hands and feet may be of vital importance to the well-being of the patient at the time and in the future. Management of leprosy thus also involves an ability to deal with deformities, advise on and perform simple physiotherapy, diagnose and treat early reactions and above all, recognize the serious manifestations of the disease that require urgent referral to hospital.

**Eyes**

**Lagophthalmos**
In the early stages, symptoms are often relieved and, in some, lid function is definitely improved by:
1. exercise of the eyelids daily;
2. prevention of drying, especially during sleep, using bland oil;
c) minimizing of infection using a mild antiseptic agent, e.g., a weak zinc sulfate ointment; and
d) the use of dark glasses to reduce glare and protect the eyes from damage as far as possible.

If corneal sensation is impaired, the cornea cannot be covered, or there is already some exposure keratitis, the patient needs attention from an eye specialist.

**Acute plastic iridocyclitis and acute phases of the chronic granulomatous form**

These conditions require:

a) full dilatation of the pupil with atropine or other mydriatics; and
b) measures to counter inflammation, such as local heat, local corticosteroids and, where necessary, anti-inflammatory drugs such as aspirin. If signs of glaucoma are present, the patient requires treatment by an eye specialist.

These principles also hold if erythema nodosum nodules develop on an eye.

Patients with severely inflamed eyes should be referred at once to a doctor.

**Nerves**

Acute or chronic inflammation of peripheral nerves results in neuritis. It is usually painful and tender and often leads to partial or complete paralysis of the muscles supplied by the affected nerves. The most commonly affected nerve trunks are ulnar, median, facial and lateral popliteal. Pain may be accompanied by tingling. Some patients develop sensory and motor deficit without having any symptoms, the so-called “silent neuritis”.

The management of neuritis will depend upon whether or not it occurs as part of an ENL reaction or a reversal reaction. The treatment of neuritis in association with ENL is essentially the treatment of ENL. Acute neuritis occurring in association with a reversal reaction should be treated vigorously with steroids. Initial doses of prednisolone could be as high as 60-80 mg per day, and could be gradually reduced as symptoms regress. The patient should be hospitalized, particularly when high doses of prednisolone are administered. Mild cases of neuritis should be managed symptomatically with drugs such as analgesics. Splinting of the affected part could help in minimizing deformity. Surgical intervention, such as decompression of the nerve, should be undertaken only when medical treatment fails.

**Hands**

The involvement of the peripheral nerve trunks—ulnar, median, and radial—in leprosy often results in muscle weakness and paralysis of the small muscles of the hand. This leads to partial or complete hand clawing or wrist drop, depending on the nerve trunk affected. Other signs of damage to the hand include swelling due to inflammation, dry cracked skin, and burns and other wounds. Most wounds are caused when patients neglect the care of their hands. It is, therefore, important that patients should be educated and encouraged to inspect their hands for wounds as a routine and not to use sharp or hot objects. If wounds or inflammation should occur, the affected hand should be rested in a position that will avoid contracture, such as in a functional position maintained with the help of a splint.

**Feet**

Destruction of the feet by trophic ulcers is one of the most common complications of leprosy, though it can be prevented if early care is taken. The greatest problem is the loss of sensation in the foot which results from the disease.

With loss of nerve supply, the skin of the foot suffers secondary effects from loss of normal secretions. The skin of the lower part of the leg becomes dry, scaly and
cracked. The foot may develop fissures and cracks which tend to admit infection and may be the cause of more serious trouble later.

**Prevention**

Prevention is more important than treatment and fortunately it is quite easy to restore dry skin to normal. The feet, including the lower leg, should be soaked in a bucket of water for 15 to 20 minutes. The excess water should be wiped off with a towel and then petroleum jelly (Vaseline) rubbed over the skin to keep the water in. This routine needs to be repeated every day. If cracks and fissures have developed the heaped up thickening of the cuticle around the edges should be excised, and the depths of the crack should be painted with gentian violet.

One of the most important causes of disability in leprosy is plantar ulceration. While the basic cause is loss of sensation, the mechanisms involved include continuous pressure during walking leading to ischaemic necrosis, and mechanical injury by sharp objects.

Three important precautions that must be taken by patients with insensitive feet are:

1) inspection of the feet at the end of each day for thorns or wounds, giving them immediate attention;
2) the wearing of shoes or sandals that are not made with nails;
3) the limiting of walking, particularly over hard paved roads, and severe limiting of the use of the foot in the event of injury or infection.

**Treatment**

Before a plantar ulcer forms as an open wound, there is usually a stage of deep inflammation. This stage will heal without leaving an open wound provided it is rested early. Every leprosy worker must inspect the feet of all patients who have loss of sensation and loss of sweating looking for swelling, redness, blisters or thorns. Corns and thick scars should be shaved with a sharp knife or softened by dressings of salicylic acid for several days and then scraped away.

When an ulcer has formed and become infected there is usually profuse discharge, slight fever, and enlargement and tenderness of the inguinal glands. The treatment at this stage is as follows: 1) bed rest with the foot elevated; and 2) daily dressing with hypertonic magnesium sulfate solution or with a mild antiseptic.

When the acute stage is subsiding and there is no sign of spreading infection, the wound must be entirely explored with a sterile blunt probe to see whether the bone is exposed. If the bone is exposed, rest should continue. If the wound is well localized, the bone is not exposed and there is no infection, a plaster of paris cast can be applied. The purpose of the plaster cast in the treatment of plantar ulcers is mainly to immobilize the foot.

**Footwear**

Shoes are important in any treatment programme in leprosy. The function of footwear is to protect the feet and to spread the strain of weight-bearing over the sole, sparing the scarred areas and the pressure points.

Protection from penetrating injuries from sharp objects, such as thorns and broken glass, may be achieved with almost any kind of shoe or sandal. If microcellular rubber sandals are being used they should always have an undersole of leather or vulcanized rubber. Microcellular rubber has now been widely used over a long period for ulcer-preventive footwear and has proved very suitable. It is important to remember that nails should not be used in the manufacture of shoes for leprosy patients.

**Physiotherapy**

Physiotherapy is a useful adjunct to medical and surgical management of lep-
rosy patients. It is of help in preserving the physiological properties of paralysed muscles and preventing atrophy, as well as strengthening the muscles during recovery. It is therefore imperative if muscle bulk and activity are to be maintained during the period of paralysis. Physiotherapy should commence early to obtain the best results and can even begin under field conditions.
Chapter 7

Reorganization of services and operational strategies for leprosy control

To meet the new challenge resulting from the increased complexity of the revised intervention strategy, the various activities relating to leprosy control will have to be reconsidered.

Case-finding

Any intervention strategy based on secondary prevention, including multidrug therapy, can succeed only if all the known sources of infection in the community are given effective chemotherapy and rendered noninfectious. Every effort must therefore be made to mobilize community resources, strengthen community cooperation and increase community awareness regarding the disease, in order to facilitate recognition of early lesions within the family unit, and promote self-reporting. Community health workers and village committees have a crucial role in identifying persons suspected of having the disease who should be referred to the health centre for more detailed clinical examination. This will require appropriate training of community health workers. The primary health care approach may well be the most difficult to achieve, but ultimately this strategy will reap the most rewards and have the greatest impact.

Diagnostic services

Clinical examination

It is essential to classify patients correctly, since recommended drug regimens are
different for multibacillary and paucibacillary patients. Patients must also be examined to exclude any contraindications prior to the commencement of treatment with rifampicin, clofazimine, or dapsone.

**Bacteriological examination**

For the purposes of diagnosis and allocation of regimens, skin smear examination is extremely important and should always be undertaken. This procedure makes it possible to identify patients who, if untreated, would have the most unfavourable prognosis in the community. It is also the principal method of monitoring progress and deciding on the end-point of treatment in multibacillary patients.

Laboratory facilities must therefore be strengthened through:

- provision of suitable equipment, e.g., microscopes, glassware, and a regular supply of reagents, slides, etc.;
- retraining of staff;
- continuous monitoring and supervision.

The laboratory facilities needed to service the leprosy control programme may be either attached to the programme, or part of peripheral laboratory services, depending upon the local situation.

It is essential that these laboratories are closely supervised by a competent technician, who should undertake periodic evaluation of the services provided, including operational evaluation and quality control through a smear check system (see Annex 3).

**Priorities for the introduction of multidrug regimens**

In countries where manpower and financial resources, including logistic support, are available, all registered multibacillary and paucibacillary patients should be given multidrug therapy, treatment being commenced in a phased manner within a specific schedule. When there are constraints, priorities must be formulated so that available resources are put to the best use. Patients requiring multidrug therapy can be classified in the following order of priority:

1) multibacillary cases clinically suspected as dapsone-resistant;
2) newly diagnosed multibacillary cases;
3) multibacillary cases that have been treated for more than 5 years but remain active;
4) multibacillary cases treated for less than 5 years;
5) paucibacillary cases clinically suspected to be dapsone-resistant;
6) other paucibacillary patients;
7) multibacillary patients rendered negative who are on maintenance therapy.

Decisions regarding priorities for the introduction of multidrug therapy must, however, be taken at the country or regional level, since they involve detailed consideration of other technical, administrative, operational and organizational factors.

**Treatment delivery**

The major emphasis in leprosy control must be placed on the provision of adequate, efficient, and flexible outpatient treatment facilities, particularly for the monthly supervised administration of drugs. Even the best available regimens will have a low success rate if treatment services are not focused on ensuring the cooperation of patients. Hence, patients must be able to receive treatment at a place convenient to them, e.g., a local primary health centre or leprosy control unit.

In certain special situations, especially in countries with rugged mountainous terrain where communications are difficult and health facilities are meagre, or in isolated
island communities, it may be necessary to use the services of traditional practitioners of medicine, school teachers, village headmen, or other means outside the conventional medical network for drug delivery.

Organizational infrastructure

With the introduction of multidrug regimens and the intensification of case-detection activities, the responsibilities and duties of the staff will increase. A disadvantage of partially supervised chemotherapy is the rather heavy workload of the treatment services.

To ensure efficient implementation of the revised strategy, reorganization of the infrastructure will be necessary to enable the staff to cope with their increased responsibilities. Since local conditions vary greatly, the final decision on how this is to be done will have to be taken at the country level, taking into account other considerations such as the multibacillary/paucibacillary patient mix, disease prevalence, population density, terrain, etc. For instance, while in some specialized programmes one medical officer can look after as many as 2000 patients, in other situations, such as in integrated programmes, it may not be possible for one medical officer to deal with more than 200 patients. Similarly, while a peripheral health worker in a specialized programme would be able to take care of up to 200 patients, in an integrated programme it would be difficult for a health worker to look after more than 50.

Where villages are scattered and the population density is low, the coverage will have to be reduced to maintain a high level of efficiency. In areas with an integrated service, a specialized intermediate level supervisor may have to supervise the work of 5–10 multipurpose workers.

In addition to the patient/population ratio, it will be necessary to consider the relative numbers of the various types of personnel in the primary health care system, e.g., community health workers, multipurpose workers, specialized staff. This information will assist in the allocation of manpower resources to strengthen the leprosy control service at the peripheral level.

Referral services

Referral facilities for temporary hospitalization will be necessary for the management of the following complications:

1) severe erythema nodosum leprosum (ENL) or reversal reactions;
2) complicated plantar ulcers;
3) deformities requiring surgical correction;
4) side-effects of drugs requiring immediate attention;
5) serious intercurrent ailments.

Hospitals and health centres must be willing and competent to admit and treat these patients in order to improve case management. It will be useful if the policy governing admission to hospitals is officially defined. It should be emphasized that patients should be kept in hospital for as brief a period as possible.

Integration with basic health services

A leprosy service cannot reach its full potential unless the medical and health skills available to leprosy patients are at the same level as those for other patients. It is therefore imperative that the full resources of basic health services become more increasingly involved in the management of leprosy patients.

Planning for integration should ensure that an effective and efficient control service is retained and fortified and does not deteriorate in scope and function. For this purpose the personnel of health centres
and their satellite units should receive adequate training concerning leprosy. The activities and the tasks involved at different levels of the infrastructure are reviewed in Table 5.

**Information support systems**

It is generally recognized that the available information on the leprosy situation in the majority of countries is unsatisfactory. Moreover, owing to lack of uniformity in the definition of terms and concepts, data from different countries are barely comparable and consequently have little epidemiological or operational value for comparisons among countries. A system providing essential clinical, epidemiological, and operational information in a standard format would permit valid comparisons of the results of control measures taken by the health services in different areas. Adequate information is essential to the whole evaluation process, and it is necessary to ensure an efficient information support system throughout the programme. The requirements must be specified at the planning stage. The system must be carefully structured to permit concise, appropriate and relevant recording of information.

Records are a practical means of obtaining information stored at the peripheral level. In integrated programmes particularly, they should be simple, practical and limited to essentials. Elaboration of any kind should be discouraged. To be useful, records must be complete, accurate and up to date.

Reports are based on records. Their purpose is to keep managers at higher levels informed about performance. Reports should be simple, clear, self-explanatory and as brief as possible. To be of value they should be complete, accurate and submitted, on time, at regular intervals.

**Recording and reporting**

The records and reports discussed below are intended as specimens to illustrate the requirements at the peripheral level. They should be modified and adapted to the health service system prevailing in each country. At the minimum, records should include a treatment card and/or treatment register, a surveillance register, and an individual patient form such as the ones developed by the Catholic University of Louvain, Brussels, in collaboration with WHO (the OMSLEP system), which summarize all the information essential for evaluation. These forms have recently been slightly modified (16).

**Patient card/register**

A separate card is maintained for each patient and is necessary for efficient management of treatment. It should contain full information on the patient’s identity, clinical details, and treatment. The same card may also be used for surveillance. An example of a treatment card is given in Annex 5. In some cases the information on treatment is maintained on a separate register, and the following is an example of the information that could be included on such a register.

| Column 1: | Serial no. |
| Column 2: | Registration no. |
| Column 3: | Name of patient |
| Column 4: | Address |
| Column 5: | Age |
| Column 6: | Sex |
| Column 7: | Type of leprosy |
| Column 8: | Date of commencing treatment |
| Column 9: | Treatment attendance |

Column 9 would contain 36–48 blocks or subdivisions for recording the dates on which monthly treatment is given. A separate register may be maintained for paucibacillary patients, if desired, in which case Column 9 would need only six subdivisions.
<table>
<thead>
<tr>
<th>Activities</th>
<th>Level</th>
<th>Person(s) responsible</th>
<th>Tasks involved</th>
<th>Competence and knowledge required</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Early recognition of suspected leprosy cases and their referral</td>
<td>1.1 Home</td>
<td>individual family members, parents</td>
<td>a) recognition of early symptoms of leprosy, hypopigmented patches, and loss of sensation, b) seeking confirmation of diagnosis and treatment</td>
<td>knowledge of symptoms of leprosy and its consequences, knowledge of availability and location of health facility</td>
</tr>
<tr>
<td></td>
<td></td>
<td>community health workers</td>
<td>a) and b) as above, c) directing patients to referral facility for confirmation of diagnosis, d) absentee follow-up</td>
<td>ability to identify symptoms of leprosy and its complications, knowledge of referral facilities, basic training in health education, ability to communicate with the people and the supervisory level</td>
</tr>
<tr>
<td>1.2 Local health facility</td>
<td></td>
<td>multipurpose workers, nurses, medical assistants, physician</td>
<td>a)-d) as in 1.1, e) confirmation of diagnosis, f) taking skin smears and microscopic examination, g) record-keeping and reporting on leprosy morbidity, h) supervision of community health workers, i) training community members and community health workers whenever possible</td>
<td>adequate theoretical knowledge and practical skills in relation to leprosy with basic elements in epidemiology, treatment, and methods of control of the disease, clinical examination of patients, testing for sensation and thickening of nerves</td>
</tr>
<tr>
<td>1.3 First referral level</td>
<td></td>
<td>nurses, physicians</td>
<td>a) adequate management of complications, b) supervision and continuing training of multipurpose workers, nurses and medical assistants</td>
<td>adequate knowledge and practical skills regarding the clinical and preventive aspects of leprosy, ability to assist in diagnosis of difficult cases, knowledge of national leprosy control strategies</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Supplies and equipment</th>
<th>Logistic support</th>
<th>Community support</th>
</tr>
</thead>
<tbody>
<tr>
<td>suitable information material, e.g., pamphlets, posters</td>
<td>community health education</td>
<td>community-generated support, e.g., health committee and volunteers; support of health education in schools and by voluntary agencies facilities for community health workers; community cooperation and acceptance; support from community development committees or similar bodies; identification, selection and training of community health workers in cooperation with health authorities</td>
</tr>
<tr>
<td>as above; checklist and/or manual of tasks as above; access to refresher training; spot map of villages and houses</td>
<td></td>
<td>assistance with transport facilities; assistance with land and building facilities; support to training of selected community members and community health workers; appropriate communication systems, e.g., public transport, telecommunications, etc.</td>
</tr>
</tbody>
</table>


<table>
<thead>
<tr>
<th>Activities</th>
<th>Level</th>
<th>Person(s) responsible</th>
<th>Tasks involved</th>
<th>Competence and knowledge required</th>
<th>Supplies and equipment</th>
<th>Logistic support</th>
<th>Community support</th>
</tr>
</thead>
</table>
| 2. Treatment        | 2.1 Home | individual family members, parents | a) motivate patient to take self-administered drugs daily  
b) motivate patient to attend health facility monthly for supervised administration of drugs  
c) watch for complications  
d) supervise simple physical exercises, e.g., oil massage, exercises  
e) promote personal hygiene within the family to prevent transmission | knowledge of health and social consequences of the disease;  
knowledge of transmission;  
knowledge of personal hygiene;  
knowledge of elementary oil massage and exercises | suitable information material, e.g., pamphlets; containers for drugs | facilities for health education  
facilities for housing, etc.: support of village health committee | community cooperation;  
health education at community level;  
village health committee |
|                     |        | community health workers | a)–e) as above  
f) home visits for tablet counts  
g) treatment delivery in special situations  
h) supervision of home tasks  
i) absentee follow-up  
j) health education  
k) referral to health facility if complications occur | as above;  
knowledge of drug administration and complications;  
recording and reporting | kit with stationery and pin and feather;  
relevant information material, e.g., pamphlets | facilities for health education;  
home visits;  
inventory/spot map of villages and houses | as above;  
facilities for housing, etc.: support of village health committee |
| 2.2 Local health facility | multipurpose workers/paramedical workers (in leprosy), nurses, midwives, medical assistants, physicians | a)–k) as in 2.1  
l) treatment and drug distribution  
m) treatment of complications  
n) referral for admission if necessary  
o) maintaining adequate stock of drugs  
p) recording and reporting system, compilation and analysis of data  
q) supervision of home task responsibilities | as in 2.1  
knowledge of epidemiology and treatment of leprosy including its complications;  
capability of participating in training of community health workers;  
group health education activities in the community | adequate drugs;  
relevant information material, e.g., pamphlets;  
slide projector and other audiovisual equipment for health education;  
material for training;  
facilities for transporting patient to first referral level | facilities for health education;  
manuals;  
preparation for training community health workers;  
transport facilities;  
inventory/mapping of villages | provision of local facilities for training of community health workers;  
transport |
### 2.3 First referral facility

<table>
<thead>
<tr>
<th>Nurses/Physicians</th>
</tr>
</thead>
<tbody>
<tr>
<td>a) treatment of complications</td>
</tr>
<tr>
<td>b) admission if necessary</td>
</tr>
<tr>
<td>c) laboratory investigation if side-effects occur</td>
</tr>
<tr>
<td>d) supply of drugs and reagents to periphery</td>
</tr>
<tr>
<td>e) supervision of community health workers and local health facilities</td>
</tr>
<tr>
<td>f) training of community health workers, health workers and local health facility personnel</td>
</tr>
<tr>
<td>g) epidemiological and operational assessment</td>
</tr>
</tbody>
</table>

### 2.2 Knowledge of all aspects of national leprosy control strategies; planning supervision and monitoring of capabilities; reports and returns analysis of data; training

### Appropriate communication system, e.g., public transport, etc.

### 3. Case-holding

#### 3.1 Home

<table>
<thead>
<tr>
<th>Individual family members</th>
</tr>
</thead>
<tbody>
<tr>
<td>a) motivate patient to attend clinic regularly for supervised treatment</td>
</tr>
<tr>
<td>b) motivate patient to take daily self-administered drugs</td>
</tr>
<tr>
<td>c) care of hands and feet</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Community health workers</th>
</tr>
</thead>
<tbody>
<tr>
<td>a) home visits for health education and tablet counts to promote treatment regularity</td>
</tr>
<tr>
<td>b) pre-clinic motivation drive</td>
</tr>
<tr>
<td>c) care of hands and feet</td>
</tr>
<tr>
<td>d) referral for complications</td>
</tr>
<tr>
<td>e) absentee follow-up</td>
</tr>
</tbody>
</table>

### Knowledge of health and social consequences of the disease; knowledge of personal hygiene

### Suitable health education material

### Facilities for health education and instruction

### Community cooperation; village health committee

### As above; knowledge of drug administration and complications; need for and importance of regular treatment; clinic dates should be known

### Relevant information material on treatment

### Facilities for home visits; spot map of villages

### As above
<table>
<thead>
<tr>
<th>Activities</th>
<th>Level</th>
<th>Person(s) responsible</th>
<th>Tasks involved</th>
<th>Competence and knowledge required</th>
<th>Supplies and equipment</th>
<th>Logistic support</th>
<th>Community support</th>
</tr>
</thead>
<tbody>
<tr>
<td>3. Case-holding (continued)</td>
<td>3.2 Local health facility</td>
<td>multipurpose workers, nurses, medical assistants, physicians</td>
<td>a) comprehensive primary health care treatment of complications, e.g., reactions, ulcers b) absentee follow-up c) family counselling d) issue of protective footwear e) screening for rehabilitation f) support of families during crises</td>
<td>knowledge and practical skills regarding diagnosis of leprosy and its treatment, including complications; appreciation of family counselling measures</td>
<td>drugs; bandages and medicines for ulcer treatment; standard size, simple footwear for ulcer prevention; records and registers</td>
<td>facilities for home visits</td>
<td>community cooperation; village health committee</td>
</tr>
<tr>
<td></td>
<td>3.3 First referral level</td>
<td>nurses, physicians</td>
<td>a) admission for treatment of complications b) domiciliary rehabilitation c) physiotherapy d) family and patient counselling</td>
<td>knowledge of all aspects of leprosy; family counselling; community rehabilitation programmes; social orientation of health workers; supporting supervision and guidance</td>
<td>drugs for treatment of leprosy and its complications; physiotherapy equipment, e.g., wax bath, infra-red lamp, etc.</td>
<td>facilities for domiciliary rehabilitation, e.g., bank loans, age pension</td>
<td>intersectoral support; community cooperation</td>
</tr>
<tr>
<td>4. Surveillance of high-risk groups, e.g., contacts, school/children, etc.</td>
<td>4.1 Home members</td>
<td>individual family members</td>
<td>a) awareness of early signs of leprosy b) undertaking preventive measures by good personal hygiene acceptance and cooperation of all family members in undergoing clinical examination</td>
<td>knowledge of health and social consequences of leprosy; knowledge of transmission of leprosy</td>
<td>suitable information material, e.g., pamphlets</td>
<td>facilities for health education; regular provision of drugs to patients to reduce infectivity</td>
<td>community-generated support, e.g., health committees and volunteers; support of health education in schools and religious institutions, etc.</td>
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<tr>
<td></td>
<td></td>
<td>community health workers</td>
<td>d) maintenance of contact register and annual examination of family members e) home visits f) health education on personal hygiene g) ensure regular treatment of cases to reduce infectivity h) school surveys</td>
<td>identification of high-risk groups, e.g., contacts, school/children; knowledge of transmission of leprosy; ability to detect early signs and symptoms of leprosy</td>
<td>kit with stationery and pin and feather</td>
<td>facilities for health education; spot map of villages and households; records</td>
<td>facilities for village health volunteers (housing, etc.)</td>
</tr>
<tr>
<td>4.2 First health facility</td>
<td>multipurpose workers, nurses, medical assistants, physicians</td>
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<tr>
<td>d) h) as in 4.1</td>
<td>adequate theoretical knowledge and practical skills, with basic elements in epidemiology, treatment and methods of leprosy control; clinical examination of patients, testing for sensation and thickening of nerves</td>
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<td></td>
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<tr>
<td>i) confirmation of diagnosis</td>
<td>kit with recording forms, stationery, and pin and feathers; essential drugs; manuals; laboratory and equipment supplies; transport facilities for supervision</td>
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<td></td>
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<td></td>
</tr>
<tr>
<td>j) taking skin smears and microscopic examination</td>
<td>records; stores; referral system; supervision; transport for home visits; spot map of villages</td>
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<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>k) record-keeping and reporting of leprosy morbidity</td>
<td>assistance with transport facilities; assistance with land and building facilities; support to training of selected community members and community health workers appropriate communication systems, e.g., public transportation, telecommunication, etc.</td>
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<tr>
<td>l) supervision of community health workers</td>
<td>m) epidemiological studies to identify high-risk groups</td>
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</table>

<table>
<thead>
<tr>
<th>4.3 First referral level</th>
<th>public health medical officer</th>
</tr>
</thead>
<tbody>
<tr>
<td>a) epidemiological and operational evaluation</td>
<td>as in 4.2; methods of leprosy control</td>
</tr>
<tr>
<td>b) promotion of health education</td>
<td>facilities for health education; facilities for evaluation</td>
</tr>
<tr>
<td>c) supervision of lower levels</td>
<td>transport facilities</td>
</tr>
<tr>
<td></td>
<td>intersectional coordination and cooperation with school health authorities, factory medical officers, etc.</td>
</tr>
</tbody>
</table>
Surveillance register
Where it is not possible to include information on surveillance on the original patient card, it may be maintained on a separate register. This information is required in order to monitor the follow-up examinations of patients who have completed their treatment. The following is an example of information to be included in a surveillance register.

Column 1: Serial no.
Column 2: Registration no.
Column 3: Name of patient
Column 4: Address
Column 5: Type of leprosy
Column 6: Date of completing treatment
Column 7: Surveillance examination
Column 8: Status

Column 7 would contain 5 blocks or columns for each of the 5 examinations due for multibacillary patients. For pauci-bacillary patients, only 2 of these blocks would need to be completed.

The OMSLEP individual patient form and related forms
The individual patient form (IPF) is simply a summary of the individual clinical record and is filled in (a) at the time of registration; and (b) at the end of each calendar year. It does not replace the treatment card/treatment register, or surveillance register which may vary according to the local context. If the clinical records currently in use provide all the information necessary to complete the IPF, no modification in these records is required. The IPF is meant to sum up the data on each individual in order to permit compilation and evaluation of information on an annual basis, using two other forms, which are filled in at the end of each calendar year—a detection form (DF), which sums up the data for all patients registered during the current year, and an annual statistics form (ASF), which sums up the data for all patients followed-up during the year (whether or not detected during that year and including those patients removed from the register during the year).

These forms are reproduced in Annex 6.

Other registers
Other registers such as contact registers, smear registers, etc., can be developed according to local needs.

Data analysis and feedback
The quality of statistics can be no greater than the quality of the information-gathering systems upon which they are based. The upgrading of these information systems at every level is encouraged, from primary sampling and recording in the field, and transcription and reporting by peripheral and more central levels, to the calculation and use of summary statistics by staff at regional and central headquarters. Attention should be paid to the quality of the forms used (are they understood by those who fill them in?), to the fact that quality and quantity of data may be inversely related (the amount of routine reporting will vary in different contexts, but it should not be assumed that more is always better), and to the necessity for frequent and appropriate feedback from central to peripheral levels (without which the quality of reporting will inevitably decline).

The summarizing of raw data in calculated statistics requires considerable care, not only for numerical accuracy but also in order to ensure quality control at every level. The statistics should be examined critically to ensure that they mean what they are supposed to mean and to detect any errors, changes, or trends in different areas and over time. The need for critical scrutiny of data by all health workers cannot be stressed too greatly.
Case-holding

An important technical requirement for successful multidrug therapy is the regularity of drug intake. Even the most effective drug regimens will fail if not administered regularly.

The attendance of patients at treatment centres depends on several factors. Some operational factors that could contribute to effectiveness of treatment are:

1) careful siting of clinics with timings convenient to the patients;
2) clinical and bacteriological reviews of patients as required, and discussion of findings with the patients;
3) simple physiotherapy, care of plantar ulcers and provision of suitable footwear;
4) appropriate referral mechanisms for the treatment of complications and deformities;
5) comprehensive medical care for the treatment of intercurrent ailments;
6) timely termination of treatment in patients who fulfil the required criteria;
7) effective supervision of the field workers at the peripheral level who are responsible for primary leprosy care; and
8) provision of appropriate welfare and rehabilitation facilities for patients who need them.

The main advantage of partially supervised regimens is that no concealed irregularity can occur in the administration of supervised doses. It is essential to ensure that the patient actually ingests the drugs. If the patient does not attend on the appointed day, the dose will be missed unless prompt action is taken. Services must, therefore, be organized in such a manner that they are convenient to the patient rather than to the health workers.

For the chemotherapy to be successful, regularity in taking the self-administered component of the regimen is also necessary. It is, therefore, essential to take both direct and indirect action to promote regularity of drug intake whether it be supervised or self-administered.

Aids to promote compliance

1) Home visits by an auxiliary worker prior to the appointed date for treatment to remind the patient to attend have been effective in promoting regularity in some countries.
2) Patients should receive the drugs in suitable damp-proof containers. The storing of dapsone and clofazimine together prevents the clofazimine capsules from sticking to each other in hot, humid climates.
3) Home visits by auxiliary or community health workers for tablet/capsule counts are a reliable and inexpensive method of monitoring the regularity of drug intake. Patients who have more or fewer tablets in their possession than they should on the day of the count should be suitably advised regarding the importance of taking their drugs regularly.
4) Generation of family pressure to promote regular drug intake can be an effective method when properly applied.
5) Health education of patients (and their families) should not be an activity limited in time and independent of treatment. It must be systematic, repeated and integrated with other health activities. Its aim is to ensure patients' full cooperation in bringing treatment to a successful conclusion.
6) Urine samples should be examined to monitor compliance where possible.
   a) The most effective method of monitoring compliance with dapsone treatment is to employ a simple laboratory procedure for detecting the drug or its metabolites in the urine. A spot test using Ehrlich's reagent has been found to be very useful in field studies. The details of the test are given in Annex 7.
b) No simple laboratory method has yet been developed for monitoring compliance with clofazimine treatment. However, among light-skinned patients the degree of pigmentation provides some indication of the extent to which the drug is being taken.
c) Since rifampicin is given under supervision it is not necessary to monitor compliance. The drug gives a characteristic orange-brown colour to the urine within 6–8 hours of ingestion.

Default from treatment

Default from treatment is a major problem in the chemotherapy of leprosy.

Some typical reasons for default are:

1) ignorance of the importance of regular treatment;
2) belief that when symptoms have subsided there is no need to continue treatment;
3) toxic side-effects of drugs or reactions;
4) skin discoloration following clofazimine treatment;
5) rude and unhelpful behaviour of health workers;
6) social prejudice deterring patients from attending the leprosy clinic;
7) symptoms not subsiding as quickly as expected;
8) distance of patients’ home from clinic and the inability to walk far because of plantar ulcers;
9) inconvenient clinic hours;
10) seasonal factors and other competing needs.

Identification of default can only be done if record cards are completed and filed correctly. The dates when the patient has to attend should, be recorded in advance on the treatment card according to an individual appointment schedule. If the patient does not attend on the appropriate date an effective mechanism for default retrieval must be initiated immediately.

Actions to follow up defaulters can be direct or indirect. Direct action implies personal contact with the patient through visits by health workers. Indirect action includes letters or messages, written or verbal, sent through an agent. Indirect actions are less expensive and more easily performed but are usually less effective than direct action.

In any leprosy control programme, a proportion of the registered patients are long-term absentees, i.e., they have not attended the treatment centre for years. Health workers should visit these patients and re-educate them to resume their treatment and complete the prescribed course.

Drugs, transport, and other supplies

Drugs

It is essential that sufficient quantities of antileprosy drugs are available at all health institutions, both at peripheral and referral levels. The quantity and type of drugs required for each centre can be calculated on the basis of the drug regimens selected and the number of patients likely to be treated, allowing a small margin for wastage and other contingencies.

A decision must be taken on central procurement or local procurement, in keeping with administrative instructions, cost, time, availability and other factors. Central procurement is generally more economical, but needs to be supported by a well planned logistics system to ensure availability at the periphery of all drugs included in multidrug therapy. Purchase orders for essential and accessory drugs must be placed at least one year in advance to ensure an uninterrupted supply, taking into account the shelf-life of the drugs. Difficulties associated with importation, finance, storage, and distribution of drugs
must never be permitted to interfere with 
the supply lines.

Storage requirements
Storage requirements for essential anti-
leprosy drugs are given below.

Clofazimine
Each capsule contains 50 or 100 mg of 
micronized clofazimine suspended in an 
oily base. The drug has a shelf-life of 5 
years and should be protected from humid-
ity and heat. The capsule consists of 
gelatin, which is known to be sensitive to 
humidity; hence the preparation is supplied 
in humidity-resistant containers which 
should be closed after use. The capsules 
may stick together when improperly stored 
but remain usable. They should be dis-
tributed to patients in small, plastic, 
airtight containers. The drug should be 
kept out of reach of children.

Rifampicin
Rifampicin is available as capsules of 150 
or 300 mg, as coated tablets of 450 and 
600 mg, and in syrup form. The capsules 
and coated tablets must be protected from 
heat and moisture. The syrup should be 
stored at temperatures below 25°C. The 
shelf-life of rifampicin is 4 years. The drug 
should be kept out of reach of children.

Dapsone
Tablets of 10, 25, 50, and 100 mg are 
available. They should be protected from 
heat and moisture. Dapsone has no par-
ticular shelf-life and can be used for several 
years after manufacture. It should be kept 
out of reach of children.

Transport
The transport requirements should be 
planned and designed before operations 
commence. Capital expenditure will be 
necessary for the provision of motor 
vehicles and other means of transportation.

Consideration should be given to: 
(a) vehicle usage, including fuel consump-
tion and maintenance, and anticipated 
spares for replacement; (b) mobility of the 
field staff for home visits and case-holding; 
(c) the mobile treatment circuit; and 
(d) supervision and other activities.

Other supplies
Supplies include microscopes, chemical re-
agents for preparing stains, scalpels, 
forceps, slides, spirit lamps, gauze and 
bandages for ulcer dressings, footwear, etc. 
The expected rate of consumption of each 
type of item and the quantity of initial 
stocks required need to be projected, their 
costs estimated, and orders placed accord-
ingly.

Supervision and 
monitoring

Supervision
This entails regular monitoring and control 
of the operational output, i.e., the activity 
provided by the service. An enlightened 
community can provide some degree of 
managerial supervision through various 
mechanisms designed to promote regularity 
of treatment, e.g., village health com-
mittees. Control of a technical nature, 
however, comes from more specialized 
levels of the health service, through guid-
ance, monitoring, and an appropriate in-
formation support system.

It is essential to ensure that programme 
activities are undertaken in accordance 
with prescribed procedures. Supervision 
must be systematic and continuous, and 
corrective action must follow wherever 
necessary. Supervision is not intended to 
assess achievement of programme targets 
or to estimate coverage. A common ten-
dency, which should be avoided, is for 
supervision to be made an exercise in
evaluation of programme activities (this is most marked when supervision is done by specialized staff).

Supervision increases the efficiency of health workers by developing their knowledge, improving their skills, and promoting positive attitudes towards work. Supervision should not be punitive and is not a one-way process, i.e., from supervisor to worker. To produce the desired effect, supervision must be well planned, regular, and consistent.

The success of the programme depends to a considerable extent on the satisfactory performance of the staff—if certain tasks that should be done are either not being done correctly or are not being done at all, programme objectives will not be achieved. An important responsibility of the programme manager is to oversee, direct and assist health workers.

Supervision is aided by programme monitoring, i.e., the process of keeping a continuous watch on programme performance through periodic reports, in order to identify areas that need supervision most urgently.

The following are prerequisites for effective supervision.

1) A manual of instruction should be available for every worker. It should be in simple language, easily understood and work-related, i.e., of an operational nature.

2) An ideal supervisor has a pleasant and friendly manner, is quick in establishing rapport with workers of all categories, knows the manual, is familiar with the problems that arise in the field, is devoted to the work, is always prepared to travel and endure personal discomforts, is ready to listen with an open mind to any problems, and, finally, has endless patience in teaching and training workers.

3) A climate propitious for supervision must prevail; those supervised should look forward with pleasure to the visit.

It can be achieved by allowing workers to feel that, in preparation for the visit, they can assemble all their problems, secure in the knowledge that the supervisor will make genuine efforts to solve them.

4) Supervisory visits should be carefully planned. Before each visit the supervisor should review the findings of the last visit and the actions taken.

5) Periodic reports should be made by field staff.

6) Periodic review meetings should be held for feedback of data analysis, planning activities, and monitoring targets.

The range of programme supervision stretches from logistics (provision of drugs, transport requirements, and maintenance of equipment) to the management of patients and their treatment.

Indicators that are characteristic of programmes that are being managed effectively are:

1) implementation of projected activities according to schedule;
2) use of resources for their intended purpose, without diversion to other activities;
3) effective utilization of resources without wasteful duplication;
4) provision of a reasonably good quality of service in all areas;
5) a system of objectives, targets, and priorities, which are periodically reviewed;
6) a structure in which the functions of the different agencies concerned are clearly defined but can adapt to change;
7) good morale and motivation of health service personnel;
8) clear policies for developing and using to the fullest extent the capabilities of all kinds of health service personnel;
9) maintenance of public confidence;
10) establishment and use of adequate channels for complaints and suggestions.


**Monitoring**

Programme monitoring is sometimes called indirect supervision. It is the observation of programme performance through examination of periodic reports. It should not be confused with programme evaluation. Monitoring may show that a particular performance is unsatisfactory, but since it is based on reports it will provide no pointer as to why the performance has been unsatisfactory.

Programme monitoring should support general supervision. Both supervision and monitoring are indispensable for good programme management.

**Community involvement**

The active involvement of the community in support of the leprosy programme is essential. The success of the strategy will largely depend on the support of the community and the enlightened involvement of village councils. However, this approach must take into consideration the social prejudice against leprosy that exists in many societies.