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International Meeting on Epidemiology of Leprosy in Relation to Control held in Jakarta, Indonesia, 17-21 June 1991, organized by the World Health Organization and cosponsored by the Sasakawa Memorial Health Foundation

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Leprosy Review

A journal contributing to the better understanding of leprosy and its control

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LEPRA

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Leprosy Review is published by the British Leprosy Relief Association (LEPRA) with the main objective of contributing towards the better understanding of leprosy and its control. Original papers on all aspects of leprosy, including research, are welcomed. In addition, *Leprosy Review* seeks to publish information of educational value which is of direct benefit to the control of leprosy under field conditions, and hence to the individual patient. The Journal aims to interpret what is being done in other disciplines, particularly for field workers.

From time to time the Editorial Board invites special articles or editorials from experts in various parts of the world, and gives consideration to the production of a supplement or special number devoted to a particular subject or theme of major importance.

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Epidemiology of leprosy in relation to control

The papers contained in this volume were presented at an international meeting held in Jakarta, Indonesia, 17–21 June 1991, organized by the World Health Organization and cosponsored by the Sasakawa Memorial Health Foundation.

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Preface

The control of leprosy in the endemic parts of the world is passing through an important phase as a result of the widespread application of multidrug therapy (MDT) as recommended by WHO. At this moment there are many unprecedented changes taking place in many countries in the leprosy situation, most of which are highly favourable. In fact, it appears that developments in disease control are overtaking the accumulation of knowledge of the epidemiology of the disease. While there has been a phenomenal increase in recent years in the basic knowledge of *Mycobacterium leprae* and the host response generated by it, including at molecular and immunological levels, there are as yet no reliable and usable laboratory tools that can be applied on a large scale for the better understanding of the epidemiology of *M. leprae* infection.

The rapidly changing situation in leprosy calls for the development of simple operational and epidemiological methods to assess the current disease situation and to predict future trends. In addition, the development of indicators for evaluating the control of leprosy at different levels, and their application, is essential for monitoring the progress. Thus the application of all existing knowledge on the epidemiology of leprosy to improve disease control is of prime importance, particularly in view of the targeted goal that leprosy should be eliminated as a public health problem by the year 2000, defining elimination as attaining a level of prevalence below 1 case per 10,000.

The International Conference on the Epidemiology of Leprosy in Relation to Control, organized by WHO together with the Sasakawa Memorial Health Foundation and the Indonesian Government, was held in Jakarta from 17 to 21 June 1991, and was able to address, in depth, several of the issues discussed above and came to useful conclusions and recommendations. The papers contributed by the various scientists were valuable, and will be of considerable interest to leprosy workers. For this reason, it was decided that the Proceedings of the Conference should be published as a special supplement to *Leprosy Review*, and this has been made possible by a generous grant from the Sasakawa Memorial Health Foundation.

The publication of the Proceedings of the Conference will hopefully generate further interest in studies of the practical problems in leprosy control, with such studies contributing to the overall goal of eliminating leprosy as a public health problem.

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Needs and prospects for epidemiological tools in leprosy control

P FEENSTRA

1. Introduction

1.1. MAGNITUDE OF THE LEPROSY PROBLEM

The suffering of leprosy is caused by irreversible damage to the peripheral nerves, which leads to sensory loss, paralysis and loss of function of the hands, feet and eyes. The resulting deformities are the main cause of the social stigma attached to the disease. This stigma especially leads to the very serious psychological, social and economic consequences for leprosy patients as well as for their families. It should therefore be realized that the magnitude of the leprosy problem is insufficiently reflected by mere data on numbers of cases.

In September 1990 3·7 million leprosy cases were registered worldwide for chemotherapy. During 1990, 576,360 new cases were reported. (WHO) This information is obtained from routine health services reports from the individual countries and should therefore be treated with caution. It is, however, the best information available on the global leprosy problem.

1.2. IMPACT OF MDT

The introduction of the WHO recommended multidrug therapy (MDT) over the last 10 years was a revolutionary event in the history of leprosy control. MDT has proven to be effective, safe and acceptable to patients and health workers and can be implemented under a wide variety of conditions. Early relapses are rarely observed. The shortened duration and the effectiveness of the treatment improves patient compliance and motivates health workers. In most programmes the introduction of MDT is included in the intensive (re)training of the health workers, health education of patients and the community as well as improved supervision; this has resulted in a considerable upgrading of leprosy control activities. These positive effects of the implementation of MDT have brought about a growing confidence in the community concerning the possibilities of leprosy treatment. Many programmes have reported that this has resulted in increased early self-reporting of patients so that in more cases nerve damage is prevented.

Because of the short duration of MDT, patients are released from treatment much earlier than with dapsone monotherapy. This has, together with the initial 'clearing of the registers' during the introduction of MDT, resulted in a striking decline of the number of

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leprosy patients registered for treatment. An impressive example is the ALERT Leprosy Control Programme in Shoa Province, Ethiopia, where the number of patients registered for chemotherapy fell from 21,138 in 1982 to 2,636 in 1990. On a global scale the number dropped from 5·4 million in 1985 to 3·7 million in 1990, although by that time only 55% of the cases were on MDT.

MDT has not only a higher efficacy than dapsone monotherapy, but as mentioned above, in many programmes patients are also diagnosed and treated at an earlier stage of the disease. This means that the period of infection is shortened. Therefore it is possible that the risk of infection will become lower in an area covered by an MDT programme than in a comparable area where the leprosy control programme relies on dapsone monotherapy. If this assumption is true and if it is further assumed that, in analogy with tuberculosis, there is a direct relation between the risk of infection and the incidence of disease, a decline (or an acceleration of an already existing declining trend) in the incidence of leprosy may be expected during the next 10 years in those areas where MDT has been widely and adequately implemented during the 1980s.

Given the long incubation time of leprosy and the fact that in most programmes wide MDT coverage of cases has not yet, or only very recently been achieved, a clear idea of the impact of MDT on the incidence of leprosy is not yet available. Nevertheless, the incidence of leprosy (as reflected by case-detection figures) is clearly declining in a number of countries where MDT was introduced in the early 1980s and where there were well organized leprosy control programmes based on dapsone monotherapy many years before the introduction of MDT, e.g. Thailand. This decline in incidence, in addition to a possible initial effect of MDT, is mainly attributed to the intensive decades-long implementation of dapsone monotherapy. However, many other known factors, (e.g. vaccination with BCG) and unknown factors (e.g. related to socio-economic improvement), may have played a role. Moreover, the decline in incidence is not observed in all countreis which have implemented MDT since the early 1980s and had a good monotherapy programme prior to the introduction of MDT.

2. **Elimination of leprosy**

The 44th World Health Assembly (1991) adopted as a resolution the goal of attaining global elimination of leprosy by the year 2000. 'Elimination' is defined as reaching a level of prevalence below 1 case per 10,000 population. The prevalence of leprosy (number of cases registered for treatment at a specified time) is equal to the product of the incidence (number of new cases detected during the year) and the average duration of treatment. Given the global number of cases annually detected (1989/1990: 576,360; case detection rate = 1·09 per 10,000 population!), it may be expected that the global elimination goal can be achieved with the present MDT regimens, provided full coverage with MDT is established within the next few years and is maintained at the highest possible level. This expectation is justified if the duration of treatment does not exceed a period of 6–9 months for PB leprosy and of 24–36 months for MB leprosy. As the global MB:PB ratio among new cases is below 2:3, the prevalence will become more or less equivalent to the incidence. For individual countries, which at present have case-detection rates above 1 per 10,000 population, the target is likely to be achieved within 10 years only if the local MB:PB ratio is very low and if full MDT coverage is established soon.

However, by the end of 1990 only 55·7% of the 3·7 million leprosy patients registered for chemotherapy was on MDT. Far too many leprosy patients do not yet have access to the benefits of MDT, especially in the African Region, which with an MDT coverage of only 18·4% is lagging behind. Successful introduction of MDT so far has been achieved mainly in those countries or regions where the conditions are relatively 'easy' for the implementation of MDT: countries or regions with a good infrastructure, or with sufficient numbers of well-trained health workers, a good coverage with health services, or with a pre-existing, well-managed leprosy control programme based on dapsone monotherapy, adequate financial resources etc. It is obvious that major efforts are required for the achievement of full global MDT coverage.

3. **Integration of leprosy control**

At various occasions, including the 44th World Health Assembly, the WHO has urged the Member States to integrate leprosy control activities within the general health services. In many countries leprosy control programmes are already integrated or are in a process of transition from a specialized, vertical structure towards integration. The concept of the integration of leprosy control is gaining wide acceptance. To a great extent this is based on considerations of efficiency. With the declining number of registered patients vertical programmes are far too expensive. However, the basic justification for integration is the principle of equity. Integration means that leprosy control becomes the integral responsibility of permanent, community-based general health services, which provide the entire community, including leprosy patients, with comprehensive and continuous health care. This has clear advantages compared to the periodical and monopurpose services of vertical programmes, which in many situations reinforce the stigma attached to the disease. A prerequisite for integration is the existence of an adequately functioning general health services infrastructure. Although at the central and intermediate levels specialized services should be maintained within the integrated programme (for training, technical supervision, referral), the day-to-day patient management and recording, registration and reporting will become the task of general health staff.

4. **Needs for appropriate epidemiological tools**

4.1. CHANGING NEEDS

In 1983, when experience with MDT was very limited, a WHO Study Group on the Epidemiology of Leprosy in Relation to Control made a number of recommendations on the application of epidemiological tools for leprosy control (TRS 716, WHO, Geneva, 1985). The needs and relevance of various aspects of epidemiology of leprosy in relation to control have undergone significant changes since the Study Group made its recommendations.

In the light of:

the decreasing prevalence of leprosy as a result of the implementation of MDT;
the WHO goal of reaching a global prevalence rate below 1 case per 10,000 population by the year 2000; and

the widely accepted policy of implementing leprosy control activities as an integrated part of the general health services based on the primary health care approach,

there is a need to review these recommendations and to identify how optimal use should be made of epidemiological tools for the management of leprosy control. Such management tools should assist in the planning, implementation, monitoring and evaluation of leprosy control programmes and should by definition be relevant for decision-making. The management tools should preferably be based on epidemiological information which can be collected by general health staff under routine field conditions.

In this context three important subjects, which are strongly inter-related, are to be considered:

the assessment of the leprosy problem in terms of prevalence and incidence of leprosy and leprosy-related disabilities;
the prediction of future trends of this leprosy problem;
the basic epidemiological data for monitoring and evaluation of leprosy control programmes under routine field conditions.

4.2. ASSESSMENT OF THE LEPROSY PROBLEM

A reasonable knowledge of the magnitude of the leprosy problem in terms of prevalence and incidence of leprosy and leprosy-related disabilities is required for adequate planning, implementation and evaluation of leprosy control activities. At present the estimated case-load ranges from 7 to 15 million worldwide. This wide range demonstrates the lack of adequate tools to measure the magnitude of the leprosy problem. The issue is further complicated by the lack of a clear operational definition for a case of leprosy.

The only method available so far for obtaining reliable estimates is the (random sample) prevalence survey. Because of the low prevalence of leprosy and its tendency to occur in clusters, the sample size has to be very large. This makes the method an expensive and time-consuming affair, which is not appropriate for application in the vast majority of leprosy-endemic countries.

There is, therefore, a need for practical methods for the assessment of the leprosy problem which are adequate for the planning and evaluation of leprosy control programmes. In this context it should be carefully considered what degree of precision is required for the planning of leprosy control activities and whether the methodology is appropriate for application under very low prevalence conditions. The methods should preferably be based on available health services data, as it may be assumed that in general the information on registered cases reflects the magnitude of the leprosy problem in a country. However, different extrapolation factors will apply for different situations.

4.3. PREDICTION OF FUTURE TRENDS

Predictions of future trends are useful for long-term health planning and are important for obtaining commitment from governments, funding agencies and health authorities. Expectations regarding the future trend of the incidence and prevalence of leprosy and leprosy-related disabilities, as discussed in Section 1.2, are mainly based on extrapolation of the trends of reported numbers of cases on register and reported numbers of new cases. It may, however, be questioned whether these expectations are based on scientifically

sound evidence. Not only are there many hazards involved in the extrapolation from routine health services data, but as there is also a lack of a standardized operational definition of a case, the reliability of these predictions is even more questionable. Moreover, the impact of MDT on the risk of infection is not known, as there are no tools available to measure infection. And even if infection could be measured, the relation between the risk of infection and the incidence of disease would still have to be identified.

There is, therefore, a need to identify or to develop scientifically sound epidemiological tools for the prediction of future trends, which can assist in the planning of leprosy control. Such tools may consist of a combination of various forecasting techniques. The issue also includes the exploration of the possible use as a management tool of epidemiological techniques, especially modelling, for the identification of optimal interventions for the reduction of the leprosy problem (e.g. surveillance of high risk groups, use of immunodiagnostic tests, chemoprophylaxis, alternative drug regimens, duration of treatment, vaccine) under varying epidemiological and operational conditions.

An important question, which has to be addressed here, is whether it will be feasible to develop tools which are of practical relevance for programme managers. What will be their limitations and how easy will they be to apply? Will they be precise enough for planning the elimination of leprosy in the individual countries?

4.4. BASIC DATA REQUIREMENTS FOR THE EVALUATION OF LEPROSY CONTROL PROGRAMMES

The basic strategy for leprosy control consists of early diagnosis and the provision of adequate chemotherapy (=a complete course of MDT) in order to:

cure the patients;
to interrupt transmission of infection, thereby reducing the incidence of disease; and
to prevent leprosy-related disabilities.

Therefore the most relevant indicators for the monitoring and evaluation of leprosy control should reflect the programme effectiveness in terms of the proportion of cases on treatment among the real number of cases, the proportion of patients cured (=completed treatment) among those who started MDT, the reduction of the incidence of leprosy and the reduction of the incidence of leprosy-related disabilities.

The indicators should be appropriate for application in low prevalence situations. They should preferably reflect directly what they are supposed to measure, e.g. proportion of patients completing treatment among those expected to complete treatment, but may also be proxy indicators, e.g. proportion of disabled patients among new cases as an indicator for the case detection performance.

Usually leprosy control programmes collect a wide variety of data. Many programmes have developed their own (sometimes computerized) information systems despite the availability of the OMSLEP system, which apparently does not fulfil everyone's requirements. Most leprosy control programmes do not make adequate use of the data, often obtained through complicated administrative procedures and a lot of field workers' and their supervisors' working time. Most of this information is not used for any decision making.

In order to improve this situation it is necessary to identify the major issues involved in the evaluation of the operational performance and of the epidemiological impact of leprosy control programmes. The decision on what events have to be reported and which data have to be collected should be based on these issues.

The indicators suggested in the report of the WHO Study Group on the Epidemiology of Leprosy in Relation to Control (TRS 716) are far too many and too many of them are not linked to decision-making or are appropriate for routine application in integrated programmes.

Therefore, there is a need to identify those indicators, including data requirements, which are the most essential as tools for the evaluation of leprosy control programmes. Moreover a number of additional indicators, which are appropriate for optional use by more advanced programmes and a number of indicators, which can be applied for special epidemiological studies, may be identified.

Some suggestions were formulated during the WHO Consultation on Technical and Operational Aspects of Leprosy, Male, Maldives, June 1990.

In order to obtain complete and reliable data the purpose and the meaning of the data should be clear to those who have to collect them: the peripheral multipurpose health workers. This implies that the data should be relatively simple to collect and that the amount of data should be limited. The same is required for the methods for patient registration and reporting. An assessment of the experience gained with the OMSLEP recording and reporting system for leprosy system for leprosy patients is expected to be very useful for this purpose.

The method and application by general health staff of the reporting of patients according to treatment cohorts needs further exploration. A major advantage of this method is that it allows cohort analysis, not only regarding the completion of treatment (which reflects, as a direct indicator, much better the patient management performance than the indicators as suggested by the WHO Study Group (TRS 716)), but also regarding the incidence of reactions, disabilities, relapses, etc.

In view of the above, the definition of a case of leprosy should be clarified. Clear and standardized operational criteria are required in deciding whether a leprosy patient is in need of chemotherapy or not. Preferably the criteria should be based on clinical evidence. In order to exclude persons with 'sub-clinical' leprosy from the case registers, it has been suggested that a time criterion for patients with single skin lesions should be added, as the majority of such lesions are self-healing and do not lead to potentially disabling nerve function impairment.

The issue of the duration of treatment has to be considered as well, especially in relation to those cases still showing signs of active disease at the time of completion of treatment. Authoritative and clear operational criteria should be identified for the definition of 'cure'.

4.5. STATE-OF-THE-ART ON EPIDEMIOLOGY OF LEPROSY

In order to address the questions mentioned above it is necessary to review first the State-of-the-Art on epidemiology of leprosy, especially in relation to the three main issues of this meeting: the rapid assessment of the leprosy problem, the prediction of trends and the identification of evaluation tools.

The most important gaps in existing knowledge have to be identified and, consequently, suggestions for research should be made.

The following questions have to be addressed:

Which knowledge on the epidemiology of leprosy has been acquired during the past decade, which saw such a revolutionary change in the approach to leprosy control?
Which are the most important risk factors for leprosy, leprosy reactions and leprosy-related disabilities? Is it possible to identify special high-risk groups which, especially under low prevalence conditions, are in need of specific interventions, e.g. clinical and/or bacteriological surveillance, prophylactic treatment, vaccination, etc.?
What might be the implications of human immunodeficiency virus (HIV) infection for future trends in the epidemiology of leprosy?
Is there sufficient scientifically sound evidence to justify the optimistic expectations concerning the elimination of leprosy? Is it justified to rely on the extrapolation of recently observed trends?
Is it appropriate to attribute the observed changing leprosy trends, especially regarding the incidence, to the impact of leprosy control programmes or is it possible (and how) to identify the influence of other, perhaps more important factors such as BCG vaccination or factors related to socioeconomic conditions?
Is it, given the limited period of post-MDT surveillance, justified to expect that the relapse rate after MDT will remain as low as is observed during the first years after stopping chemotherapy? Can it be predicted what will happen with the leprosy trends if, for example, relapse rates will progressively increase 10 years after release from chemotherapy?

5. **Scope of the meeting**

The purpose of this meeting is to identify or to develop scientifically sound and practical management tools for leprosy control based on appropriate epidemiological information. The tools should be appropriate for application in integrated leprosy control programmes and under low prevalence conditions. The outcome of the meeting is expected to contribute significantly to the improvement of leprosy control through the rationalization of the use of epidemiological information for the planning, monitoring and evaluation of leprosy control programmes.

In order to achieve its purpose the meeting will first review the State-of-the-Art on the epidemiology of leprosy. After this review the specific needs for tools for the assessment of the leprosy problem and for the prediction of trends will be addressed. Finally the meeting will concentrate on the identification of the most appropriate data requirements for the monitoring and evaluation of leprosy control programmes.

Based on the identified needs for management tools and the required epidemiological information, as part of the group discussions on the four main issues we should attempt to identify the priorities for research which are relevant for the improvement or development of such tools. This involves questions such as:

Is our present knowledge of the epidemiology of leprosy adequate for the identification and development of appropriate methods for the rapid assessment of the leprosy problem, for the prediction of trends and for the management and evaluation of leprosy

control programmes under varying operational conditions and, if not, which research is needed to develop such tools?
Which research, especially in the field of health systems research, is needed for the better application of the available epidemiological knowledge of leprosy? Is it possible to evaluate the effectiveness of leprosy control programmes with routinely collected health services data or is there a need for special studies? What degree of precision is required of such data?
Which other new tools for leprosy control, such as a vaccine, new drug regimens, immunodiagnostic tests, etc., can be expected or should be developed during the next 10 or 20 years? What will their additional contribution, and thus their relevance, be in terms of potential benefit, efficiency and feasibility of implementation?

Practical and operationally feasible management tools are important in order to enable countries to participate effectively in the global elimination strategy for leprosy. The tools must be relevant for decision making and should preferably be based on data which can be collected routinely by multipurpose health workers at the peripheral level of the general health services. The meeting should keep in mind continuously that its aim is the identification of practical tools. Therefore we should not deviate into issues which may be very interesting, but are only of academic interest. Again and again we should ask ourselves: why and for what do we need the information and is it really needed for the improvement of leprosy control?

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Issues involved in the rapid assessment of the leprosy problem

T K SUNDARESAN

Summary Sample surveys for estimation can prove very expensive and time-consuming because of the enormous sample sizes usually required.

Where sample surveys have to be undertaken, diagnoses should be limited to detecting a case of leprosy, without attempting skin smears etc. in order to classify by types. Usually enough knowledge is available on the approximate proportion of multibacillary (MB) cases in most communities, and this knowledge could be utilized for estimating the caseload by types of leprosy. Again intensive tracing of nonrespondents could be limited to either males or females depending on convenience, and well-known sex ratios among patients utilized for deriving estimates for the other sex.

The type of rapid methods of estimation depend on three types of situations: (1) before multidrug therapy (MDT); (2) 5 years or more after MDT; and (3) less than 5 years after MDT.

In the first situation one or more of the following methods are suggested:

(i) extrapolation from registered cases;
(ii) extrapolation from child prevalence; and
(iii) conducting rapid village surveys.

In situations where MDT has been introduced for 5 years or more the registered cases plus a small number, depending on local experience, would seem to be adequate.

When MDT was introduced less than 5 years before, it is suggested that the prevalence rates be obtained by statistical interpolation drawing on the experience from areas which have had more than 5 years of MDT.

Introduction

Most of the information now available on the magnitude of the leprosy problem in the world is based on registered cases. Reports from most countries give the numbers actually on the registers and invariably there is comment that the true prevalence of the disease should be at least 50% or 100% more. The World Health Organization has underlined the need for reliable baseline information on the prevalence of the disease before introducing MDT. The need for reliable information on the true magnitude of the problem is well understood. This paper will discuss various methods that could possibly be used and highlight the advantages and shortcomings of each such method.

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Estimation and case-finding

At the outset, a clear distinction needs to be made between case-finding for control purposes and estimation. In case-finding and control, an effort is made to find all possible cases in a community and treat them. On the other hand, the purpose of estimation is generally to get an idea of the caseload in large areas such as a country or a district. The purpose is 2-fold: (1) to obtain baseline information on the magnitude of the problem; and (2) to assess periodically the progress of the control programme. This paper deals only with problems of estimation.

It may be relevant to mention two concepts which should be constantly kept in mind in connection with problems of estimation. The first is 'nonsampling errors'. This can arise due to differences in the definition of a case, observer variations in the diagnosis and classification, incomplete coverage of the population, etc. It is most important to keep these variations to a minimum otherwise the estimates will not be 'valid'. The second consideration is the 'precision' with which the estimates are required. These are the 'sampling errors' and have a direct bearing on the sample size, in the case of sample surveys, and will be discussed more at length in a subsequent section.

Medical issues involved in estimation

There is not yet a universally accepted definition of a case of leprosy, notwithstanding the recommendation of the WHO Sixth Expert Committee[1] that introduced a new category—'cases needing treatment'. Some investigators would like to count even very minimal lesions with a good prospect of self-healing, while others would like to leave them out. The specificity of diagnosis in early cases is likely to be less than in established cases. Again there are the usual intra- and inter-observer variations in diagnosis of early disease and in the classification of the disease as paucibacillary or multibacillary, depending mostly on the accuracy of bacteriological examinations. It may be easy to categorize patients on the registers according to this criterion, but when enumerators meet cases in surveys, they have to depend on the information of the patients themselves to decide whether they need further treatment or not and this may not be accurate.

Total population surveys

This procedure should in principle give the exact situation in the community, but it is too expensive, time-consuming and demands a lot of resources in terms of personnel and equipment, and even assuming that resources are available this method is not necessarily the best. The disease is 'rare' in a statistical sense and occurs unevenly or in 'patches'. Nonresponse due to various reasons is all too common. If the nonresponse is related to the occurrence of the disease, as is likely in many situations, this could greatly bias the results. The fact that 99% of the population has been examined can give a confidence in the findings, but the 1% not covered could be hiding a disproportionate number of cases. Again there is the question of 'what is a case?' It is well known that a substantial number of paucibacillary cases are self-healing. After all, the main interest is in knowing the numbers needing treatment. Thus a repeat visit may be necessary to exclude the cases that have healed in the meanwhile. For this purpose it is necessary to lay down rules for the periodicity, i.e. at what interval.

Table 1

Expected Prev. rate (per 1000)	Sample size
5	230,000
4	287,000
3	384,000
2	576,000
1	1,152,000

SAMPLE SURVEYS

Since the aim is only to estimate the prevalence of the disease, sample surveys are to be preferred to total enumerations because:

(1) they are cheaper;
(2) the results can be obtained in a shorter time; and
(3) intense effort can be put into controlling the non-sampling errors referred to in the previous section.

However an adequate sample size depends on: (1) the expected prevalence of the disease; and (2) the precision with which the estimates are required. Given the degree of precision required the sample size will increase when the prevalence decreases. Cluster sampling is the usual design of choice, being the most practical, and the design effect is assumed to be about three. (This means that the sample size will be about three times that for simple random sampling.) Table 1 will give an idea of the minimum sample sizes for different 'expected' prevalences for a precision of 20%.

Second, for the same expected prevalence the sample size will increase even more rapidly when the degree of precision demanded increases. Table 2 will give an idea of the order of magnitude of the increases for a prevalence rate of 2 per 1000.

With the sort of prevalence rates expected in low and moderately endemic areas, the sample sizes have to be very large. Securing improved coverage once the sample has been chosen, and keeping down other nonsampling errors, can be enormous tasks.

'Rapid' methods and suggested simplifications

Long years of experience in leprosy control in the world have highlighted certain patterns

Table 2

Relative precision (%)	95% C. limit		Sample size
	upper	lower	
40	2·4	1·6	144,000
30	2·3	1·7	256,000
20	2·2	1·8	576,000
10	2·1	1·9	2,310,000

in the distribution of the disease in the community and the numbers coming to the knowledge of the leprosy services. These are related to the general attitude of the population and the adequacy of the leprosy services. The epidemiological pattern is seen in the age and sex distribution and the proportion of multibacillary patients among all cases of leprosy. Bechelli *et al.*[2] have suggested making use of observations on these patterns to predict the prevalence of the disease.

The introduction of MDT on a large scale is known to affect the patterns referred to above and hence the approach to 'rapid' methods has to visualize three situations:

I The situation before the introduction of MDT on a large scale. Baseline information on the magnitude of the problem is often a prerequisite for introducing MDT and a good part of the endemic areas of the world are in this situation. As MDT is being introduced rapidly there is an urgent need for a method to obtain the information quickly.

II The situation where it is 5 years or more since the introduction of MDT with adequate coverage.

III The situation where it is less than 5 years since MDT has been introduced.

I. BASELINE INFORMATION BEFORE INTRODUCING MDT

(*i*) *Sample Surveys*

If there is no information to go by, a sample survey may have to be undertaken. The methodology for such sample surveys in leprosy has been elaborated by Sundaresan *et al.*[3] However, the following simplications are suggested:

One of the components of medical examination is the taking of skin smears and testing them bacteriologically. This is an expensive operation and calls for trained personnel. However, from observations of registered cases and limited surveys, the proportion of multibacillary cases seems to be fairly constant in each society although the proportion can vary from country to country. For example, before the introduction of MDT, it was between 16 and 23% in Nigeria, India and Ethiopia. Bechelli *et al.*[4] have reported that in the sample surveys in Cameroon, Northern Nigeria (Katsina) and Thailand (Khon Kaen), in the 1960s, lepromatous and borderline cases constituted 8%, 8% and 37% of all cases respectively. However, the prevalence of indeterminate forms was much higher in the first two countries. Information of this nature could be utilized for obtaining first approximations to prevalence rates by limiting the examination of patients to a minimum, without attempting to classify them as MB or PB, in the first instance.

Table 3

Country	Prevalence rates (Male:Female)
Cameroon[4]	1·3
Thailand[4]	1·3
Nigeria[4]	0·84
S. India (Tirukoilur)[5]	1·5
Myanmar (Regd. 1989)[6]	1·75

Again the sex ratio of patients in any society seems to be relatively constant, males having in general a higher prevalence rate. Table 3 gives the sex ratios from a selected number of countries.

Although, in population surveys, by house-to-house visits both males and females can be examined, there are some special problems with regard to each sex. For example, to examine females completely, one may need to recruit female workers. In sample surveys it is important to cover the population selected. At least a sample of the nonrespondents in the first round have to be traced to see how their nonresponse is related to the presence of the disease. This tracing of nonrespondents is usually time-consuming and needs a lot of effort. A knowledge of the approximate sex ratio of cases could facilitate limiting the tracing of nonrespondents to one of the sexes, according to the circumstances. For example, if the nonresponse from males is essentially due to their being away at work, complete coverage can be sought for women and the rates for males extrapolated. On the other hand if there are practical difficulties in examining women, it may be better to extrapolate from the male prevalence rates. It is understood that for practical reasons, in general, both males and females will be examined. The suggestions for extrapolation are applicable only at the analysis stage, when for some reason there are reasons to conclude that survey of one of the sexes is not perfect.

(*ii*) *Extrapolation from registered cases*

Practically all countries report the number of cases on their registers. In many situations there are comments by leprologists that the true number of cases could be so many times

Table 4. Kohn Kaen, Thailand,[8] sample survey, 1962

Sample	Population examined	Registered cases	All cases	Reg./All	Block (%)
1	3019	25	34	73·5	
2	2448	34	49	69·4	
3	2457	36	56	64·3	
4+5	3711	20	31	64·5	
6	3291	4	5	80·0	
7+8+9	3932	22	30	73·3	
	18,858	141	205	68·8	All 18,858

Table 5. Orissa, India, 1988–89[9]

District	Total cases	Voluntarily reporting (%)
Ganjam	4090	47·3
Puri	3602	43·7
Cuttack	4998	57·9

those on the registers. For example, in 1987 Chitimba[7] reported for Nigeria that 'there are 282,000 registered patients out of a population of 100 million people and it is estimated that there are one million sufferers. An appraisal conducted in 1975 puts the prevalence rate of registered cases between 0·1 and 17 per thousand with a mean of five per thousand'. Thus the prevalence of registered cases was 2·82 per thousand and the national estimate is 5 per thousand. Tables 4 and 5 show examples from certain other areas of the world where there is a possibility of comparing the prevalence rates of registered cases with the true rates in the population.

What emerges from these comparisons is: (1) given a country's situation as regards leprosy services, the registered cases are a fairly constant proportion of all cases in that area, year by year and locality by locality (provided each locality is sufficiently large); (2) the proportion of MB cases or proportion of children can be quite different among the registered group when compared to all the cases. It is just that the total numbers seem to be well correlated irrespective of the composition of the two groups.

The merit of this approach is that it is least expensive. In many countries, limited surveys in selected areas already provide the type of relationship that exists between registered cases and all cases, and this relationship can be used to provide an extrapolating factor to derive the true prevalence from known registered cases. Undoubtedly, this would be a first approximation but may be adequate for planning purposes.

Issues involved in this approach are:

(1) there should be a leprosy service in the area with reasonable registration procedures;
(2) there should be a means to estimate the extent of multiple registration in different centres or services;
(3) a distinction should be made between areas or centres where the case-reporting is voluntary or passive and areas where there is an active case-finding programme. The extrapolation factors could be vastly different in the two types of area; and
(4) a distinction may have to be made between the population living within accessible distance of a leprosy service and others.

In any case pilot studies on a small scale should be carried out to derive an extrapolating factor or confirm the validity of one already being used.

(*iii*) *Extrapolation from child prevalence*

In many areas of the world, especially in hyperendemic areas under dapsone monotherapy, the prevalence rates of leprosy among children, 5–14 years of age, were closely correlated to the overall prevalence rates as Table 6 illustrates.[8]

Table 6

Country	Child prevalence rate/Total prevalence rate
Myanmar (69–72)	0·79
Shwebo (Myanmar) (63)	1·04
N. Nigeria (60)	1·14
India (62–67)	0·92

The above relationship suggests that the total prevalence rates can be extrapolated from child prevalence rates if the latter can be ascertained. It should be noted that the proportions of MB and PB cases could be different for the two groups although the overall rates for all types may be closely related as above. Dr E Declercq[8] has pointed out that 'there seems to be a strong correlation between the prevalence rate of leprosy for children and the total prevalence rate if studied in different areas of the same country and that the rates remain stable over the years within one area. However this relationship is not similar in different countries'.

If not already known from past experience based on prevalence surveys, etc. this should first be established or ascertained from pilot investigations. The advantage of extrapolating from child prevalence rates is that it is relatively quicker and less expensive to examine a large number of children, e.g. school surveys.

As an illustration of the savings involved, suppose it is known that the overall prevalence rate is about 1·25 times that of the child prevalence rate. If by examining 30,000 children we obtain a rate of 5 per 1000 we might be able to state that the overall rate is 6·3 per thousand with a 95% confidence interval between 5·3 and 7·3. To make a similar statement by actual population surveys, with cluster sampling, we might need a sample size of 50,000. Of course the 30,000 children may be drawn from a population of 150,000, but house-to-house visits are avoided and large numbers are examined at selected places such as schools. Further it is easier to examine children completely and nonresponse rates can be reduced considerably.

The issues involved in this approach are:

(1) it is important to know the proportion of children that attend school and the social strata from which they are drawn;
(2) one should make sure that the children attending school do not represent a 'selected' segment of the population;
(3) in the above case other possibilities such as co-operation with the immunization services, should be explored so as to obtain a good representation; and
(4) the school-starting age could vary from country to country. A choice should be made of the most appropriate age-group to be studied. Perhaps for operational reasons all children in the school should be examined recording the ages at the same time. The splitting by appropriate age-group could be done at the analysis stage.

(*iv*) *Rapid village surveys*

In this procedure an intensive effort is made to educate the population of the villages on symptoms of leprosy and the efficacy of modern drugs. The team visits the villages after this preparatory phase and with the help of key local personnel, individuals with suspected symptoms are asked to present themselves in a central place for examination. The method is easy to carry out as it does not require house-to-house visits, and the efficiency of the procedure should be estimated by comparing it with the traditional type of survey, at least in a few settings.

Any of the above methods, preferably a combination of them, could provide estimates of prevalence with a degree of precision acceptable for planning purposes.

II. SITUATIONS WHERE IT IS 5 YEARS OR MORE SINCE THE INTRODUCTION OF MDT

In this situation, from the experience obtained so far, it is seen that there is a drastic reduction in the prevalence of registered cases, while the numbers of newly detected cases year by year continues undiminished at least for a number of years. Sometimes, voluntary reporting of hitherto undetected cases is prompted by the knowledge of the possibility of cure with MDT and an upsurge in 'newly detected' cases is seen during the first few years after MDT is introduced. In this situation the epidemiological pattern of the disease such as the proportion of MB cases, proportion of child prevalence and even ratio of registered cases to all cases, can change from year to year and the rapid methods suggested above may not be applicable.

The following procedure is suggested in such situations. It is assumed that because of treatment by MDT there is a drastic reduction in transmission of the disease at least from those treated. The new cases that are reported are presumably drawn: (1) from a pool of hitherto undetected cases coming now, often voluntarily, for treatment; (2) from cases infected prior to MDT but developing manifest disease only now; and (3) cases infected and developing the disease after the introduction of MDT. Data from two typical situations are presented in Table 7 to illustrate the dramatic reduction in prevalence rates

Table 7

Ethiopia[10]

Year	Number of registered cases	New cases
1983	80,927	6,243
1984	70,809	5,306
1985	59,822	5,113
1986	51,983	4,589
1987	40,170	4,753
1988	31,753	4,725
1989	24,399	3,714
1990	15,976	3,606

N. Arcot District, India[11]

Year	Prevalence per 1000
1983	20·38
1987	4·0
1988	1·68
1989	1·27

Yearly survey findings

Year	Case detection rate per 1000
1983	3·56
1984	2·82
1985	2·17
1986	8·2
1987	1·6

after MDT and the relatively slower rate of reduction in the annual new-case detection rate.

Thus in areas where there has been a vigorous implementation of MDT the prevalence over a period of 5 years drops dramatically. From the North Arcot experience it would appear that a good many of the cases that remained undetected (and unregistered) earlier have reported for treatment. Thus the numbers on the registers at the end of 5 years of MDT should be close to the actual number of cases in the community. On making enquiries from the leprosy workers in Tamil Nadu, the missing cases should at the most be 30% of those on the register. Thus the prevalence rate in N. Arcot at the end of 1989 should not be more than 1·7 per thousand—information that should be adequate for future planning of the leprosy programme.

In Ethiopia it has always been assumed that the registered cases as at 1985 represented half the number of true cases. In 1985 there were 59,822 cases on the register and this has been reduced to 15,976 cases in 1990. If it is assumed that there is no reduction in the cases *not* on the register in 1985, an upper limit to the caseload in 1990 would be 75,798 or 1·5 per 1000.

Thus in areas with MDT for 5 years or more the cases on register plus a small percentage should provide as good an estimate as any that can be obtained. The small 'correction factor' can usually be provided by the leprosy workers in that area and could well serve as an upper limit. At the expected rate of prevalence any imaginable sample survey could not provide estimates more precise.

III. AREA WITH MDT OF LESS THAN 5 YEARS

For estimation purposes this is perhaps the most difficult situation. The rate of reduction

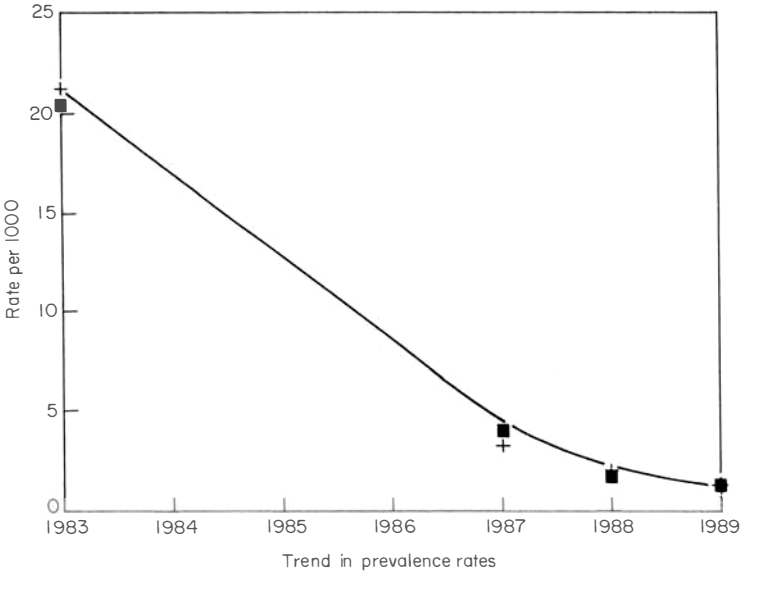

Figure 1. Leprosy prevalence rates per 1000 N. Arcot, India. ■, observed; +, expected.

Table 8

No. of years after MDT	Prevalence as a % of prevalence before MDT
0	100
1	62
2	39
3	24

in prevalence is rapid and steep. The rate of reduction would be substantial even during the period of a sample survey so that the result of the survey would no longer represent a 'point-prevalence'. The epidemiological pattern of the disease changes drastically from year to year. For example, because of the longer duration of treatment for MB cases the proportion of such cases still on the registers would appear to be increasing. Thus the rapid methods suggested above may not be satisfactory. On the other hand one can draw from the experience from areas where MDT has been introduced for more than 5 years. Figure 1 shows the exponential regression curve fitted to the available data from N. Arcot in India. Interpolating from this curve the trend in the prevalence rates would seem to be as in Table 8.

Experience with MDT is fast growing in many areas of the world. The above type of statistical analysis based on larger databases and in different country situations could improve the accuracy of the interpolations.

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Summary of 'Estimation of the leprosy problem through health services data'

K JESUDASAN

When estimating the leprosy problem in countries and areas, often the only available data are gathered as part of routine health service data collection.

Reviews of country situations in the Western Pacific Region of the World Health Organization indicate that in spite of some drawbacks, routine health service data provide very useful information on the epidemiology of leprosy and can also be used to plan leprosy elimination programmes.

Estimation of the leprosy problem in countries is usually the basis for the following:

1 understanding the epidemiology of leprosy;
2 evaluation of the impact of leprosy control measures;
3 estimation of the problems of disability;
4 measuring the effectiveness of MDT on leprosy control, and
5 planning intervention for leprosy elimination.

Epidemiological data collected

Initially, the data for the calculation of the prevalence and incidence rates are collected. These rates by population units such as provinces or subdistricts are worked out to obtain a geographical profile of the leprosy situation.

Additional data on the age, sex, type, disability rates and contact factors provide information on the current status of the leprosy problem. It would be expected that in a high endemic area the prevalence and incidence would be high, the age group with leprosy would be younger with a predominance of PB cases and low deformity rate. However, much would depend on the effectiveness of case finding.

Analyses of secular trends over a period of time provide invaluable data on changes in the epidemiological situation of leprosy. Consistent changes validate observations made at different times.

Operational information

Then data on the operational aspects of leprosy control are collected. This includes information on the organizational structure of leprosy control, whether vertical, semivertical or integrated; case detection activities; health education; treatment and

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surveillance including relapses on monotherapy and MDT; bacteriological enumeration; hospitalization facilities; rehabilitation; training inputs; monitoring and supervision.

Analysis of operational information provides information on programme function.

This information provides valuable clues to the estimation of the leprosy problem through data routinely available in most countries and provides programme managers with a rapid assessment. This has been demonstrated by experience gained in India, the Philippines, Papua New Guinea, Fiji, Western Samoa, Tonga, the Cook Islands and also Vanuatu.

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The epidemiology of disability in leprosy including risk factors

W C S SMITH

Introduction

It is disability which sets leprosy apart from other diseases,[1] and a control programme cannot be successful if it fails to control disability. Disability is a very relevant measurement of progress in leprosy control.[2] To the lay person leprosy means deformity[3] and leprosy without disability is often not recognized as leprosy by the general public, even in the untreated lepromatous stage. It is quite clear that disability is an important measure in the evaluation of control—however, to be able to use this fact, it is necessary to be able to define disability, and correctly measure it, and to understand its determinants and distribution. In particular, it is important to understand the evolutionary process of disability in individuals and populations in order to estimate the impact of various interventions on disability in leprosy.

Definition and measurement of disability

It is rare to find in the leprosy literature a definition of disability other than the alteration of function as opposed to deformity which is defined as the alteration of shape. Most of the disability literature in leprosy lists items rather than considers definitions and these lists include deformity as well as disability, and changes in anatomy and physiological function.

An International Classifications of Impairment, Disability and Handicap (ICIDH) has been developed[4] in parallel to the development of the use of the term disability in the leprosy world. This classification introduces concepts of disability related to rehabilitation in contrast to the strictly descriptive definition used in leprosy. The International Classification uses the following definitions:

a. Impairment—'Any loss or abnormality of psychological, physiological, or anatomical structure or function'—WHO, 1980;
b. Disability—'Any restriction or lack (resulting from an impairment) of ability to perform an activity in the manner as within the range considered normal for a human being'—WHO, 1980;
c. Handicap—'A disadvantage for a given individual resulting from an impairment or disability, that limits or prevents fulfilment of a role that is normal, depending on age, sex, and social and cultural factors for the individual'—WHO, 1980.

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It can be seen from these definitions that what leprologists call disabilities are probably regarded by the ICIDH definition as impairments.

Thus the whole system of approach to disability terminology in leprosy differs from that now recommended by the World Health Organization. The approach used in leprosy is suitable for measurement and description of disabilities, and for epidemiological purposes, however, it fails to incorporate the concepts of rehabilitation, which is a major deficiency. Thus a weakness in a muscle group may be seen as a disability to be corrected surgically rather than developing an understanding of what this functional loss means to that individual patient, if anything at all.

A number of scales of disability assessment have been developed[5–7] and it is clear that none are considered adequate by all as new modifications are developed.[8] It may be considered that no system is ideal when so many have been developed or, perhaps, that different scales are developed for different purposes. There are two major purposes for measurement of disability and each require different tools. The first is the simple grading of the level of disability—this can be carried out quickly in the field and gives a rough assessment of disability. The second is a measurement tool which is sensitive enough to measure change in disability. The first tool cannot do this but if the first purpose is the one required then the more detailed assessment is unnecessary. The exact measurement tool used for the assessment of change depends on what changes the observer wants to examine. However, there is still the need for a standard measure which can be used to compare disabilities between places and over time. The use of a variety of measurement tools makes it difficult to compare the experience in different programmes.

A very different approach to surveying disability is taken by the ICIDH system from that generally used in the field of leprosy. The survey begins with questions to the individual about function ability to see if that person has a disability. When a disability is identified in this way then further investigation is carried out to identify which impairment gives rise to the disability and whether the disability constitutes a handicap. This is an interesting approach which would identify the disabilities that are important to the patient rather than those which are important to the health worker. This approach certainly merits consideration by leprologists.

Epidemiology of disability (impairment) in leprosy

The well-recognized risk factors for disability in leprosy are listed in Table 1. In common with most disease processes, disability in leprosy increases with age. (See Figure 1, based on a data set from India.[2]) This observation is well known and well documented,[9,10] as is the fact that disability rates are higher in men than in women.

Classification of leprosy is also related to the frequency of disability, being highest towards the lepromatous end of the spectrum (Figure 2). This is not a surprising observation given the pathogenesis of the disease. The age effect, however, is independent of the type of leprosy. Duration of disease is also noted to be a risk factor.[10]

The treatment of leprosy is related to disability in many studies, which show that those who are receiving treatment are more likely to be disabled than those who are not receiving treatment.[10,11] Two explanations have been proposed, first that those disabled are more easily detected and more likely to be motivated to take treatment; and secondly that treatment may cause disability. This later controversial explanation has been

Table 1. Risk factors for disability in leprosy

1	Age
2	Sex
3	Classification
4	Duration of disease
5	Site of skin lesions
6	Reversal reactions
7	Treatment
8	Socioeconomic factors
9	Educational attainment
10	Geographical factors
11	Ethnic group
12	Occupation
13	Method of case detection

Figure 1. Percentage with impairment.

proposed during the monotherapy era and there is evidence that nerve damage occurs during MDT,[12] but whether this is more frequent than during monotherapy or when untreated is not known (Figure 3).

Poor socioeconomic status and low educational attainment have both been identified as disability risk factors,[10,11] but whether this is cause or effect is unclear, and may in individual patients be either or both. Occupation has also been identified as a risk factor, and this is not unexpected where those with heavy manual jobs or with occupations which

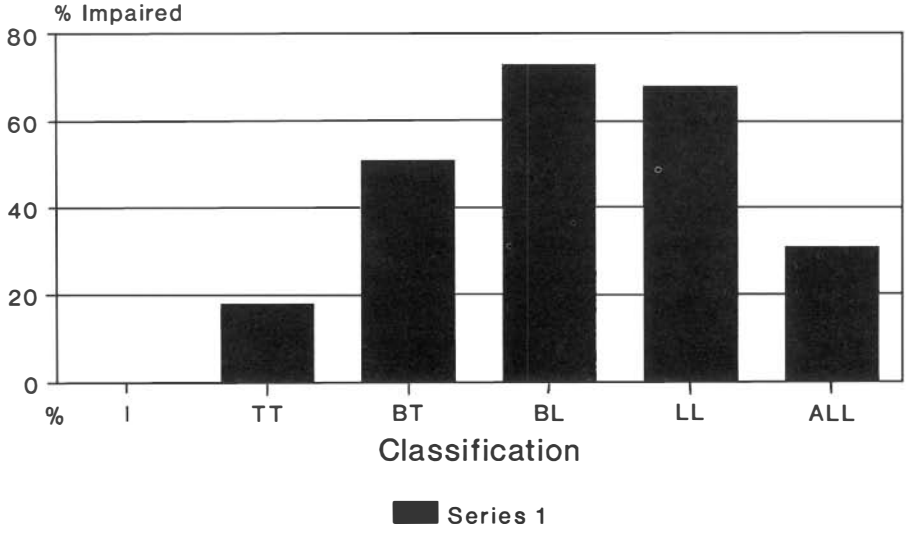


Figure 2. Impairment by classification.

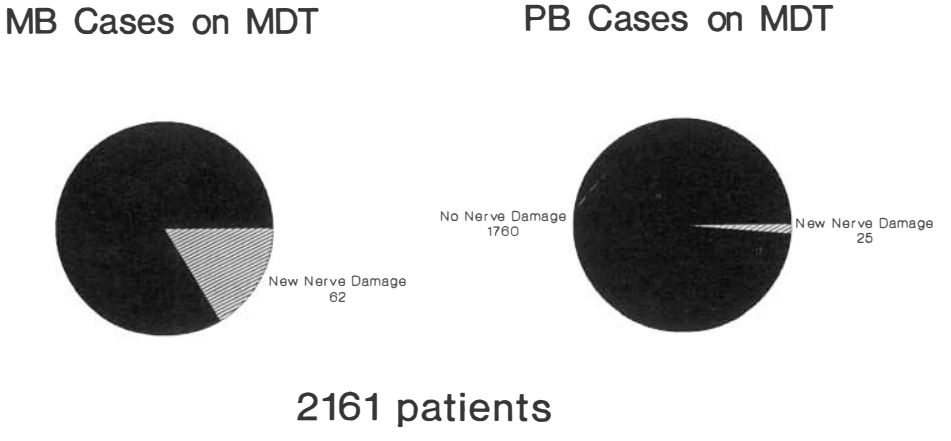


Figure 3. New nerve damage during MDT.

involve walking for long distances are more susceptible to secondary disabilities. Ethnic group and geography have both been noted as important in disability rates within individual countries, but lack of standardization of methods is often a problem in interpreting studies between countries. Factors such as different distribution of classification may confound geographical differences in disability.

Different disability rates are noted by method of case detection (Figure 4) where voluntary reporting shows the highest rates.[2]

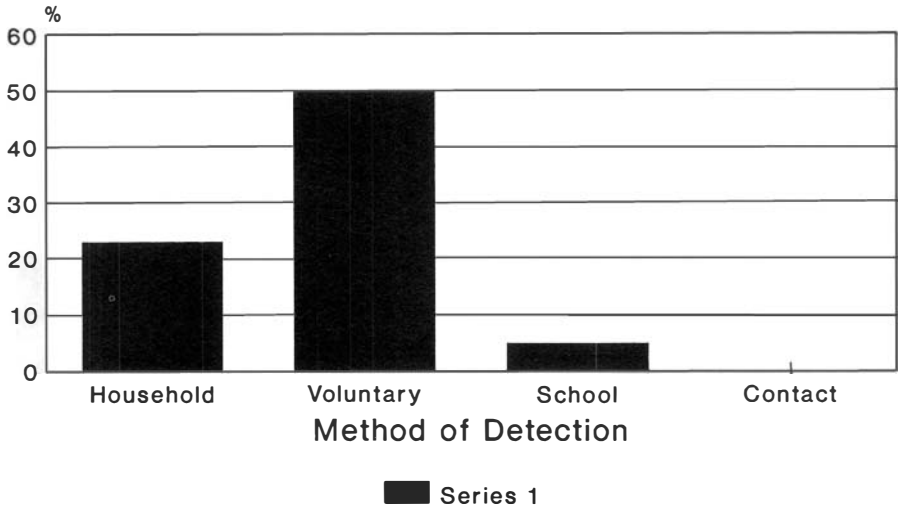


Figure 4. Impairment rates.

Trends in impairment rates

The trends in impairment rates are important in evaluation of leprosy control programmes and a number of important points need to be emphasized. Firstly, as control programmes develop the impairment rates in newly-detected patients (Figure 5) decline.[13] This would happen even if the treatment programme had no effect on disability and it is a mistake to attribute the effect to the programme without using a control group. This is because disabled patients are more easily detected and as programmes develop most new patients added are diagnosed earlier.

A second important point to note is that those with impairment naturally tend to deteriorate (Figure 6). The rate of deterioration varies by classification.

The current practice of deleting from treatment registers and releasing from control patients with impairment disguises the problem of disability in leprosy in a community, and this is especially true with the use of MDT. Figure 7, again based on data from India, shows the rapid decline in registered cases after the introduction of MDT but no similar decline in the prevalence of patients with impairment.[13, 14]

Prevention of disability

This is an important element of control programmes which has recently been studied,[15] where attention was focused on the leprologists' approach to disability. The ICIDH classification would suggest a broader approach to disability prevention at three levels: (1) prevention of impairment by early detection and treatment of disease and of acute nerve damage; (2) limitation or reversal of disability due to impairment using aids, appliances, surgery and patient education; (3) prevention of the transition from disability to handicap by public education, social and cultural adaptation and vocational training.

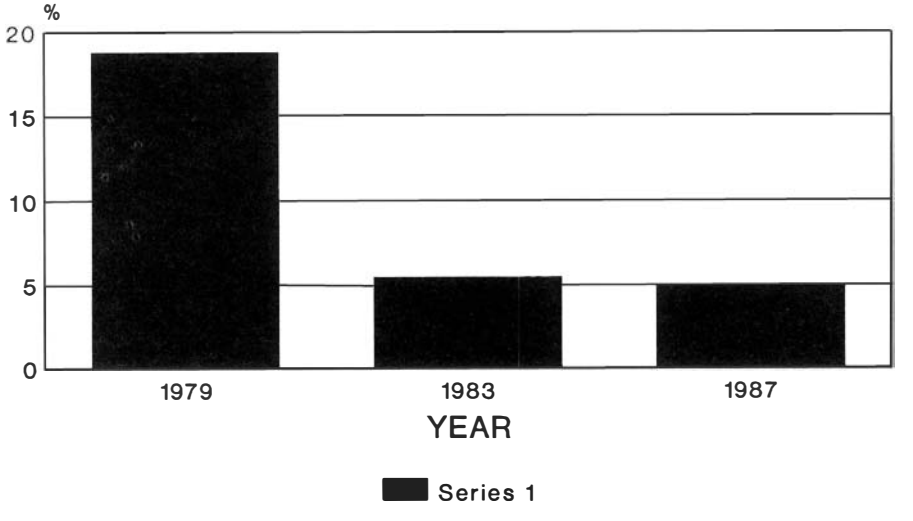
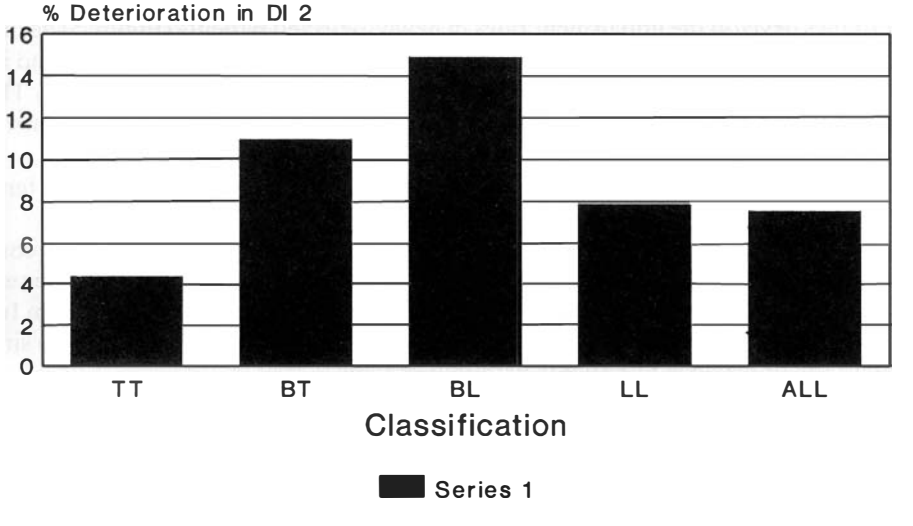


Figure 5. Impairment in new patients.



19 improved, 28 Deteriorated

Figure 6. Deterioration in impairment (118 patients followed over 4 years).

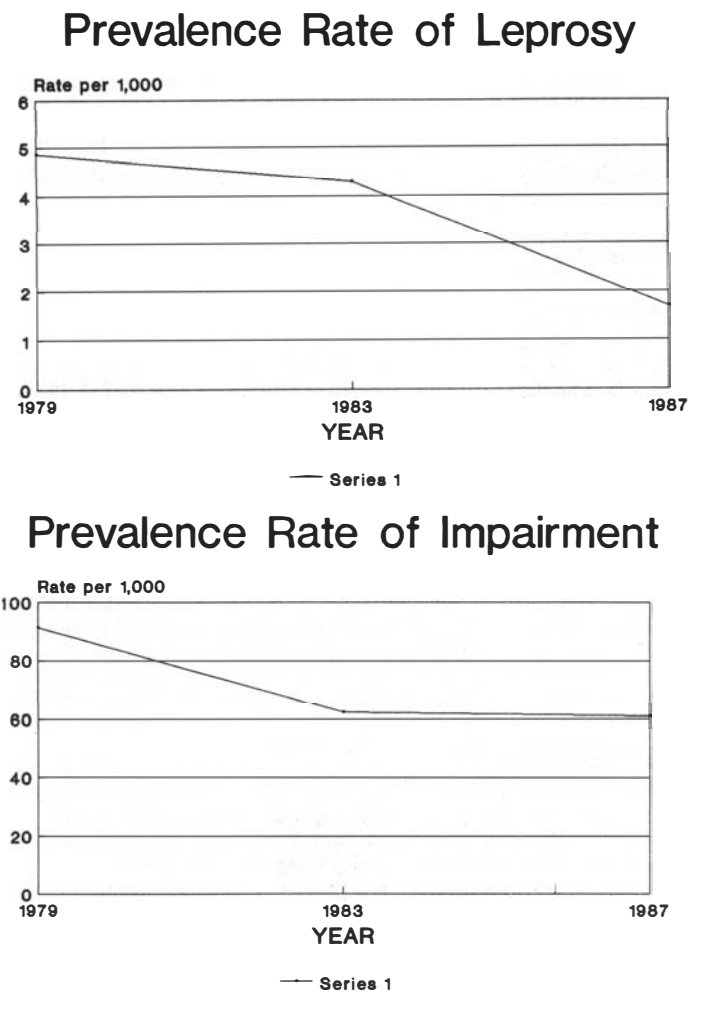


Figure 7. Prevalence changes—leprosy and impairment.

Important research questions are now being addressed as to the effectiveness of different methods of disability prevention and in particular to their cost-effectiveness. Studies are currently under way to look at these issues but it is important that analysis of these studies take account of the natural trends in disability and that proper controlled studies are designed.

Conclusions

Disability in leprosy is extremely important because to the patient and the public it is the disability that sets the leprosy patient apart. Standardized methods of measurement of

disability still need to be developed and the approach adopted by the new International Classification of Impairments, Disability and Handicaps needs to be given consideration by those in the leprosy field. Measures of disability are important for evaluation of programmes, evaluation of treatments, to identify needs for patient education and for rehabilitation. Approaches to disability prevention need to be evaluated in terms of cost-effectiveness which take into account the natural progression of disability and must be based on controlled trials. Disability is the measure of progress in leprosy control which is relevant to the general public.

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Epidemiometric modelling in leprosy based on Indian data

M F LECHAT

Introduction

Today, I suppose, any moderately bright child who has had a minimal exposure to computers could programme an epidemiometric model on a rainy Sunday afternoon using existing softwares and a technologically basic machine, but the situation was quite different in the early 1970s when the leprosy epidemiometric model was first designed.

The problem addressed was clearly circumscribed. After 20 years of large scale, mass control campaigns based on dapsone monotherapy, leprosy had not been eradicated, and even worse, it was not known whether the disease was or was not on the decrease. International funding agencies such as UNICEF, nongovernmental organizations, as well as governments, all were getting tired of emphatic promises and overdue delays. There were talks of a vaccine which could revolutionize the control strategy.

The concerns at that time were: (1) was it reasonable to expect a decline of the leprosy problem in the next 20 years, using current control methods? How much of a decline? How long would this take? (2) Could some improvements in the implementation of control, such as earlier detection or better compliance, speed up the decline? (3) Could some radical changes in the strategy, such as old-fashioned isolation or futuristic vaccination, modify the prediction? In what direction, and by how much?

The model aimed at predicting the trends in incidence over 20 years by using the control methods of that day. It also attempted to simulate the trends which resulted from changes in the control parameters. The indicator used was incidence, i.e. the number of new cases per year in the population.

Structure

As a first step, the development of the model required the definition of a structure and the identification of the various population subgroups (stages) as well as the permitted transitions and their directions (Figure 1). The stages were:

healthy susceptible;
latent;
multibacillary patients, nontreated, treated for less than 1 year, treated for 1 year or more, dropped from treatment, discharged;
paucibacillary patients, with the same categorization as the multibacillary patients.

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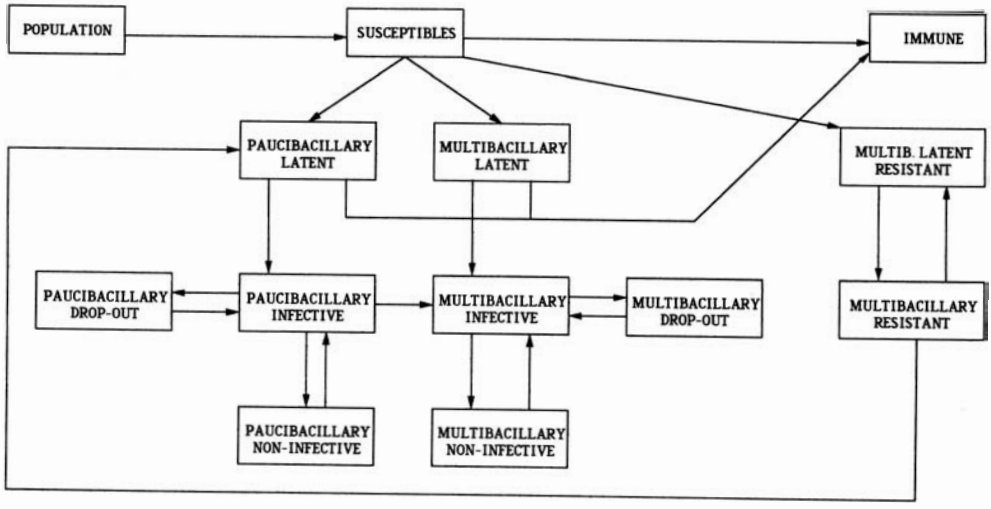

Figure 1. Model structure. Reproducted by kind permission of the *Bulletin de l'Organisation mondiale de la Santé*.[2]

For the sake of keeping it simple, the structure of the model is based on a number of epidemiological assumptions, such as no discharge without treatment, no reversal reaction, no extra-human reservoir, a constant age distribution of the population, and no migration out of or into the area.

The model is macroscopic and deterministic. It is macroscopic since it intends to describe the evolution of incidence and prevalence of the disease in the entire population, or in subpopulations, rather than in foci or at the individual level. It is deterministic because it only considers the prevalences and incidences as averages, and does not take their variability into account.

Estimation of parameters

The equation of the model was based on actual data. We were quite fortunate to have access to the files that had been assembled for nearly 16 years (1955–70) at the Leprosy Centre, Polambakkam, South India. They were allocated first by Dr F Hemerijckx, then by Dr C Vellut and their respective staffs, on 35,262 patients, representing 320,000 person-years of observation. These data had distinct characteristics.

1 They were population based, i.e. the whole population of 500 villages in a circumscribed area was regularly surveyed during the period.
2 No individuals from outside the area were included.
3 Detection was carried out in a standard way by personnel trained in the same manner over the whole period.
4 Treatment remained unchanged, based on dapsone monotherapy at a weekly dose.

It is possible that some occasional divergences from this ideal pattern occurred during the period. The consensus was that such divergences, which could not be controlled a

posteriori, were minimal. Data validation for various types of internal inconsistencies caused the rejection of less than 0·5%.

There were 28 parameters calculated from the observed data or estimated by a statistical approach. Those parameters calculated from observations were the annual population in each stage, the transition rates, the birth and death rates, and the respective proportion of multi- and paucibacillary patients.

To represent the transition from one stage to the next, 2 types of equation were used.

Equations of the first type were based on a negative exponential probability function of staying in the initial stage. They were in the form of a negative exponential. They were used to calculate the transitions from undetected cases to detected, treated to drop-out, drop-out to retreated. The second type included conditional probabilities of transition from 1 stage to another but no special function of duration in the initial stage was used.

A negative exponential function was also used to model the delay at detection. It was set up in such a way that 75% of the new patients could be detected after 1 year from the onset of the disease. To the best of the knowledge of the field staff this estimation was reasonable.

Two major parameters could not have been directly derived from actual observations and had to be estimated by a least-square method. They were (1) the latency period between infection and onset of disease for both multibacillary and paucibacillary patients, and (2) the specific infective power of these 2 patient types. The latency period was estimated to be shorter for multibacillary than for paucibacillary patients (respectively 2·4 and 4·0 years). These values are in clear contradiction to the periods calculated from a few actual observations in Louisiana and among US War Veterans. Estimation of the infective capacity by considering the type of leprosy yielded more consistent estimates. The risk of a person developing leprosy through contact with a multibacillary case is higher than through contact with a paucibacillary one. This agrees with the epidemiological studies of Doull.[1] However, due to the high proportion of paucibacillary patients among the diseased population, those patients constitute a nonnegligible source of infection.

Simulations

A number of simulations were carried out, either at the initial stage of the model, or later by changing some of the basic epidemiological assumptions.

Incidence depending on multibacillary or paucibacillary types of leprosy was predicted over a period of 20 years with ongoing control methods. The results indicated that with dapsone monotherapy a reduction of 50% incidence could be expected after 12 years (Figure 2). We believe this conclusion was important as it showed that control of leprosy requires perseverance, firm financial commitments, and unyielding efforts. Eradication cannot be achieved overnight.

Earlier detection, resulting in an increase to 90% from 75% of the annual input of new patients detected within 1 year of onset (assuming a negative exponential detection rate over time) does not significantly change the incidence in the long run (Figure 3). Intensifying case detection, a costly and fastidious method, had been repeatedly advocated as one of the more efficient ways to improve control. Long-term incidence is slightly more sensitive to the rate of compliance to treatment. After decreasing by 50% the

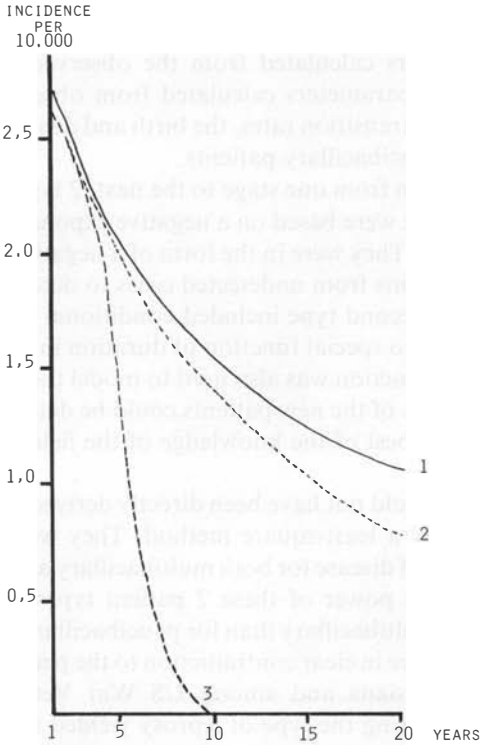

Figure 2. The incidence of 20 years:

(1) present control methods;
(2) reduction to 50% drop out; and
(3) vaccination of 100% of the population with immunoprophylactic vaccine.

annual proportion of patients who abandon treatment, incidence is reduced by 50% after 20 years (Figure 2). A cost-benefit analysis has shown that the latter method is much more advantageous than increased efforts to achieve earlier detection.

The effects of isolation were also simulated. This confirmed the largely held belief that the isolation method is futile in reducing long-term incidence (Figure 3).

The initial simulations suggested that vaccination was by far the most promising method (Figure 2). This conclusion is one of the major drawbacks of the exercise. It could have encouraged investing resources in a long-term research programme on the basis of a much too simplified model. Subsequent simulations draw a distinction between a prophylactic and a therapeutic vaccine and show that the effect of a vaccine preventing infection is delayed for several years. In the long run it is quite effective though slow for decreasing incidence (Figures 4 and 5). On the other hand, a vaccine active in preventing the appearance of leprosy in those individuals already infected has an immediate effect. It must be repeated at periodic intervals to catch those recently infected, which reduces its long-term effectiveness. In addition, the respective efficacy of using either one of these types of vaccines depends on the prevalence of infection in the population.

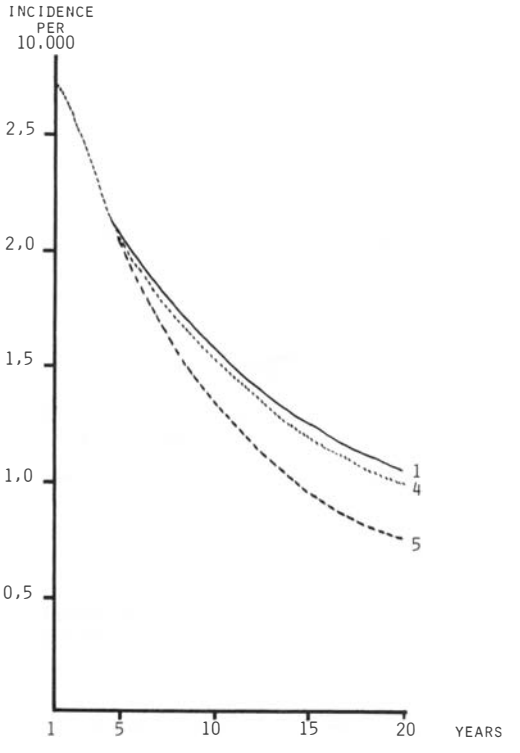

Figure 3. The incidence of 20 years:

(1) present control methods;
(4) 90% detection within one year of onset; and
(5) isolation of multibacillary cases at detection.

Simulation of various treatment regimens—dapsone monotherapy for all patients, multiple drug therapy (MDT) for all patients, MDT for multibacillary cases and dapsone therapy for the paucibacillary ones—showed that because of the ratio of multi- to paucibacillary patients which prevails in South India (about 13% of multibacillary cases), MDT treatment for all patients, including paucibacillary, is imperative (Figure 6). Restricting MDT to the multibacillary patients is of little or no avail (for the paucibacillary patients, in spite of their low infectivity, constitute a significant source of infection because of their large numbers). This introduces the paradox that if MDT is restricted to only one type of leprosy, in this model it is most effective when only applied to paucibacillary patients.

An obvious conclusion is that it would be incorrect to restrict treatment to the paucibacillary patients even when resources are scarce. This demonstrates the paradox of individual risk vs population risk.

Simulation of various *relapse rates* (10–100%) in multibacillary cases with various treatment regimens indicate that relapse with MDT is not a major problem (Figure 7). The declining trend of incidence slows down (with a 20% relapse rate) or is slightly

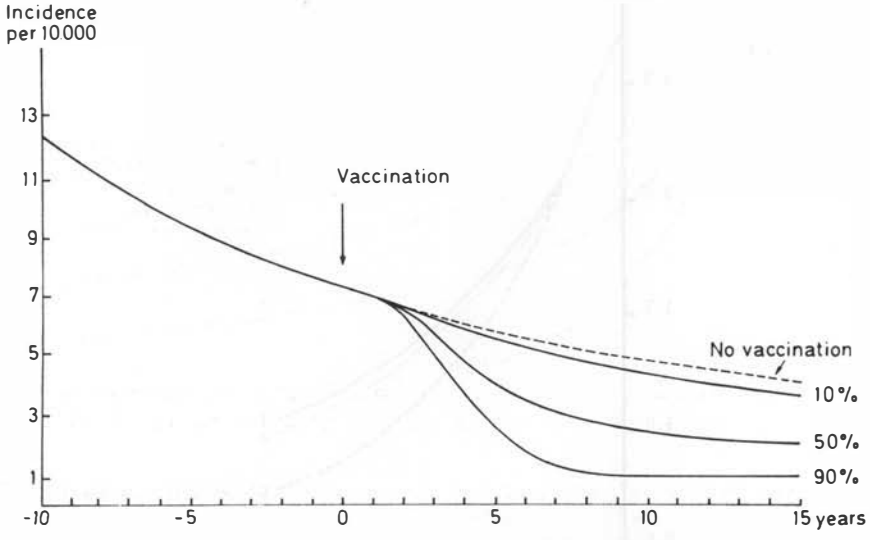

Figure 4. Prediction of incidence for both types of leprosy with an immunoprophylactic vaccine covering 10—50—90% of the population. Reproduced by kind permission of the *International Journal of Leprosy*.[3]

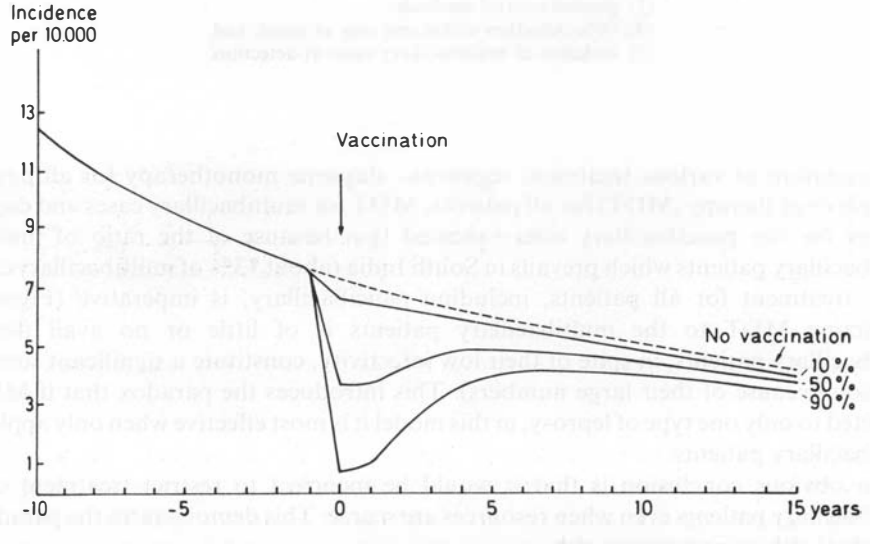

Figure 5. Prediction of incidence for both types of leprosy with an immunotherapeutic vaccine covering 10—50—90% of the population. Reproduced by kind permission of the *International Journal of Leprosy*.[3]

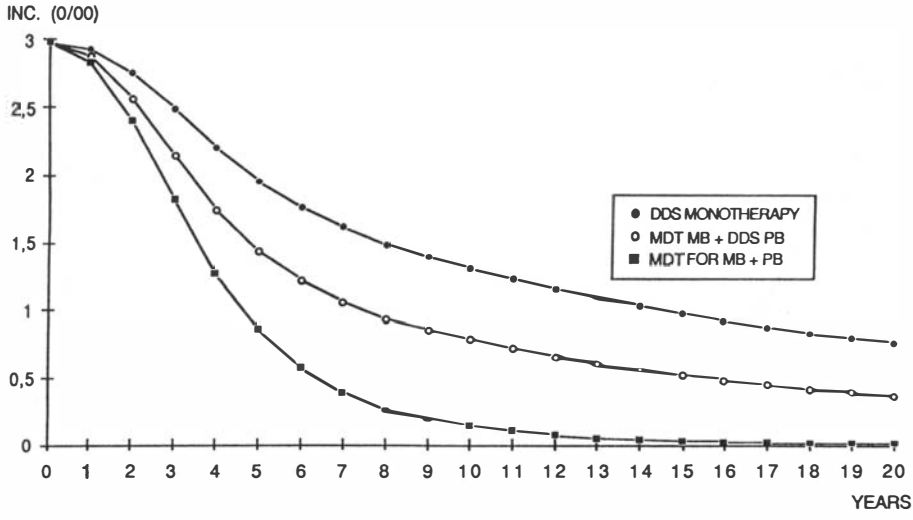

Figure 6. Computer simulation of incidence of leprosy with three different therapeutic regimens. Reproduced by kind permission of the *International Journal of Leprosy*.[4]

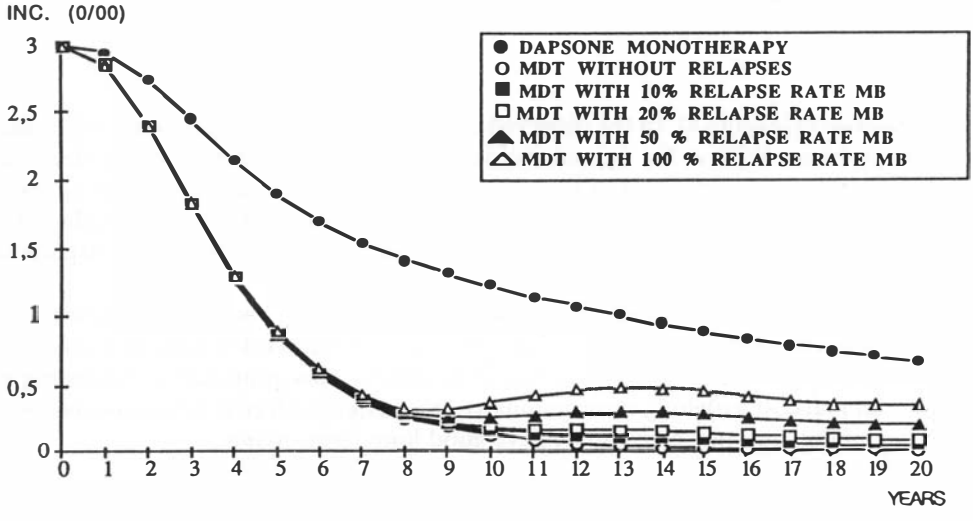

Figure 7. Computer simulation of incidence with dapsone and MDT with different relapse rates.

reversed for a period (with a 50–100% relapse rate) only after 8 years. These results are important in view of a popular claim that multibacillary patients under MDT should continue treatment after 2 years even when they become bacillary negative. Some say they should even be treated for life. As for control, relapses are not significant as long as they are detected early; in other terms, all treatment requires a close surveillance system.

Simulation of resistance required the introduction of new compartments in the model and an extension of 50 years (which probably has little justification due to the long-term

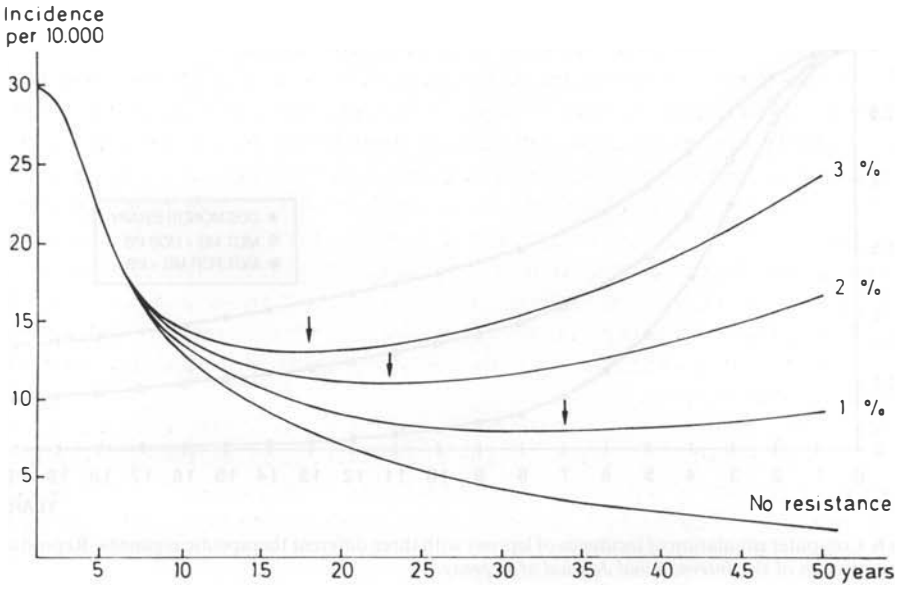

Figure 8. Prediction of incidence for both types of leprosy with 1—2—3% secondary drug resistance. Reproduced by kind permission of the *International Journal of Leprosy*.[3]

unpredictability) (Figure 8). In the observed conditions, secondary resistance constitutes a major problem. With a 3% annual incidence of secondary resistance, the declining trends in incidence slow down after 6 or 7 years and then begin rising at increasing speed after 15 years. These results are more forboding because no provision was made in the very simplified model for the contribution of subsequent cases with primary resistance to incidence in subsequent years.

Cost-benefit analysis can also be simulated by introducing various cost-parameters. Such econometric analysis should be subject to caution, for it is often difficult to calculate the various components of different control strategies. This approach is interesting to compare annual cost with long-term cumulative cost. Highly effective strategies are costly at the beginning, but may prove to achieve good long-term saving.

Conclusion

Overall, we must consider the possible uses and drawbacks of the model. It was developed in a specific area, South India, which presents its own special epidemiological contexts. Therefore it has clear limitations.

The resulting figures should be viewed with caution. The results are highly sensitive to a number of parameters, either directly observed or derived through statistical estimation. The model is based on a number of assumptions, not all verifiable and possibly too simplified. The quantitative results should not be generalized for use in other areas which might have different conditions of prevalence, incidence, multi/paucibacillary ratios,

birth and death rates. It is not certain that epidemiological data with an equal value to those collected in South India could be found in many places.

The model serves its own purpose and might not be best used when repeating the exercise exactly in different places. It acts as a type of grammar or structure. The model helps to clarify epidemiological concepts as exemplified by the existing differences between immunoprophylactic and immunotherapeutic vaccines or the epidemiological similarity of noncompliance and treatment-sensitive relapse albeit on different time scales. The model's most important purpose is to list the problems it tackles in the order of importance and make various comparisons. It could consider whether every patient should receive MDT, or only multibacillary patients; it could compare the relative insensitivity of incidence to early detection (despite the complete and early detection in the study area); or it could stress the importance of resistance in the long term as compared to nondrug resistant relapses.

Due to the present success of MDT-based control, this modelling approach in leprosy is no longer a part of basic research. The future belongs to microscale modelling for disappearing diseases. What can be expected in terms of limited foci, clusters, and erratic time fluctuations? This could be called, to use a fashionable new avenue of research, fractal epidemiology.

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Epidemiological modelling for tropical disease control

J H F REMME

Introduction

The epidemiology of tropical diseases depends on the dynamic interaction of a multitude of biological, ecological, demographic and behavioural factors and processes, many of which cannot be measured directly. This makes it difficult to arrive at a comprehensive quantitative understanding of the epidemiology and control of tropical diseases without the aid of special epidemiometric tools. Epidemiological modelling can be helpful in this respect by providing a framework for the quantitative description of the dynamics of transmission, infection, disease and the impact of control.

Advances in model development and application have been modest for most tropical diseases and the practical value of models has often been questioned. In this paper I will briefly review a few examples of modelling in tropical diseases, with special reference to the case of onchocerciasis, and then identify what I consider to be the potential advantages and disadvantages of epidemiological modelling for tropical disease control. I will try to argue that epidemiological modelling can have great operational value if a number of conditions are met.

Previous modelling in tropical diseases

A good epidemiologial model is a simplication of reality which is nevertheless elaborate enough to give a realistic description of the main processes under study. The difficulty in epidemiological modelling is to strike a proper balance between simplification and realism. In the early days of modelling the emphasis was on simplification, but more recently the balance has started to swing back in favour of realism.

The first generation of models aimed at giving a simple and elegant description of the transmission and natural history of disease. These models were purely mathematical models which had to be simple to keep them mathematically tractable. However, their application involved the study of very complex issues such as the definition of breakpoint levels for the prevalence of infection or the vector density below which transmission cannot maintain itself and the infection will die out naturally.[1] The often bitter experiences of eradication programmes and the results of detailed analysis of epidemiological data has shown that these early models were just too simple for these types of application. The subsequent generations of mathematical models have tried to explain

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why this was so by demonstrating the importance for transmission of such factors as density dependent regulation, heterogeneity in exposure and susceptibility to infection, and nonuniform impact of interventions.[2,3] These mathematical models have been quite useful by clarifying concepts and improving the understanding of the transmission process.

The computer revolution has allowed a recent shift from purely mathematical models to computer simulation models which are less restricted by mathematical limitations and can better fulfil the requirement for realism. As a result, modelling has become more accepted among public health specialists and there are now several examples of the successful application of epidemiological simulation models for the prediction of epidemiological trends and for the planning and evaluation of tropical disease control programmes.

THE EXAMPLE OF MALARIA

The first model for malaria was a simple mathematical model developed during the first decade of this century by Sir Ronald Ross and highlighted the role of the vector in the transmission process. It indicated that not all vectors needed to be eliminated to ensure the interruption of transmission but that it was sufficient to reduce the vector density below a certain breakpoint level. Following this early start, further modelling development was slow and had to await the work of MacDonald in the 1950s and the major attempt of modelling malaria transmission as part of the WHO research project on the epidemiology and control of malaria in the Sudan savanna in West Africa, the so-called Garki project. The Garki model, in which the concept of immunity had been introduced, was quantified and tested using the parasitological and entomological data from the Garki project and proved to be a major improvement compared to previous malaria models.[4] Its major drawback was that it was only a transmission model and did not address the question of morbidity and its control. In a review of their work, the investigators concluded that the Garki model has had important educational value even though it has not been used directly for planning of control.[5]

THE EXAMPLE OF LEPROSY

Modelling has played an important role in leprosy research because of the work by Lechat, who developed an epidemiometric model which used computer simulation.[6,7] The emphasis in this work was on the relative comparison of alternative control options by simulating their long-term impact, and it has helped considerably to clarify the thinking about leprosy control. Further information about this model and its application are given in another article in this volume.[8]

THE EXAMPLE OF LYMPHATIC FILARIASIS

Since the 1960s, so-called catalytic models have been used extensively in the analysis of age-specific data on microfilaraemia. This work has resulted in estimates of the duration of microfilaraemia and of the force of infection. Comparison of the estimated force of infection and entomological data highlighted the inefficiency of transmission in lymphatic

filariasis and indicated that only a very small proportion of inoculated larvae managed to develop into adult worms. Catalytic models have also been used to support alternative hypotheses on the natural history of disease which challenge the generally accepted theory and the role of immunological factors.[22]

Recently a new TDR initiative was launched for the accelerated development of epidemiological modelling in lymphatic filariasis for the purpose of steering research and to help the design of more effective control strategies.[9] This initiative was partly a result of the success with epidemiological modelling for another filarial disease, onchocerciasis.

THE EXAMPLE OF ONCHOCERCIASIS

The Onchocerciasis Control Programme in West Africa (OCP), which is one of the largest tropical disease control programmes in the world, started its operations in 1975. The strategy of the Programme was to interrupt transmission by vector control for a period of 20 years, a period which was supposed to exceed the lifespan of the parasite even though the actual lifespan was not known. Epidemiological modelling was not used in the planning phase of the project and only after several years of control did it become obvious that there was a definite role for modelling in the OCP. After 8 years of control there was great uncertainty about the epidemiological impact of the control operations. The entomological evaluation results suggested that transmission had been interrupted but the epidemiological evaluation showed only a little decline in the prevalence of infection. This uncertainty about the impact of control, together with the lack of reliable predictions of future epidemiological trends and funding requirements, caused considerable nervousness in the donor community and it became urgent to resolve this issue. As a first step a simple force-of-infection model was developed to help interpret the extensive epidemiological data collected.[10] With the new analytical approach it could be concluded from the epidemiological data that vector control had been successful in interrupting transmission in 90% of the OCP area and that the parasite reservoir was dying out rapidly. A first estimate of the average lifespan was arrived at and it was concluded that the required period of vector control was considerably less than 20 years. Subsequently, a more sophisticated computer simulation model was developed for the detailed prediction of future epidemiological trends under vector control and of the remaining vector control period required. The predictions of this model have been useful in securing funds for the third financial phase of the OCP[11] and 5 years later it could be shown that the predictions were correct.[12,13]

In 1987 there was another development which prompted further epidemiological modelling. A new drug, Ivermectin, had successfully passed the clinical trials and become available for the treatment of onchocerciasis. Ivermectin is a microfilaricide which does not affect the adult worm but only kills its offspring, the microfilariae. This development required a review of the control strategy and a decision whether the future control strategy should be based on chemotherapy, vector control or a combination of the two. To help resolve this question, ONCHOSIM, a sophisticated computer simulation model for the transmission and control of onchocerciasis, was developed.[14] This model has been used extensively in the OCP, not only for the comparison of the alternative control strategies but as a powerful epidemiological tool in day-to-day operational planning and evaluation of onchocerciasis control.

Advantages and disadvantages of epidemiological modelling

Based on the rather unique experience with the operational application of modelling in the OCP I have listed below what I consider to be the potential advantages and disadvantages of epidemiological modelling for tropical disease control.

ADVANTAGES

Comprehensive quantitative approach to epidemiology and control

Because of the complexity of tropical diseases, epidemiological research is often designed to study a well-defined part of the overall problem in order to keep the study manageable and to obtain clear and unambiguous results. The disadvantage of this approach is that epidemiological research tends to be fragmented and not directly designed to address questions of control. Modelling forces a comprehensive approach to the main factors which determine the epidemiology and control of a disease, and to their interaction, and facilitates epidemiological reasoning focused on disease control.

Integrated analysis and synthesis of knowledge and information

It is often believed that modelling can only be meaningful for diseases for which the natural history is fully understood and can be quantified in detail. However, this belief is completely mistaken and the lack of quantitative information on important factors in the transmission and disease process may actually be a good reason for embarking on modelling. Different sets of information can, when analysed integrally using an epidemiological model, provide an estimate for important parameters which can otherwise not be quantified. An example in the OCP was the integrated analysis of the results of routine epidemiological evaluation data on infection levels, results on the viability of adult worms removed surgically from patients in a few selected villages, and entomological information on transmission levels. This analysis allowed a very satisfactory estimation of the parasite lifespan, an unknown but crucial factor which determines the required duration of the vector control programme.[12,15]

Identification of research priorities and planning of research

During the design and quantification of a model it soon becomes evident what the relative importance is of the different factors which determine the transmission and disease process, and what the most important information is which is lacking and requires (field) research. During the development of ONCHOSIM it became very clear that the relationship between vector infectivity and intensity of infection of the human host was extremely important for the dynamics of infection and special field experiments were undertaken to quantify this relationship. Without the modelling work this relationship would probably never have been studied in such detail. The relationship proved to be particularly important for predicting the impact of Ivermectin based control[16] and it is currently believed that the observed difference in effectiveness of Ivermectin treatment for transmission control in the West African savanna and in Central America is due to the fact that the above relationship is very different for the vector species from these two

areas. In West Africa, the vector is already highly efficient when the microfilarial loads of the human hosts are still low, such as after Ivermectin treatment, while the Central American vector hardly transmits at low microfilarial loads.

Prospective evaluation of control strategies

Prospective evaluation is usually seen as the most valuable application of modelling. It involves the prediction of the long-term impact of alternative control strategies and the prospective comparison of their (cost-)effectiveness.[17] In some situations it may be sufficient to compare the relative effectiveness of alternative control strategies without requiring great accuracy in the predictions of the epidemiological trends over time. However, such accuracy becomes much more important when issues like long-term planning and cost considerations are considered. The most important OCP example of prospective evaluation was the comparison between the predicted long-term impact of chemotherapy and larviciding. The conclusion was that chemotherapy is useful for morbidity control if it can be sustained over a long period but that only larviciding for transmission control can achieve definite control within a time limited period. Vector control is therefore still the basis of the control strategy in the OCP.[13,18]

Appreciation of uncertainty through sensitivity analysis

A problem with detailed epidemiological models is that they involve many parameters which cannot be measured accurately but which do affect the model predictions. However, with modelling the uncertainty due to this can be studied in so-called sensitivity analyses. A practical example in the OCP was the sensitivity analysis of the risk of recrudescence if vector control would be stopped after a given number of years. This risk depends among others on the true biting rate and the variability in the parasite lifespan. The sensitivity analysis showed that the remaining uncertainty about the lifespan variability was not very important but that the risk of recrudescence was highly sensitive to variation in the biting rate, a conclusion which has had practical implications for the design of surveillance strategies.[19,20]

Planning of control and evaluation activities

Modelling can even be valuable for the planning of actual control and evaluation activities by indicating when and where it is most efficient to do what. An example in the OCP is the planning of surveillance activities after cessation of vector control. During the first 2 years this will involve only entomological surveillance for residual transmission at selected high-risk locations (the model was also used to predict which transmission levels would be acceptable and which not) but after 2 years this will be replaced by epidemiological surveillance for incidence of infection.[20]

Prediction of epidemiological trends and funding requirements

As mentioned above the prediction of trends is among the most important applications of epidemiological modelling. It involves the prediction of epidemiological changes during

the control period but also of trends without control for the purpose of comparison and estimation of the benefit of control. These type of predictions are not only important for planning purposes but equally valuable for informing funding agencies and securing long-term funding. An important example in the OCP was the prediction of the trends in infection levels under vector control and the conclusion that 14 years of successful vector control were required.[11,21] This conclusion was accepted by the donor community which made the required long-term funding commitment to the OCP.

Evaluation of impact of control

The predicted trends give a reference for the analysis of evaluation data on the impact of control. In the OCP this is the most common and routine application of modelling. An example is the epidemiological evaluation of the impact of vector control on transmission which was based on the comparison of observed trends in prevalence and intensity of skin microfilariae in the population of 187 indicator villages,[5] which are surveyed at intervals of 3 years, with predicted epidemiological trends assuming complete interruption of transmission.[13]

Continuous review

The operational application of modelling involves continuous review of current epidemiological understanding through continuous testing of model predictions and analysis of evaluation and field research data. This process results in feedback and regular updating of the model to incorporate the new information and in improved understanding of the quantitative aspects of transmission and disease process.

Interdisciplinary communication and collaboration in research and control

Epidemiological modelling can be a great tool for improving communication between scientists of different disciplines involved in the epidemiology and control of tropical diseases. Model development in the OCP has brought together epidemiologists, entomologists, biostatisticians, parasitologists, ophthalmologists, managers, immunologists and behavioural scientists. There have been special multidisciplinary meetings for model development, and there are always extensive sessions during OCP research meetings to discuss simulation results and to review proposed model updates and planned applications.

DISADVANTAGES

Oversimplification

Oversimplification is the classical problem of modelling[23] and, as mentioned before, the difficulty in modelling is to strike a proper balance between simplification and realism. Excessive simplification can be avoided by discussing the model assumptions with specialists in the various disciplines concerned and through detailed testing of the model against field data.

Overdose of mathematics and magic

A classical problem with mathematical models is that an advanced mathematical description of an epidemiological problem is of limited use when attempting to communicate with public health specialists. The potential clients may be scared off by the formulas and not accept the conclusion of a model which they do not understand. This may also be a problem with simulation models, but less so if the model structure can be explained in a clear flow diagram which is epidemiologically meaningful.

Uncritical interpretation

A completely opposite problem occurs when those responsible for disease control operations start believing everything a model predicts. This may happen when some model applications have shown to be successful, as in the OCP example, and disease controllers lose their critical attitude to the model. It is the responsibility of the modeller to highlight the limitations of the model and to stress the need for continuous testing of assumptions and predictions.

Cumbersome

Serious epidemiological modelling involves a lot of work. This is particularly so for computer simulation models which require extensive computer programming, testing, debugging, quantification etc. It also requires specialized skills in mathematics and computer science, and scientists with experience in the application of modelling.

High risk research

It is always possible to make an epidemiological model for a disease, and it is very likely that a serious attempt at modelling will benefit the planning of epidemiological research. However, it is much less certain whether model development and testing will result in a model which is sufficiently valid and reliable to be directly useful for tropical disease control. Much will depend on the availability of epidemiological data on which the model can be tested.

Conclusion

Based on my experiences I would conclude that epidemiological modelling can be very valuable for tropical disease research and control if the following conditions are met. In the first place there should be a clear practical need and interest for epidemiological modelling among those involved in research and control of the disease. Secondly, model development, testing and application should be a truly multidisciplinary effort closely associated with control and field research activities. Thirdly, the structure of the model should be transparent and meaningful for all collaborating scientists. The actual transmission and disease process should therefore be modelled as closely as possible, preferably by computer simulation. Fourthly, it is very important that modelling is seen as a continuing process and that a model evolves continuously through testing, application

in analysis and updating when required. This implies that the initial model design should be flexible enough to allow future updating. Finally, those involved in field research and control should have direct access to the model and know how to use it as a practical epidemiological tool.

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Towards the use of decision sciences in leprosy control

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Introduction

The planning and evaluation of disease control is extremely complicated because of the many factors and uncertainties that are involved in predicting and explaining trends. In leprosy, for example, the impact of control measures on the epidemiological trends is not precisely known. In spite of this, multidrug therapy (MDT) is now the first-choice treatment for leprosy. In countries where MDT is implemented on a large scale, a marked reduction in the prevalence rate has been achieved. It is also noticeable that treatment compliance is improved. These positive effects are mainly attributed to the short duration and low toxicity of MDT.[1] But even when MDT is chosen, there are many ways in which MDT-strategies can be organized. Planning and evaluation tools would be most welcome.

At our Institute we have developed methods and tools for assisting decision making in disease control programmes which are based on epidemiological simulation modelling. Based on our experience in the control of non-communicable diseases, we started analysing tropical disease control problems in a joint project with the Onchocerciasis Control Programme (OCP). In this project simulation models have been developed which are now used routinely by the OCP in the planning and evaluation of river blindness control measures.

In this paper we will first summarize our approach to developing and using decision aids, and then consider the possibility of using this approach in leprosy control.

Guidelines and approach

We suggest, with our experience of over 10 years in epidemiologic modelling, that the following guidelines should be followed in developing model-based decision aids in disease control programmes:

- health outcome should play the central role;
- the models should be based on a rational and medically sound basis;
- resource use, economic and cost-effective calculations should be studied when indicated, but always in relation to the health outcome;
- the primary goal is to support decision making, but a secondary—intimately linked—goal is to increase our knowledge and understanding of the disease and the possibilities for its control;

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- a modelling approach is necessary because many interacting factors play a role in the problems that are to be addressed. High quality data and expert knowledge is necessary in developing a satisfactory model;
- development and application of decision models should be a collaborative enterprise with existing control programmes, involving scientists and health workers from different disciplines.

Control questions that should be addressed by epidemiometric models developed according to the above guidelines include:

- what will be the impact of the current or a proposed control strategy on trends in incidence, prevalence, morbidity and mortality of the disease concerned;
- what are the implications for resource use of executing alternative control strategies;
- can the optimal control strategy for a given amount of resources be indicated;
- what will be the favourable and the adverse effects of a specified control strategy from a public health point of view;
- can our knowledge of the natural history and the epidemiology of the disease be improved, either by careful analysis of available data or by conducting special studies;
- are observed trends during control significantly different from the predictions. And if so, in what way has the control programme to be adapted, if at all?

All the above questions should be answered for the specific situation of the country or area where the control programme is carried out.

A number of conceptual and practical requirements should be satisfied in order to develop models that are able to address such diverse questions. Conceptually, they should have the seemingly contradictory properties of being comprehensive and detailed. They should be appropriate for assessing the effects of different control measures on epidemiological and population health trends. They should also be suitable for detailed data analysis and prediction within a control programme. From an organizational point of view, modelling should be an integral part of the disease control programme. This calls for an approach which is easy to use and which can be adapted to new results and to changes in control policy.

The way in which we have tackled model building has been proven successful for both cancer screening,[2,3] and onchocerciasis control.[4–7]

Epidemiological models for leprosy control

The first step in the development of decision-oriented epidemiological models is the description of all factors and their inter-relations that are important for the control of leprosy. These can be classified as follows:

- epidemiological indicators: incidence and prevalence, both of infections and of disability; other indicators are the age-distribution of the incidence, and the distribution of type of leprosy. Leprosy mortality is very low and directly linked to disability and can usually be deleted;
- natural history of leprosy, e.g. self-healing;
- diagnostic tools: intensive use is made of clinical diagnosis, and of bacteriological, histopathological and immunological diagnosis;
- the type of control: multidrug therapy has a high cure rate and is quite promising. Health education and contact tracing helps to decrease the secondary cases. In addition, BCG vaccination provides a certain degree of protection;

- surveillance (early detection of cases, case surveillance);
- behaviour of patients, e.g. compliance, alertness of symptoms. At the level of the control programme this is expressed as coverage and completion rate;
- effectiveness of therapies. Cure and relapse rates, duration of treatment, impact on transmission.

The way and the detail in which these factors and their inter-relations are taken into account, and the way in which they are embedded in a population–disease–intervention model, determines the possibility of their use for addressing control problems. Lechat[8] has contributed most to leprosy control modelling. We have considerable experience with so-called microsimulation modelling.[2,3,6,7] This implies simulation of individual human life histories. Together, the simulated individuals constitute a community, e.g. a village population. In the onchocerciasis control model ONCHOSIM, the life-histories of parasites in man are also simulated individually. Stochastic microsimulation enables a realistic formulation of the mechanisms of transmission, which is important in predicting the epidemiological trends associated with different policy options. When a validated, decision-oriented model has been developed, the important questions concerning leprosy control can be addressed.

LEPROSY CONTROL: QUESTIONS AT STAKE

Prediction of trends

Decision analytic tools can be used to predict leprosy-related public health trends concerning the prevalence of registered cases, the incidence of new leprosy cases, cases under treatment, RFT cases, relapse rates, and incidence and prevalence of disability. The predictions can be made both for an existing situation and for different (alternative) control options.

Planning of resource requirements

The short- and mid-term predictions of incidence and prevalence may in turn be used to make projections of the necessary resources, especially financial, that are needed for leprosy surveillance and control.

Choice of control strategies

The control methods which give the best public health results when resources are limited can be identified. For example, a detailed investigation of MDT could lead to recommendations to ensure a more efficient use of available resources, by analysing the trade-off between (shorter) duration of MDT-treatment and (more) relapse treatment. On the other hand, the conditions and circumstances that make it possible to attain certain goals (for example, 1 case per 10,000 population with a minum of resource use) can be researched.

An essential aspect of control strategies is the organization of leprosy control programmes, and their integration into the general health services. The different integration strategies, which are country-specific, can be compared in terms of effectiveness and costs.

Explanation of observed trends, and identification of research priorities

Careful analysis of observed trends and results of existing control programmes can be used for monitoring the performance of a programme. This may also contribute to the improvement of our knowledge of the natural history and the transmission of leprosy. In this way, the approach may be used to identify research priorities. A better understanding of leprosy will in turn lead to better possibilities for rational decision making.

SCIENTIFIC REQUIREMENTS

It must be emphasized that a decision analytic approach to control questions does need validated models. Thus, two stages can be distinguished: (1) model development, and (2) model application (see Figure 1).

The development of validated models (stage 1) requires a collaborative effort with leprosy control projects which have longitudinal data. The use of such databases is indispensable. An ideal database comprises complete longitudinal data on diseased and also on healthy persons. It covers a complete and sufficiently large region, for which additional information, e.g. demographic, is available.

The data from such projects should first be used to estimate the parameters of the model, and then to test the joint action of all the factors. For example, models that are to be used for making predictions about trends (stage 2) should be validated by predicting historical trends as observed in the control projects. In practice, the initially validated model will be upgraded whenever new knowledge or relevant data become available.

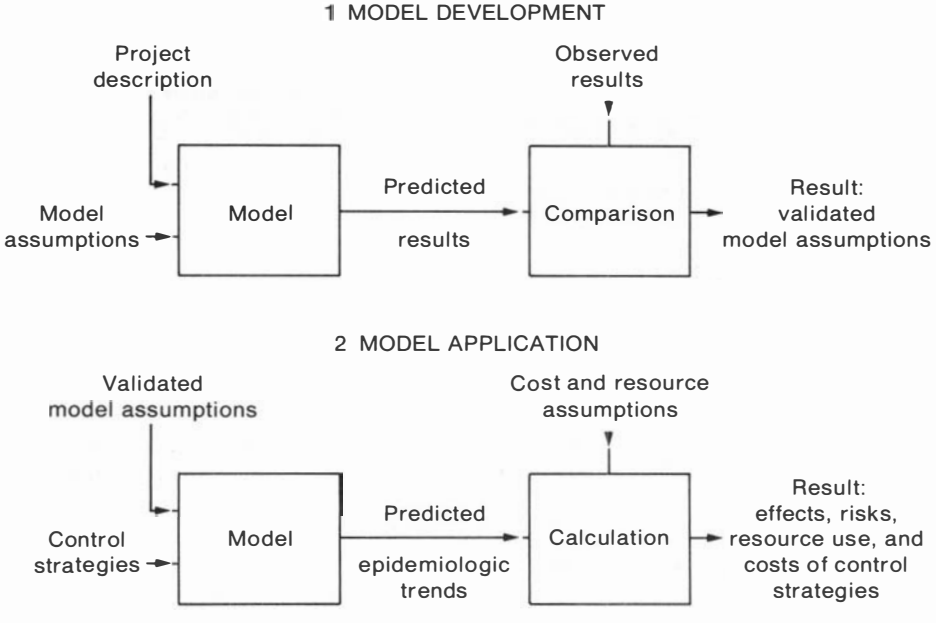

Figure 1. Model development (1) and application (2).

Conclusions

The success of decision models as an aid in leprosy control cannot be guaranteed beforehand. But applied modelling could be important when addressing questions in prediction, planning, monitoring and evaluation. There are excellent control programmes with longitudinal data which could form the backbone for constructing validated simulation models. Those in charge of leprosy control programmes should seriously consider a collaboration with scientists and decision makers for jointly developing practical decision aids.[9,10,11]

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Figure 1. Model development (1) and application (2).

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Major issues involved in the evaluation of leprosy control programmes through MDT

C K RAO

Introduction

In the past 4–5 years countries where leprosy is endemic have increasingly adopted multidrug therapy (MDT) in the treatment of leprosy. The broad aim of MDT is to interrupt the transmission of infection through early case detection and regular and complete treatment, and also to prevent disabilities and deformities. Reports on effectiveness, safety and patient acceptability from countries implementing MDT have continued to be positive, and also show that MDT has increased community confidence in the curability of the disease, which promotes voluntary self-reporting of patients.

Planning and evaluation are managerial tools that contribute to the success of leprosy control programmes. Evaluation helps further prospective planning to be effective by identifying achievements or shortcomings and highlighting the points that could improve programme performance.

The implementation of MDT for leprosy cases demands a highly sensitive monitoring and evaluation system to ensure the programme's smooth and coordinated progress. The use of expensive and effective drugs under supervision for relatively long periods makes treatment monitoring a crucial component of the programme. The correct time of programme inputs, including drugs and educational material, is ensured through programme monitoring. Monitoring also helps in reshuffling priorities, dropping unproductive efforts and in indicating neglected areas.

In this paper evaluation has been taken to include both monitoring (day-to-day follow-up of activities) and evaluation. Monitoring is also referred to by some programme designers as internal evaluation and is often in-built in leprosy control programmes. Unlike monitoring, external evaluation is periodic and independent of the programme personnel, which ensures lesser individual bias and greater reliability of data reported.

My experience in planning and participating in the independent evaluation of leprosy programmes in India and Myanmar in recent years is the basis for delineating important issues involved in the evaluation exercise.

Issues

OBJECTIVES OF EVALUATION

The objectives of the programme may vary from country to country, depending upon the

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aims, strategies, infrastructure, and duration of the MDT operations, and may include some or all of the following:

—Assessment of case detection progress, case treatment, drug delivery and reasons for patient default.
—Validation of reported data through examination of records and field visits.
—Assessment of the ongoing information system in terms of its promptness and completeness.
—Ascertainment of the technical competence and devotion of the staff involved.
—Determination of the impact of health education, if any, in dispelling ignorance/prejudices in the community, in promoting regularity of treatment and in retrieving the defaulters.
—Examination of the impact of the measures on the disease.

KEY COMPONENTS IN MDT DELIVERY

Treatment delivery

MDT is delivered once a month by the health personnel at predetermined points near the patient's home or in health centres/dispensaries/out-patient departments of hospitals, either to all eligible patients or only to selected patients, as decided in a country's programme.

Case detection

This is achieved through the promotion of voluntary self-reporting of patients, through active surveys, or by both methods, envisaged under the programme chosen.

Patient card maintenance

This should indicate the clinical/bacteriological status before, during and after MDT.

Case treatment

It should be specified which MDT regimes are followed for multibacillary (MB) and paucibacillary (PB) cases, and the regularity of MDT and monitoring drug intake by patients under the programme.

Record maintenance

Data recording and reporting systems should be maintained at different levels and there should be officers responsible for this, and feedback should be given to the senior officers clarifying the strong and weak points in the reports.

Health education

This occupies a high priority in the success of MDT—though it is the responsibility of every health worker involved in the programme to educate the patients, their families and

the community, this may receive very little attention from most of them, especially in integrated programmes. Voluntary self-reporting of cases, a high compliance rate and a high rate of treatment completion reflect how effective the education component is in the community, considering patient awareness, patient participation and community acceptance.

Leprosy profile

General information on leprosy prevalence and other epidemiological indices in the area before and during MDT should be available.

Infrastructure

Enumerating general health services personnel and/or special leprosy workers involved/ available for a leprosy programme and designating their job training status.

Voluntary organizations

These have to be active participants in monitoring and evaluation from the programme planning stage when working for leprosy control in a country

Monitoring methodology

The existing information recording and reporting procedures followed to monitor a leprosy control programme may vary from country to country. Most programmes that originated as strong vertical programmes continue to have a comprehensive reporting system compatible with/adopted from OMSLEP. Appropriately most integrated programmes have a simple and practical reporting system that include the core activities of case detection and case treatment as a part of health care reporting. The aim of leprosy information systems is to give timely though roughly correct figures rather than unduly precise but delayed data.

Sources of information

These should be leprosy patient cards and registers, leprosy survey data, surveillance information and supervisors' reports.

Training of monitoring personnel

All health workers responsible for monitoring data collection and for supervision should obtain their skills during job training for leprosy control.

Selection of indicators for monitoring leprosy programmes

These may vary from country to country based upon the programme aims, strategies and the infrastructure implementing it. The broad goals of MDT in leprosy control programmes should be to provide in full the course of MDT to leprosy cases, therefore

certain minimum indicators must be monitored. The following five indicators suggested to be 'required' at the WHO Consultation on Technical and Operational aspects of leprosy in Male, Maldives, in June 1990, are considered appropriate as minimum indicators: (i) prevalence; (ii) case detection; (iii) the proportion of patients with disability grade II among newly detected cases; (iv) MDT coverage, i.e. the proportion on MDT against all registered cases for chemotherapy; and (v) MDT completion, i.e. the proportion who have completed MDT among those put on MDT. Advanced programmes could develop additional indicators that were suggested in the report of the WHO Study Group on the Epidemiology of Leprosy in Relation to Control (TRS716). Operational criteria for definition of an active case for computing prevalence suggested by the Sixth Expert Committee on Leprosy (TRS768) would be appropriate to ensure uniformity, to define the targets for MDT and to determine the disease trends following MDT programmes.

Supervision

This is central to monitoring. Supervision ranges from validation of disease diagnosis, classification, activity, treatment delivery, treatment intake, detection and the management of reactions, skin-smear results and also logistics—delivery of drugs and transport. Part-time or full-time supervisors at different levels are identified and trained in the supervisory skills and techniques of leprosy control programmes.

Feedback on reports

Regular feedback from supervisors on their observations concerning both strong and weak points of the programme and comments on reports to lower reporting echelons, though not involved in decision-making, improves the programme performance.

STRENGTHENING MONITORING SYSTEM

An in-built monitoring system is often subjected to decay, and becomes less effective with time. However, the decay could be minimized and delayed by the periodic training of workers in skills to review critically the data and initiate corrective actions, maintenance of patient cards, encourage effective supervision, a periodic programme review of different levels by the highest administrative authority, listing priority indicators for monitoring, issuing a periodic news letter, maintenance and storage of records, etc.

The Indian programme appears to be unique in having a system of internal evaluation of leprosy programmes by creating regular assessment teams supported by the central programme at the state level and hiring full-time/part-time consultants supported by the WHO at national level. Though a formal review of their contributions has not been done, it is considered that they help to improve the quality of reported data, as well as tackling the operational/administrative problems in time. The programme is considering ways and means of keeping internal evaluators on a continuous basis.

EXTERNAL EVALUATION

The existence of a leprosy information system is basic to evaluation and monitoring. As

mentioned earlier, an evaluation undertaken by an expert who is independent of the programme planning and implementation, ensures lesser individual bias and a greater reliability of data.

Objectives

The objectives of evaluation listed above are perhaps relevant for external evaluation as well as with varying priorities. Broad objectives of evaluation are two-fold; one is determination of operational efficiency, i.e. to examine if what was planned or expected was in fact carried out, and the other is the determination of the impact of the control measures on the selected indices, i.e. whether what was expected in terms of selected indices did actually happen.

Collateral benefits

An element of healthy competition among the staff, especially middle-level managers, raises the morale of the peripheral staff, motivating health administrators, health planners and politicians for their increased support. Through their active participation it educates the administrative medical officers at state/division level on the strengths and weaknesses of the programme in their area *vis-à-vis* at the national level.

Sources of data

Records and reports maintained at all (peripheral to national) levels on the programme activities to delineate the leprosy profile.

Annual reports of the programme for the last 2–3 years.

Monthly/quarterly reports, if any, for the current year and previous year.

Leprosy patient data/cards maintained at villages/health centres.

Data obtained from discussions with programme managers—national, provincial, divisional, township/regency/district levels.

Interviews with health workers, supervisors, leprosy patients and community members.

Questionnaires for data collection

Appropriate questionnaires are constructed and pretested by the country programme manager taking account of the terms of reference for independent evaluation and the time available for evaluation. The questionnaires are used for interviewing programme managers, medical officers, supervisors and health workers involved in leprosy control at different levels to determine their competence and contribution. Questionnaires are also used for interrogation of leprosy patients and community members to determine the level of their awareness, participation in the programme activities, perception on social aspects of leprosy, etc. Questionnaires are also developed to collect appropriate data on leprosy control programmes at different levels. About 14 or 15 questionnaires were used in the three Indian programme evaluations and 7 in the Myanmar programme evaluation. Questionnaires to ascertain the leprosy profile from the states in India and divisions in Myanmar were sent to all concerned with the central programme 2 weeks before the

proposed field visits with a request to place the data at the disposal of the evaluators, should they visit that particular state/division. This ensured a timely submission of data and self-review of the data in the states/divisions irrespective of the actual visit of evaluators.

Sample selection

Effective evaluation, unlike monitoring, can only be carried out in a small sample because of time and funding constraints. Samples for field visits were selected by a WHO consultant independent of the programme managers both in India and Myanmar. Random samples of states and then districts were selected in India to ensure wide coverage of the country after stratification by levels of leprosy endemicity, varying organizational infrastructure and duration of MDT activities in force. A total of 10 multibacillary (MB) and 10 paucibacillary (PB) patients and 20 community members in 2 villages selected by the evaluators were interrogated in each of the districts assigned for evaluation in India.

In Myanmar 5 MB and 5 PB patients were chosen to be interviewed in 2 villages in each township selected for evaluation. Voluntary organizations involved in leprosy control efforts in the districts selected for evaluation were also included for evaluation of the Indian programme. No voluntary organization was involved in leprosy control work in the townships selected for evaluation in Myanmar.

Selection of evaluators

In India teams of 3 experts each have helped to improve competent evaluation of programme management (by a health administrator), impact assessment (by an epidemiologist), and validation of reported data (by a leprologist) besides giving other administrative and operational advantages of a team approach. In India 9–12 teams were formed for the three evaluations of the programme in 1986, 1987 and 1989. As mentioned above, each team had the services of a leprologist/leprosy control expert provided by the WHO from outside India. National evaluators were drawn from directors of health services of states or the equivalent, professors of community health or the equivalent and similar experts working with voluntary organizations whose involvement motivated them to support the programme.

In Myanmar, regional leprosy officers from outside their divisions were involved as evaluators along with a WHO consultant, the latter having selected the divisions and townships on a random sampling basis, and 2 teams of 3 experts were formed.

Should in-depth evaluation of some areas or some component of the programme be considered necessary, suitable experts as evaluators have to be recruited.

It is necessary to ensure that the evaluators are adequately briefed at the start of the evaluation so that they are able to fill the questionnaires and collect the requisite data correctly and uniformly. Briefing was given for 2 days both in the Indian and the Myanmar evaluations.

Duration of evaluation

It is convenient to complete the evaluation—travel, briefing and report—in 10–15 days.

With appropriate planning and preparation this period was found to be satisfactory. Disruption of routine programme activities are marginal in brief evaluations. When a smaller number of evaluators/teams are available, evaluation has to be prolonged over a relatively longer period. The Indian and Myanmar programme evaluations were all completed within 15 days. Funds for these evaluations were available from their respective WHO country budgets.

Collection of data

Appropriate data are collected by the evaluators from the reports using the assigned terms of reference. Information on the infrastructure availability against the sanctioned strength, training status of personnel, leprosy prevalence, case detection, case treatment, MDT coverage, MDT completion, health educational activities and their impact, quality of laboratory services, quality of supervision, supply of drugs, mobility, etc. are collected by the evaluators on a sample basis. Evaluators also validate a small sample of reported data on diagnosis, classification, treatment schedules, regularity of drug delivery and drug intake, disease activity, skin-smear results, etc. and record the data on the appropriate questionnaires.

Analysis and interpretation of data

Evaluators are expected to present orally their findings to the senior health officer of the state/division at the end of the visit. Hence data collected will have to be analysed before leaving the assigned states/divisions. It is a good strategy first to highlight the strengths of the programme, if any, before indicating the areas that need strengthening by the state/division health administration. On return to the central programme headquarters to report and deliver the duly completed questionnaires the points of view of the state/division, if any, have to be considered to see if it is necessary to relay them to national level. During oral presentation and debriefing the strengths found are to be projected while also suggesting areas that require urgent corrective action at all levels of the programme, including the central level.

Report and recommendations

Each evaluator/team has to give a narrative report with the completed questionnaires using the terms of reference assigned for evaluation. Brief, lucid and timely reports including positive features of the programme are helpful to improve/strengthen the programme performance. The evaluation reports have provided valuable support to the Indian programme—strengthening laboratory services; making possible the rapid extension of MDT to a large number of districts; the timely release of funds for health educational activities; giving priority to the filling of vacant posts; the training of personnel; and increasing the budget.

Actions taken on the report

The major aim of leprosy programme evaluation is to improve its performance. Evaluation guides in decision making. This purpose will not be achieved if the report is

unduly delayed or timely corrective actions are not initiated. Hence it is necessary to review the actions taken on the recommendations of earlier evaluation, if undertaken.

Conclusion

It may be stated that leprosy evaluation procedures followed in one country could be adopted in another country with only minor modifications, where warranted, to suit the local conditions.

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Defining a case of leprosy

V K PANNIKAR

Introduction

In leprosy, as in many other diseases, there are situations where the definition of a 'case' is uncertain. Some diseases can be diagnosed with certainty at autopsy only, such as Alzheimer's disease, and hyaline membrane disease. For some other conditions, such as cervical dysplasia and the adult onset of diabetes, there is a continuum from normal to abnormal with no clear demarcation line between them.

A Dictionary of Epidemiology[1] defines a case as 'a person in the population or study group identified as having a particular disease, health disorder, or condition under investigation'.

There have been attempts to provide an operational definition by assigning levels of certainty to the diagnosis of a number of different diseases. The Expanded Programme for Immunization (EPI) has produced guidelines to grade various EPI diseases as 'suspect', 'probable' or 'certain'.[2] To formulate a definition of a 'case' that would cover all aspects of a disease would be difficult, since it would be voluminous and academic, and probably of very little practical value. The usefulness of a definition that is meant to serve as a basis for action—an operational definition—may be determined by its practical applicability, not by the degree of its completeness. An operational definition must be judged in the light of its stated purpose, and what is relevant is whether it contributes to meeting the agreed purpose, which is control of leprosy in the community. It is widely recognized that the diagnosis of leprosy is often difficult. It has even been said that the absence of a clearly-stated 'case' definition calls into question much of the leprosy literature in so far as it renders results incomparable and unreproducible. Newell[3] remarked that 'there is no definite, finite or absolute test, sign or finding which can be said to divide a person with leprosy infection or leprosy illness from the rest of the population'.

The disease

Leprosy is often defined as 'a chronic disease of man resulting from infection with *Mycobacterium leprae* and affecting primarily nerves, skin and mucosa of the upper respiratory tract'. In the absence of any reliable tools for detecting the subclinical stages of the infection process, the emphasis for diagnosis of the disease is on clinical manifestations. The most remarkable thing about leprosy is the enormously wide variation in the

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way the disease affects different individuals: in some patients the disease involves only one peripheral nerve, or causes a single skin lesion which persists indefinitely or disappears of its own accord, while in others it produces a variety of skin lesions, together with destruction of several peripheral nerve trunks and damage to organs such as eyes, larynx, or bones, etc. Every conceivable variation occurs between these two extremes.

The diagnosis

Most clinical leprosy comes to our attention through the recognition of certain skin or nerve lesions. The very slow onset, history of long duration, absence of any irritation or itching and history of contact are very suggestive. Leiker[4] states that: 'it is a general rule that the diagnosis of leprosy would always be considered as a possibility whenever in a chronic skin disease or neurological disorder, another diagnosis cannot be made with full confidence, or the patient does not respond to the treatment which is normally effective'. The diagnosis of leprosy is based on the demonstration of one or more of the following cardinal signs:

- characteristic skin lesions;
- sensory loss in the lesion or area;
- thickened nerves; and
- presence of AFB in skin smears.

The histopathological diagnosis of leprosy is based on cellular infiltration of nerve branches and/or the presence of intracellular acid-fast bacilli.

The definition

The Sixth WHO Expert Committee on Leprosy[5] defined a case of leprosy as 'a person showing clinical signs of leprosy, with or without bacteriological confirmation of the diagnosis and requiring chemotherapy'.

The problem

a A long history of disease, a slow and insidious onset combined with the absence of irritation and itching are highly suggestive of leprosy but not diagnostic unless supported by signs like sensory loss, thickened nerves, or AFB in the skin smears. However, in practice, eliciting partial sensory loss and judging thickening of nerves is difficult and services for skin-smear examinations in leprosy endemic areas is generally unsatisfactory.

b Leprosy control programmes, as well as field-based epidemiological studies, have relied on the identification of leprosy by clinical diagnosis. There is considerable inter- and intra-observer variation observed in the diagnosis of leprosy, especially in PB cases. This has serious implications when comparing leprosy situations in different areas or in the same area at different points of time.

c Histopathological examination does not always help in the diagnosis of early leprosy.

d There is no independent 'gold standard' for the diagnosis of leprosy. Neither serology nor skin tests have a high enough degree of sensitivity and specificity to be useful in confirming or eliminating all suspect cases of leprosy.

e The clinical diagnosis of leprosy as observed in a total population survey seems to present greater difficulties than it does among self-reporting patients. In a survey, in about 35% of actively-found suspects, leprosy could not be confirmed. The difficulty applies almost entirely to PB leprosy, because diagnosis of MB leprosy could usually be established on the basis of results of skin smears.

f Under field conditions, the diagnosis and classification of leprosy are generally the responsibility of paramedical workers. It is necessary to determine the proportion of underdiagnosis and misdiagnosis in the findings of paramedical workers.

g In countries with a specialized programme for leprosy there is a tendency towards overdiagnosis, especially if case detection targets are imposed. In countries with integrated programmes, leprosy is often underdiagnosed because of lack of training and motivation.

h At present leprosy patients 'needing' or 'underoing' treatment, those who have 'completed MDT treatment', those who 'require surveillance', those who are 'under surveillance', those with 'deformities and disabilities', and those who 'need care' are sometimes grouped together as 'cases of leprosy'. Lack of distinction between these categories continues to be a source of error in computing and comparing statistics necessary for planning and organizing leprosy control programmes.

i The clinical diagnostic criteria often vary with individual examiners and their diagnostic prejudices.

j In a vast majority of PB cases the disease manifests itself as one or two inconspicuous skin lesions, which may disappear spontaneously.

k In the minimal lesions, there appear to be a real doubt as to whether many of the lesions are indeed those of leprosy, especially in areas where the prevalence of other dermatological conditions causing changes in the colour and texture of the skin are common.

l The initial 'indeterminate' class, though widely used, often in the absence of cardinal signs to diagnose 'early' or 'suspect' lesions in the field, is poorly defined and a constant source of disagreement between leprologists and pathologists.

Points for discussion

a The differential diagnosis in the absence of positive skin smears is often based on the examination of peripheral nerves. In such cases the diagnosis of leprosy should not be considered unless definite loss of sensation can be demonstrated in skin areas innervated by the corresponding nerve.

b Patients in whom a presumptive diagnosis is made on the basis of other evidence (such as non-anaesthetic skin lesions, history of contact, etc.) may be kept as 'suspect cases'. Wherever possible, these can be entered in a separate register to facilitate follow-up procedures.

c An individual who had been afflicted by the disease, presenting without any sign of clinical activity and with negative bacteriological findings should not be referred to as a 'case', and not even as an 'ex-case'.

d The programme should promote self-detection through health education, as self-reported patients generally have established disease and also are more inclined to attend for treatment regularly. In practice, the majority of established cases (both PB and MB) self-report. It is only the minimal or doubtful lesions which are detected by active surveys.

e It is important that standardized diagnostic criteria are laid down, which will be as valid, unambiguous, reproducible and simple enough to be adopted by the field workers.

f The real issue for control is rather an operational one:

Who is at risk of developing deformities and disabilities?
Who is capable of transmitting the disease to his/her contacts?

This calls for a definition which is robust enough to minimize false 'positive' diagnoses.

g In established leprosy, there is firm agreement between clinical and histopathological diagnoses. However, in early disease there is much disagreement.

h The diagnosis of leprosy is a serious matter and a wrong diagnosis may unnecessarily put the patient and his family through great mental agony. Therefore, if there is even the slightest doubt, the patient should be kept under observation until further evidence confirms the disease.

The self-healing

The majority of patients with one or two lesions self-heal with no sequelae, do not need chemotherapy, and run the risk of stigmatization. In Cochrane's study 70% of indeterminate leprosy cases self-healed. Lara & Nolasco,[6] reported that all types of lesions showed a tendency towards healing. Nearly 78% of the lesions healed spontaneously and 12·5% showed incomplete healing.

Noordeen[7] reported that 103 of 270 (38%) tuberculoid cases showed spontaneous healing. Sirumban[8] found that the rate of healing in untreated PB leprosy to be 22·4% per year. The healing time in these studies was about 2 years.

If we take the analogy from tuberculosis, only 10% of infections may manifest as clinical disease. This may also be true for leprosy.

The 'initial' or 'early' or 'minimal' or 'indeterminate' lesions are probably signs of infection rather than early signs of the disease itself.

Summary

The biological and technical hurdles confronting the development of new diagnostic tools are manifestly great in leprosy. Leprosy diagnosis in the field, for control as well as for research purposes, will have to remain, for the time being, predominantly clinical.

It is important that the significance and relevance of diagnosing so-called 'early' lesions must be viewed in the context of the objectives of leprosy control. All evidence suggests that the majority of these 'cases' are not likely to progress in the individual, nor is there any evidence that these 'cases' are of any importance for the transmission of the disease. At its best, such 'cases' may be a sign of temporary infection which will disappear

spontaneously within a few months without leaving any residual signs. It is more likely that the majority of these are not cases of leprosy.

In making such a diagnosis its ethical implications on the individual, his family and the local society must be considered, given the intense social stigma this diagnosis will generate; besides the cost of treatment and the potential risk of serious side-effects due to treatment.

It may be justifiable to have a broad definition if the incidence of leprosy is still high and all reported cases are to be accepted as valid. But once the backlog of cases has been detected and, as a result of control efforts, the number of new cases begins to decrease, there is a need to narrow the case definition for national statistics. When the disease is on the verge of elimination, the case-definition may be more rigorous (by adding verification procedures/investigations before accepting for inclusion in the national statistics).

It is evident that active case-finding programmes and sample surveys detect a large number of self-healing early lesions or non-leprosy conditions which do not contribute to the main objective of leprosy control. It is unjustified to continue with active case-finding programmes if the proportion of progressive/advanced new cases has reached a low level. Moreover, in integrated programmes, based on the PHC system, the customary distinction between active and passive case-finding is no longer valid, as the health infrastructure is expected to have reached the doorsteps of the population.

This is not an attempt to advocate 'late' case detection, because it is well known that in many diseases, including leprosy, the cost of treatment for advanced cases is high and the success rate is low. What is important is to develop standardized and valid criteria for the diagnosis of leprosy, so that those who need treatment are easily identified and treated, and those who are not affected by leprosy escape the unnecessary burden of stigmatization. In general, leprosy progresses very slowly and it is possible to detect established cases before they develop serious deformities or disabilities, through community health education programmes. Additionally in programmes where MDT has been implemented vigourously, it has renewed the community's confidence in health services and has promoted self-reporting to a great extent.

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Surveillance and monitoring of multidrug therapy using cohort analysis

D DAUMERIE

1 Surveillance of the leprosy situation

The twin goals of leprosy control programmes are to interrupt the transmission of infection by detecting cases as early as possible and treating them in order to achieve complete cure. A leprosy control programme also aims to prevent the development or occurrence of deformities and disabilities among detected patients. Therefore the most relevant indicators are those which reflect the programme's effectiveness and efficiency in the detection and management of leprosy patients.

The main purpose of leprosy surveillance is to assess continuously the epidemiological situation using some selected indicators, in order to enable decision-makers, programme managers and health workers to take public health action at the correct time. At the international and national levels, data should be used to monitor trends, set priorities, allocate resources and raise funds. At district level, the data should be used to target interventions, monitor and evaluate programme effectiveness.

The existence of a leprosy information system at global level is essential. It should be able to give reliable information on selected indicators. Its purpose is not necessarily for research, or evaluation of MDT efficacy, or programme monitoring or assessement at country level. The main purpose is to provide clear data on the epidemiological trends of leprosy at different levels (worldwide, WHO regions, subregions and countries). Considering the elimination purpose, the need for good information on prevalence and incidence becomes a priority and considering that the MDT strategy is the main tool for leprosy control, monitoring of its implementation and coverage is relevant.

Data collected should provide information on 3 different topics:

1.1 OCCURRENCE OF THE DISEASE, MAGNITUDE OF THE PROBLEM

- Prevalence of the disease and monitoring changes over time.
- Populations at risk.
- Leprosy morbidity in terms of time, place and population.
- Disabilities.
- Attitudes, practices, behaviours and stigma.

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1.2 MANAGEMENT AND MONITORING INFORMATION

- Availability and distribution of resources.
- Distribution and quantity of supplies.
- Coverage.
- Access to the programme, acceptability.
- Quality of the programme.
- Cost-effectiveness.

1.3 RESEARCH ON AETIOLOGY, RISK FACTORS, DEVELOPMENT OF NEW INTERVENTIONS AND EVALUATION OF THE EFFICACY OF THE PROGRAMME

This includes clinical, epidemiological, social, economic and operational research. The data needed for such research are many and vary according to the objectives of the study. Therefore this topic will not be discussed in this paper.

All different types of data can be collected separately or in conjunction with:

—routine reporting systems;
—sentinel systems;
—special surveys;
—special studies.

However, it should be kept in mind that the collection and analysis of data have to be relevant, reliable, flexible but standardized and done at the right time. The implementation of a surveillance system should not create additional work for programme managers and health workers.

2 Technical issues related to leprosy surveillance

2.1 A CASE OF LEPROSY: OPERATIONAL STANDARD CASE DEFINITION

The definition of a case of leprosy as recommended by the 6th Expert Committee on Leprosy is widely used and has dramatically improved the standardization and interpretation of the available information. It would be useful to determine the sensitivity and specificity of this case definition through special studies and/or sentinel systems.

2.2 CLASSIFICATION

The 6th Expert Committee on Leprosy recommends classifying patients in control programmes as either having multibacillary (MB) or paucibacillary (PB) leprosy. This classification is mainly based on clinical and bacteriological criteria. However, in most leprosy control programmes the absence of laboratory services, or the poor quality of smears and microscopy, make standardization difficult and increases the risk of misclassification.

2.3 PREVALENCE OF LEPROSY

This is the main indicator used worldwide to assess the magnitude of the problem, to monitor trends and to assess the impact of the control measures. In addition to the issues

related to the definition of a case of leprosy, it is very often not easy to define the population under surveillance in a given area due to the lack of updated statistics, weakness of health services coverage, migration, etc. In assessing the magnitude of the problem, the point prevalence has to be reviewed in conjunction with incidence or new case detection over a given period of time if it is to be meaningful. The monitoring of trends requires consistent information in order to detect changes in the disease rate. Assessing the indicators in determining the impact of the control measures, i.e. MDT on the epidemiology of the disease, the decrease in the point prevalence is not sufficiently robust. The temporal changes could be explained by various factors such as the deterioration of the surveillance system, the deterioration of the control programme, the natural trend of the disease, the impact of confounding factors, etc.

The point prevalence is generally used, which is defined as the number of leprosy cases among a given population in a defined area on a specific day. Point prevalence is appropriate for chronic diseases with low incidence. In the past, with the long duration of treatment, a case of leprosy was a 'case' for almost the rest of his/her life. The point prevalence was reflecting an acceptable picture of the leprosy situation.

Nowadays, with the implementation of MDT, leprosy is becoming a short-term disease for a large proportion of patients. Therefore it would be necessary to question the relevance of continuing with point prevalence as a measure of reflecting the magnitude of the problem.

In this respect, the use of period prevalence may be more appropriate, as it offers some advantages and seems to reflect better the magnitude of the problem, the workload and the impact of the control programme.

2.4 ELIMINATION OF LEPROSY

Elimination is defined as a prevalence below 1 per 10,000 population. When determining the prevalence target, we have to differentiate point and period prevalence. We have also to define the level of elimination (global, regional, country, district).

In terms of prevalence of registered cases, it will be relatively easy to monitor the elimination using essential indicators based on prevalence, focusing on the surveillance in some selected countries and checking/assessing the results of surveillance with small size sample surveys. However, taking into consideration the 'true prevalence', it would be necessary to conduct surveys to determine the number of estimated cases. For the time being such surveys are not standardized, and are not cost-effective.

3 Essential indicators

3.1 ESSENTIAL INDICATORS TO ASSESS THE MAGNITUDE OF LEPROSY

The following indicators have to be calculated according to global, regional, country and district levels:

Prevalence rates: Registered cases

Numerator: The operational case definition recommended by the 6th Expert Committee is appropriate and we should continue to encourage its use.

Denominator: The mid-year estimated population during the current year should be utilized, as published by 'World Population Prospects' (UN).

Detection rates: New cases

Calculated for the considered period of time and using as the numerator all new cases registered for treatment and for the denominator the population as defined above.

—proportion of PB and proportion of MB among registered cases;
—proportion of PB and proportion of MB among new cases;
—proportion of children among new cases;
—proportion of patients with disabilities rated as grade 2 among new cases.

3.2 ESSENTIAL INDICATORS TO MONITOR MDT IMPLEMENTATION

MDT implementation and MDT coverage are discussed below.

Proportion of registered cases (MB and PB) treated with MDT (MDT coverage)

This statistic is defined as the number of registered cases (PB or MB) receiving at least 1 month's dose of MDT during the year among the total number of cases (PB or MB) appearing on the register during the year.

Theoretically, data needed to calculate this indicator are easy to collect. However, the numerator and denominator are a type of period information, and this introduces confusion and explains some inconsistencies in the data provided by countries and the poor reliability of this indicator. In addition, MDT coverage does not reflect the quality of the coverage and should be analysed in conjunction with geographical coverage, compliance and the proportion of registered MB and PB cases cured with MDT.

Proportion of registered cases (MB and PB) cured with MDT

This indicator would be extemely useful to monitor MDT at district, national and global levels. It can be calculated using cohort reporting, a cohort being defined as a group of persons sharing one or several characteristics at the same period of time.

3.3 OTHER INDICATORS

According to the existing situation, the objectives of each leprosy control programme and the standards defined at national level, leprosy control managers can define a set of specific indicators in order to monitor and/or evaluate the various components of the programme. In addition to the essential indicators, additional data can be collected for specific purposes such as special studies, risk factors, health system research, trials, etc.

4 Cohort analysis for surveillance in leprosy

In the surveillance of patients with long-term diseases, it is generally admitted that certain characteristics of the patient and his/her disease may be analysed using powerful yet

flexible statistical methods based on regression models and life-tables. These methods were developed to analyse survival data and their use was generalized to all data related to time and trends. The concept is to collect and analyse information on the occurrence, or the non-occurrence, of special events. This approach is used for calculating rates (descriptive epidemiology) or probabilities. With respect to leprosy control, these statistics offer a number of advantages in monitoring and analysing relevant indicators such as MDT coverage, patients cured with MDT, reactions, relapses etc.

4.1 DEFINITIONS

The term cohort refers to a group of individuals who are exposed to the same risk at the same time. Analysing cohorts helps to dissociate potential confounding factors such as age, secular trends, etc.

Cohort analysis should involve collecting information on each individual that details:

—the reference date (date of commencement of observation);
—the date of the last examination and the patient's status at that date;
—the surveillance duration (the time between the date of the start of observation and the date of the last examination);
—the point date (the date of the analysis, i.e. when the status of each patient is ascertained);
—lost for follow-up (a patient for whom it is impossible to know the status at the point date).

4.2 MDT COVERAGE AND CURE RATE

Cohort reporting of treatment outcomes is the most informative technique for evaluating case-holding and treatment effectiveness. It avoids biases that occur in retrospective and cross-sectional methods. Cohort monitoring could be carried out at district level to provide immediate feedback of the results to staff. It is based on analysis of data obtained from the leprosy patient register, or other forms used to monitor treatment.

Here the cohort is constituted by all patients registered during a given period of time (reference date), say a quarter. The duration of the follow-up period is chosen in such a way that all patients have had the chance to complete the prescribed treatment period, according to the criteria of regularity (2/3 rule), and the final examination. The items (status) will represent the numerator and the number of input-patients will represent the denominator.

The treatment results can be expressed using 2 main indicators calculated with the data collected from the cohort:

MDT coverage

The proportion of patients treated with MDT among patients registered for treatment in the cohort.

Cure rate

The proportion of patients who completed treatment (according to the definition of

completion of treatment), have been examined and declared cured (according to the definition 'cured patient') in the cohort.

Some other indicators can be calculated using the same method/data such as: MDT attendance rate, new disability rate, defaulter rate, fatality, etc. In practice, we need to follow 2 types of cohorts—PB cohort and MB cohort: the PB cohort should be analysed every 9 months and MB cohort should be analysed every 36 months.

4.3 RELAPSE RATE

The relapse rate is mainly used to judge the results of clinical trials and the efficacy of new regimens and new combinations. Though it can be estimated using person/years of follow-up as the denominator, the use of cohort life-tables offers a number of advantages in estimation of probability to relapse; computation of the probability taking into account; patients lost to follow-up; comparisons between various groups using non-parametric tests, etc.

The use of cohort life-tables gives a reliable estimation of the evolution of the relapse risk during the time, and authorizes the use of non-parametric tests to compare several cohorts.

4.4 SCOPE AND LIMITATIONS OF COHORT ANALYSIS AND SURVIVAL STATISTICS

Current data are generally used to calculate rates at a given time: prevalence, detection, incidence, ratios, etc. This is appropriate in assessing the magnitude of a problem as it is at present and permits a glimpse of the future, if present rates continue. The data needed to calculate such rates are relatively easy to collect. However, these rates are of limited value if they are atypical of the general time period, or if future rates fluctuate greatly.

Cohort analysis and cohort life-tables give us a way of assessing events as they are experienced and related to populations exposed to the same risk at the same time. Their disadvantage is that it may often only be of historical value: to generate cohort and life-tables we need to collect information appropriate to each time period and to perform the results retrospectively. Information collection and summary appears more complicated as they involve the calculation of date intervals. This problem can be solved by the use of appropriate registers and forms, and by the use of microcomputers that are often available these days at intermediate and central levels in monitoring health problems.

The use of cohort reporting to monitor MDT coverge and cure rate is recommended as a control. Cohort analysis for prevalence, detection and incidence should be used only to carry out epidemiological studies, life-tables to follow relapse rate in clinical trials, or in comparing the efficacy of several regimens.

5 Conclusions

The information collected in a surveillance system should be the minimum necessary to achieve the objectives of the system. The fewer data collected, the more likelihood there is that these will be collected and reported correctly. For leprosy control, a basic surveillance system might collect data annually on the magnitude of the problem (existing cases and new cases) including information on the type of leprosy, age and disabilities and

on the controi measures (number of patients cured with MDT). The information generated by the system has to be carefully analysed for decision-making, and feedback information should be given to the users.

The quality of the surveillance system should be regularly assessed to ensure that it is based on a good understanding of the epidemiology of leprosy. The surveillance system should facilitate rapid action which in turn leads to a reduction in the prevalence and incidence of the disease.

Information collected routinely at the periphery is usually considered to be of poor quality and inadequate. However, this is often a misconception. Most leprosy control managers are aware of the fact that health workers in the field are faithfully collecting, recording and reporting the data. Unfortunately, this vast amount of painstakingly collected data is neither compiled nor analysed at the intermediate or central level. Moreover, whenever information is required, there is an attempt to conduct fresh surveys or demand the completion of new sets of forms. This has often resulted in an increase in the workload without any potential benefit to the programme. If we study carefully the available data, we can see that it is more than adequate and of a reasonably good quality. If the data are compiled properly and analysed they provide a very powerful tool for decision-making. Cohort analysis will be able to do this efficiently for the various needs of leprosy control, without overburdening the routine activities.

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Indicators for use in leprosy control programmes

MYO THET HTOON

The leprosy control measures currently being undertaken in almost all the control programmes in the world are based on the two main strategies of case-finding and treatment. These two measures have been the cornerstone of leprosy control activities since the era of chemotherapy with dapsone. Unless a major breakthrough occurs in the development of a vaccine, these two measures will be the main strategy used in the elimination of leprosy as a public health problem by the year 2000.

Most of the leprosy control programmes operating in endemic countries are to be monitored and evaluated using these two activities. Depending on the type of the health care delivery system and availability of resources, each country or even each region in a country have developed their own unique case-finding and treatment activities. Indicators to be used for either monitoring or evaluation are going to differ from programme to programme, depending upon the type of control programme (specialized vertical or integrated), nature of activities undertaken and the availability of resources.

Generally it is felt that as leprosy control measures are integrated into the primary health care services (which means that less specialized persons are to be used) the amount of data routinely to be collected needs to be reduced as well as simplified. Certain information that was routinely available during the years when leprosy control was a specialized service activity will no longer be routinely available. A trade-off between information that is thought to be essential and that which is not essential must be made. The operational and epidemiologic indicators to be used for the monitoring or evaluation of a leprosy control programme will also differ between that of a central or intermediate level programme manager and a peripheral programme manager. Some of the indicators intended for use by the peripheral programme managers may not be of use for the central planners.

Since the programme managers at the peripheral levels are the ones who are mainly involved in the day to day implementation of the case-finding and treatment activities it is important that a set of minimum indicators be identified which could be routinely collected and used by the personnel at the peripheral level. Indicators are to be divided into two categories. One set of indicators are intended for the peripheral programme managers and the second set for the central or intermediate level programme managers. Each set of indicators is then to be subdivided into operational and epidemiologic indicators.

The formula for the calculation of each indicator is as shown in the OMSLEP,

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Recording and Reporting Systems for Leprosy Patients, edition 3.[1] The list of indicators recommended for use in integrated leprosy control programmes is as follows.

REGISTERED PREVALENCE

The registered prevalence is a very useful indicator and has been used by almost all control programmes. It is also easy to calculate since almost all control programmes have the total number of registered cases. Usually the registered prevalence is calculated as a point prevalence. Since the treatment duration for paucibacillary (PB) patients is now much shorter under the MDT regimen, in programmes where MDT treatment activity is efficient the registered number of cases may be comprised of only multibacillary (MB) cases. If the true magnitude of the problem of leprosy in an area is to be estimated, the period prevalence may be more appropriate.

With the introduction of MDT in most control programmes the registered prevalence has drastically declined in a very short period and it may no longer reflect the true situation in areas where the detection rates do not approximate the incidence rate.

PROPORTION OF REGISTERED CASES AMONG ESTIMATED CASES

This is a very useful indicator for central or intermediate level programme managers, especially if one aims at cutting the transmission through MDT. As pointed out in the OMSLEP, the problem is finding the denominator for this indicator which is the total number of estimated leprosy cases. If future leprosy control programmes are to have a specific time frame target, this indicator will highlight the success of the control measures in an area. It is possible that an area may report a very low registered prevalence but the present registered caseload could be only a small fraction of the total estimated cases as a result of poor case-finding activities.

TOTAL NUMBER OF SCHOOLCHILDREN SCREENED FOR LEPROSY, SCHOOL DETECTION RATE, TOTAL CONTACTS EXAMINED, CONTACT DETECTION RATE, TOTAL POPULATION MASS SURVEYED, MASS SURVEY DETECTION RATE AND ACTIVE CASE-FINDING PROPORTION

The indicators concerned with the operational aspect of the active case-finding activity are the total numbers of schoolchildren screened for leprosy, the school detection rate, total contacts examined, the contact detection rate, the total population mass surveyed, the mass survey detection rate and the active case-finding proportion. In programmes where the registered cases are almost equal to the number of estimated cases or if the incidence of leprosy is too low the active case-finding measures may be very inefficient and costly. In such programmes these indicators need not be used on a routine basis. In programmes where the proportion of registered cases is still low compared to the estimated number of cases, these indicators are helpful in monitoring the operational aspect of the case-finding activities with the aim to increase them.

PROPORTION OF REGISTERED CASES ON MDT

This indicator is useful in monitoring the MDT coverage of an area. The proportion of

registered cases on MDT will become obsolete as the MDT coverage expands in an area and reaches 100%. This indicator is useful during the transition period from dapsone monotherapy to MDT in assessing the operational coverage of MDT, especially in programmes introducing MDT on a phase-by-phase basis.

The numerator for this indicator is the total number of cases obtaining treatment during a given period. The denominator is the total number of cases registered for treatment in that specific area during the same period. This is a kind of period prevalence, where the total number of prevalence cases at the start of the period of reporting is added to the total number of cases that are newly treated during the same reporting period.

PROPORTION OF CASES ON REGULAR MDT

This indicator could be calculated for all cases on MDT or separately for PB and MB cases. Regularity of treatment is to be taken as those who receive at least two-thirds of the recommended number of MDT doses during the year as defined in OMSLEP. Though this information is important for assessing whether patients are receiving sufficient treatment, this information could not be collected routinely through monthly reports and should only be calculated on a yearly basis.

NEW CASE MB PROPORTION AND NEW CASE UNDER 14 YEARS PROPORTION

These two indicators are useful in assessing the transmission of the disease when incidence could not be calculated easily. As stated in OMSLEP, when the MB proportion stabilizes the detection rate approaches the incidence rates.

These two indicators could be influenced by the mode of case-finding activities conducted in a specific area. A programme which stresses school surveys will have a high proportion of new cases under 14 years of age. Programmes with only passive case-finding activity may be picking up relatively more MBs than PBs and so in such areas the new case MB proportion will be high.

Assuming that no drastic change in the mode of case-finding has occurred in the past, these two indicators are useful in assessing the transmission of the disease.

PROPORTION OF GRADE II DISABILITY AMONG NEW CASES

This indicator reflects the effectiveness of the case-finding activity. It is a good operational indicator, especially when used together with other case-finding indicators. Since the numerator of this indicator includes only visible disability (grade II) this indicator will approach zero as cases are being detected at an early stage as a result of a good case-finding programme.

TOTAL CASES COMPLETING MDT DURING THE YEAR

The total number of cases completing MDT during the year is to be used as a crude indicator to measure the efficiency of the MDT activity. This figure is easy to obtain and though it reflects MDT activities carried out in the past it nevertheless gives a rough estimate of the outcome of the MDT activity in an area. Assuming that the regularity of

Table 1. Indicators for use in control programmes

Indicators	Peripheral programme managers		Central/ intermediate programme managers	
	Op:	Epi:	Op:	Epi:
1 Registered leprosy prevalence	++	++	++	++
2 Proportion of registered cases among estimated cases	+		++	+
3 Total schoolchildren screened for leprosy	++		+	
4 School detection rate	++		+	
5 Total contacts screened	++		+	
6 Contact detection rate	++		+	
7 Total population mass surveyed	++		+	
8 Mass survey detection rate	++		+	
9 Active case-finding proportion among new cases	+		++	
10 Proportion of registered cases on MDT	+		+	
11 Proportion of cases on regular MDT during the calendar year	+		+	
12 New case MB (proportion)	+	+	+	++
13 New case under 14 years (proportion)	+	+	+	++
14 Proportion of grade II disability among new cases		+		++
15 Total cases completing MDT during the year	+		+	
16 Relapse rate (MDT)	+		+	

treatment has not changed during the period under study, it could be assumed that this indicator reflects the MDT activity carried out in the past.

RELAPSE RATE

The relapse rate to be estimated is based on the clinical relapses detected. As pointed out in the OMSLEP, the problem with this indicator lies in the validity of the denominator. The total accumulated discharged cases are difficult to review during a given year, especially in programmes where the on-going MDT caseload is still high. The majority of the relapses will be self-reported and the denominator will be made of all discharged cases. This makes the interpretation of the relapse rate a little difficult since a cohort analysis of the discharged cases will be impossible to calculate from routine data collection forms, especially in an integrated leprosy control programme. The programme managers will have to use this as a rough measure to assess the effectiveness of the MDT in an area.

Reference

[1] OMSLEP, *Recording and Reporting Systems for Leprosy Patients*, edition 3.

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OMSLEP as an evaluation tool

E DECLERCQ

If leprosy is to be controlled, those in charge of the programmes at the local, regional or global levels should be able:

—to check whether the control measures, that is the strategies and targets that have been planned, are effectively and efficiently implemented. This is the operational evaluation; and
—to evaluate whether the programme has reached its medium- or long-term objectives, that is the reduction of the problem in terms of the numbers of patients in need of the health services. That is the epidemiological evaluation.

The evaluation process should be based on the use of objective indicators. These indicators need also to be simple to allow health workers at all levels, even the most peripheral, to collect the data necessary to calculate them.

The need to use standardized indicators is evident at the national level. It is also advantageous at the regional or global level. For instance it would allow the epidemiological trend to be analysed in relation to the control strategies used locally.

From the start this has been the objective of the OMSLEP system in the recording and reporting of leprosy patients: to propose not only a set of standard indicators for the operational and epidemiological evaluation, but also a system for collecting the data necessary to calculate them.

When it was decided to create the system in 1976, the first step was to make a review of the information systems used in 78 leprosy control projects from 45 countries. This enabled a list to be drawn up of indicators whose value had been thoroughly reviewed by a group of experts. Then the data that needed to be collected were listed, and an individual patient form and two annual statistical forms designed. A booklet was published, explaining how to fill in the form, how to calculate the indicators, and how to interpret them.

From the start, the OMSLEP system was also designed to facilitate the transfer of data onto microcomputers.

In the years following its conception, a second edition of the booklet was published, with some minor modifications. In 1987 the third edition was published in order to adapt the system to evaluate MDT programmes, based on the list of 25 indicators recommended by a WHO Study Group in 1985. The design of the system remained basically unchanged, with an individual patient form, and two annual statistical forms:

—the individual patient form is a summary of the patient's clinical chart, which only takes into account the data necessary to calculate the indicators (Appendix 1);
—the detection form, which is a summary of the status at detection of all the patients

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newly detected during the year; its purpose is to help calculate the indicators dealing with incidence or detection (Appendix 2);
—the annual statistics form gives the data of all the patients who have been registered at one time or another during the year. It allows the calculation of the indicators dealing with prevalence or with the status of the patients after detection (Appendix 3).

The software for PC computers was also adapted for the evaluation of MDT programmes. At the same time it was made compatible with the requirements of ILEP.

The underlying philosophy of the system has always been to be as simple as possible, so that it could be used by polyvalent health workers at the peripheral level. It was to permit both the management of the project locally, and the monitoring of the programme at national level. At the same time, as it is based on the collection of individual patients' data, it also allows some sophisticated analyses such as cohorts or survival analyses to be carried out. This is of course particularly easy when the system is computerized.

From the information available, OMSLEP has been introduced in either its standard or in an adapted form in 54 countries at the national level. The ILOMSLEP software is also used in a number of programmes, but only in 5 countries at the national level.

The use and impact of MDT is of course among the most important aspects of leprosy control that need to be monitored. This monitoring should not pose any problem where an adequate information system exists. An attempt to monitor MDT at the global level has been made by the Department of Epidemiology of the Catholic University of Louvain in Brussels, Belgium, through the 'Leprosy Epidemiological Bulletin', which is published every 6 months.

The data are mainly collected through a standard questionnaire sent to the Ministries of Health of leprosy endemic countries. In case no information is sent by the Ministry of Health, other sources of information are also used, such as:

—ILEP and ILEP representatives at national level;
—papers published in scientific journals that deal with prevalence, case detection or MDT coverage at national level;
—the WHO Leprosy Unit at Headquarters, with whom there is a regular exchange of information.

The data requested are the following:

—total population of the country;
—year of introduction of MDT in the country;
—MDT regimens used;
—registered cases at the end of the year;
—MDT cases;
—newly detected cases during the year;
—additional MDT cases;
—completed MDT;
—cumulative MDT cases;
—cumulative completed MDT cases.

The data concerning the leprosy patients are requested by type of leprosy. These data are presented by country, WHO Region and at the global level. They are also used to calculate the following 4 indicators (Appendix 4):

Table 1. *Leprosy Epidemiological Bulletin.* Last year for which the requested data were available

	1989	1988	Before 1988	Not available
Registered cases	92	47	30	5
MDT cases	85	48	20	21
New cases	73	51	23	27
Additional MDT cases	59	29	22	64
Completed MDT	56	28	23	67
Cumulative MDT cases	52	30	24	68
Cumulative completed MDT cases	53	44	24	53

—prevalence rate;
—case-detection rate;
—proportion of patients on MDT;
—proportion of patients who have completed their treatment among the cumulative MDT cases.

The data presented in the 'Bulletin' concern 174 countries and territories. However, not all the data are available from every country. Even when they are available, the data are often not consistent. Obviously, with the exception of a number of very well-structured control programmes, the number and quality of the data available at national level are rather limited (Table 1).

Some possible reasons for this lack of reliable information could be:

—that there is a lack of interest from the peripheral health workers to collect information whose usefulness has not been made clear to them;
—there is no regular feedback to the periphery;
—the number of data requested is too large;
—the frequency of reporting requested is too high.

Thus there is an urgent need to redefine a very limited set of basic indicators, for which the data could be easily and reliably collected by primary health care workers and which should thus be within the capabilities of all control programmes and countries.

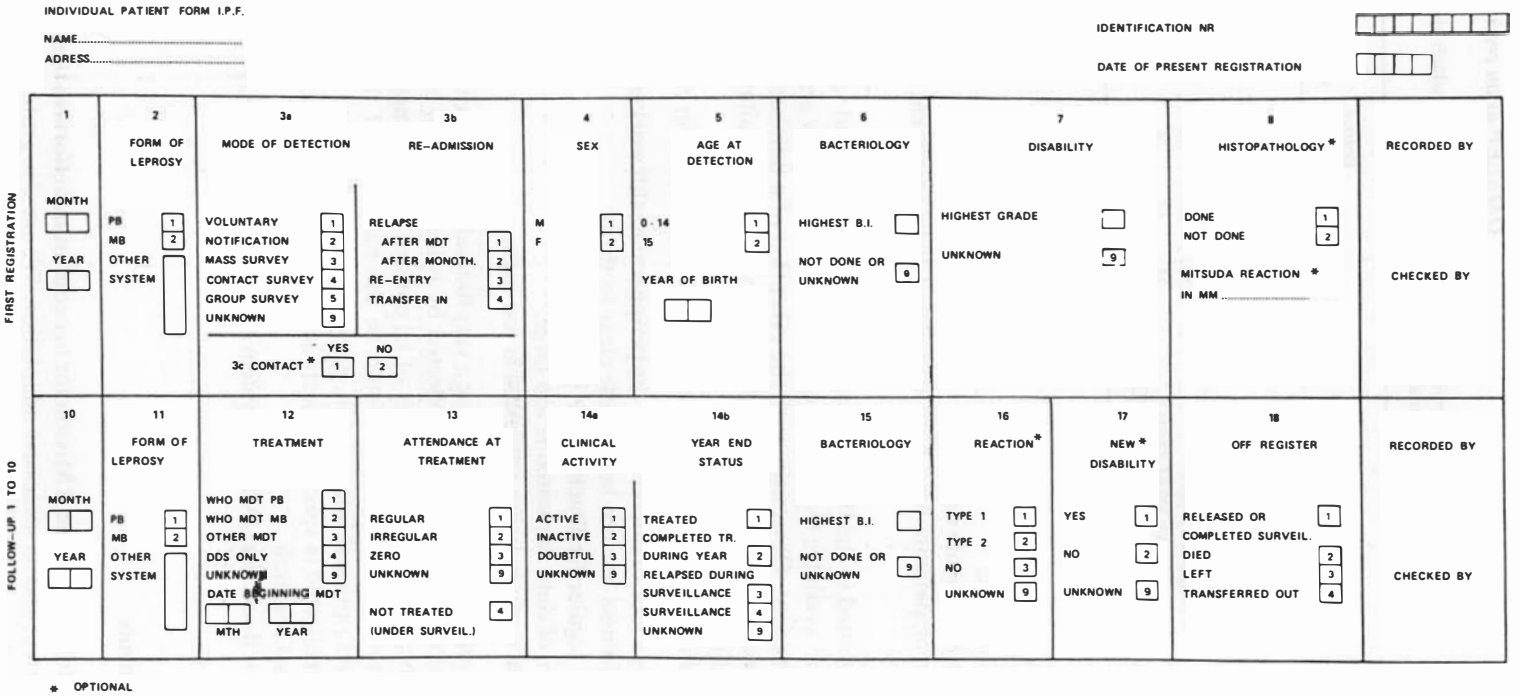
This limited set of indicators would be the backbone of the information system. Additional and optional information, allowing more elaborate analyses, could also be defined to be collected in specific projects according to local possibilities, and particularly for operational research.

Once this is done, the OMSLEP system could be easily adapted to provide appropriate support.

Acknowledgments

We are grateful to Claudine B Misson for her continuous efforts in the development of the OMSLEP system and its successive adaptation. We are also grateful for the services given to users in the leprosy-endemic countries.

Appendix 1. OMSLEP individual patient form.



Appendix 2. OMSLEP DF—detection form (total number of new patients registered).

CENTRE / DISTRICT.....
PROVINCE.....
COUNTRY.....

YEAR 19.....

	1. MODE OF DETECTION						2	3		4		5	6	7				8
	A	B	C	D	E	F		SEX		AGE				A	B	C	D	
	VOLUNTARY	NOTIFICATION	MASS SURVEY	CONTACT SURVEY	GROUP SURVEY	UNKNWON	TOTAL NEW PATIENTS	A MALE	B FEMALE	A 0-14	B 15	BACTERIOLOGICALLY POSITIVE	DISABLED	RELAPSE AFTER MDT	RELAPSE AFTER MONOTHERAPY	RE-ENTRY	TRANSFER IN	GRAND TOTAL
PB																		
MB																		
Total																		
PERSONS TO BE EXAMINED																		
PERSONS EXAMINED																		

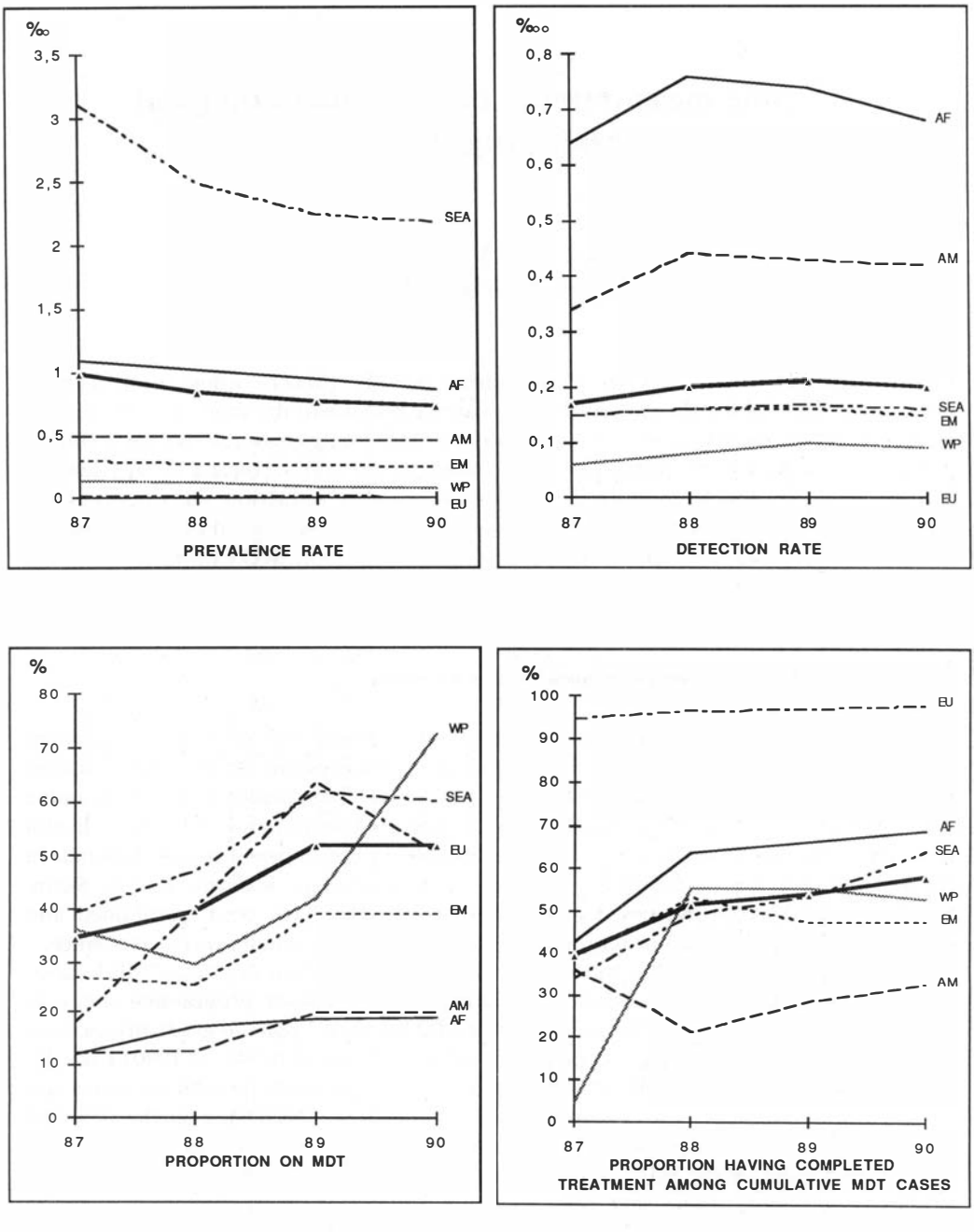
Appendix 3. OMSLEP ASF—annual statistics form (total number of registered patients).

YEAR 19.....

CENTRE / DISTRICT.....
PROVINCE.....
COUNTRY.....

		1	2	3 OFF REGISTER				4	5 YEAR END STATUS					6 ATTENDANCE AT TREATMENT					7.1 CLINICAL STATUS				7.2 CLIN. SURV.		8.1 BACT. STATUS			8.2 BACT. SURV.	
				A	B	C	D		A	B	C	D	E	A	B	C	D	E	A	B	C	D	A	B	A	B	C	A	B
		TOTAL PATIENTS REGISTERED AT END OF PREVIOUS YEAR	NEWLY REGISTERED CURRENT YEAR	RELEASED OR COMPLETED SURVEILLANCE	DIED	LEFT	TRANSFERRED OUT	TOTAL PATIENTS REGISTERED AT END OF CURRENT YEAR	TREATED	COMPLETED TREATMENT DURING THE YEAR	RELAPSED DURING SURVEILLANCE	UNDER SURVEILLANCE	UNKNOWN	REGULAR	IRREGULAR	ZERO	NOT TREATED (UNDER SURVEILLANCE)	UNKNOWN	ACTIVE	INACTIVE	DOUBTFUL	UNKNOWN	DONE	NOT DONE OR UNKNWON	POSITIVE	NEGATIVE	NOT DONE OR UNKNOWN	DONE	NOT DONE OR UNKNOWN
MDT	PB																												
	MB																												
	Total																												
Monoth.	PB																												
	MB																												
	Total																												
Total	PB																												
	MB																												
	Total																												

NOT RELEVANT



Appendix 4. Annual trends by WHO regions (*Leprosy Epidemiological Bulletin*).

Lepr Rev (1992) **63,** Supplement, 84s–92s

The measurement of the epidemiological impact of multidrug therapy

CHAROON PIRAYAVARAPORN &
SOMCHAI PEERAPAKORN

One of the well-known effects of multidrug therapy (MDT) when using a mass programme approach is the reduction of prevalence because of the shortened duration of treatment. It is still not known if the application of MDT helps to accelerate the cessation of leprosy transmission in the community, which is the major concern of any leprosy control activities, and be quantified in terms of incidence reduction. This paper is not aimed at giving the unequivocal answer to the question but it presents the current changes in the observed pattern of leprosy in Thailand in relation to the MDT implementation of our leprosy control programme.

1 MDT and the leprosy control programme in Thailand

Modern leprosy control programmes based on case-finding and domiciliary treatment was established in Thailand in 1955 as a specialized programme. At that time dapsone monotherapy was the only standard treatment available. The revision of the programme approach from a specialized programme to an integrated programme of the basic health service system was fully effective in 1977, covering 67 of the 73 provinces of Thailand. In the remaining 6 highly endemic provinces, Mahasarakham, Kalasin, Roi-et, Surin, Saraburi, and Nakhon Sawan, leprosy control activities have been maintained and directed using a specialized programme approach by leprosy zonal centres ever since.

MDT implementation was started in 1984 in 3 northeastern provinces (Mahasarakham, Kalasin and Roi-et) which are among the specialized programme areas as mentioned above. From the implementation of MDT it took 7 years to gradually increase the coverage rate among all leprosy patients in Thailand from 11 to 94% in 1990 (Table 1).

Such an achievement in MDT implementation has been made possible by active and sincere support from many non-governmental organizations (NGOs), since the allocated government annual budget for leprosy control activities alone could not meet the enormous expenses of the MDT implementation programme. For instance, the supply of rifampicin and clofazimine have been adequate because of timely donations from the World Health Organization (WHO) and the Sasakawa Memorial Health Foundation (SMHF), which were in addition to the purchase of drugs from the Government budget. Some other contributions which were also equally important are cars, microscopes, health personnel training expenses, etc. These have been granted by the German Leprosy

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Table 1. Cumulative MDT coverage by year. Thailand, 1984–1990

Year	Province covered		Case covered	
	No.	%	No.	%
1984	3*	(4)	5,008	(11)
1985	16	(22)	13,673	(33)
1986	29	(40)	18,901	(55)
1987	49	(67)	18,075	(63)
1988	61	(83)	14,605	(65)
1989	73	(100)	13,695	(82)
1990	73	(100)	11,308	(94)

* Mahasarakham, Kalasin, Roi-et/Northeast of Thailand.

Relief Association/Hartdegen Fund (GLRA/HF), The Netherlands Leprosy Relief Association (NSL), the American Leprosy Mission (ALM), and innumerable other domestic and international NGOs as well.

Case-finding methods in Thailand consist of household contact surveillance, rapid village surveys (mobile clinic), school surveys, and skin clinic services. All methods have been practised regularly since the vertical programme of 1955 with various degrees of intensification in some methods during that time. Figure 1 shows the annual achievement in terms of the number of persons examined from 1976 to 1990.

2 Changes in the observed pattern of leprosy: a nationwide comparison and the findings of 3 provinces

The data mentioned here are from routine recording and reporting of all governmental health service units which are parts of the leprosy control programme. Data are collected nationwide from all 73 provincial health offices, 12 leprosy zonal centres, and 13 government-run leprosy settlements. Data from the 3 provinces, Mahasarakham, Kalasin and Roi-et, are grouped as one unit to make comparison with the nationwide data more meaningful.

The years 1984–1990 should be considered as a transition period during which MDT gradually replaced dapsone monotherapy in Thailand (as mentioned above) on a nationwide scale. Hence it may be too early to claim, in 1991, that any change in the occurrence of new cases as represented by the nationwide leprosy detection rate is due to MDT. On the contrary, for the 3 provinces where MDT coverage of leprosy cases was high from the start and exceeded 95% within 1 year of operation owing to the vertical programme settings, any change in the new case profile there could possibly be originated from MDT implementation. In addition, even though the leprosy control programme has been operating for some time in Thailand without major changes in case-finding measures, the so-called 'backlog effect'[1] in the time trend interpretation of the concerned rate should still be kept in mind.

Changes in the observed pattern of leprosy are as follows:

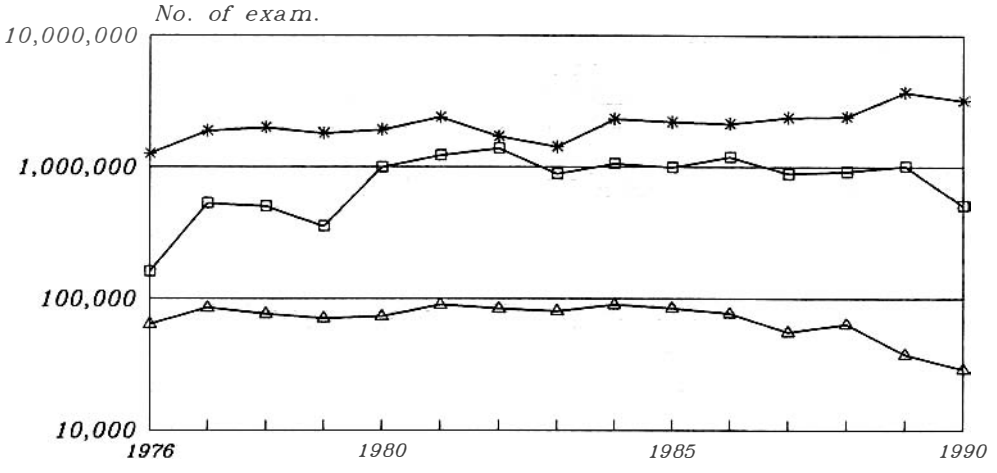

Figure 1. Leprosy case-finding activities, Thailand, 1976–90. —△— Household contact, —□— Mobile clinic, —×— School survey.

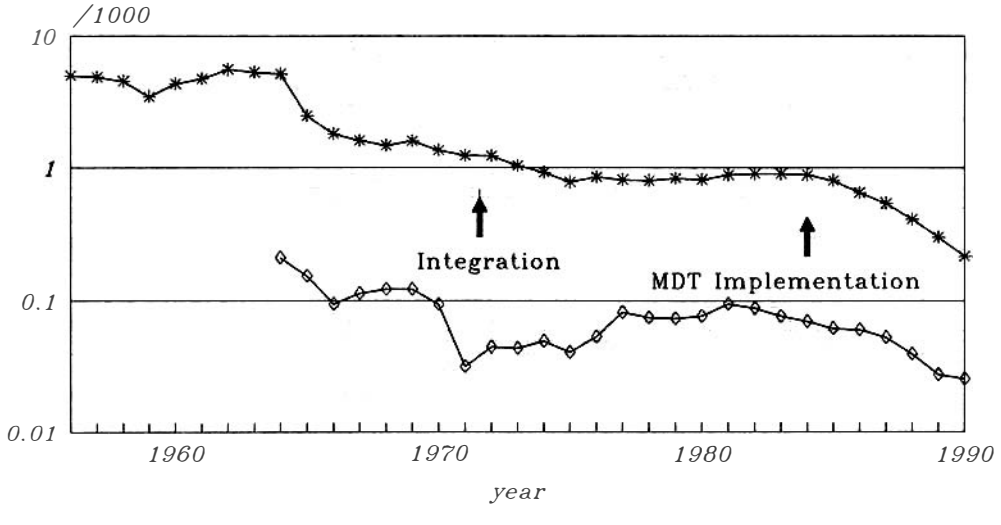

Figure 2. Leprosy in Thailand, 1956–90. —×— Prevalence rate, —◇— Detection rate.

2.1 *Prevalence and detection rate reduction* (Figures 2–5)

Since the beginning of the integration programme in 1976, a marked prevalence rate reduction was observed after the implementation of MDT in 1984. It is observed both on a nationwide scale and in the 3 provinces with, not surprisingly, a greater rate of decline in the latter due to the said historical background of MDT implementation.

An interesting finding is the regular decline of the detection rate which showed up before MDT. The detection rate decline in Thailand began in 1982 and in 1983 in the 3 provinces, which is definitely before MDT could have had any effect. Additionally, the

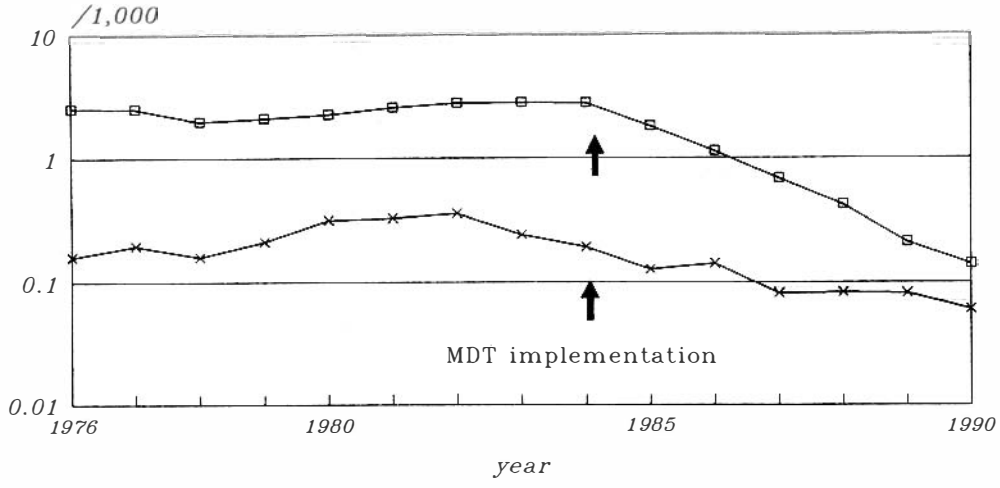

Figure 3. Leprosy in 3 provinces, Mahasarakham, Kalasin and Roi-et, of North-east Thailand, 1976–90. —□— Prevalence rate, —×— Detection rate.

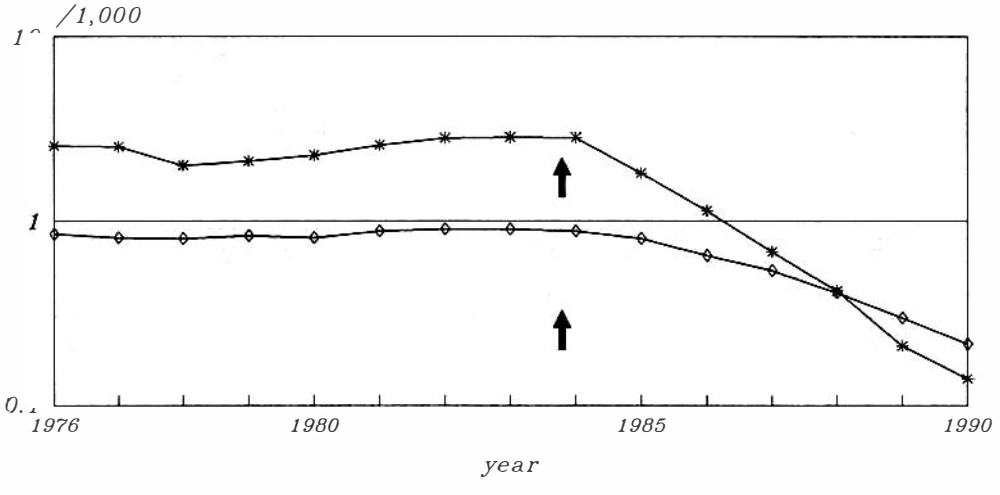

Figure 4. Leprosy prevalence rate in all provinces vs 3 provinces in Thailand, 1976–90. —×— 3 provinces, —◇— All provinces.

falling rate of the detection of leprosy is greater in the 3 provinces than in Thailand. Anyhow, the decline still continued after the introduction of MDT.

Theoretically, the prevalence to detection ratio under a MDT programme should be less than the ratio under a dapsone monotherapy programme due to the shortened period of treatment. This theory has been confirmed since the ratio in the 3 provinces has reduced from 14·7 in 1984 to 2·4 in 1990, whereas in the case of Thailand the ratio was 12·5 in 1984 and 8·4 in 1990.

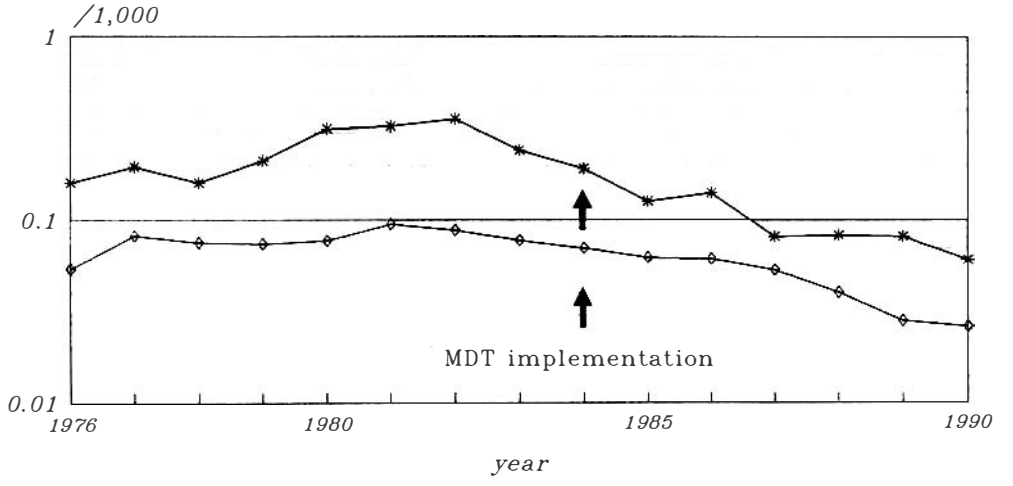

Figure 5. Leprosy detection rates in all provinces vs 3 provinces in Thailand, 1976–90. —✶— 3 provinces, —◇— All provinces.

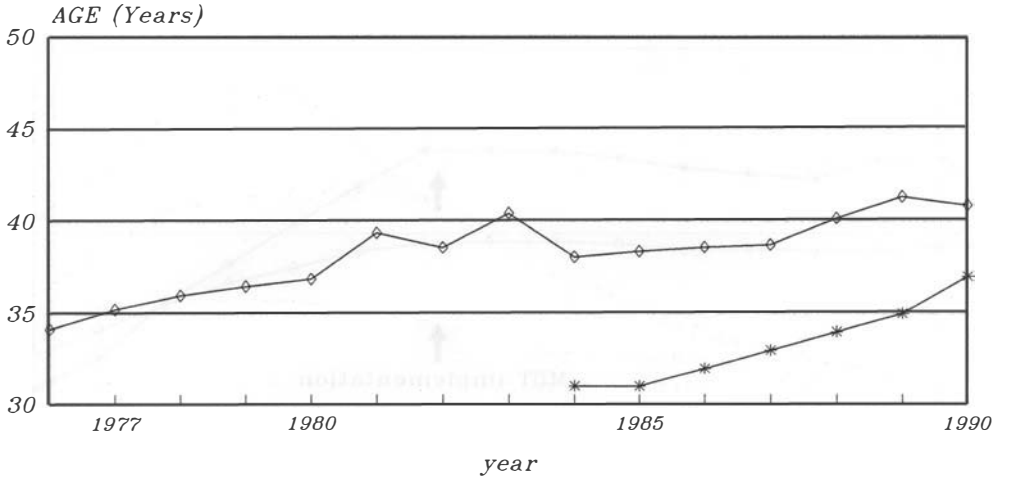

Figure 6. Mean age at onset among new cases of leprosy, Thailand, 1976–90. —◇— All provinces, —✶— 3 provinces.

2.2 *An increase in mean age at onset and a shift in the peak age incidence* (Figures 6–10)

There is a gradual increase in the mean age at onset among new leprosy cases in Thailand from 34·16 years in 1976 to 40·87 years in 1990 and in the 3 provinces from 31 years in 1984 to 37 years in 1990.

Analysis of the age-specific leprosy detection rate in Thailand and the 3 provinces using 5-year average data during 1976–1990 reveals a similar pattern. There is a general decline in the detection rate in every age group during that period. The peak age of

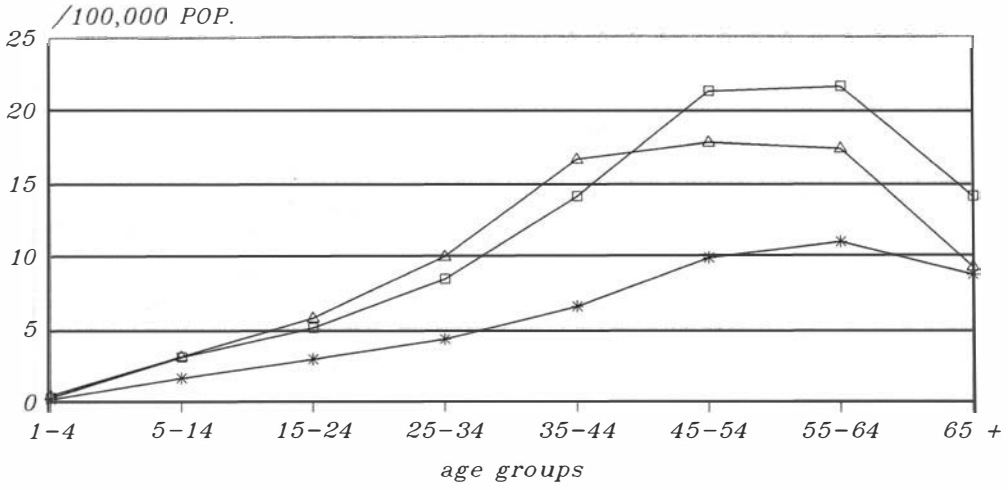

Figure 7. Age specific annual detection rate of leprosy, Thailand, 1976–90. (MDT started in 1984 and)—△— Year 1976–80, —□— Year 1981–5, —×— Year 1986–90.

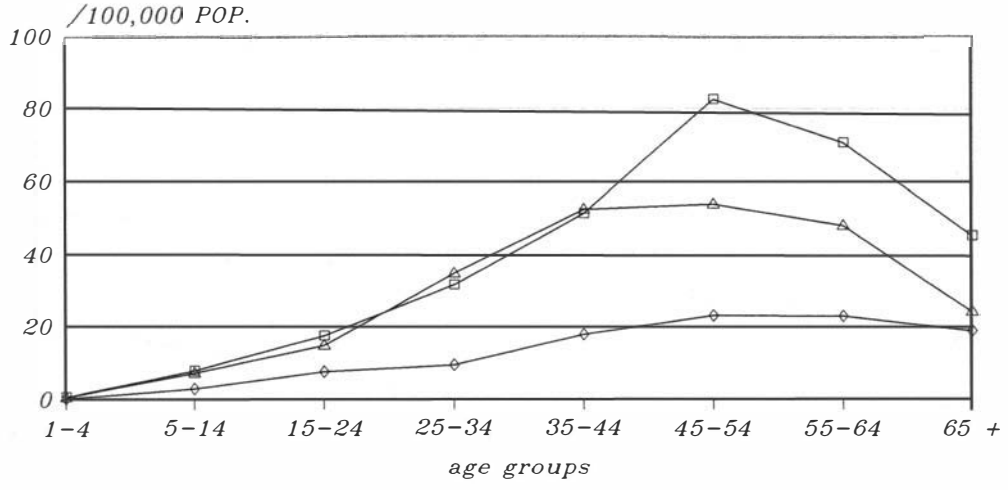

Figure 8. Age specific annual detection rate of leprosy, 3 provinces in Thailand, 1976–90. (MDT started in 1984.) —△— Year 1976–80, —□— Year 1981–5, —◇— Year 1986–90.

incidence is in the older adult population in Thailand and also in the 3 provinces. A shift in peak age incidence to the older age group is clearly observed in Thailand and in the 3 provinces as well by comparing the data of 1980, 1985 and 1990.

2.3 *An increase in the lepromatous ratio among new cases* (Figure 11)

A clear, steady increase of the lepromatous ratio among new leprosy cases has been observed both in Thailand and in the 3 provinces after the implementation of MDT. In

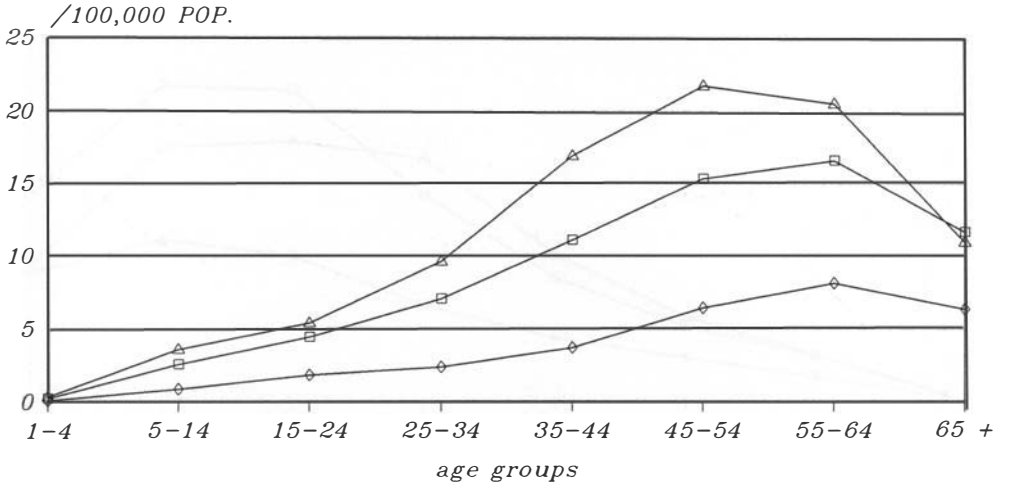

Figure 9. Leprosy detection rate by age group, Thailand, 1980, 1985 and 1990. —△— Year 1980, —□— Year 1985, —◇— Year 1990.

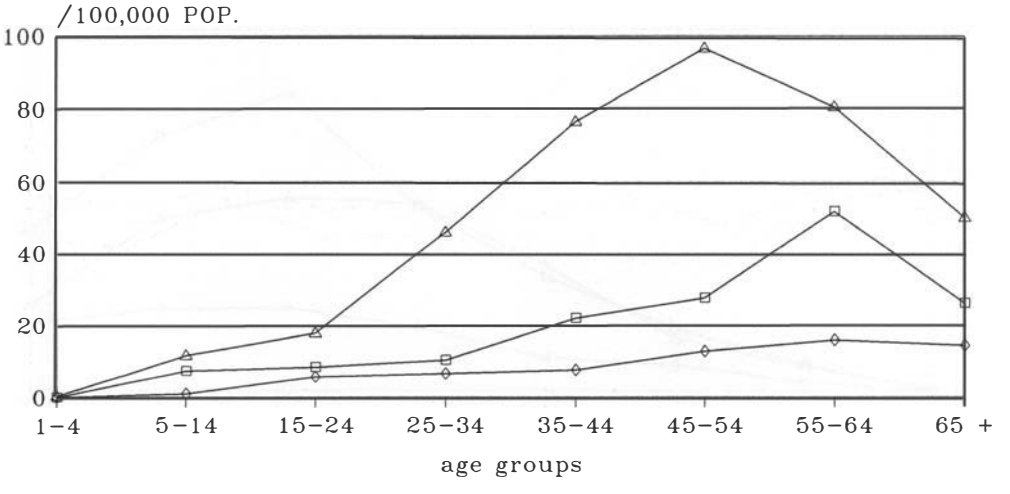

Figure 10. Leprosy detection rate by age group, 3 provinces (Mahasarakham, Kalasin and Roi-et), Thailand, 1980, 1985 and 1990. —△— Year 1980, —□— Year 1985, —◇— Year 1990.

the case of Thailand the increase has been for a long while and in the 3 provinces it only began in 1985.

The lepromatous ratio in the 3 provinces, together with the average age-specific detection rate pattern of the 'pre-MDT' period (1981–1985) has reminded us of the 'backlog effect' possibility.[1]

2.4 *A steady trend of disability rate among new cases* (Figure 12)

The rate of leprosy disability (grade 2 and over) among new cases is lower in the 3

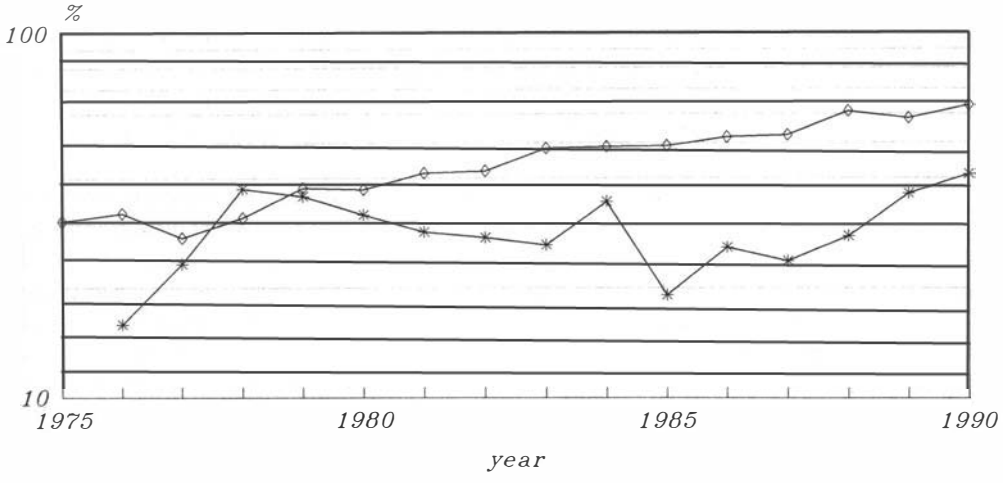

Figure 11. The lepromatous ratio among new cases of leprosy, Thailand, 1975–90. —◇— All provinces, —×— 3 provinces.

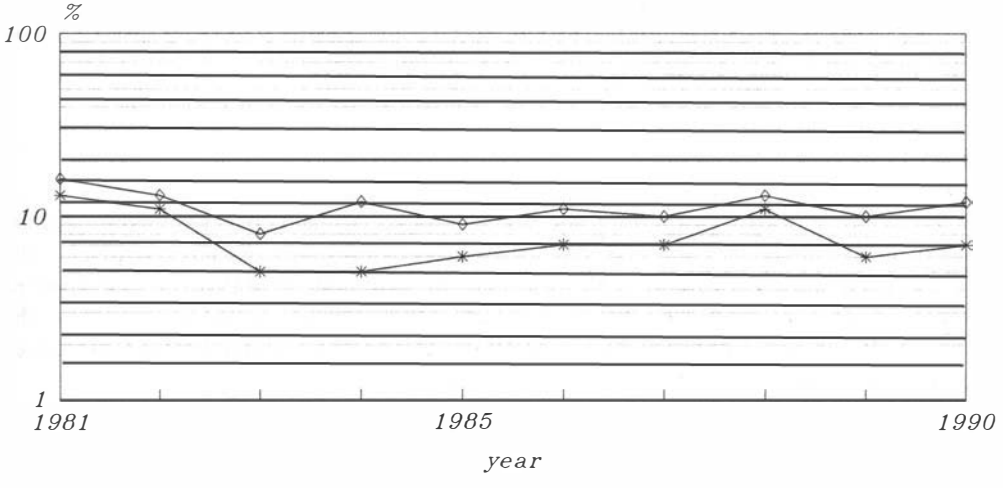

Figure 12. The disability rate among new cases of leprosy, Thailand, 1981–90. —◇— All provinces. —×— 3 provinces.

provinces than in the nationwide data implying earlier case detection. Due to the laborious effort in case detection activities under the vertical programmes of the 3 provinces, a single figure disability rate has been achieved and quite successfully sustained during the period.

3 Conclusion and Discussion

Today Thailand can be regarded as one of the low endemicity areas of leprosy, because of

the low prevalence and detection rates. The secular trends of major epidemiological indicators such as the increase of the mean age at onset, the increase of the lepromatous ratio among new cases, and the shift to the older age group of the peak age of incidence, all of which are quite definite, imply that at present the occurrence of leprosy is the result of post-primary infection of earlier days and that leprosy transmission in Thailand is now inactive.

Since the case detection rate serves as an estimate of incidence and is greatly influenced by the type and intensity of case-detection activities,[2] the validity of the detection rate as an indicator of incidence should be assessed first. According to Lechat,[3] when the proportion of lepromatous subjects become constant and when the proportion of new patients with disabilities approaches zero, the detection rates can be considered as a valid estimation of the incidence rates. Based on these criteria, the decline in the detection rate in our study could not be validified as the decline in leprosy incidence since the L-ratio is not constant and the disability rate among new cases is not approaching zero. However, the said findings in the 3 provinces, together with the subjective impression of the leprosy control team there, convinced us that the said criteria may not be practical or sensitive enough for the situation of low endemicity in our case.

Should a new set of epidemiological indicators be identified regarding the assessment of active leprosy transmission in the community of low leprosy endemicity?

Should there be some studies trying to make use of modern technology in the field of seroepidemiology and immunology to assess the dynamics of leprosy transmission as supplementary data to the study of epidemiological indicators?

Acknowledgments

The authors would like to thank Mr Sinchai Kachend of the Leprosy Division and Dr Yongyuth Wangroongsarb of the Malaria Division for their excellent work on the graphic presentation in this article. We are also indebted to Mr Piya Piyasilp, the Director of the Leprosy Zonal Centre, 6 Khon Kaen and Dr Pieter A M Schreuder of the Netherlands Leprosy Relief Association (NSL) for their contributions on the 'three provinces' data set.

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Lepr Rev (1992) **63,** Supplement, 93s–98s

Treatment failures with multidrug therapy

D LOBO

1 Introduction

Multidrug treatment (MDT) for leprosy has been in extensive use in India since 1982–83. A study of patients who received MDT in programmes run by 15 non-governmental voluntary organizations (NGOs) in India since 1983, is presented here. These NGOs are located in different geographical regions in the following States of India—Andhra Pradesh, Karnataka, Kerala, Maharashtra and Tamilnadu.

The main aim of the study was to measure the overall success of MDT using the following simple parameters:

a Number and proportion of patients declared as cured and released from treatment or released from control.
b Number and proportion of treatment 'drop-outs'.
c Number and proportion of treatment failures including relapses.

Patients and methods

A total of 67,472 patients from 15 NGOs who received MDT from 1983 to date, are included in the study.

The patients received the treatment regimens described below.

PAUCIBACILLARY (PB)

This includes patients that have polar tuberculoid (TT), indeterminate (I), primary neuritic (PN) and borderline–tuberculoid (BT) with less than 10 skin/nerve lesions and who are skin-smear negative.

Rifampicin (RMP), 600 mg once/month supervised;
Dapsone (DDS), 100 mg daily unsupervised;
Duration, 6–12 months.

MULTIBACILLARY (MB)

This includes patients that have mid-borderline (BB), borderline lepromatous (BL), polar

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lepromatous (LL) and borderline–tuberculoid (BT) and who are skin-smear positive and/ with more than 10 skin/nerve lesions. Either:

1 Standard WHO regimen (all mg):

Supervised once in 28 days
RMP 600
CLOF 300
DDS 100

Unsupervised daily for 27 days
CLOF 50
DDS 100

or

2 Modified WHO regimen as recommended by the National Leprosy Eradication Programme (NLEP):

Supervised daily for 14 days
RMP 600
CLOF 100
DDS 100

Followed by the Standard WHO regimen as in 1 above.
Duration: minimum 2 years or until bacteriologically negative.

TREATMENT FAILURES

The treatment failures have been classified into 4 groups:

1 PB cases who showed active signs at the end of 12 doses and were given MB treatment with 3 drugs for a minimum of 2 years thereafter.
2 MB cases who showed clinically active signs with or without bacteriological reduction at the end of 36 doses of MB treatment with 3 drugs.
3 PB or MB cases who have been classified as relapse and re-started treatment during or after surveillance.
4 PB or MB cases who manifested severe Type I or Type II reactions, which necessitated temporary or permanent stoppage of MDT.

CRITERIA FOR SIGNS OF ACTIVITY

The criteria for signs of activity have not been uniform. However, the following signs in general have been considered as active:

1 Increase in the size of the lesion or anaesthetic area;
2 appearance of new lesions;
3 erythema;
4 tenderness of nerves;
5 Type II reactions;
6 increase in the bacteriological index (BI).

RELAPSE

Relapse has been defined as the re-appearance of the signs of activity and/or appearance of new lesions and/or bacteriological positivity during or after surveillance.

Results

Table 1. Cases under study and proportion of drop-outs

Patient details	PB	MB	Total	Proportion (%)
1 Total number of patients who received MDT	52,398	15,074	67,472	
2 Patients eliminated as drop-outs (incomplete treatment)	2,523	1,709	4,232	06·28
3 Patients remaining for the study	49,875	13,365	63,240	93·72

Table 2. Analysis of study cases

Patient details	PB	MB	Total	Proportion (%)
1 Patients available for study	49,875	13,365	63,240	
2 Patients declared RFT/RFC	41,729	9,488	51,217	81·0
3 Patients presently under treatment	8,146	3,877	12,023	19·0

Table 3(a). Analysis of treatment failures excluding relapses

Patient details	PB	MB	Total	Proportion (%)
1 Patients availabe for study	49,875	13,365	63,240	
2 Patients recorded as treatment failures	1,424	269	1,693	2·7

Table 3(b). Profile of different groups of treatment failures excluding relapses

				Proportion to	
Patient details	PB	MB	Total	Failures (%)	Study cases (%)
1 PB cases-active after 12 doses—received MB (regimen thereafter)			1,426	84·2	2·25
2 MB cases who showed clinically active signs (after 36 doses)			197	11·6	0·31
3 PB/MB cases who manifested Type I/Type II reactions prompting stoppage of MDT	57	13	70	4·2	0·11
4 Total number considered as failures			1,693		2·67

Table 4. Proportion of relapses

Patient details	PB	MB	Total	Proportion (%)
1 Total number of patients declared RFT/RFC	41,729	9,488	51,217	
2 Patients recorded as relapsed	123 (0·29%)	31 (0·32%)	154	0·3

Table 5. Profile of MB relapses (Available for 17 out of 31 recorded cases)

Duration (months) RFT	Relapse	No. of cases	Percentage
6–12		4	23·6
12–18		3	17·6
18–24		2	11·8
More than 24		8	47·0
Criteria for diagnosis			
Clinical only		8	47·0
Bacteria only		1	6·0
Clinical & bacteria		8	47·0

Note—the balance of 14 relapses are from one centre, the Sacred Heart Leprosy Centre, in Tamilnadu.

Table 6. Profile of PB relapses (Available for 108 out of 123 recorded cases)

Duration (months) RFT	Relapse	No. of cases	Percentage
6–12		27	25·0
12–18		31	28·7
18–24		20	18·5
More than 24		30	27·8
Criteria for diagnosis			
Clinical only		107	99·1
Bacterial only		—	—
Clinical & bacterial		1	0·9

Note—the balance of 15 relapses are from one centre, the Sacred Heart Leprosy Centre, in Tamilnadu.

Discussion

The study proves that most patients who receive MDT satisfactorily complete the

treatment and are declared as cured and released from treatment within 6–12 months in PB leprosy or 24–36 months in MB leprosy.

A deliberate attempt was made to give a much wider definition of treatment failures that included apart from relapses, patients who did not become inactive within the stipulated duration of 12 months in PB and 36 months in MB cases and 77·2% of cases recorded as treatment failures belong to this category. Most of them are not really failures but required additional treatment with 3 drugs instead of 2 drugs in PB cases or additional duration of treatment (beyond 36 months) in MB cases. About 6·3% of the cases are recorded as drop-outs. The percentage of relapses is only 0·3% and those where a stoppage of treatment was prompted is 0·1%.

It needs to be emphasized that the diagnosis of relapse has been made on clinical and/or bacteriological (skin-smear) grounds only. No case was subjected to mouse-footpad inoculation. About 25% of the MB as well as PB relapses (Tables 5 and 6) were diagnosed between 6 and 12 months after release from treatment (RFT) and another 17·6% of MB relapses and 28·7% of PB relapses were diagnosed between 12 and 18 months after RFT. It is likely that most of these cases recorded as relapses were late reversal reactions. This is further corroborated by the fact that 47% of the MB relapses were made on clinical grounds alone. Out of 55,449 cases due for release from treatment, 51,217 (92·2%) were duly declared as RFT.

Conclusions

A study of 67,472 patients from 15 NGOs working in India who received MDT has been presented. The large majority of patients (92·2%) completed satisfactory treatment, were declared as cured and released from treatment, within the stipulated duration, thus proving that the MDT standard of WHO or the modified WHO/NLEP (India) regimen is:

—effective;
—acceptable to patients; and
—easy to implement in India.

About 2·56% of the patients required treatment for longer or required additional treatment with 3 drugs instead of 2.

The percentage of relapses was 0·3%. MDT can thus be expected to produce a steady decline in the quantum of leprosy infection in the community and a steady decline in prevalence/incidence rates. The goal of eradication is achievable if MDT is properly implemented.

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12 The Sacred Heart Hospital, Kumbakonam 612 401, Thanjavur District, Tamilnadu State—Dr S Thomson.
13 Sagayamatha Hospital & Leprosy Centre, Pulambady 621 711, Tiruchy District, Tamilnadu State—Dr S M Kabiruddin.
14 St Joseph's Leprosy Hospital, Tuticorin 628 002, Tamilnadu State—Dr T S Petro.
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The relevance of future leprosy vaccines to disease control

M D GUPTE

The concepts on leprosy control vary widely, according to different perceptions of the problem, the technology available to meet the targets and the commitment to achieve the final goal. The Executive Board of the World Health Organization, in its 82nd session in January 1991, and the World Health Assembly in May 1991 passed resolutions to eliminate leprosy, i.e., to achieve a prevalence of less than 1 per 10,000, by the year 2000. Leprosy is a public health problem because of the associated deformities and the resultant negative social overtones. Worldwide, leprosy control programmes were aimed at the early detection and treatment of leprosy, to enable the prevention of disabilities. As a secondary effect of chemotherapy, it was hoped that the transmission of leprosy infection would be lowered, resulting in better control of the disease. Multidrug therapy, as a newer strategy, essentially focuses on the same theme.

In the 1950s dapsone was the first drug to be used in public health practice for leprosy control. With dapsone, a comparatively rapid decline in leprosy prevalence was observed in several sets of population-based data. It was unclear whether the recorded decline and eventual incidence stabilization was because of backlog clearance or was the effect of dapsone.[1] Dapsone was also tested as a chemoprophylactic agent in several places—in this role it could be considered only in individual situations, and not as a general public health measure for mass prophylaxis.[2] The probable role of dapsone in neuropathy[3] and the widespread problem of dapsone resistance[4] further emphasized the limitations of the application of dapsone therapy in respect to leprosy control.

BCG was considered as a potential tool for leprosy control following the observations of Fernandez that demonstrated lepromin conversion.[5] Encouraging results of its protective efficacy are available from Uganda, New Guinea and Malaŵi—a prophylactic efficacy of 50–80% was observed there,[6]—but results from Burma have shown an efficacy of about 20%.[7] A similar moderate level of protective efficacy was observed from the recently analysed data from the South Indian BCG trial.[8] In this trial, a 0·1 mg dose of BCG consistently gave higher protection than a 0·01 mg dose, the overall efficacy being 24% and 17%, respectively, for these two doses. It was also seen that protective efficacy was highest in the youngest age group, indicating the probable efficacy of BCG in the uninfected population. Both sexes had the same protection. Protective efficacy of BCG did not differ greatly in PPD-S and PPD-B positive and negative groups. Protective efficacy against various clinical forms of leprosy was similar, except in the pure neuritic type, where it was somewhat lower. The smear positive incidence cases detected in the trial were uniformly distributed among those receiving doses of 0·1 mg BCG, 0·01 mg BCG or

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a placebo. This indicates that smear positive leprosy cases were not prevented by BCG. Thus BCG does not appear to be a vaccine which could be used for the general prevention of leprosy, although it might prevent leprosy in some parts of the world.

Multidrug therapy campaigns have recorded remarkable success in terms of prevalence reduction in several parts of the world.[9] We examined district level data in India, where MDT campaigns were operative for over 8 years, but there was no apparent indication that a declining incidence could be attributed to MDT. If leprosy is eventually controlled or 'eliminated' by the use of MDT, it will be the second disease to be overcome by chemotherapy, the first being yaws.

It seems obvious, considering these facts, that an effective vaccine against leprosy is needed. At the moment there are three or four antileprosy vaccine candidates being tested, and field trials with these vaccines are underway. The advances in molecular biology have made it possible for there to be second generation vaccines. Hence, when vaccines for preventing leprosy are considered, ICRC, *Mycobacterium welchii*, *M. leprae* combined with BCG and possible second generation vaccines are favourites as the candidates. One more vaccine, *M. habana*, is in the process of development, but there is not enough information available yet on its possible role as an immunoprophylactic agent against leprosy.

M. LEPRAE (A) IN COMBINATION WITH BCG

Kirchheimer & Storrs[10] in the early 1970s reported a major advance in experimental leprosy—the nine-banded armadillo, *Dasypus novemcinctus*, model for the cultivation of *M. leprae*. Following this large quantities of *M. leprae* have become available, and scientists have begun to develop *M. leprae*-based vaccines. A safe supply of *M. leprae* for immunological studies in man was obtained.[11] There is no single batch for *M. leprae* preparations, they are all harvests and lots.[12] Lots tested in various vaccine trials in the world have demonstrated the capacity of the vaccine to produce sensitization against *M. leprae*. Various lots of *M. leprae* vaccine have also demonstrated protection in the mouse footpad model. Characterization of different harvests are difficult.

Since 1989, we have used varying doses of BCG+*M. leprae* in vaccine studies in Thiruthani Taluk, Chingleput district, Tamilnadu. In several other studies on man in different parts of the world, a *M. leprae*+BCG combination has also been observed to have sensitizing potential in terms of lepromin and soluble antigen skin test conversions.

Sensitizing potential and protection against footpad infection in mice following inoculation with *M. leprae* was demonstrated by Shepard.[13] Studies in the Central JALMA Institute for Leprosy (CJIL), Agra, demonstrated that the combination of BCG and *M. leprae* was effective in preventing *M. leprae* infection in the mouse model.[14]

Convit[15] demonstrated the immunotherapeutic effect of combined killed *M. leprae* and BCG in a study involving 155 inactive BL/LL patients, 351 active BL/LL patients, and 46 indeterminate leprosy patients, findings that were independently confirmed by a group of histopathologists.

M.W. VACCINE

Talwar's group in Delhi looked for a mycobacterium that not only contained desirable cross-reactive antigens with *M. leprae* with respect to the immune reactivity of TT

patients, but also contained antigens evoking response in LL patients. Based on their studies. *M.w.* was selected as a candidate for vaccine production.[16]

Safety

Talwar carried out animal toxicity studies for *M.w.* vaccine and the product was found safe. *M.w.* has been used in several parts of India on patients, and is also being tested in a field study at Kanpur. *M.w.* vaccine has been well tolerated by the vaccinees and there are no reports of side- or toxic effects. Being a cultivable organism, it is possible to identify various characteristics of the bacillus and quality control is easy.

Animal studies

The CJIL studies demonstrated a heightened DTH response and strong protection in the mouse model.[14]

Sensitization studies

Talwar observed the conversion rate following *M.w.* vaccination was 90–98% in the lepromin negative contacts of LL patients.[17] In a study we carried out, *M.w.* vaccine was used in a dose of 10^9 bacilli and 5×10^9 bacilli. We found that with the increased dose of 5×10^9 *M.w*, post-vaccine responses to Rees' skin test antigen and lepromin-A were marginally higher than the responses observed in the normal saline group.

Immunotherapy

Phase-I clinical trials revealed that 20 of 32 BL/LL patients, persistently negative to Dharmendra and Mitsuda lepromins, were converted to a lepromin positivity status with a single intradermal injection of 5×10^7 autoclaved *M.w.* This was still manifest 8–11 months after the initial immunization.[18] Hospital-based Phase-II immunotherapeutic clinical trials have been in progress since December 1986 in two hospitals in New Delhi. Talwar observed success, based on results on 103 patients belonging to the 'single blind' portion of this study.[19]

ICRC VACCINE

ICRC bacilli were first isolated in 1958 by Bapat *et al.*[20] ICRC vaccine was first produced in 1979, and Bapat and Deo registered a patent for ICRC vaccine (C-44 strain) in 1981. The initial hospital-based studies were conducted from 1979 at the Acworth Leprosy Hospital, Bombay. A prophylaxis study has been in progress in Maharashtra State since February 1987.[21]

Safety

Extensive animal toxicology studies were conducted on the ICRC vaccine at the Cancer Research Institute, Bombay. ICRC vaccine has been used on leprosy patients since 1979. In the immunoprophylaxis trial in Western Maharashtra, India (30,000 population),

leprosy patients developed no complications following ICRC vaccine, apart from an extremely small number of individuals who developed regional suppurative adenitis. ICRC vaccine, like *M.w*, is a product developed from cultivable bacilli. The quality of this product should be maintained easily.

Animal studies

Bhide found that ICRC vaccine provided protection against *M. leprae* infection in the mouse model,[22] but these results were unconfirmed by Sreevatsa & Desikan.[14]

Sensitization

A total of 11 (92%) out of 12 lepromin negative individuals were converted following ICRC vaccine.[23]

Immunotherapy

In 1981, Deo and colleagues published their findings on the potential antileprosy vaccine from killed ICRC bacilli.[24] The 'vaccine' was administered to 46 LL and 11 BB/BL patients who were on dapsone treatment, and 10 lepromatous patients with high BI also received rifampicin for varying periods. Similarly treated 9 LL patients, who received saline, served as controls. A total of 14 of 46 LL vaccinated patients developed ENL. Histopathological examination of skin biopsies from vaccinated LL patients revealed regressive changes, and 4 months after vaccination, lepromin conversion was observed in 50% and 80% of LL and BB/BL cases, respectively. Bhatki *et al.*[25] reported 5 cases of reversal reactions induced by ICRC vaccine in LL patients, providing additional evidence of the immunotherapeutic potential of ICRC vaccine. A group of LL patients is being investigated for T-cell responses of ICRC and *M. leprae* antigens before and 6–10 months after vaccination with ICRC vaccine. It was observed that in 12 out of 16 vaccinated patients, there was a drop in the bacillary index after vaccination—6 of them showed parallel increase in the proliferative responses to both ICRC and *M. leprae* antigens.[26]

Field trials

Field trials using ICRC, *M.w.* and *M. leprae*+BCG vaccines have been launched worldwide. *M. leprae*+BCG is being tried in Venezuela and Malawi. ICRC and *M.w.* vaccines are being tried in Maharashtra and Uttar Pradesh respectively for their prophylactic efficacy. In January 1991, a comparative vaccine trial involving all these vaccines was launched by the Indian Council of Medical Research in the Chengalpattu-MGR district of Tamilnadu. The first results from Venezuela are expected in the near future. Results from the other trials can be expected after 1994. Vaccine trials are very demanding exercises and results from field trials will be awaited with great interest.

Possible second generation vaccines

A number of mycobacterial antigens (70KD, 65KD, 31KD, 18KD and 10KD) have been

identified. Natural or recombinant forms of these proteins are now available. Choosing antigens with possible prophylactic efficacy could prove to be a very deceptive exercise. Activity is focused on secretory proteins which are also the most prominent proteins in bacterial extracts. Defining 'protective antigens', and 'protective and pathologic immunity' are some of the questions that are being investigated (D B Young, 'Defining protective antigens', working paper for Joint PVD/TDR Meeting on Mycobacteria, Geneva, 1 May 1991). Promising approaches for inserting different DNA sequences in BCG have been developed.[27] As with other second generation vaccines, other carriers such as Canary-pox virus, salmonella, attenuated listeria, etc., could also be considered. The use of alum and other adjuvants is generally the initial approach used. The work on second generation vaccines is still very much at the exploratory stage. The studies based on cytokine liberation may be employed to identify some of the potential antigens in a comparatively short period of 1 or 2 years. However, it is difficult to postulate the availability of second generation vaccines and their potential role in the near future, even for field trials.

Effects of therapy and vaccine

The direct or primary effect of chemotherapy in leprosy is antimicrobial. The bacteria are killed rapidly, which leads to a cure. As the bacteria in patients are killed, the load of infection is reduced. This effect is expected to lead to the reduction in the risk of infection and also to lessen risk of disease—both secondary effects of chemotherapy. However, in view of the long latent/incubation period, new cases will keep occurring for some years. Therefore some time will elapse before the full impact of chemotherapy on the incidence of leprosy will be established. But as can be seen from the available data, no perceptible impact has been noticed even after 7 or 8 years of MDT. Thus the secondary effect of therapy on reducing transmission of leprosy cannot be presumed, though it is theoretically possible.

Therefore, prophylactic vaccines have a place in controlling leprosy transmission. BCG acts against leprosy by preventing primary infection and also reinfection. BCG may not be effective against reactivation. The candidate vaccines presently available are supposed to have immunotherapeutic efficacy. Hence they might be effective in infected individuals and they may also prevent the reactivation type of disease. A vaccine that is effective in both uninfected and infected individuals is likely to have the direct and rapid effect of reducing the incidence of leprosy in an area with active *M. leprae* transmission. In an area with a low level of transmission, vaccination will be a potent tool in reducing the number of those susceptible.

Relevance of a vaccine

The available parameters of animal studies, sensitization to *M. leprae* antigens following vaccination and immunotherapy, are only indirect measures of the probable prophylactic efficacy of the vaccines that are being developed. There are now vaccine trials testing each different vaccine. Several recombinant and native antigens as well as mycobacterial components are being investigated for their role in immuno-modulation. It is not

impossible to conceive the emergence of effective antileprosy vaccines one day. Perhaps a single antileprosy vaccine may not be effective in all the geographical areas or in different epidemiological situations. It would be essential to understand the possible roles of these vaccines in different situations, if they are found to be effective prophylactic agents. Whether the measure could be applied generally to the total population, or only to certain high risk groups needs to be ascertained. The assessment of the risk of disease and the risk of complications following vaccination is needed. The possible benefits of prevention will have to be considered. A vaccine may prevent only the early and less infectious forms of leprosy. It may be necessary to have a vaccine that will also prevent serious and highly infectious forms. Alternative approaches and priorities for disease control will have to be taken into account. Case detection and case holding in controlling disease transmission, costs of case detection and case holding and the cost of preventing leprosy cases will need consideration in an overall context. Clearly leprosy vaccine is a distinct research goal and an area of high research priority.

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The role of health systems research in leprosy control

INDRA PATHMANATHAN

Multidrug therapy and leprosy control

The development of multidrug therapy (MDT) has provided the technology that could reduce leprosy to the level where it will no longer be a public health problem. However, although this technology is available, there are many problems in effectively applying it for the benefit of all leprosy patients.

At present only 55% of registered cases are on MDT and there is considerable variation in MDT coverage in different countries. Several issues have to be addressed in order to strengthen leprosy control programmes (Table 1).

A review of progress in MDT shows that in most countries:

some policies are not appropriate;
some aspects of many programmes are inadequate or unsuitable and
the implementation is less effective than desired.

Changes are needed that enable all patients to be detected early and receive adequate MDT. These changes include the development of appropriate policies, the design of suitable programmes and the effective implementation of activities at the operational levels.

In order to be effective when making such changes, there is a need for detailed and accurate information to support decision making. However, such information is often lacking, inadequate or unreliable. As a result, decision making is often based on assumptions and unjustified opinions, and can result in inappropriate choices and decisions, which and discovered too late. The undesirable consequences are then usually corrected through a system of trial and error, without any factual assessment being made of the causes.

The various levels of decision making in the health system are well described in the WHO publication 'Managerial process for National Health Development' (1981). The policy and planning level determines the priorities, policies, broad objectives and strategies for control and involves politicians and higher level managers in the health and health-related services. The programme management level involves programme managers at midlevel, e.g. state, regional, district levels, NGOs, etc, and determines the activities, distribution of resources, etc. The technical and operational level determines the day-to-day activities, sets targets and monitors achievement relative to these targets. This level includes managers and supervisors at district level, clinical level, health teams, etc.

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Table 1. Multidrug therapy coverage: September, 1990

WHO region	No. of registered cases × 1000	% on MDT
African	483	18·4
American	302	23·7
E. Mediterranean	100	38·7
S.E. Asia	2,693	66·2
W. Pacific	153	63·4
European	7	49·7
All	3,738	55·1

In addition to these managerial levels within the health and health-related services, it should also be remembered that decision making also involves families, community groups, etc.

INFORMATION FOR DECISION MAKING

Decision making at the policy level, programme management level and operational level each deals with different aspects of the major issues that are involved in implementing MDT for leprosy control. Appropriate information is needed for each level of decision making. As was stressed in the editorial published in *Leprosy Review* in 1989 entitled 'Priorities in Leprosy Control', research to provide suitable and accurate information for decision making in programme management should receive as much attention as research to provide information, for example, on immunological aspects of leprosy. Some examples of the types of information needed at the different levels of management are given in Table 2.

Currently the existing health information systems (HIS) routinely generate a great deal of data but much of this is not analysed and interpreted to provide meaningful information for managers to use in decision making. Health systems research (HSR) provides the means to analyse and interpret the masses of data routinely available from HIS to respond to the specific information needs of managers. Some of the information that is needed may not be routinely available and needs to be collected through specially designed studies. These are HSR studies.

Purpose and uses of HSR

HSR is the scientific method for acquiring information which can be used for rational decision making in health management. It is concerned with populations, organizational structures and the interaction between them. It provides information to identify health needs in specific contexts, to set priorities on an informed basis to facilitate the allocation of resources and foster a more equitable population-based approach that responds to the health needs of high risk and vulnerable groups. It also provides information to enable more effective application of available technology, to evaluate policies and programmes

and suggests priorities for new research directions. HSR places health and disease in a larger context that takes account of social, economic and cultural factors.

Several illustrative examples of the types of information HSR studies have provided are given by the contributors to the WHO publication, 'Health Systems Research in Action' (1988).

In Botswana a study in a new agricultural development with large-scale migration provided information to determine appropriate stopping places for mobile dispensaries and developed a system for continued monitoring of health problems, particularly of migrants from other parts of the country who were at special risk in an unfamiliar environment. In Indonesia, a research project identified risk factors among pregnant women and developed a screening system which is used in 11 provinces to detect high-risk mothers and manage them at appropriate levels in the health system. In the USA, a number of studies influenced the debate and decisions on adaptation of the existing health systems by the consolidation of the health insurance system, financing of medical care for

Table 2. Examples of information needed for decision making in leprosy control

Type of decision making	Examples of some types of information needed which can be provided by health systems research
At the policy level	
Determining the relative priority for MDT in the national expenditure on drugs	The relative mortality, morbidity, social and economic burden of the major health problems; and the relative effectiveness and acceptability of various drugs.
Integration of leprosy workers into general health services	Educational, sex and age profile of leprosy workers; relative wage and service structures of leprosy workers in comparison with general health service workers; functional analysis of roles that can be reassigned and the type of training needed; attitudes of general health workers and leprosy workers towards integration, etc.
At the programme management level	
Selection of appropriate strategies to improve case holding, e.g. what type of health educational approaches should be used? Should accessibility be improved through mobile health teams or community workers or both?	Attitudes and perceptions of various community groups in relation to leprosy and MDT; geographic patterns of the prevalence of leprosy and of defaulters from treatment; and the relative accessibility of health services; geographic distribution of health personnel in relation to the prevalence of leprosy; availability of local community resources that can supplement the health services, etc.
Operational level	
Improvement of accessibility of health services	Attitudes of general health services personnel and the community towards leprosy and integrated lerposy services; knowledge of the community on availability of services; existing workload of peripheral staffmobile health teams, etc., and their potential to undertake management of MDT, etc.
Improvement of case detection	Proportion of cases registered in advanced stages; knowledge and attitudes of community; knowledge and skills of relevant health staff; availability of adequate laboratory backup for peripheral health staff etc.

the poor, the development of 'health maintenance organizations', and the adoption of medicare, all of which were intended to provide more equitable access to health care.

In Malaysia, a study on the low utilization of a mobile dispensary's services showed that the functions it originally served were now taken over by health subcentres and community nurse clinics that had been constructed subsequently and were now easily accessible to the 40 villages visited by the dispensary because communications had improved. This study led to a review of the mobile dispensary and clinic services in the area and a redeployment of resources.

In another study on the effectiveness of management of hypertensive patients in an outpatient clinic, it was found that for many patients the prescribed treatment regimens were inappropriate; and because of the rapid turnover of doctors, most were unaware of the criteria for management of hypertensives that had been established in that clinic. There was also no system to identify drop-outs, to recall defaulters, or to provide information and counselling for patients and their families. This study formed the basis for a series of planned interventions that improved the percentage of effectively managed hypertensive patients from 55% to 90%.

Many of the problems addressed in the above examples are similar to the issues that affect the implementation of MDT in leprosy control. It is evident that HSR can provide valuable assistance in improving the effectiveness of leprosy control.

HSR USED IN DECISION MAKING AT THE OPERATIONAL LEVEL

The value of HSR in providing information for policy levels and for programme planning is rapidly gaining credence. However, at the midlevel management and operational levels there is little evidence that decision making is based on facts.

Research is often perceived as a grand venture that contributes to a major breakthrough in human knowledge or provides information for far-reaching changes in the health system. The examples quoted above show that HSR is equally useful in providing information for rational decision making at every level in the health system, including the operational level. Decision making at the operational level, e.g. the district medical officer of health, public health nurses, medical assistant, clinical supervisor etc., is affeced by fewer and less complex factors than it is at the higher levels. Therefore the type of information required is generally less complex, and the type of research that can provide such information is also simpler. Experience has shown that many such studies can be designed and conducted by health personnel at district and hospital level, provided they are appropriately trained and are supported and guided by experienced researchers who understand the concept and approaches of HSR.

DO SIMPLE STUDIES' DONE AT HEALTH DISTRICT LEVEL DEMEAN THE LABEL RESEARCH?

It is important to note that simple research should not mean poor quality. HSR studies done at the operational level can be easier to design and execute but will need to adhere to the same basic principles of research as other more sophisticated research.

When more and more health staff become competent in such research and use the findings it will be posible to ensure that the 'scientific method pervades all decision-making in health' and that data and information will be used as the 'rational basis of

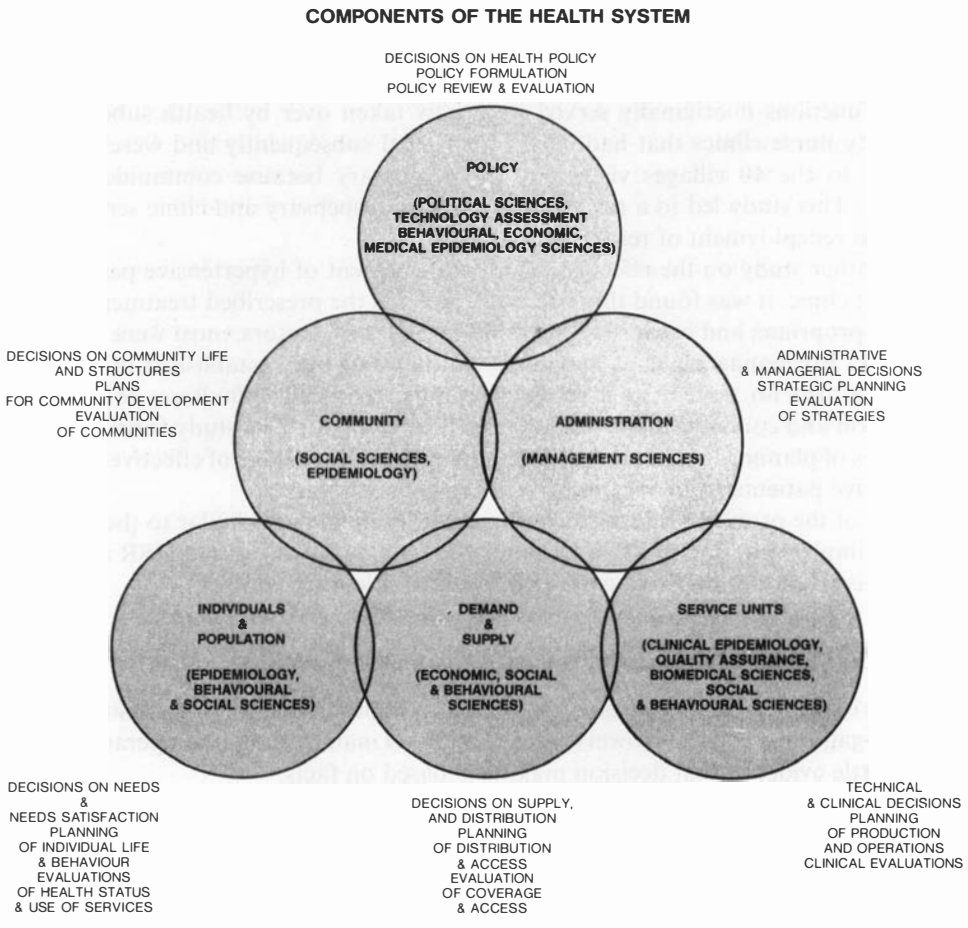

Figure 1. Components of the health system.

health care' as recommended by the Nobel Conference on Health Research and Development (1989).

The nature of HSR

HSR IS MULTIDISCIPLINARY

Since the purpose of HSR is to provide appropriate information for decision making in the health system, it is first useful to consider the health system itself and how various components of the health system interact and are inter-related, so that the design of HSR studies will focus on appropriate and relevant aspects of the problem that is being studied.

One way in which the different inter-related and interaction components of the health system may be depicted is illustrated in Figure 1. For example, a study aimed at reducing 'treatment failures' will need to obtain information on factors within the 'Service Units' (Figure 1) e.g. clinical decisions, health education, drug availability, etc.; 'Administra-

tion', e.g. supervision, monitoring practices, etc; 'Supply and demand', e.g. clinic schedules, transport availability; 'Individuals and populations', e.g. attitudes and beliefs towards leprosy and MDT, economic pressures, etc.

In each of the components it is evident that decision making relates to a different set of concerns, and therefore the nature of the information that is needed is also different. In order to provide the appropriate type of information on issues in each component, the approaches and research techniques from different scientific disciplines, e.g. epidemiology, sociology, health economics, management, etc., are needed. Figure 1 illustrates some of the disciplines that are relevant to concerns in the various components of health system.

It is evident that HSR is multidisciplinary. In large and complex studies this may mean that researchers from different disciplines may need to co-operate, each contributing the relevant concepts and research techniques from their own disciplines in designing and executing the study. In simpler studies, it would be possible for researchers to be trained to apply the basic concepts and techniques from several disciplines, e.g. epidemiology and behavioural sciences, in their research projects.

HSR IS PARTICIPATORY

The participatory nature of HSR is one of its major characteristics. In order to ensure that the research is relevant and appropriate, everyone directly concerned with a particular health or health care problem should be involved in the research project(s). This could include policy-makers, health managers from the health services involved, health care providers and, if relevant, the community itself. This involvement is critical if the research activities are to make a difference:

- if decision makers are only involved after completion of the study, the report may just be shelved ;
- if health staff are only involved in data collection and not in the development of the proposal or in data analysis, they may not be motivated to collect accurate data or carry out the recommendations;
- if the community is only requested to respond to a questionnaire, the recommendations from the study may not be acceptable;
- if professional researchers are not involved in the implementation of recommendations, they may have little concern for the feasibility of the recommendations.

HSR MUST LEAD TO ACTION

Since the purpose of HSR is to provide information for decision making in the health system it must be focused on priority problems and the results must be utilized in decision making.

There are several features that will enhance the likelihood that research findings will be utilized.

Studies should be scheduled so that the results are available when needed for key decisions, otherwise the research loses its usefulness, i.e. *research must be timely.*

Emphasis should be placed on comparatively simple, short-term research designs which probably will yield practical results relatively quickly. Simple but effective research

designs are difficult to develop, but much more likely to yield useful results within the desired time.

The principle of cost-effectiveness is important in the selection of research projects. Research should focus, to a large extent, on low-cost studies that can be undertaken by health personnel at the management and services level in the course of their daily activities.

Results should be presented in formats most useful for administrators, decision-makers and the community. Each report should include:

- a clear presentation of results with a summary of the major findings adapted to the interests of the target audience for the report;
- honest discussion of practical or methodological problems that could have affected the findings;
- alternative courses of action that could follow from the results and the advantages and drawbacks of each.

Evaluation of the research undertaken should not be by the number of papers published but by its ability to influence policy, improve services and ultimately lead to better health.

HSR in leprosy control

Until now the focus of research in leprosy control has been in furthering an understanding of the disease and its epidemiology; and in developing the technology to cure and prevent the disease. The stage has now been reached where it is necessary to focus research on ensuring that the benefits of the progress that has been achieved in terms of knowledge and technology are applied effectively for the benefit of all and not just some leprosy patients. It is HSR that provides the approaches that are needed for this purpose.

HSR is applicable and useful for providing information for the policy making, programme planning and operational levels of leprosy control programmes. It will be an extremely useful support for decision making in relation to implementation of MDT and is highly relevant with regard to current developments in leprosy control.

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Report on the group discussions on the needs and prospects for epidemiological tools in leprosy control

1. State of the art on the epidemiology of leprosy

1.1 INTRODUCTION

The major gaps in the knowledge on the epidemiology of leprosy in relation to control and, consequently, recommendations for epidemiological research and for health systems research were identified.

The recommendations for epidemiological research in leprosy have been divided into the epidemiology of infection, disease and disability. New studies will be required to address some of the recommendations, but, wherever possible, existing data sets (including vaccine trials, drug trials and good control programmes) should be exploited.

1.2 EPIDEMIOLOGY OF INFECTION

There is a continued need for a sensitive and specific assay for *Mycobacterium leprae* infection. New developments in PCR technology and in immunodiagnostic tests may ultimately permit studies of the distribution and determinants of infection in communities, thereby identifying potential sources of transmission, and groups at particular risk of disease, and allowing transmission to be monitored. Efforts should be made to encourage relevant basic research towards such tools, and to facilitate their rapid evaluation in field contexts.

1.3 EPIDEMIOLOGY OF DISEASE

1.3.1 The known determinants of clinical leprosy include age, sex, household contact, geographical location, genetics, BCG and 'socioeconomic factors'. It may be useful to express the associated risks in terms of attributable risks, to define the proportion of clinical cases associated with various factors, for example, what proportion of cases in various communities are attributable to household contact.

1.3.2 The relative importance of intra- versus extra-household contact as a risk factor may change (increase?) as leprosy declines. This could have practical implications for the role of (household) contact surveys in leprosy control. The extent to which present and past household contact with cases, and different family relationships to cases, affect the risk of leprosy thus should be studied in different epidemiological contexts. Efforts should be made to define the proportion of cases which might be

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identified by expanding the definition of contact to include, for example, past household contact and distant relations to known cases.

1.3.3 It is important to analyse the distribution of cases by place of birth as well as by place of residence at onset of disease or registration. These distributions should be interpreted with relation to a control group and/or to information on patterns of migration within the population concerned. This is particularly important for urban areas.

1.3.4 The implications of HIV infection for leprosy (in particular multibacillary disease) incidence, reaction and relapse should be further evaluated. Case control studies are appropriate, with attention to confounding, for example by nonleprosy morbidity and by social factors.

1.3.5 Socioeconomic factors and different ecological conditions are obviously important in leprosy. Efforts should be made to distinguish between various factors associated with low socioeconomic status, for example overcrowding, which may be associated with leprosy risk.

1.3.6 Efforts should be made to identify (immunological) correlates of BCG-induced protection, in order to explain observed differences in vaccine efficacy. The identification of such correlates would have great utility both in predicting the efficacy of BCG in different populations and for the screening of potential vaccine reagents.

1.3.7 The cost-effectiveness of different vaccines and different vaccination strategies, different treatment regimens and treatment strategies including new drugs should be investigated. The use of epidemiological models should form part of the evaluation of cost-effectiveness.

1.4 EPIDEMIOLOGY OF DISABILITIES

Leprosy associated disability is a critically important but understudied aspect of leprosy epidemiology and control. Descriptive studies of the patterns of disabilities in representative samples or populations of leprosy patients should be encouraged. Even more useful would be longitudinal studies of the natural history of, and risk factors for, reactions and their outcome, and clinical trials of various interventions to control reaction and to prevent or reverse disabilities.

1.5 HEALTH SYSTEMS RESEARCH

Leprosy programmes at different levels face operational problems in implementing control. Problem-solving has often been based on nonsystematic and intuitive approaches. It is here that health systems research (HSR) could play an important role by introducing scientific methods for acquiring information which can be used for rational decision making at the operational level. HSR is multidisciplinary, which means that programme managers responsible for such research should seek collaboration from appropriate experts such as social scientists before embarking on HSR. HSR is participatory so that persons concerned and dealing with the problem participate in the research projects. HSR should lead to action and results must be utilized for decision making.

2. Prediction of future trends in leprosy

2.1 NEEDS FOR THE PREDICTION OF FUTURE TRENDS

The ability to predict future epidemiological trends is an important requirement for disease control programmes. At present this is particularly important for leprosy control because of the rapidly changing epidemiological situation as a result of the introduction of MDT. The prediction of trends in leprosy is required for the following purposes.

2.1.1 *Planning*

The prediction of trends in the prevalence of registered cases and in the incidence of new leprosy cases provides a time-frame for future epidemiological changes and a basis for the planning of resources. The estimation of the benefits of control and resource requirements will help to mobilize sustained political and funding commitments in the long term.

2.1.2 *Evaluation*

The comparison of predicted and observed trends facilitates the interpretation of evaluation results in terms of effectiveness of control, both at the global and the local level. The cause of possible unsatisfactory results can be analysed and the control strategy adjusted accordingly.

2.1.3 *Research*

Prediction techniques such as modelling can be a powerful tool to improve the comprehensive understanding of the quantitative aspects of transmission, disease and the impact of control. Another application is the prospective evaluation of alternative control strategies to identify the optimal approach. Prediction of the impact of potential new tools for control, such as vaccination and immunodiagnosis, may help to secure the required funding for the development of such tools.

2.2 METHODS FOR THE PREDICTION OF FUTURE TRENDS

A series of methods are applicable.

2.2.1 *Extrapolation*

Conventional extrapolation has until now been the standard method for prediction. Extrapolation should preferably be based on incidence rates (or case-detection rates, adjusted to the extent possible for the delay between onset and registration). Extrapolation of prevalence rates will often be misleading.

2.2.2 *Proxy trend indicators*

In many areas, population based rates are unavailable or cover only a very short period of time. In such situations, the need arises for a quick assessment of secular trends based on

rather rough data. Previous analyses have shown that age at onset, the proportion of multibacillary cases and sex ratio can be used as proxy indicators of changing trends.

2.2.3 *Simulation modelling*

Simulation modelling combines demography, epidemiology and control measures in one coherent framework. This makes these methods appropriate for the assessment and adjustment of control measures. This includes the explanation of deviations from predicted trends as a result of differences between executed and planned control policies. Computer simulation models can also be useful in optimization by studying the combined impact of different control methods (vaccination, MDT, early case-detection, rehabilitation) on population health.

2.2.4 *Expert opinion (Delphi)*

Expert opinion, such as the Delphi technique, is necessary when data are lacking. These methods are being used increasingly in health planning but they are of limited value for quantitative predictions of trends.

2.3 REQUIRED DATA FOR TREND PREDICTIONS

To enable the prediction of trends, the following data are required: Minimal requirement (data to be collected at registration):

—Date of registration
—Date of birth (or estimated year of birth)
—Sex
—Place of residence
—Multibacillary or paucibacillary

If feasible, the following data should also be collected:

—Stated year of onset
—Disability at registration
—Date of start of treatment
—Type of treatment
—Treatment compliance
—Date of discharge or death
—Reasons for discharge
—Date of relapse
—Treatment of relapse
—Date of discharge after relapse

Information on the progression of disability would be of additional value for estimating the public health importance of leprosy.

Preferably all methods should be based on incidence rates necessitating population data on age and sex. However, in the lack of such data, proxy indicators could be based on proportions calculated on the basis of the patients registered.

2.4 CONCLUSION

A situation of declining incidence rates together with the large scale introduction of MDT calls for the utilization of methods for the prediction of future trends. Conventional extrapolation is the simplest prediction method but it is limited in scope. Methods based on proxy indicators give more refined predictions and better possibilities for interpretation. Simulation modelling, the most complex method, can in addition address questions about changing epidemiological trends resulting from the effect of control measures applied to the target population.

Given the importance of reliable trend predictions, the considerable expenditures involved in collecting large amounts of evaluation data, and the relatively modest investments required for further development and application of prediction methods, the meeting considered that further research in this field should be cost-effective. The following specific recommendations for further research were made.

2.5 RECOMMENDATIONS

2.5.1 Methods for prediction of trends should be further developed and validated, and be used in a more systematic manner in the monitoring and evaluation of leprosy control. In each instance the least complex method should be used which is valid for that particular purpose.

2.5.2 Simulation models for leprosy control should be further developed by incorporating current simulation techniques and decision sciences methodology. The development and testing of these models should be a multi-disciplinary effort, involving at least scientists responsible for epidemiological field research and control of leprosy, and scientists with experience in epidemiological modelling.

2.5.3 In implementing the above recommendations, optimal use should be made of existing epidemiological data sets for leprosy.

3. **Assessment of the leprosy problem**

3.1 INTRODUCTION

The issues relating to the assessment of the leprosy problem were limited to the quantitative estimation of prevalence and incidence of leprosy.

3.2 DEFINITION OF A CASE

The Sixth Report of the WHO Expert Committee on Leprosy (Technical Report Series 768, 1988) defined a case of leprosy as 'a person showing clinical signs of leprosy with or without bacteriological confirmation of the diagnosis, and requiring chemotherapy'. There was a consensus that for quantitative assessment a leprosy case was a person needing chemotherapy. It is recognized that it is difficult to predict which lesions would self-heal and that keeping such persons under observation would pose problems for assessment; therefore they should be considered as cases needing chemotherapy. Relapses should also be considered as cases but those who had completed chemotherapy should no longer be considered as cases.

3.3 ASSESSMENT OF INCIDENCE

As the incidence cannot be assessed by direct measurement it should be inferred by indirect methods. Detection rates should be taken as the best estimate of incidence until better methods are developed.

3.4 ASSESSMENT OF PREVALENCE

The prevalence is an index which is more amenable to direct measurement. There is a need for methods of estimating prevalence which would be rapid and economical. The period following the introduction of MDT poses special problems because of the rapid decline in prevalence, improved ascertainment of cases, and increased sensitivity of diagnosis.

3.4.1 Total population examination is both extremely expensive and unnecessary.

3.4.2 Sample surveys are the standard method of obtaining information about disease prevalence—however, the required sample sizes are extremely large because of the uneven distribution of leprosy. Sample surveys in leprosy are expensive and both sampling and non-sampling errors are likely to be large. Therefore such sample surveys should be carried out with extreme care and in exceptional circumstances.

3.4.3 Methods of estimating prevalence through extrapolation from registered cases should especially be considered. The number of cases in registers have been shown to correlate with estimated cases, as revealed by sample surveys. The extrapolation factor will be different following the introduction of MDT.

3.4.4 Rapid community surveys is another economical means to assess prevalence. In this procedure an intensive effort is made to educate the population of the community on the signs of leprosy and the efficacy of modern drugs. The survey team then visits the community, and with the help of key local personnel, individuals with suspected signs are examined in a central place.

3.5 ASSESSMENT IN THE LATER PHASES OF ELIMINATION

Towards the elimination stage, priorities will shift towards the rehabilitative needs of patients, both under treatment and those who have completed treatment but have disability. The emphasis will be on the assessment of disability due to leprosy.

4. **Basic data requirements for the evaluation of leprosy control programmes**

4.1 INTRODUCTION

The Report of the WHO Study Group on Epidemiology of Leprosy in Relation to Control (TRS 716, 1985) listed standardized indicators to evaluate leprosy control activities. Many of these were found to be extremely useful during the initial few years of MDT implementation. However, the number of indicators is far too many for routine applications under field conditions in most leprosy endemic countries. By now the efficacy of MDT regimens for both PB and MB has been clearly established by leprosy control programmes. There is now need to focus on the most essential indicators which could assist in decision making for leprosy programmes implementing MDT.

Essential indicators need to be relevant to assess the magnitude of the leprosy problem

and the effectiveness of leprosy control measures. Based on recommendations made during the Consultation on Technical and Operational Aspects of Leprosy held at Male, Maldives, in June 1990, six indicators are recommended as the most essential. A number of other important indicators which are considered useful are suggested for application in programmes which are capable of collecting and reporting the data required for the compilation of these indicators. These are listed as optional indicators.

4.1.1 *Essential indicators*

The essential indicators have been identified based on their relevance and feasibility at both national and peripheral levels. Data required to calculate these indicators should be collected by all leprosy control programmes. It is recommended that these indicators are calculated once a year. The first two indicators should not only be reported as rates, but also in absolute numbers.

4.1.1.1 *Prevalence rate.* The prevalence rate is defined as the number of registered cases at the end of the year divided by the population in which the cases have occurred. The population should refer to the most recent, consistent and reliable source. This indicator reflects the magnitude of the problem, and helps in planning and evaluation of control measures. It is also necessary for evaluating workload, but in that respect it must be interpreted in conjunction with the new case detection.

4.1.1.2 *Case detection rate.* This rate is defined as the number of new cases detected during a year divided by the population in which the cases have occurred. This indicator is the most appropriate to estimate the true incidence of the disease in a given population, when analysed in conjunction with the proportion of disabled patients (grade 2) among newly detected cases. This should be specified by the type of the disease (PB/MB).

4.1.1.3 *Disability rate among newly-detected cases.* This is defined as the proportion of newly-detected cases with grade 2 disability among the total number of newly-detected cases during the year. This indicator reflects the effectiveness of the programme in terms of early case finding and the level of community awareness of the disease.

4.1.1.4 *MDT coverage.* This is defined as the proportion of cases registered for multidrug therapy at any time during the year, among the total number of cases appearing on the register during the year. The denominator is the total number of cases that was on the treatment (=monotherapy+MDT) register at any time during the year.

This indicator reflects the programme performance in achieving full MDT coverage and helps to set targets.

4.1.1.5 *Number of patients having completing MDT during the years.* In those programmes in which the recording and reporting system does not yet allow the collection of such information or the duration of MDT is ill-defined, the number of patients completing MDT during the year could be used as a proxy indicator.

Where possible, the MDT completion rate should be calculated. It is defined as the proportion of patients who have completed their MDT among patients expected to complete their MDT. This must be calculated separately for MB and PB cases.

This indicator is important to evaluate the patient compliance to treatment as well as the programme performance in providing adequate MDT.

4.1.1.6 *Number of patients relapsing after MDT.* Careful recording and reporting of relapses is important for use as a crude marker of treatment failures which could indicate the need for a special study.

4.1.2 *Optional indicators*

These indicators may be used for specific purposes wherever possible. Additional resources may be needed for collection of some data required for these indicators.

4.1.2.1 *Prevalence rate by type—PB/MB*
4.1.2.2 *Proportion of children among newly-detected cases*
4.1.2.3 *New cases, specified by mode of detection*
4.1.2.4 *Incidence of new disability among registered cases*
4.1.2.5 *MDT coverage in new patients*

4.1.3 *Indicators for use in the later phases of elimination*

In this situation the most relevant indicator is the total number of new cases and relapsed cases detected during the year. In this era indicators reflecting the prevalence of leprosy related disabilities will be important because of the shift in priorities towards monitoring and managing rehabilitative needs of patients.

Appendix

This table illustrates how the indicators are calculated. It is not intended to replace existing reporting forms.

	Population			Year			
	Registered cases at the end of the previous year	New cases detected during the year		Cases on MDT during the year	Completed MDT during the year	Registered cases at the end of the year	Relapses after completion of MDT
		With disability grade 2	Without disability grade 2				
PB	a	b	c	e	j	p	l
MB	f	g	h	i	k	q	m
Total	a+f	b+g	c+h	e+i	j+k	p+q	l+m

1. Prevalence (rate)

   —prevalence $p+q = \frac{p+q}{\text{population}} \times 10{,}000$

2. Case detection (rate)

   —total number of new cases $= b+g+c+h$

   —percentage of MB cases $= \frac{g+h}{b+g+c+h} \times 100$

   —case detection rate $= \frac{b+g+c+h}{\text{population}} \times 10{,}000$

3. Disability rate among newly detected cases

   $= \frac{b+g}{b+g+c+h} \times 100$

4. MDT coverage

   $= \frac{e+i}{a+f+b+g+c+h} \times 100$

5. Number of relapses after MDT during the year (Absolute number)

   $= l+m$

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Major Conclusions and Recommendations

The WHO International Meeting on Epidemiology of Leprosy in relation to Control reviewed the state-of-the-art of epidemiology and discussed issues relevant to leprosy control, particularly in terms of changing needs following the widespread implementation of multidrug therapy (MDT) and the declining trends in prevalence of the disease. The following are the major conclusions and recommendations of the meeting.

1 The need for rapid assessment of the leprosy prevalence situation, particularly before introducing MDT, was recognized. As sample surveys are not feasible in most situations other methods of estimating prevalence through application of extrapolation factors were considered suitable.
2 The need for making predictions for the future trends was recognized for the purpose of planning, including resource mobilization, evaluation and research. It was recommended that methods for prediction of trends, including simulation models, should be further developed through a multidisciplinary effort and by making optimal use of existing epidemiological data sets.
3 The leprosy evaluation indicators developed at earlier WHO meetings were reviewed and six essential indicators were recommended for routine programmes. Optional indicators were also recommended for more developed control programmes.
4 The meeting identified some of the more important research areas in epidemiology of leprosy including risk factor studies for the disease and leprosy-related disabilities, the influence of HIV infection in leprosy, cost-effectiveness of different vaccine and therapy strategies, and correlates for protective effect of vaccines.
5 In view of the leprosy elimination goal adopted by the World Health Assembly and the rapidly changing situation the meeting strongly recommended strengthening of epidemiological capabilities of leprosy control programmes. It also recommended that problems at the operational level of leprosy control should be solved through systematic approaches such as health system research.

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