

REPORT

of the

INTERNATIONAL LEPROSY ASSOCIATION

TECHNICAL FORUM

Paris

25 – 28 February 2002

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Summary of the Report of the ILA Technical Forum

Introduction

Tremendous progress has been made in the control of leprosy, particularly since the adoption of multi-drug therapy (MDT) as standard treatment policy. However, despite a dramatic reduction of the number of leprosy patients registered for treatment, the number of newly detected cases at the global level has not shown a comparable decline. Moreover, other problems remain to be solved. In recent years, a number of new technical policies aimed at simplifying the diagnosis and treatment of leprosy have been recommended for application in the field. The implications of some of these policies appeared to require further discussion, in the light of evidence from research. To accomplish this, the International Leprosy Association (ILA) organized a Technical Forum, consisting of 16 experts in leprosy from 11 countries, to review critically the strategic issues related to leprosy control and the major technical policies being applied in the field.

Methods

An organizing committee developed a set of questions addressing important issues in the field of leprosy. A systematic search of the literature was carried out, using these questions to define the parameters of the search, and searching four health-related bibliographic databases covering the literature from the year 1966 onwards, as well as the bibliographies of papers already identified and the “gray literature”, and contacting key researchers.

Some 7000 titles and abstracts were read, from which more than 800 studies were selected as relevant. The critical studies have been graded in terms of the strength of the evidence, based on an objective assessment of the design and quality of each study, and a subjective judgment of the consistency, clinical relevance and external validity of the entire body of evidence. The Forum has produced evidence-based recommendations for leprosy control activities (graded EB). For those issues for which evidence was found to be lacking, the Forum has produced recommendations based on best practice (graded BP). Finally, the Forum has identified those areas requiring further research (graded R).

Conclusions and recommendations

Global situation of leprosy

Actual prevalence is likely to differ significantly from available figures, which are based on the patients registered for treatment. In addition, there are many people living with the consequences of leprosy. Despite a dramatic reduction of the number registered cases, the global new-case detection-rate has not declined. Furthermore, there is no evidence that, once a predefined level of prevalence rate is reached, leprosy will necessarily die out.

It is very likely that significant numbers of new patients will continue to present for many years. Thus, it is essential to ensure that leprosy control activities be sustained, even in countries or areas that have officially reached the elimination target (BP).

Diagnosis and classification

Approximately 70 per cent of leprosy patients can be diagnosed by means of the single sign of skin patches with sensory loss, and this sign of leprosy should be taught as widely as possible. However, 30 per cent of patients, including many multibacillary (MB) patients, do not present with this sign. Enlargement of one or more nerves is an important additional sign, to be supplemented by skin-smears, if these are available and of assured quality. This has implications for training: peripheral health workers should be taught to suspect leprosy, by becoming familiar with the typical appearance of leprosy skin lesions. Patients with suspicious lesions that are not anesthetic should be referred. Health workers at the first referral level must be able to diagnose almost all cases of leprosy among suspects referred to them (EB).

The skin-smear remains the most accurate means of classifying leprosy in the field. In practice, however, classification can be based on counting the number of skin lesions: paucibacillary (PB) ≤ 5 patches; MB > 5 patches (EB).

Further research into easily applicable and cost-effective tests that would be useful for identifying *Mycobacterium leprae* infection and diagnosing leprosy should be continued (R).

Chemotherapy

The 24-month MDT regimen for MB patients and the six-month regimen for PB patients have been found to be highly effective for routine application in the field (EB). Currently, almost all MB patients are being treated by 12-month MDT; however, very little information is available regarding the rate of relapse among patients treated by this regimen. Therefore, field programs with adequate facilities should monitor the relapse rates. Surveillance among relapsed patients for the emergence of rifampicin resistance should be carried out by special centers (R).

Although a shorter, common regimen for both PB and MB leprosy is desirable, such a regimen must first be studied in controlled trials, with relapse as the outcome, before it can be implemented (R).

Nerve function should be included as an outcome measure in chemotherapy trials in leprosy (R).

The system for delivery of MDT should be patient-friendly. Flexibility is important, but regular contact between the patient and the health worker should be maintained. Only in exceptional cases, in which the patient cannot be seen monthly, should more than a one-month supply of MDT blister-packs be provided (BP).

Health workers should actively trace absentees and encourage them to complete their treatment as early as possible, instead of passively awaiting their return and removing them from the register as defaulters after an absence of 12 or more consecutive months (BP).

Prevention of disability and rehabilitation

Early diagnosis of leprosy and treatment with MDT reduces the frequency of nerve function impairment (NFI). However, MDT will not prevent all NFI, and the magnitude of the impact of MDT on NFI is dependent on *early* case-detection and treatment (EB).

During MDT, nerve function should be assessed regularly using standard methods. PB patients with existing NFI and MB patients should be carefully monitored for new NFI, as they are at greatest risk. Steroids are recommended for the treatment of reactions and NFI of recent onset; the expected recovery rate for nerve function is approximately 60 per cent (EB). Relevant training and a supply of steroids should be assured.

Research is recommended to identify the optimal steroid regimen, to develop alternative and more effective treatments for reactions and recent NFI, and to determine indications for treatment. Further research is recommended on the use of prophylactic steroids in preventing NFI (R).

Teaching and empowering patients in self-care is an effective activity, which should be part of all leprosy programs. The use of locally acceptable, appropriate footwear is a cost-effective intervention for those with loss of plantar sensation (EB).

Socio-economic rehabilitation, which requires participation by client, family and the community, is valuable for selected clients, and is best delivered through general, community-based rehabilitation programs (BP).

Epidemiology and organization of leprosy services

There is no consistent evidence that the introduction of MDT has accelerated the decline of the incidence of leprosy. Whereas early diagnosis and regular treatment by MDT will remain the cornerstones of leprosy control for the foreseeable future, additional strategies should be developed, based on better understanding of the epidemiology of the disease (R).

Vaccination with BCG as part of childhood immunization must be continued in countries in which leprosy still exists. Repeated BCG might be considered for individual protection of contacts of leprosy patients (EB).

Because chemoprophylaxis with dapsone has been shown to be an effective way to reduce the incidence of leprosy, particularly among household contacts, the possible role of chemoprophylaxis based on bactericidal drugs should be further studied (R).

More research is needed, particularly on transmission of *M. leprae*, the role of subclinical infection, progression from infection to disease, and trends of incidence of the disease, including the impact of MDT (R).

Prevalence alone is of limited value as an indicator of leprosy control. The new-case detection-rate may be a better indicator; this rate should be analyzed in conjunction with other indicators. The treatment completion rate is an important indicator of the effectiveness of patient management (BP).

To guarantee sustainable leprosy services, leprosy control programs should be integrated within the general health services. The process of change from a vertical to an integrated program should be carefully planned and adapted to the local situation. An uninterrupted supply of anti-leprosy drugs must be guaranteed. Field procedures, including recording and reporting, must be simplified (BP).

Where case-detection rates are low, a focused approach is appropriate, whereby services are provided mainly in selected general health facilities in the areas in which leprosy still occurs. The skills of health workers will be limited mainly to suspecting leprosy. Referral facilities should confirm the diagnosis and begin treatment. Continuation of treatment could be delegated to the peripheral health facility serving the community in which the patient resides. The resources devoted to leprosy must be in balance with those required for other, often much more serious, public health problems (BP).

Training of all categories of staff involved in leprosy control should be task-oriented. Leprosy should be included in the curricula of medical faculties and paramedical schools. Every major leprosy-endemic country should have at least one center with expertise for training of specialized staff (BP).

Information-education-communication (IEC) activities, especially those employing participatory approaches, result in increased knowledge, change of behavior, and reduction of stigma (EB). Studies should be carried out to identify the methods that are most cost-effective under different conditions (R). Before IEC activities can be implemented, effective MDT services should be already available in the area. Combining IEC for leprosy with that for other health problems is cost-effective, and does not set leprosy apart (BP).

Leprosy-elimination campaigns (LECs) can play an important role in the process of integration. Case-finding in LECs must be based on self-reporting to the general health staff (BP). In leprosy endemic areas in which there is no health infrastructure, innovative, situation-specific strategies for diagnosis and delivery of MDT should be developed.

These activities should be combined, wherever possible, with other special initiatives to address other health problems (BP).

Preface

As the President of International Leprosy Association (ILA), which is in the process of making major changes of its structure and activities, in order to become more sensitive, relevant and capable of meeting the changing needs of global leprosy problems, I am happy to present the outcome of one recent innovative undertaking, the ILA Technical Forum, which was convened in Paris in late February, 2002.

As the introduction of this report states, the ILA felt it imperative to organize such a Forum now, in order to respond to the need for clear and sound guidance for their activities primarily in the area of leprosy control in the field, felt by leprosy workers, for whom the 7th Report of the WHO Expert Committee on Leprosy, published in 1998, was no longer adequate.

Before deciding to organize the Forum, we requested that WHO hold the 8th meeting of the Expert Committee soon, rather than waiting for another five years to maintain the usual 10-year interval. A negative response from WHO compelled us to organize our own meeting of experts in leprosy from different parts of the world, experts whose individual and collective expertise is fully comparable to that of any group of experts that WHO has convened in the past, or was capable of organizing now or in the near future.

As stated in the Summary of the Report, we were particularly keen to obtain and summarize the available evidence, which would serve as the basis of the recommendations produced by this Forum, so that the recommendations would be both trustworthy and useful. In the search for, and the selection of the documentary evidence, the Forum received excellent and critically important support from INFOLEP in Amsterdam and from the Department of Public Health of the University of Aberdeen Medical School in Aberdeen, Scotland. We are most grateful for this support.

The ILA is proud to publish the Summary of the Report of the Technical Forum in English, French Spanish and Portuguese, and the full Report in English as a supplement to the March number of the International Journal of Leprosy (IJL), its official organ. In addition to the subscribers to the IJL, all of the participants in the forthcoming XVIth International Leprosy Congress, to be held in Brazil in August, 2002, will receive a copy at the time of registration.

I am most happy to acknowledge the decisions by Leprosy Review; Indian Journal of Leprosy and Bulletin de l'ALLF to publish, along with their regular publications, the full Report of the Technical Forum, simultaneously with its publication in the IJL, thus ensuring the wide distribution that this Report deserves. In addition to publication of the full Report in English, Leprosy Review is publishing Spanish and Portuguese versions of the Summary of the Report, while Bulletin de l'ALLF is publishing the entire Report in French.

I wish also to extend our thanks to the ten member organizations of ILEP, who generously supported the Technical Forum financially, and I sincerely hope that the Report we have produced meets their expectations.

If this publication contributes to the strengthening and improvement of the multitude of leprosy activities undertaken in the world as we hoped, all of us involved in this undertaking will feel our effort, which was not inconsiderable, well rewarded.

Dr. Yo Yuasa
President, ILA

Introduction

1 Background and Objectives

Since the seventh meeting of the WHO Expert Committee on Leprosy (¹), held in 1997, a number of new technical policies aimed at simplifying the diagnosis and treatment of leprosy have been recommended for application in the field (^{2,3}). The implications of these new policies for leprosy control have not been systematically examined. In addition, a number of important issues that may have profound impact on leprosy control -- *e.g.*, the basic concept of leprosy elimination -- require further discussion.

Currently, an appropriate forum in which to review these issues and to prepare recommendations and technical guidelines does not exist. However, the effort to control leprosy cannot afford to await the eighth meeting of the WHO Expert Committee on Leprosy. For this reason, the convening of a technical forum, in which important issues related to leprosy control may be discussed, was urgently needed.

That the International Leprosy Association (ILA) had never organized technical meetings other than international or regional leprosy congresses by no means suggests that it should not or could not take such an initiative. During the past few years, its members have been seriously discussing reform of the ILA, and many have expressed their beliefs that, as a professional association, the ILA should play a more active role in the day-to-day activities of leprosy control. Organizing a technical forum not only conformed perfectly with one of the objectives of ILA -- *i.e.*, “...to help in any practicable manner the antileprosy campaign throughout the world” (⁴), but also marks an important step in its reform.

There are numerous precedents for technical recommendations or guidelines for a number of diseases being issued by professional associations rather than by governmental or inter-governmental organizations. If the ILA has any strength, it is the technical expertise of its members; virtually all of those recognized as experts in leprosy, regardless of affiliation, are members of the ILA, including many who have played leading roles in the major international and regional meetings on leprosy, including those of the WHO Expert Committee on Leprosy. Therefore, the ILA is very favorably situated to convene a high-level technical meeting with participation of the most recognized experts.

The objectives of the technical forum are to:

- review critically the important issues related to leprosy control and the major technical policies being applied in the field;
- produce evidence-based recommendations for leprosy control activities;
- where evidence is lacking, produce recommendations based on best practice; and
- identify those areas requiring further research.

2 Methods

An organizing committee, which met twice during 2001, was charged with the responsibility of preparing a working document, which would form the basis of the discussions of the Forum. The committee developed a set of questions that were considered to represent important areas of change in the field of leprosy. These questions are listed in Annex 1.

In preparing the working document, a systematic search of the literature was carried out by researchers at the University of Aberdeen, working in collaboration with INFOLEP, using the set of questions to define the parameters of the search, and using four health-related bibliographic databases covering the literature from the year 1966 onwards, as well as the bibliographies of papers already identified, searching the “gray literature”, and contacting key researchers in the various disciplines. A potential limitation of this approach is the so-called publication bias, as a result of which studies with positive or significant findings are more likely to be published.

Approximately 7000 titles and abstracts were read for relevance. From among these, 837 studies were selected and distributed to the committee members who were responsible for writing the relevant chapters of the working document. Thus, the recommendations contained in the working document are supported by a variety of published papers and studies. These critical studies were examined in order to grade the strength of the evidence supporting each recommendation, based on an objective assessment of the design and quality of each study, and a subjective judgment of the consistency, clinical relevance and external validity of the whole body of evidence (5).

The guidelines used in this review are those recommended by SIGN⁽⁶⁾, having been developed by the U.S. Agency for Health Care Policy and Research⁽⁷⁾ and employed extensively in systematic reviews. The grading system is explained in more detail in Annex 2; briefly, recommendations graded “A” are based on evidence from randomized controlled trials, those graded “B” involve evidence from other well-designed studies, and those graded “C” are based solely on expert or experienced opinion.

For this report, a systematic review of the literature was carried out for each of the questions posed. The computerized information retrieval systems used to search for relevant information were Medline, Cinahl, EMBASE and Healthstar, covering the period 1966-2001, and restricting the search to studies on humans. The key words used differed for each of the questions posed. Experience in other fields has indicated that searches of the electronic databases identify only about half of the relevant studies⁽⁸⁾, so this approach was augmented by:

- searching the ‘gray literature’, the non-significant research findings, which are rarely accepted for publication, and which tend to remain in internal departmental reports;
- searching bibliographies of studies identified from the computer-based searches;
- contacting key researchers in the field;
- hand-searching key publications; and
- exploiting other resources (*e.g.*, speaking with colleagues and other experts).

The abstracts identified by the electronic search were assessed to determine whether each article met predetermined eligibility criteria. All abstracts or titles that appeared to meet the eligibility criteria were retrieved. If, given the information available, it was determined that the abstract definitely did not meet the criteria, it was rejected. If, on the other hand, the title or abstract left room for doubt in the reviewer’s mind, the full article was retrieved.

For abstracts that had been identified as potentially eligible, the complete articles were assessed to determine if the inclusion criteria had been met. A relevance form (Annex 2) was used to insure that the criteria had been applied in a standard way, and a data-extraction form was employed to record data from the studies included.

Literature cited

¹WHO Expert Committee on Leprosy. Seventh Report. WHO Technical Report Series no. 874, World Health Organization, 1998, Geneva.

²World Health Organization. 2000. Guide to the elimination of leprosy as a public health problem. WHO/CDS/CPE/CEE/2000.14.

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Table. Numbers of abstracts and complete articles reviewed

Question	Database							
	Medline		Embase		Healthstar		Cinahl	
	Abstracts	Complete articles	Abstracts	Complete articles	Abstracts	Complete articles	Abstracts	Complete articles
1-3	234	55	310	41	0	0	0	0
4, 5	476	79	346	43	3	0	3	1
6	255	74	128	40	0	0	1	0
7	37	12	27	2	0	0	0	0
8	16	3	24	11	0	0	0	0
9	106	32	113	27	0	0	0	0
10	448	49	255	27	2	0	0	0
11, 12	142	34	115	14	1	0	1	0
13	597	50	272	22	2	0	1	0
14	362	13	597	44	3	0	0	0
15	57	18	105	21	0	0	1	1
16	4	2	14	5	0	0	1	0
17	382	48	333	49	3	0	4	0
18	807	31	410	19	6	0	7	0
Total	3923	500	3049	365	20	0	19	2

ANNEX 1. QUESTIONS

Diagnosis

1. What are the sensitivity and specificity of the diagnosis of leprosy based solely on skin lesions with loss of sensation?
2. What are the sensitivity and specificity of classification based solely on counting the number of skin lesions, using skin smear positive cases as the gold standard?
3. Can the slit skin smear be replaced for field use by any other tool for the purposes of diagnosis and classification?

Treatment

4. What is the treatment completion rate in patients given unsupervised, accompanied MDT, under different field conditions?
5. What is the risk of new nerve damage in these patients?
6. What are the relapse rates in patients with various initial BI's, after 12 or 24 months of MDT?

Prevention of Disability

7. Is early detection of leprosy cases, with prompt MDT, effective in prevention of impairments?
8. Does early detection and treatment of reactions and new nerve damage prevent impairment? If so, what are the best methods of detection and the thresholds for treatment?
9. Does steroid prophylaxis prevent impairment?
10. How effective are interventions in self-care, footwear provision and socio-economic rehabilitation?

Epidemiology and Control; Organization of Leprosy Services

11. Are untreated MB cases the only significant source of infection?
12. What evidence is there for the effectiveness of interventions to stop or reduce the transmission of leprosy? Consider BCG, MDT, chemoprophylaxis, segregation and increased living standards.
13. What are the best indicators of trends in incidence of leprosy?
14. How can leprosy control activities best be sustained? What place can LEC's play in promoting sustainable services? What can be done where there is no health care infrastructure?
15. What is the evidence that IEC interventions can change the knowledge, attitudes and behavior of the public with regard to leprosy – especially with regard to self-reporting, reduction of stigma and compliance?
16. Which methods are most cost-effective?

17. How can appropriate and effective training be developed for all grades of staff involved in leprosy control?

18. For evaluation purposes, what are the minimum program data that must be recorded in an integrated setting?

Annex 2. DATA EXTRACTION FORM

BIBLIOGRAPHIC DETAILS

Authors:

Journal:

Title:

Year Volume Issue Page Numbers Country of origin

Reviewer 1

Reviewer 2

SECTION:

QUESTION:

SEARCH DETAILS

MEDLINE EMBASE CINAHL Healthstar OTHERS

Identified from reference checking (which article?)

Refman Database/s

ID No.

TYPE OF STUDY

- Systematic review with meta-analysis of randomized controlled trials
- Randomized control trial
- Non-randomized study
- Quasi-experimental study
- Review article
- Comparative study
- Cross sectional study
- Correlation study (ecological study)
- Case-control study
- Expert committee reports or opinions
- Clinical experiences
- Others with details

QUESTION ADDRESSED:

Sample size:

Setting of the study:

Age and sex of the patients:

Methodology:

Results:

Conclusions:

Reviewer's Comments:

GRADE OF RECOMMENDATIONS

- Grade A
 - Ia Evidence obtained from meta-analysis of randomized controlled trial
 - Ib Evidence from at least one randomized controlled trial
- Grade B
 - IIa Evidence from at least one well-designed controlled study without randomization
 - IIb Evidence from at least one other type of well-designed quasi-experimental study
 - III Evidence from well designed non-experimental descriptive studies, such as comparative, correlation and case studies
- Grade C
 - IV Evidence obtained from expert committee reports or opinions and/or clinical experiences of respected authorities

The Global Situation of Leprosy Control at the Beginning of the 21st Century

In May 1991, the World Health Assembly adopted as an objective the “elimination of leprosy as a public health problem by the year 2000” ⁽¹⁾, elimination being defined as a prevalence of less than 1 per 10,000 population. Ten years later, at the World Health Assembly in May 2001, it was claimed that this target had been attained at global level ⁽²⁾. The most recent statistics on registered and new cases reported at country level, published by WHO in January 2002 ⁽³⁾, showed totals of 597,232 registered cases and 719,330 new cases detected during the year 2000. Although these data take into account only those countries with more than 100 registered cases, the global prevalence of registered leprosy cases is now slightly below 1 per 10,000. This is indeed a great achievement, because it represents a reduction of 90 % from the prevalence of 12 per 10,000 reported in 1985. Today, virtually all registered patients are treated by MDT, thanks to which a total of approximately 11 million patients have been cured. Altogether, 107 of the 122 countries considered to be endemic in 1985 have achieved the elimination target. Approximately 83 per cent of the registered cases live in only six countries -- India, Brazil, Myanmar, Indonesia, Madagascar and Nepal.

In interpreting these data, however, the following points must be considered:

- the figures representing the situation at the global level take the global population as denominator, whereas leprosy is virtually absent from a number of (mainly the industrialized) countries;
- some countries had not reached the elimination target by the end of 2000, and may have difficulties reaching it by the year 2005;
- the figures mentioned represent the prevalence of registered cases. However, this can be very different from the actual prevalence, because coverage of the population by health services is far below 100 per cent in some countries, leading to gross under-detection in certain areas ⁽⁴⁾, and because, even when the population is reasonably well covered by the health services, there may be significant under- or late detection ^(5,6);
- it is obvious that leprosy remains an important problem in some countries with a registered prevalence less than 1 per 10,000, either at the national level because of gross under-detection, or in provinces or states within countries, in which the prevalence may remain high;
- the decrease of prevalence is attributable primarily to “cleaning” of the registers (discharge of cured or defaulting patients) and to shortening the duration of treatment, and is not a consequence of reduction of the transmission of *Mycobacterium leprae*;

- the number of new cases detected annually has remained quite stable during the last 15 years. It reached a maximum in 1998, and then slowly decreased in the course of the two following years. However, it is still significantly higher than it was five to ten years ago. The increase of the annual new-case detection-rate observed during the recent years may be attributed primarily to massive case-detection campaigns carried out in several endemic countries, most notably India, and to the expansion of geographical coverage by the leprosy services (⁷⁻⁹).

Leprosy is a disease of importance to the public health mainly because of the disabilities it causes. It has been estimated that, at the global level, there may be 3 million people with leprosy-related impairments and disabilities (¹⁰). For the year 2000, it was reported that 4 per cent of the newly detected patients for whom information was available presented with grade 2 disabilities (³). That proportion was smallest (3 per cent) in South-East Asia, but reached 9 per cent in that region when India was excluded. It was 11 per cent in Africa and 5 per cent in the Americas; however, no data were available from Brazil, where that proportion reached 7 per cent in 1998 (¹¹). Although grade 1 disabilities are important, because patients with disabilities of this degree are at serious risk of developing more serious impairments, data are usually not available.

Literature cited

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The Diagnosis and Classification of Leprosy

1 Introduction

The accurate diagnosis of leprosy is of fundamental importance to all aspects of leprosy epidemiology, case management and the prevention of disability. Under-diagnosis will allow the continued transmission of the disease and much needless individual suffering, whereas overdiagnosis will involve overtreatment with antibiotics and unnecessary stress and stigma for some people; both will lead to misleading epidemiological statistics.

The diagnosis and classification of leprosy have traditionally been based on the clinical examination, frequently with additional information from skin-smears. Histopathologic examination, inoculation of the mouse foot pad, serologic tests, skin-testing and PCR have been largely confined to research studies, but attempts are being made to develop new tools that will make the tasks of diagnosis and classification easier and more reliable in the field.

The ideal diagnostic test would be simple, would identify all cases (100 % sensitivity), and would be negative in people who do not have leprosy (100 % specificity). Combining individual tests may improve the precision of a diagnostic procedure. Using the “OR” connector (only one sign of several is required for the diagnosis), sensitivity is increased at the expense of specificity, whereas using the “AND” connector (a combination of two or more signs must be present for the diagnosis) increases specificity at the expense of sensitivity.

The sensitivity and specificity of a test can be determined only by comparison with another test known to be reliable -- a so-called “gold standard”. The gold standard is rarely infallible, so the results will always possess a degree of error. It should be noted that, whereas the histopathologic examination may be the most reliable method for confirming a diagnosis of leprosy, it is by no means a perfect test in itself (¹⁻⁴). Similarly, many practical problems affect the reliability of skin-smears (^{5,6}).

2 What are the sensitivity and specificity of the diagnosis of leprosy based solely on various combinations of clinical signs, using biopsy as the gold standard? What contribution can skin smears make to the sensitivity and specificity of the diagnosis?

Three cardinal signs remain the basis for the clinical diagnosis of leprosy (⁷):

- anesthetic skin lesions;
- enlarged peripheral nerves; and
- acid-fast bacilli in the skin smear.

Any one of these signs has been regarded as sufficient for the diagnosis of leprosy (the “OR” connector), so that sensitivity is high. Each sign is also quite specific in itself, so that specificity is high. The most important potential source of error is the reliability of the examination of the individual patient, referred to as inter-observer variation.

This was affirmed by the WHO Expert Committee on Leprosy (⁸) at its seventh meeting in 1997, which defined a case of leprosy as follows: “A case of leprosy is a person having one or more of the following features, and who has still to complete a full course of treatment:

- hypopigmented or reddish skin lesion(s) with definite loss of sensation;
- involvement of the peripheral nerves, as demonstrated by definite thickening with loss of sensation;
- skin-smear positive for acid-fast bacilli.

This definition includes retrieved defaulters with signs of active disease, as well as relapsed patients who have previously completed a full course of treatment, but does not include cured persons with late reactions or residual disabilities” (⁸).

A widely quoted study in India (⁹) examined the agreement in the diagnosis of suspicious skin lesions in 811 children, who were examined separately by two experienced leprologists. Approximately half of the children were eventually diagnosed with leprosy, whereas half were found not to have leprosy. In this group of patients, in which the leprosy was mainly tuberculoid or indeterminate, and which would be expected to include many doubtful cases (^{10, 11}), the leprologists concurred in 90% of cases, indicating that, in experienced hands, these signs represent a reproducible means of diagnosing leprosy.

In a study of the diagnostic efficiency of paramedical workers (PMW) in India, the results were considered disappointing (¹²). However, reexamination of the data reveals that the sensitivity of the PMWs’ examination was 97 % and the specificity 92 %. The 55 cases that were wrongly diagnosed were almost all children with few lesions, the most difficult group to diagnose accurately. The weakness of this study is that the gold standard was the diagnosis made by a medical officer, rather than the results of examination of a biopsy specimen. It can therefore be stated with some confidence that, as traditionally practiced, the cardinal signs represent good diagnostic tools.

As the clinical management of leprosy becomes integrated into the general health services, the majority of patients will be diagnosed and managed by non-specialists. For this reason, attempts have been made to simplify the guidelines for diagnosis by field staff using a single sign – the finding of a skin patch or patches with definite loss of sensation (¹³). Other suspect cases, not diagnosed by this single criterion, may be referred to an appropriate center for further examination. Such suspects will be people with skin

lesions suggestive of leprosy, but without anesthesia; health workers can be taught to recognize such suggestive lesions by the use of photographs and atlases.

This simplified strategy for diagnosis, which could be used in especially difficult situations, and is being routinely applied in many national programs, may lead to significant underdiagnosis, particularly of multibacillary (MB) disease. Underdiagnosis of MB patients is important for two principle reasons:

- MB patients are thought to represent the major source of infection, so further transmission of *Mycobacterium leprae* may occur; and
- because they are at greater risk of reactions and consequent nerve damage, they may succumb to preventable disability, with the accompanying psychosocial sequelae.

Overdiagnosis will result in unnecessary treatment, but, more importantly, the psychosocial consequences of the diagnosis of leprosy should never be minimized. Therefore, the contribution of each of the cardinal signs will be examined.

2.1 Skin lesions with sensory impairment

Hypopigmented or erythematous macules are present in many newly diagnosed leprosy patients, and are often the first clinical sign of the disease. Many other conditions produce similar lesions, however. Therefore, to be specific for leprosy, the lesions must be accompanied by definite loss of sensation. This greatly reduces the sensitivity of the test, especially in MB cases, in which macules are less distinct and less likely to be anesthetic.

The most rigorous study performed in this area was carried out in Malawi, where sensory loss in paucibacillary (PB) lesions proved by histopathologic examination was examined (¹⁴). Although this study may reflect some of the limitations of the histopathologic examination already mentioned, the sensitivity as a diagnostic test of loss of light touch sensation in a lesion was 48.5 % and the specificity 72 %.

Other published studies give higher figures for the sensitivity of this test among PB patients. Figures of 93 % in India (¹⁵), 92 % in Bangladesh (¹⁶) and 86 % in Ethiopia (¹⁷) have been reported. It is likely that the mixture of cases and the stage of disease at which they were examined account for some of these differences. Specificity was not calculated in these studies, as they were not population surveys. However, it is clear that hypesthetic lesions are occasionally seen in conditions other than leprosy, such as chronic dermatitis (¹⁸), which may lead to some overdiagnosis.

Fewer studies have examined anesthetic lesions in MB cases, because there is less perceived difficulty in the diagnosis, using the traditional cardinal signs, including skin-smears (¹⁵). Published figures for the sensitivity of anesthesia in the skin lesions in MB patients are remarkably similar: 49 % in Bangladesh (¹⁶) and 54 % in Ethiopia (¹⁷).

In Ethiopia, the sensitivity of this single criterion taken alone was 70 % for all patients. A large proportion (74 %) of those whose lesions were not anesthetic were smear-positive, and, therefore, represented potential sources of *M. leprae* in the community⁽¹⁷⁾. In other words, employing anesthetic skin patches as the single diagnostic criterion, 30 % of patients may be missed, most of whom will be smear-positive.

2.2 Peripheral nerve enlargement

Thickened nerves generally appear later than do skin lesions. They were found in a greater proportion of new patients in Ethiopia (ulnar nerve enlargement in 68 %) (17), where the patients typically present late, than in India (ulnar nerve enlargement in 23 %) (20), where detection is generally much earlier. The finding of one or more enlarged nerves is more common among MB than among PB patients: in Bangladesh the figures were 96 % and 86 % respectively (16), whereas, in Ethiopia, the corresponding figures were 91 % and 76 % (17). One study in India, which included only early PB patients, found that only 20 % had enlarged nerves (15).

The reproducibility and specificity of the examination for nerve enlargement have been questioned (21). One study in India found good agreement among three experienced senior examiners; it is interesting that the agreement for thickened nerves was better than that for typical macules with sensory loss (22). A second study in India found only moderate reproducibility among eight experienced PMWs (20).

False positive findings may occur because of poor examination technique (21) or because of non-specific enlargement of a nerve, seen in some manual workers (23, 24). A compromise proposed in the recent ILEP Learning Guide (25) is to teach health workers to examine just two nerves, the ulnar and the peroneal, thereby enabling them to detect the vast majority of cases of nerve enlargement (17, 25). The data show that, in Ethiopia, 451 (91 %) of 496 new cases with nerve enlargement had involvement of either the ulnar (137 patients, 27.5 %) or the peroneal nerve (48 patients, 10 %) or both (266 patients, 53.5 %). A balanced view may be to accept as diagnostic of leprosy a thickened nerve with at least one of the following additional signs (17, 26):

- a typical, hypopigmented skin lesion, with or without sensory loss; or
- nerve-function impairment (NFI) typical of leprosy, in particular, sensory loss on the palms of the hands or soles of the feet.

2.3 Neuritic leprosy

Primary neuritic (“pure neural”) leprosy presents as a peripheral neuropathy, in which there are no skin lesions suggesting leprosy. The diagnosis depends on finding definite nerve enlargement and, often, NFI. In general, these patients would be diagnosed by the classical cardinal signs, but not by the single criterion of an anesthetic skin patch. In one study in India, biopsy of a cutaneous nerve was confirmatory in all 158 cases in which it could be done (27), indicating that, in experienced hands, the clinical diagnosis is

very specific. In Ethiopia, this diagnosis was made in 3 (0.5 %) of 594 newly detected patients ⁽²⁸⁾, whereas in India, 179 (4.6 %) of 3853 patients exhibited this form of the disease ⁽²⁹⁾. In Nepal, 8.7 % of new patients in the field were found to have neuritic leprosy ⁽³⁰⁾.

2.4 Slit-skin smears

Skin-smears have traditionally represented one of the cardinal signs of leprosy: when positive, they directly demonstrate the presence of *M. leprae*. The specificity of this examination therefore approaches 100 %. However, the sensitivity of smears alone is low, because smear-positive patients rarely represent more than 50 %, and, sometimes, as few as 10 % of all patients. On the other hand, positive smears indicate the most infectious group of patients. Smears are useful in diagnosing MB patients and relapses; their disadvantages are related to the logistics and reliability of taking, staining and reading the smears.

Whereas the standard of smear-taking and microscopy may not always be very high ⁽⁵⁾, every effort should be made to improve their quality by supervision and continuing education ⁽⁶⁾. The increased use of acid-fast microscopy for the diagnosis of tuberculosis may permit skin-smears for leprosy to be performed with greater reliability.

2.5 Sensitivity and specificity of combinations of cardinal signs for the diagnosis of leprosy

When all three cardinal signs were used in Ethiopia, the sensitivity was 97 % ⁽¹⁷⁾. Specificity was not determined in this study, but the positive predictive value was 98 %. Although few published studies contain sufficient data to permit calculation of the sensitivity of each cardinal sign, the figures presented in Table 1 suggest that any single sign is inadequate as a diagnostic test. The skin-smear does not add greatly to the sensitivity of the diagnosis, because the clinical diagnosis of MB leprosy employing two signs -- anesthetic patches and enlarged nerves -- is generally regarded as straightforward. Specificity is much more difficult to measure, because of the need to include details of all subjects examined who did not have the disease. Thus, it is rarely possible to determine the specificity of diagnostic tests for leprosy from published data.

A study in Malawi ⁽²⁶⁾ examined the certainty of diagnosis, particularly of PB leprosy, assuming that the cardinal signs possess a high degree of specificity when used correctly. It was suggested that the diagnosis is “extremely likely” if any one of the following was found:

- a skin lesion of typical appearance, and definite anesthesia to light touch within the lesion;
- a skin lesion of typical appearance without evidence of anesthesia, but with a definitely enlarged nerve (near to or distant from the lesion);

- a skin lesion of typical appearance without evidence of anesthesia or nerve enlargement, but in a person with sequelae typical of leprosy neuropathy;
- a definitely enlarged nerve together with signs of damage to that nerve; or
- a skin lesion of typical appearance without evidence of anesthesia, but on the face.

Unfortunately, “skin lesions of typical appearance” were not defined. These criteria are very similar to a recent suggestion to use any two of five signs to make a firm diagnosis⁽¹⁷⁾.

2.6 Biopsy

Material from a biopsy specimen may be used for a variety of purposes, including histopathologic examination, studies of immunohistopathology, and “culture” of *M. leprae* in the mouse foot pad. As already indicated, histopathologic examination cannot be regarded as the gold standard: even in the best of hands, a significant proportion of clinically obvious patients will yield negative or doubtful histopathologic pictures. In practice, most studies employ a combination of clinical and histopathologic criteria. The specificity of the histopathologic criteria is high, although it must be noted that it may be difficult to distinguish relapse from reaction in treated PB patients⁽³¹⁾.

Immunohistopathologic techniques offer the possibility of significantly increased sensitivity and specificity of the diagnosis of leprosy. A recent study of PB patients in China showed⁽³²⁾ that staining for the PGL-I antigen was very specific, whereas routine histopathologic examination was generally non-specific; this preliminary finding needs confirmation by additional studies.

2.7 Serology and PCR for diagnosis

The only serological test that has been widely studied is that for anti-PGL-I antibodies. Two methods have been employed: the *M. leprae* particle agglutination assay (MLPA); and an ELISA assay, which has been further refined into a “dipstick” assay. The ELISA or dipstick assay is preferred because of greater specificity⁽³³⁻³⁵⁾. The disadvantage of this assay is its lack of sensitivity, especially for PB leprosy, although studies vary in how close a correlation is found with skin smears^(36,37).

PGL-I antibody testing has been reported to be helpful in the early detection of MB relapse⁽³⁸⁾. It may also provide an overview of the epidemiology of subclinical infection, as opposed to active disease⁽³⁹⁻⁴¹⁾. What has thus far proved more uncertain is application of this test to the early diagnosis of clinical cases⁽⁴²⁻⁴⁶⁾, and to the prediction (either among contacts of known cases or in the general population) of who will develop clinical disease in the future⁽⁴⁷⁻⁵⁰⁾. Newer serological tests based on recombinant technology may eventually overcome these difficulties and be useful in the field⁽⁵¹⁾.

Tests based on the polymerase chain reaction (PCR) are potentially highly sensitive and specific (⁵²), but because they require a sophisticated laboratory, they are not currently applicable except as research tools.

3 What are the sensitivity and specificity of classification based solely on counting the number of skin lesions, using the skin-smear examination as the gold standard?

The spectrum of disease in leprosy has been characterized in a number of clinico-immunopathological classification systems, the most widely used of which is the Ridley-Jopling classification (^{7,53}). Since the introduction of MDT, however, the division of patients simply between PB and MB treatment groups has become normal practice. The most rigorous method of assigning patients to a treatment group is bacteriological, employing the slit-skin smear or biopsy. It should be noted that classification is required because there are two treatment regimens; if developments in chemotherapy lead to one regimen for all, classification will not be needed for this purpose, but it is important to remember that PB and MB cases have been shown to have very different risks for subsequent impairment and disability; classification may therefore remain an important tool.

When MDT was first introduced in 1981, the Ridley-Jopling classification was used as the basis of the new system of classification, with TT and BT cases termed PB, whereas BB, BL and LL cases were termed MB. A BI of 2 or more at any site required that the patient be classified MB, thereby changing the classification of some BT patients. By the time of the Sixth WHO Expert Committee Report in 1988, it was concluded that there were clinical and operational reasons for considering all smear-positive cases MB (⁶). Since then, skin-smears have been done on all patients in some programs, with all smear-positive patients classified MB, and smear-negative TT and BT patients PB.

Because of the unavailability or unreliability of skin-smears in many programs, clinical methods of classifying patients have been developed. The recent WHO Guide asks the health worker to count the number of skin patches; if there are ≤ 5 patches, the patient is classified PB, whereas if there are > 5 patches, the classification is MB (¹³).

The relevant published data comparing clinical classification with bacteriologic classification are presented in Table 2. Note that the exact criteria for classification (both clinical and bacteriologic) vary slightly among the studies. The sensitivity and specificity of the clinical criteria are stated with reference to the bacteriologic criteria as the gold standard.

Further analysis of data from Bangladesh showed (¹⁶) that specificity cannot be very much improved by any combination of purely clinical criteria. The authors also pointed out that the results of such studies vary in different countries according to the case-mix, making it difficult to set global standards. The lower sensitivity and higher specificity found in the last three studies, compared with the first three studies in Table 2, may be attributed to the greater proportion of smear-negative PB patients with ≤ 5 lesions

in the samples (in the last three studies, PB patients comprise 41 % - 83 % of all patients, compared with only 19 % - 23 % of all patients in the first three studies).

As pointed out in a recent review (⁵⁴), “The WHO system of classifying leprosy cases as MB is simple to apply and has a reasonable balance between sensitivity and specificity. However, it must be recognized that the system will lead to a small but significant number of smear-positive MB cases being treated with a PB treatment regimen.” A study from Thailand also suggested that the risk of relapse may be greatest in the small group of MB patients wrongly classified PB and, therefore, undertreated (⁵⁵). Also, there are larger numbers of PB patients who are unnecessarily treated with the MB regimen.

In a study carried out in Brazil (⁵⁶), the anti-PGL-I antibody assay was found to have a sensitivity of 77 % and a specificity of 93 %, whereas the combination of the anti-PGL-I antibody assay and the number of lesions demonstrated a sensitivity of 94 % and a specificity of 77 % in the detection of true MB patients. However, a small group of patients remains who will be undertreated.

Another problem is identification of the small group of patients with an initially high BI ($BI \geq 4$), who may be at greater risk of subsequent relapse (⁵⁷). A study in Nepal (⁵⁸), in which different methods of identifying highly smear-positive patients were examined, found three clinical features in various combinations (LL classification, more than five body areas involved, and skin infiltration) to be sensitive ($> 95\%$) but not specific predictors of this condition; by combining these features using the “AND” connector, specificity could be greatly increased, but sensitivity would be greatly reduced. Whereas the skin smear is the gold standard (*i.e.*, it is taken to have 100 % sensitivity and specificity), anti-PGL-I antibody assay in the same study demonstrated sensitivity of 84 % but very low specificity (⁵⁸).

Conclusions

It is clear that at least two of the traditional cardinal signs are necessary to achieve a reasonable degree of sensitivity in the diagnosis of leprosy; using anesthetic patches as the only sign of leprosy is inadequate. One or more enlarged nerves is an acceptable additional sign, to be supplemented by skin-smears when available.

This has implications for training: peripheral health workers should be taught to suspect leprosy from the typical appearance of leprosy skin lesions; they should be able to diagnose leprosy in those patients with anesthetic skin patches. Patients with suspicious patches but without anesthesia should be referred, and health workers at the first referral level should be able to diagnose almost all cases of leprosy among suspects referred to them; therefore, they must know how to examine for enlarged nerves.

For classification, no other test, either clinical or serological, approaches the reliability of the skin-smear in classifying patients. However, because it is not reasonable to expect that all new patients will be smeared for the purpose of classification,

classification should be based simply on the number of skin lesions, as recommended by WHO.

Recommendations

The following recommendations are based on the evidence just described:

- Approximately 70 % of leprosy patients can be diagnosed using the single sign of anesthetic skin patches, and this sign of leprosy should be taught as widely as possible.
- 30 per cent of all patients, including many MB patients, do not present with this sign, and health workers must be taught to suspect and refer other possible cases.
- Referral of suspects who do not have anesthetic patches, to a person with greater experience who has been taught to palpate the peripheral nerves, must be straightforward. Palpating just two nerves (the ulnar and the common peroneal) may permit diagnosis of as many as 90 % of patients with any nerve enlargement.
- Classification should be based on the number of skin lesions: PB \leq 5 patches; MB $>$ 5 patches. Skin-smears on a sample of new cases could provide quality control.
- Research into laboratory tests (for example, serological or skin tests) that could be useful in the field in identifying *M. leprae* infection, diagnosing active disease and classifying cases of leprosy, should be continued.

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Table 1. Sensitivity (%) of various combinations of the cardinal signs in the diagnosis of leprosy

Author	Signs						
	#1	#2	#3	#1 or #2	#1 or #3	#2 or #3	#1 or #2 or #3
Ponnighaus ¹⁴	49 (PB)						
Groenen ¹⁵	92 (PB)	86 (PB)	36	100	95	91	100
	49 (MB)	96 (MB)					
Saunderson ¹⁷	86 (PB)	76 (PB)	45	95	92	87	97
	54 (MB)	91 (MB)					
Lefford ⁵⁹			41	82			84
Sirumban ¹⁵	93 (PB)	20 (PB)					

Abbreviations: #1 - anesthetic skin lesions; #2 - enlarged peripheral nerves; #3 - acid-fast bacilli in the skin smear.

Table 2. Sensitivity and specificity of various clinical criteria for classifying leprosy patients, compared with a bacteriological method as the standard

	Criteria for classification as MB		Sensitivity (%)	Specificity (%)
	Clinical	Bacteriological		
Becx ⁶⁰	> 5 lesions	BI > 1	92	42
Groenen ⁶¹	> 10 lesions or 4 - 9 lesions and > 1 nerve	BI > 0 (biopsy)	92	41
van Brakel ³⁰	> 2 body areas	BI > 0 (biopsy)	93	39
Croft ⁵⁴	> 5 lesions	BI > 0	89	88
Dasananjali ⁵⁵	> 5 lesions	BI > 1	88	88
Buhrer-Sekula ⁵⁶	> 5 lesions	BI > 0	85	81

Chemotherapy

1 Introduction

1.1 MDT

Multidrug therapy (MDT) was first recommended by a WHO Study Group ⁽¹⁾ in 1981. Its chief characteristics were the following:

- the regimens included several drugs acting by different mechanisms, in order to prevent the emergence of drug-resistance, and to be effective even for strains of *Mycobacterium leprae* resistant to dapsone;
- the duration of MDT was limited, in contrast to the life-long duration of dapsone monotherapy, in order to improve compliance of the patients. To make this possible, only bactericidal drugs were included as components;
- rifampicin (RMP) was included as a key component because of its powerful bactericidal effect against *M. leprae*. It was to be administered only once monthly under supervision, both to insure compliance and because of its high cost;
- the recommended regimens were the minimal effective regimens; there was no recommendation against the use of stronger or longer regimens.

1.2 Official regimens ^(1,2)

To date, three regimens have been officially recommended: (i) WHO/MDT for paucibacillary (PB) leprosy; (ii) WHO/MDT for multibacillary (MB) leprosy; and (iii) a single dose of the combination RMP-ofloxacin-minocycline (ROM) for single-lesion PB leprosy, this last to be employed in those countries in which the proportion of single-lesion PB patients is large.

The composition of the first two regimens, which were recommended by a WHO Study Group ⁽¹⁾, has remained unchanged. However, the definitions of PB and MB leprosy have been modified several times, and the cut-off point between PB and MB leprosy has been simplified from a bacterial index (BI) of $\geq 2+$ in the initial skin smears at any site ⁽¹⁾ to more than five skin lesions ⁽²⁾. Consequently, a larger proportion of newly detected patients are classified as MB leprosy than in the past. At the same time, the duration of MDT for MB leprosy has been gradually shortened, from "at least 2 years, and ... whenever possible, until skin smears negativity" ⁽¹⁾, to a total of 24 months ⁽³⁾. At its seventh meeting, the WHO Expert Committee on Leprosy stated that 24-month duration for MB leprosy remained valid, while suggesting that "it is possible that the duration of the current MDT regimen for multibacillary leprosy could be further shortened to 12 months" ⁽²⁾. This careful wording clearly indicates that the recommended duration of MDT for MB leprosy is either 24 or 12 months.

The third regimen, a single dose of ROM for the treatment of single-lesion PB leprosy, which possesses obvious operational advantages, was recommended as an alternative by the Expert Committee on Leprosy at its seventh meeting (²), and has subsequently been applied widely in India, Bangladesh and Brazil (⁴).

1.3 New MDT regimens

The need for new regimens that are more effective and operationally less demanding may be summarized as follows:

- from the operational point of view, the recommended duration of treatment, particularly for MB leprosy, is still too long;
- two of the components of the current regimen for MB leprosy -- dapsone and clofazimine -- are only weakly bactericidal against *M. leprae* (⁵). Because it is these weaker drugs that determine the minimal, effective duration of the current regimen, further shortening the duration of treatment by this regimen might result in higher relapse rates;
- administration of the daily components, dapsone and clofazimine, cannot be supervised, as a result of which the MDT regimen for MB leprosy is not resistance-proof, should patients fail to comply with treatment;
- patients who do not tolerate clofazimine because of its skin coloration, or who cannot take dapsone or RMP because of allergy, or cannot benefit from RMP because of intercurrent disease or the emergence of RMP-resistance, require a safe and effective alternative;

The discovery of new drugs (⁶) that demonstrate very promising bactericidal activity against *M. leprae* has made possible the formulation of new MDT regimens. A highly desirable new regimen is one that would permit all of the components to be administered once monthly under supervision, significantly reducing the risk of emergence of RMP-resistance caused by irregular administration of the daily components. ROM is the first fully supervisable, monthly-administered regimen. The efficacy of multiple monthly doses of ROM for treatment of MB and PB leprosy has been tested in field trials in three different countries (⁴); however, two of the trials have been terminated prematurely. It is critically important that post-treatment follow-up of the patients treated in the only remaining trial be carried out as originally scheduled. Furthermore, because of the success of a single dose of ROM for the treatment of single-lesion PB leprosy, the treatment of multiple-lesion PB leprosy with a single dose of ROM should be evaluated. Should this treatment be successful, the chemotherapy of PB leprosy could be much simplified, saving significant resources that may be used for other important activities.

The bactericidal activities of both ofloxacin and minocycline are rather weak, compared with that of RMP; the combination ofloxacin-minocycline is significantly less

active than is RMP alone, and ROM is no more bactericidal than is RMP alone (⁷). Replacing the components of ROM with more powerfully bactericidal drugs would make possible a fully supervisable, monthly-administered MDT regimen. Recent findings from experiments in mice indicate that rifapentine and moxifloxacin are significantly more bactericidal than are RMP and ofloxacin, respectively, and the combination rifapentine-moxifloxacin-minocycline (PMM) is far more bactericidal than is ROM (⁸). The efficacy of PMM is currently being measured in a short-term clinical trial among lepromatous leprosy patients. If the trial confirms the stronger bactericidal effect of PMM, a field trial to evaluate the efficacy and side-effects of PMM over the long term should be carried out.

1.4 A common regimen for both PB and MB leprosy

A common regimen for the treatment of both PB and MB leprosy is desirable. However, because PB and MB leprosy differ so greatly in terms of the size of the bacterial population and the underlying immunological response, the requirements for chemotherapy, especially in terms of the number of drugs and the duration of treatment, are bound to be very different. If a common regimen is formulated on the basis of the available drugs, it appears likely that it would overtreat PB or undertreat MB. The dream of a common regimen might be realized only if the new regimen contained several very powerful bactericidal drugs, which were capable of shortening the duration of treatment for MB leprosy to only a few doses or even to a single dose.

Recently, the WHO Technical Advisory Group (TAG), at its third meeting, recommended that all leprosy patients, both PB and MB, be treated by the MDT regimen for MB leprosy for a period of only six months (⁹) The TAG stated, in support of this recommendation, that:

- MDT has been proven to be robust in terms of treatment efficacy and safety;
- relapse rates are very low, less than one percent; and
- resistance to MDT has been virtually non-existent.

However, that a regimen is effective and safe is not sufficient to justify shortening its duration. A good example is THELEP regimen C, which was composed of a single dose of RMP *plus* daily dapsone administered for a period of two years; this regimen was highly effective and safe, but 20 per cent of the patients allocated to this regimen relapsed after an average of five years of follow-up (¹⁰) Since 1998, almost all MB patients have been treated with 12-months MDT; however, no information is available regarding the 5-year relapse-rate following 12-months MDT. Therefore, at least for the time being, there is no justification for further shortening of the duration of MB chemotherapy to 6 months. Moreover, it appears hazardous to state that resistance does not exist, because post-MDT surveillance has not been carried out in routine programs for almost 10 years (³). For these reasons, before any proposal to shorten further the duration of treatment for MB leprosy by the current MDT regimen or of a common regimen for both PB and MB

leprosy may be implemented in control programs, these proposals must be studied by controlled trials, with relapse at the outcome.

2 Magnitude of MB relapse after MDT and possible existence of a higher risk subgroup of MB leprosy

Among MB patients, the efficacy of MDT is best assessed by measuring the relapse rate after completion of treatment (¹). The relapse rate was reported to be about 0.1 % per annum among MB patients administered MDT for 24 months (^{2, 12-17}). Because of the low relapse rates, post-MDT surveillance (¹) has been discontinued (³). However, reports from the Institut Marchoux in Bamako and the Central JALMA Institute in Agra indicate the existence of a subgroup of MB patients who demonstrate a high frequency of relapse after 24-months MDT (¹) -- as high as 4 to 7 per 100 patient-years among patients with initial mean BI ≥ 4.0 , and far higher than that among patients with initial BI < 4.0 , suggesting that the high initial BI is a most important risk factor for relapse. In addition, relapse was observed to occur late -- 5 years after stopping treatment, on average (¹), suggesting that follow-up of these patients may be important. Because there is no ready explanation of the discrepancy between the two estimates of the risk of the relapse among MB patients after 24-months MDT, and the possible existence of a subgroup of MB patients who are more prone to relapse, it is necessary to collect more information from the long-term follow-up of MB patients after completion of 24-months MDT. However, a number of difficulties are encountered in attempting to follow former MB patients after completion of MDT:

- in more and more routine programs, the patients are removed from the register as soon as they have completed MDT, and, very often, essential records -- *e.g.*, identity, address, initial BI and history of treatment -- are lost, making it difficult to retrieve patients for follow-up and analysis;
- because of integration of the leprosy program into the general health services, responsibility for the detection of suspected relapse rests upon general health workers, many of whom do not possess the necessary skills. In addition, the general health services often lack the manpower and resources required to follow former patients who have already completed their treatment with MDT, because they are no longer considered "cases" (²); and,
- because of the poor quality of skin-smears in the past, and because a skin-smear service is no longer available in many programs, it is difficult to identify members of the higher-risk subgroup and to detect relapse.

Because no information exists with respect to the 5-year relapse rate among MB patients after 12-months MDT, determination of the relapse rate following 12-months MDT should be considered a high priority in those treatment centers in which post-treatment surveillance is possible. In addition, the results of ongoing trials, in which the relapse rates after treatment by various regimens, including the 12-month regimen, are compared (⁴), should be published as soon as they become available.

3 The needs for both flexibility and reliability of MDT treatment

To guarantee that all newly detected leprosy patients receive treatment with MDT, the MDT services should be available and accessible to the patients. To accomplish this goal, a flexible, patient-friendly system for delivery of MDT must be implemented. However, at the same time, the principle that monthly RMP is to be administered under supervision^(1,2) should not be compromised, because RMP is the single, most important component of MDT, and non-compliance of leprosy patients with treatment has been well documented⁽¹⁸⁾. In addition, the importance of regular contact between patient and health worker for the purpose of prevention of impairment must not be underestimated.

In areas in which the infrastructure is weak, there are patients who may find it difficult to visit the health center once monthly. Current policy states that, "in such cases, more than a month's supply of MDT blister-packs may be provided to the patient"⁽²⁾, and that with "accompanied MDT", blister-packs for a full course of MDT should be provided at the time of diagnosis⁽¹⁹⁾. Consequently, in an increasing number of national programs, it has become the routine to provide the entire quantity of MDT blister-packs - - *i.e.*, a 6-months supply for PB and a 12-months supply for MB patients -- to all newly detected patients. However, in many programs, those responsible for "accompanying" the patients' treatment either have not been recruited, or lack proper training, as a result of which many of them fail to carry out their mission. As a consequence, it is difficult to be certain that the MDT drugs are indeed self-administered by the patients, notwithstanding the fact that the success of MDT could be seriously jeopardized, should patients be non-compliant.

Because the monthly component was expected to be administered under supervision, studies of compliance with MDT undertaken since the introduction of MDT focused on regularity of self-administration of the daily component, chiefly dapsones, by urine testing. Whereas the results demonstrated better compliance with MDT than with dapsones monotherapy⁽²⁰⁾, only 70 to 80 % of patients were found in compliance with the daily component⁽²⁰⁻²²⁾, suggesting that the assumption that "patients who report for diagnosis and treatment may be considered as sufficiently motivated to take full responsibility for their own care"⁽²⁾ may not be valid. Although one of the advantages of the blister-pack over the supply of MDT drugs in bulk was assumed to be improved patient compliance with the self-administered component⁽²³⁾, this assumption has been tested in only a few studies; these studies have demonstrated that blister-packs either did not improve compliance^(24,25), or improved it only marginally⁽²⁶⁾.

Because the monthly component is no longer administered under supervision to a significant proportion of patients^(19,27), it appears very likely that reduction of the frequency of contact between patients and health workers will affect the regularity of drug administration; therefore, compliance with both the monthly and daily components of MDT is certainly an issue far more important and complicated than before. It is important to measure the degree of non-compliance among those who are treated under the policy of flexible drug delivery with both the daily and the monthly components of

the MDT blister-pack. This may have significant impact on MDT delivery policy, and even on the strategy of the chemotherapy of leprosy.

“Accompanied MDT” is the term applied to a program in which a family or a community member supervises the monthly administration of drugs to the patient ⁽²⁷⁾. This concept appears reasonable, but before its wide implementation, this approach should be tested under field conditions, to identify the requirements for its success. However, even with the best program of accompanied MDT, the justification for providing the total quantity of MDT drugs to the patient may be disputed, because the family or community member cannot replace the health worker.

4 Absenteeism and default

A defaulter has been defined as a patient who has not collected MDT treatment for 12 consecutive months ⁽²⁸⁾. It has been recommended that defaulters who cannot be retrieved be removed from the register ⁽²⁸⁾, and that the register be updated at least annually ^(27, 28). In a number of national programs, as many as 40 % of newly detected patients have been considered defaulters ⁽²⁹⁾. Since introduction of the “flexible MDT delivery” strategy, increasing numbers of patients have received the entire quantity of MDT drugs at the time of the first dose of treatment. Although it has been stated that the percentage of defaulters has declined dramatically as a result of this approach, it is difficult to assess the actual rate of completion of treatment.

Whatever the reason for default, every effort should be made to prevent it. A serious attempt should be made to trace absentees beginning at the time of their first absence. Absentees who return to treatment should be treated according to WHO recommendations: six doses of MDT within nine months for PB; and 12 doses within 18 months for MB. In addition, tracing and persuading the defaulters to return for treatment is most important.

For those patients who have become defaulters, those who have died or migrated from the country should be removed from the register, whereas those who have moved out of the district or are taking treatment elsewhere should be transferred rather than simply removed from register. As long as the defaulters continue to live in the district and have yet to complete the full course of MDT treatment, they remain, by definition, “cases” ⁽²⁾, and may continue to represent sources of transmission. Instead of removing these defaulters from the register, health workers should be encouraged to retrieve them actively, with assistance from the community. A new course of MDT should be given to every defaulter after his retrieval or return.

5 Drug resistance

To date, all of the official MDT regimens contain RMP, which is significantly more bactericidal than any other antileprosy drug or any combination of ofloxacin, clarithromycin and minocycline ^(7, 30). Emergence of RMP-resistance would create

tremendous difficulty for the treatment of individual patient, and its widespread dissemination would pose a serious threat to the achievement of leprosy control.

RMP-resistant leprosy was first documented in the 1970s⁽³¹⁾. It was rare^(31, 32), probably because, in that era, RMP was seldom employed for the treatment of leprosy. Later, it was reported that, among a total of 404 MB patients who had been treated with various RMP-containing regimens, 39 relapsed and 22 were found to harbor organisms resistant to RMP, as proven by the mouse footpad technique⁽³³⁾. Virtually all of the resistant strains were isolated from patients who had been treated with RMP only after they had relapsed after long-term monotherapy with dapsone or other sulfones, and almost all of the strains were also resistant to dapsone, indicating that these patients had in effect been receiving RMP monotherapy. Because many of the 22 patients developed RMP-resistance in the decade after beginning treatment with RMP⁽³³⁾, it appeared that RMP-resistance could emerge rather rapidly among patients whose treatment regimens were inappropriate.

Although more than 10 million leprosy patients in the world have completed treatment with MDT, and RMP-resistant leprosy has not been reported among these patients⁽²⁾, one must be cautious in interpreting the findings. First, post-MDT surveillance for relapse is no longer carried out in most routine programs. Second, the standard means of diagnosing drug-resistant leprosy has required use of the mouse footpad technique; however, the great majority of the mouse footpad laboratories established for surveys of dapsone-resistance have disappeared during the last decade, which coincided with intensive implementation of MDT. As a result, RMP-susceptibility testing is rarely carried out, and the results are not always reliable. In fact, one cannot exclude the possibility that a number of RMP-resistant leprosy patients are currently undetected. Before RMP-resistance becomes so frequent that it threatens leprosy control, more solid information about its magnitude should be collected in different parts of the world.

Although it is no longer feasible to undertake a relatively large-scale survey of RMP-resistant leprosy by means of the mouse footpad technique, PCR-based DNA-sequence analysis of the *rpoB* gene of *M. leprae* represents a cost-effective alternative technique⁽³⁴⁻³⁶⁾. At this stage, surveys of RMP-resistance should focus on MB patients who have relapsed after completion of MDT, and surveillance for the emergence of RMP-resistance among relapsed MB patients should be carried out by special centers. For this purpose, a proportion of MB patients should be systematically examined clinically and bacteriologically after completion of MDT, and skin-biopsy specimens should be obtained from those patients suspected of relapse for DNA sequence analysis of the *rpoB* gene of *M. leprae*⁽³⁴⁻³⁶⁾.

MDT was developed mainly because of the widespread emergence of dapsone resistance, and the MDT regimens were designed on the principle that they would be effective against all the strains of *M. leprae*, regardless of their susceptibility to dapsone^(1, 2). Hence, in the MDT era, whether the global prevalence of dapsone-resistance is

increasing or declining is virtually irrelevant to the therapeutic effect of MDT, and there is no need to monitor trends of resistance to dapsone.

Recommendations

- To guarantee the quality of leprosy services, training in leprosy should be strengthened among general health workers.
- The skin-smear remains an important tool for diagnosing MB relapse; wherever possible, it should be reintroduced, particularly in areas in which there are a significant number of MB patients who have completed MDT, or the prevalence is greater than 1 per 10,000 population.
- Currently, almost all MB patients are being treated by 12-months MDT; however, no information is available regarding the 5-year relapse rate among MB patients treated by this regimen. Therefore, field programs with adequate facilities should monitor the relapse rates. Surveillance among relapsed MB patients for the emergence of rifampicin resistance should be carried out by special centers.
- A flexible, patient-friendly system for delivery of MDT must be implemented. At the same time, the principle that monthly RMP is to be administered under supervision should not be compromised. Only in exceptional cases, in which the patients cannot be seen monthly, should more than a one-month supply of MDT blister-packs be provided.
- Health workers should actively trace absentees and encourage them to complete their treatment, instead of passively awaiting their return and removing them as defaulters from the register after an absence of 12 or more consecutive months.

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Prevention of Disabilities and Rehabilitation

1 Introduction

Leprosy results in a wide range of impairments, the most important of which is damage to peripheral nerves. Damage to peripheral nerves causes loss of sensory, motor and autonomic nerve function to the affected region, leading in turn to deformity, secondary deformity resulting from repeated trauma to as well as dryness and cracking of the skin, and inability to perform important activities of daily living. These consequences of nerve damage have an impact on the quality of life of those affected by the disease and also generate stigma. Societal attitudes towards those affected by leprosy, often based on religious, traditional and cultural beliefs, may limit participation of people affected by leprosy in their own communities. Prevention of impairment is therefore a high priority in the management of leprosy. Prevention of nerve damage and the management of impairments are important components of any leprosy program. Rehabilitation in leprosy should be fully integrated within existing community-based rehabilitation programs on an equal basis as those with disabilities due to other causes.

0.0 Prevention of Disability

Approaches to prevention and treatment of nerve damage, as well as to limiting secondary effects, such as the increasing deformity caused by trauma, are now a standard part of all leprosy programs. Guidance on the prevention of impairments and management of nerve damage is included in publications from the World Health Organization (^{1,2}) and ILEP (³⁻⁵), and in most national guidelines on leprosy control. The components of prevention of impairments in leprosy programs include measurement of impairment, detection and treatment of reactions, self-care, footwear and eye-care.

The most commonly used measurement of impairments is the WHO Disability Index (⁶), which has been in use for several decades. It is robust and simple to use as an indicator of early case-detection. However, it is not responsive to change over time, and has limited value in monitoring the progress of individual patients. Ball-point pens are frequently used in the field by health workers to assess sensation. Other approaches to assessment of nerve function, based on voluntary motor testing (⁷) and sensory testing using monofilaments (⁸), are more appropriate for monitoring the progress of individual patients. Most guidelines describe how to detect and treat reactions.

Detection of reactions is based on acute changes of the skin lesions and deterioration of nerve function; reactions are treated by fixed-dose steroid regimens. Self-care routines are taught, and patients are empowered to develop daily routines for inspection of limbs with sensory and motor impairment for signs of injury or infection, treatment of injuries, active and passive exercises to prevention joint stiffness, and soaking and oiling to minimize drying of the skin. Instruction on protective clothing, adapted tools, and the use of footwear is also provided. Recommendations on footwear are provided, aimed usually at individuals with sensory impairment of the plantar surface of the foot. Earlier documents stressed the design and characteristics of specialized

footwear with cushioned insoles; however, more recent recommendations are for cheap, available and locally acceptable footwear. The sensory and motor impairments that affect the eyes, combined with the inflammatory processes of iridocyclitis, render the eye potentially vulnerable in leprosy. Examination of the eyes is recommended, as well as protection and lubrication.

1.0 Rehabilitation

Surgery plays an important role in the correction of deformities and in reconstructive procedures to improve function. Surgical correction of foot-drop and lagophthalmos can prevent secondary impairments such as ulceration and deformity of the foot and corneal scarring. Case-selection for reconstructive surgery is very important. Physiotherapy support is essential both pre- and post-surgery, as are facilities for occupational retraining. In the past, rehabilitation in leprosy has tended to be physically oriented and isolated from general and community-based approaches to rehabilitation. This is now changing, as more integrated approaches are adopted, and better linkages to existing community-based and community-oriented rehabilitation are established. More recently, social and economic rehabilitation have been advocated.

1 The evidence-basis for prevention of impairments and rehabilitation

Guidelines for preventing and managing nerve function impairments (NFI) and for rehabilitation have been based largely on the experiences of individuals and programs. This section focuses on a systematic review and critical appraisal of the evidence for the effectiveness of specific aspects of prevention and treatment of impairments, and rehabilitation. The following four key questions, which were selected by discussion within the organizing group and by consultation with those in the field, are identified as priorities:

- Is early detection of leprosy, followed by prompt initiation of MDT, effective in prevention of impairments?
- Does early detection and treatment of reactions and new nerve damage prevent impairments? If so, what are the best methods of detection and the thresholds for treatment?
- Does steroid prophylaxis prevent impairment?
- How effective are interventions in self-care, provision of footwear and socio-economic rehabilitation?

2.1 Is early detection of leprosy, followed by prompt initiation of MDT, effective in prevention of impairments?

Many publications assume that early diagnosis of leprosy and treatment with effective chemotherapy will prevent nerve damage (^{9,10}). That early diagnosis of leprosy, prior to the development of NFI, and treatment with effective chemotherapy that interrupts the disease process prevents nerve damage appears plausible. However, the process of nerve involvement in leprosy may commence long before the disease is clinically manifest. Moreover, NFI occurs before diagnosis, during MDT and after completion of MDT (^{11,12}), either as a gradual process or as part of a reactional episode. Therefore, it is important to appraise critically the evidence that early detection and MDT is effective in preventing NFI, and to estimate the magnitude of such an effect.

The evidence may be based only on observational data, because it would be unethical to withhold effective chemotherapy in a controlled study of intervention. Trials of chemotherapy regimens could provide an opportunity to examine possible differences of impact on nerve function; regimens that include clofazimine may result in fewer episodes of reaction. To date, however, few chemotherapy trials have included nerve function as an outcome. Current trials may include nerve function as an outcome, but any difference of effect is likely to be small, compared to the differences between treatment and untreated control groups. It is important that trials of different chemotherapies for leprosy include nerve function as an outcome.

Observational data on the occurrence of NFI before, during and after MDT have been used to estimate the magnitude of the potential effect of early diagnosis and MDT on NFI. Using such data, a study in Bangladesh (¹²) estimated that early detection and initiation of MDT could prevent more than three quarters of impairments, whereas efforts to prevent disability employed during and after MDT could prevent only one quarter. This estimate is based on a number of assumptions regarding the effectiveness of MDT and the frequency of impairments expected in untreated leprosy. Nevertheless, the study provided an estimate of the magnitude of the effect, and demonstrated that it may not be possible to prevent all impairments by MDT. Failure to achieve early detection limits the potential of MDT to prevent NFI.

In Ethiopia, it was shown (¹³) that, as late as 10 years after MDT, one-third of patients never developed impairments. However, this study, which was conducted among a group of MDT-treated patients, of whom 55% were found to have impairments at diagnosis, raises the question of whether all patients would develop NFI if left untreated. There were 39 episodes of neuropathy per 100 person years in the first year after commencing MDT in this AMFES cohort (¹⁴). In the BANDS cohort in Bangladesh 2.6% of PB cases and 37% of MB cases developed new nerve function impairment in the 2 years following detection and MDT treatment (¹⁵). A series of estimates (¹⁶) of the potential impact of implementing MDT on disability in leprosy have been attempted, based on a number of assumptions.

Recommendations

- Early diagnosis of leprosy and treatment with MDT are recommended to reduce the frequency of NFI. This recommendation is supported by observational studies and estimates, and on a number of assumptions (such as that untreated cases would develop NFI).
- It should be noted, however, that MDT will not prevent all NFI, and that the magnitude of the impact is dependent on “early” case-detection and treatment.
- Nerve function should be included as an outcome measure in trials of leprosy chemotherapy.

2.2 Does early detection and treatment of reactions and new nerve damage prevent impairments? If so, what are the best methods of detection and the thresholds for treatment?

A recent review suggests that, overall, 60 per cent of patients treated with steroids regain nerve function (¹⁷), and a number of studies that assess the effectiveness of steroids in terms of recovery in NFI show recovery rates of a similar magnitude (¹⁸⁻²⁰). Surgical interventions such as nerve decompression have been considered. Two trials of steroids *vs.* steroids *plus* surgical nerve decompression showed no added benefit of surgical intervention (^{21, 22}) in terms of nerve function. Larger, well-designed, controlled studies of early surgical interventions are indicated.

Defining early detection is difficult: “early” may be considered in terms of the duration of the history of symptoms and signs. However, studies also consider the severity of the presenting signs and symptoms in terms of the magnitude of the change of nerve function. A study in Nepal, based on a retrospective cohort design, demonstrated the outcome to be related to the severity of nerve damage at diagnosis, which may itself be related to timeliness of detection (¹⁹). A pilot study demonstrated benefit from steroid therapy even when administered 6 months after onset of NFI (²³).

An important controlled trial that addresses early detection using monofilaments as part of the TRIPOD trials (²⁴), showed that detection of early change in nerve function by monofilaments did not result in any additional benefit over detection based on careful use of a ball-point pen to assess sensory change.

2.2.1 Methods of early detection

The need for early detection and the development of more sensitive diagnostic methods for early detection of neuritis has been recognized (²⁵). Because of a lack of consensus on the best methods, a study was conducted to assess five different methods (²⁶): two weights of monofilaments, pinprick, temperature sensation, and palpation of nerve thickness. The study reported that the two best methods were palpation of nerve thickening and the 0.2 mg monofilament.

Predicting NFI and reactions is another approach to early detection. A review of the literature on type 1 reaction identified as risk factors BCG, pregnancy, and MDT (²⁷). The review also attempted to estimate the proportion of disability that may be prevented by early detection and treatment of reactions. Facial skin lesions have also been identified as a potential risk factor for facial nerve damage, carrying almost a ten-fold greater risk (²⁸). Previous nerve damage and MB classification were found to be very strong predictors of nerve damage and reactions in a large cohort study in Bangladesh, which suggested a prediction rule that could be used in the field (¹⁵). Analysis from the AMFES (²⁹) cohort in Ethiopia suggested that nerve function should be assessed by standardized methods every month.

Serological tests have also been proposed as a method of predicting nerve damage and reactions. Anti PGL-I antibodies were not found to be predictive (³⁰), whereas serum levels of neopterin may be an indicator (³¹). This possibility must be tested in large, prospective studies.

2.2.2 Threshold for treatment

The threshold for commencing steroid therapy in early reactions or NFI may be based on the magnitude of the change of function or the duration of the change. NFI is not always associated with skin signs or symptoms of neuritis, such as pain or tingling in so-called silent neuropathy (³²). Thus, reliance on symptoms and self-reporting is not sufficient. It must also be recognized that there is a degree of variation of nerve function assessment among methods and among observers using the same methods (^{8, 33}). A threshold for treatment based on change of nerve function must be higher than the expected variation in nerve function assessment.

Recommendations

- Steroids are recommended to treat reactions and nerve function impairments of recent onset; the expected recovery rate for nerve function is approximately 60%.
- MB patients and those with existing nerve function impairments should be carefully monitored for new nerve function loss, as they are the groups at greatest risk.
- Assessment of nerve function using standard methods every month during MDT is recommended.
- Research is recommended to identify the optimal steroid regimen, to develop alternative and more effective treatments for reactions and recent nerve function loss, and to determine nerve function change thresholds for treatment.

2.3 Does steroid prophylaxis prevent impairment?

Steroids represent the accepted method⁽¹⁹⁾ of medically treating NFI and reactions in leprosy. However, would steroids, if given prophylactically along with MDT, prevent NFI and reactions⁽³⁴⁾? A number of studies that have investigated this question have recently been reviewed⁽³⁵⁾.

The results of two trials of steroid prophylaxis have been published. A small (150 participants) randomized trial, conducted in India and reported⁽³⁶⁾ in 1985, showed that 10 mg of a steroid administered daily along with chemotherapy for one month was effective in preventing nerve damage in PB patients. The second, an open controlled trial conducted in Bangladesh⁽³⁵⁾, also showed a significant beneficial effect of 20 mg prednisolone daily for 3 months. Both studies suggest that such an intervention may prevent NFI and reactions.

A large scale, double-blind trial of low-dose prophylactic steroids, has been conducted in Bangladesh and Nepal^(24, 37). The dosage of prednisolone, 20 mg daily for the first three months, was tapered during the fourth month. Patients with previously untreated MB leprosy were randomly allocated to steroids or placebo along with MDT. The preliminary report⁽³⁸⁾ of the results of this trial, presented at the ILA Congress in Agra in 2000, confirmed a significant beneficial effect at 4 months, but the effect at 12 months follow-up was no longer statistically significant.

Recommendation

Further research is recommended on the use of prophylactic steroids in preventing NFI. It is not only important to demonstrate, by means of a randomized, double-blind controlled trial, that steroid prophylaxis is effective in preventing nerve damage, but also that the benefits outweigh the costs, including those of adverse reactions to steroids. The results of the trial should also indicate the magnitude of the effect, and whether the effect varies among identifiable subgroups.

2.4 How effective are interventions in self-care and provision of footwear?

Interventions to promote self-care among people with NFI, to provide protective footwear, and to stimulate socio-economic rehabilitation have become standard parts of leprosy programs over the last few decades. This section provides a review of the evidence for the effectiveness of each of these components. In practice, the components are usually delivered in an integrated manner. Some of the evidence addresses single components, whereas other evidence evaluates the effectiveness of packages of interventions.

2.4.1 Self-care

Self-care is the management, on a daily basis, of the effects of nerve function impairment, and is the responsibility of the individual. Many papers describe self-care, but do not evaluate its effectiveness. The role of health-care workers is to educate and enable patients in the self-care process. A major survey⁽⁴⁾ of self-care activities in ILEP-supported projects in 1995 revealed that 90 per cent or more of projects train patients in self-care and give advice on footwear.

Four papers that evaluate self-care and an additional five that evaluate self-care and footwear together have been identified. Seven of these studies are based on before-and-after study designs, and two employ a comparison group. The four studies that evaluate only the self-care component are the following. First, a study conducted in India⁽³⁹⁾ demonstrated that a self-care intervention for a period of 4 months improved the quality of the skin, and considerably reduced both hand and plantar ulceration. The second study, a before-and-after study also conducted in India⁽⁴⁰⁾, showed physical, functional and social improvement after self-care, as assessed by the patients themselves. The third study, a controlled trial in which two different approaches (patient education and community education) to self-care were compared to a control group⁽⁴¹⁾, also demonstrated benefit. Conducted in Nepal, the fourth study⁽⁴²⁾, which was a comparative trial of a 14-day self-care training program, showed that those trained were significantly less likely to be admitted for an infected plantar ulcer than were the controls. Each of these four studies showed benefit from self-care; the two comparative trials, in which the two interventions were compared to a control group, provided more robust evidence.

2.4.2 Footwear

The importance of appropriate footwear for feet lacking plantar sensation was recognized in the 1950s and 1960s. The use of adapted and modified footwear, using both molded shoes and insoles cushioned with micro-cellular rubber, was advocated. However, this approach was criticized because such footwear is difficult to produce and because of stigma⁽⁴³⁻⁴⁵⁾. Treatment centers were unable to produce sufficient shoes for those who needed footwear, and, because the shoes were fragile, to repair and to replace them. Also, because the shoes were also obviously different from that worn by the rest of the community, they became a symbol of the disease. During the last decade, this approach has been superseded by one of encouraging appropriate, locally acceptable footwear.

Three studies evaluate footwear programs, five evaluate combined programs of self-care and footwear, and one evaluates footwear and socio-economic rehabilitation. The first study, a before-and-after investigation of footwear, was conducted in Ethiopia⁽⁴⁶⁾. The second, a trial of foot orthoses in India⁽⁴⁷⁾, demonstrated a large difference in impairments between the intervention group and the control group (58 % *versus* 14 %). The third trial is a randomized, controlled trial of different footwear conducted in Ethiopia⁽⁴⁸⁾ that also demonstrated benefit; this study demonstrated that canvas shoes with cushioned insoles were both cost-effective and acceptable.

Recommendations

- Teaching and empowering patients in self-care is an effective activity, which should be part of all leprosy programs.
- Use of locally acceptable, appropriate footwear is a cost-effective intervention for those with loss of plantar sensation.

2.5 Socio-economic rehabilitation

Many of the earlier initiatives in rehabilitation focused on physical approaches. That the importance of social and economic aspects of rehabilitation is now being emphasized is evidenced by the recently produced guidelines for socio-economic rehabilitation (^{49, 50}). Most publications describe examples or case-studies in socio-economic rehabilitation. Two studies that describe an evaluation of such an approach were conducted in India. The first reported (⁵¹) benefits from restoration of social and economic status. The second was an evaluation of a community-based rehabilitation initiative (⁵²). Both studies stress the importance of participation of the client as well as involvement of the family and the community.

Self-care, footwear and rehabilitation activities are often combined within a program. Six published studies, all of which employed before-and-after designs, represent evaluations of the effectiveness of combined programs, and one considers a footwear and loan program. The six studies analyzing self-care and footwear programs were conducted in China (^{53, 54}), India (⁵⁵), and Senegal (⁵⁶⁻⁵⁸). The footwear and loan project was based in Chad (⁵⁹). The two studies in China showed beneficial effects, the study in India showed a 50% reduction of plantar ulcers, and the studies in Senegal showed improvement of between 33 and 62 per cent. The study of loans also reported a beneficial outcome.

Recommendations

- Socio-economic rehabilitation, which requires participation by client, family and the community, is valuable for selected patients.
- Socio-economic rehabilitation for those affected by leprosy are best delivered through general community based rehabilitation programmes.

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Epidemiology and Control

1 Introduction

Leprosy elimination was defined in 1991 as a prevalence smaller than one per 10,000 inhabitants. Underlying the elimination strategy was the hypothesis that, because leprosy patients are assumed to be the sole source of infection (¹), early detection and treatment of the cases by MDT would reduce transmission of the organism. Once the prevalence fell below a certain level, incidence would be reduced; in the long term, the chain of transmission would be broken, and leprosy would disappear naturally (²).

It is now necessary to seek evidence to verify this hypothesis. Some important questions must be answered concerning the effectiveness of interventions to reduce transmission of *Mycobacterium leprae* and the sources of infection. Evidence concerning these issues will be reviewed here. The validity of several indicators for leprosy epidemiology and control will also be discussed.

2 Are untreated MB patients the only significant source of infection?

Untreated MB patients are most probably the most important source of transmission of *M. leprae*. Household contacts of multibacillary patients have been estimated to have a risk of developing leprosy 5 - 10 times greater than that of the general population (³⁻⁵), and a positive association exists between smear positivity and infectiousness. In low endemic situations, the relative risk associated with household contact could even be greater.

Several studies have shown that untreated MB patients excrete large quantities of *M. leprae* from the nose and mouth (⁶⁻⁸). However, many studies have suggested that untreated MB patients do not represent the sole source of infection. Household contacts of paucibacillary (PB) patients have also been shown to be at greater risk of developing the disease than are non-contacts (^{3,4}), although the risk is smaller than that to contacts of MB patients. It is possible that the PB patients are not themselves the source of transmission; rather, the household contact has had contact with some outside source of infection (⁴). Those who join the household of an MB patient after treatment has been started have been shown to be at lower risk than the contacts of untreated MB cases, but at greater risk than the general population. If MDT renders the index case noninfectious, it appears likely that the source of infection is not the index case directly, but the environment of the household (⁹).

Because, in many areas, the numbers of MB patients are very small, they may not represent the most important source of infection. There is increasing evidence that subclinical transmission may occur. Nasal excretion of *M. leprae* by subclinically infected individuals could be responsible for transmission, although this is not proven. DNA sequences apparently unique to *M. leprae* have been isolated on nasal swabs from many apparently healthy individuals residing in endemic areas (¹⁰⁻¹⁵), and large proportions of those who live in areas endemic for leprosy have been shown to

demonstrate seropositivity against *M. leprae*-specific antigens (^{11, 14-16}). Even in highly endemic countries, no history of close contact with a leprosy patient can be established for many patients (⁴), although a study carried out in one endemic village in Indonesia showed that some contact with a leprosy patient could be demonstrated for most incident cases (⁵).

Direct spread is certainly important, but infection may also be indirect (¹⁷). *M. leprae*, which have been said to be capable of survival outside the human body for as long as several months under favorable conditions (¹⁸), have also been found in the soil (^{19, 20}), and insect-bites have also been said to be capable of transmitting the organism (²¹). This latter route of infection is probably not very efficient (²²), but it cannot be completely dismissed as a possibility. The existence of extra-human, animal reservoirs of *M. leprae* has been demonstrated (²³⁻²⁷) but, with the possible exception of the nine-banded armadillo, there is no evidence that these animals are of epidemiologic significance. *M. leprae*-specific DNA has been reported to be present in water, and the risk of leprosy was said to be correlated with the use of contaminated water for bathing and washing (²⁸). Leprosy lesions following dog-bites (²⁹), vaccinations and tattooing (³⁰) have also been reported. Nude mice, the feet of which had been smeared with *M. leprae* and also pricked with contaminated thorns, developed leprosy lesions (³¹), and infection of wild armadillos through thorn pricks has also been suspected (³²); such a route of infection cannot be completely excluded for humans. Finally, in some settings, the anatomical distribution of the lesions in patients with a single macule strongly suggests transcutaneous infection through wounds (³³). Other studies of the anatomical distribution of lesions are not consistent with this hypothesis, but could be consistent with infections through insect-bites (³⁴).

3 What evidence is there for the effectiveness of interventions to stop or reduce the incidence of leprosy?

3.1 Impact of MDT on transmission

MDT greatly reduces the infectiousness of leprosy patients in a matter of a few days (³⁵), a period of time much shorter than that required by dapsone monotherapy (approximately three months). Although incidence rates have been observed to have declined in many settings, evidence that MDT caused an acceleration of that decline is rare (³⁶⁻⁴⁰). In many places, the decline of incidence began before the introduction of MDT, or could be explained as well by other factors (⁴¹⁻⁴⁶). In other settings, no decline of incidence has been observed, despite the routine administration of MDT to all newly detected patients for a number of years (⁴⁷⁻⁴⁹).

Several explanations can be advanced for the apparent lack of acceleration of a decline of incidence following the introduction of MDT:

- the long incubation period of leprosy;
- the increased case detection efforts; or

- detection too late to effect very much of a reduction of transmission (⁵⁰).

3.2 Impact of other interventions

3.2.1 Immunoprophylaxis

In several randomized controlled trials that have been carried out, vaccination with BCG was shown to reduce the risk of developing leprosy (⁵¹⁻⁵⁶). The level of protection varied among trials from 20 to 80 %, for reasons that remain unclear. Repeated vaccination with BCG is capable of enhancing protection against leprosy (^{54, 56}), and addition of heat-killed *M. leprae* (HKML) to BCG does not appear to increase the protection conferred by BCG alone (^{54, 57}). However, this has not been true of all of the trials; in one trial in South India, the combination of BCG + HKML conferred protection that was almost double that conferred by BCG alone (⁵⁸). Protection conferred by BCG appears greatest if the vaccine is administered before 15 years of age (^{51, 54}). The ICRC vaccine was also shown to confer significant protection against leprosy (⁵⁸). Current research suggests the possibility of producing vaccines for leprosy that are more effective (⁵⁹).

3.2.2 Chemoprophylaxis

Chemoprophylaxis against leprosy has been studied in several trials. A systematic review and meta-analysis of these trials has shown that chemoprophylaxis based on dapson or intra-muscular acedapson conferred an overall protection against leprosy of about 60 % (⁶⁰). However, the protection appeared to wane over time after administration of the chemoprophylactic regimen. An uncontrolled trial with rifampicin administered in a single dose at a dosage of 25 mg per kg yielded an estimated protective efficacy of 35-40 % (⁶¹⁻⁶³). Finally, a program of chemoprophylaxis employing single doses of the combination rifampicin-ofloxacin-minocycline, was launched in the Federated States of Micronesia, Kiribati and the Republic of the Marshall Islands as part of their elimination program (⁶⁴). Because this was not a controlled trial, but rather an attempt to prevent the disease in an entire population, it is difficult to draw conclusions regarding the degree of protection conferred by this chemoprophylaxis.

3.2.3 Other factors

Socio-economic conditions are thought to play an important role in leprosy, their improvement resulting in a decline of incidence. One of the best demonstrations of such an influence was provided by a study of trends of incidence in mainland Japan and Okinawa (⁶⁵). Although the factors contributing to this decline are not known, housing conditions, the number of persons per household or per room, and family-size are thought to have been most important. A study in Malawi found an inverse relationship between the number of years of schooling and the risk of leprosy, and good housing conditions were also associated with a decreased risk of leprosy (⁶⁶). Nutritional factors could also influence individual susceptibility (^{67, 68}).

4 What are the essential indicators for leprosy epidemiology and control?

Indicators are tools for measuring progress in achieving the objectives of a program. Ideally, these indicators should be valid (measure effectively what they are supposed to measure), simple, easy to measure and to interpret, responsive to changes, and give information that could be used to reorient activities. This section concerns the usefulness of a number of indicators often employed in leprosy control programs.

4.1. Prevalence

Prevalence should deal with the actual number of people in need of, or receiving chemotherapy. There were several reasons for choosing prevalence, and not incidence, as the indicator of elimination:

- the incidence of leprosy is not easy to measure employing routine reporting systems, which generate information only on case-detection;
- detection of new cases may correlate very poorly with incidence, because of operational changes in activities;
- because of the long incubation period, current incidence reflects transmission that had occurred several years earlier and, therefore, does not reflect the effectiveness of current anti-leprosy activity ⁽⁶⁹⁾;
- it was hoped that reduction of prevalence to very low levels would lead, in time, to reduction of transmission of infection and, therefore, to reduction of incidence;
- the target of a prevalence of less than 1 in 10,000 at the national level and the target date of the end of the year 2000, although arbitrary, provided sufficient challenge to build political commitment and intensify activities ⁽⁷⁰⁾.

However, prevalence possesses limitations as an indicator of elimination:

- the data collected refer in practice only to those who are registered for treatment. Undetected leprosy patients are not taken into account;
- it is directly dependent upon the duration of treatment;
- prevalence of registered cases is directly influenced by detection activities, and thus by operational factors.

4.2 Incidence

The annual incidence is the number of new cases of a disease that occur in a population in the course of a year. In theory, it represents the best estimate of the current

risk of developing leprosy within the specified population. It also reflects the transmission pattern of *M. leprae* in the population during preceding years⁽⁷¹⁾. However, it is very difficult to measure in practice: clear and undisputed criteria for the diagnosis of leprosy are required, and total populations must be examined at regular intervals. Even in an ideal situation, because some leprosy lesions are evanescent, the number of leprosy patients detected in a program depends upon the frequency at which the population is surveyed^(72, 73). Even if incidence cannot be measured accurately, its trends can be estimated by a set of indicators.

4.3 New-case detection-rate

The rate at which new cases are detected is the most logical proxy-indicator of incidence. However, the new-case detection-rate poses some problems of interpretation:

- it is directly influenced by the intensity and frequency of detection activities and the quality of services;
- a number of newly detected cases may have developed leprosy several years earlier;
- at the same time, some people who develop symptoms will be detected only after a number of years, and thus will not be included in the current year's case detection rate.

In spite of these limitations, one may assume that trends of case detection reflect trends of incidence, on condition that there has been no important change of detection activities, including coverage, self-reporting behavior, diagnostic procedures and criteria^(74, 75).

4.4 Proportion of newly detected patients with grade 2 impairment

This is a highly relevant indicator. The proportion of newly detected patients with impairments has been shown to be related to delay before detection⁽⁵⁰⁾. A large proportion of patients with deformity among newly detected patients indicates that these include old cases⁽⁷⁶⁾, whereas a small and stable proportion of new patients with impairments among the newly detected cases is a sign that the delay between onset of the disease and its diagnosis is stable, and that trends of case detection reflect trends of incidence⁽⁷⁷⁾. However, the validity of this indicator depends upon the thoroughness of the examination of the new patients at the time of detection.

4.5 Proportion of children

A large proportion of children among the newly detected patients is a sign of active and recent transmission of the infection. Thus, it is an important epidemiological indicator, even though the proportion can also be influenced by operational factors, such as active campaigns among specific sub-groups of the population -- school surveys, for example. As transmission of *M. leprae* decreases in a population, the proportion of

children among the newly detected cases may also be expected to decrease. However, this is a slow process (^{43, 46}). Therefore, it would be informative to monitor age-specific case-detection rates (⁷⁵) or mean age at detection; this should increase in the situation of declining incidence.

4.6 Proportion of MB patients

This indicator is particularly difficult to interpret: the proportion of MB patients among newly detected patients differs from country to country, and is directly influenced by the criteria used for classification (bacteriological or clinical) and by detection efforts (⁷⁵). Its usefulness for interpretation of trends of case-detection rates is also questionable: the proportion of MB patients among the newly detected cases has been shown both to increase and to decrease in situations of declining incidence (^{78, 79}). However, as long as treatment differs for PB and MB patients, the proportion of MB patients will remain useful for estimating drug requirements. It may also be important to collect information on new smear-positive patients; this may be accomplished by the use of “sentinel” sites.

4.7 Treatment completion rate

This should be calculated, by cohort analysis, as the proportion of patients who have completed treatment among those expected to do so. As long as treatment differs for PB and MB patients, this indicator must be calculated separately for each type of patient.

4.8 Relapses

Although relapses appear to be very rare after MDT, it remains useful to monitor relapses at the program or country level. If a sizeable proportion of the patients starting treatment consists of relapses, the situation is worth investigating (⁸⁰).

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Organization of Leprosy Services

1 The need for sustainable leprosy services

Leprosy will remain a problem for decades to come. Significant numbers of new cases of leprosy will continue to occur; they must be detected at an early stage and given regular and complete treatment with MDT. Some of the new patients will demonstrate evidence of disability at diagnosis, and some will develop disability after diagnosis. In addition, all patients with nerve function impairment (NFI), both those on treatment and those already cured, will be at risk of developing additional impairments. Although leprosy will continue to be a disease of low endemicity, and may even be rare in many areas, leprosy services (diagnosis, treatment, prevention and care of disabilities, rehabilitation) will need to be sustained far into the 21st century (¹).

2 The WHO elimination strategy

The WHO elimination strategy possesses two major components -- early case-detection, and treatment (by MDT) of all patients. The core elements of the strategy focus on improving community access to MDT by means of the delivery of MDT by the general health services (²), including:

- capacity building to enable all health facilities in endemic countries to diagnose and treat leprosy;
- insuring easy and uninterrupted access to free MDT by improving logistics; and
- motivating people to seek timely treatment by creating increased community awareness of the early signs and by changing the social perception of leprosy (³).

The elimination goal and the activities undertaken to achieve it, especially in the field of advocacy, have contributed greatly to the fight against leprosy. Strategically, it has been an excellent choice. Never before has such a broad and strong commitment to the fight against leprosy been found as during the past decade. This has contributed greatly to the rapid achievement of full MDT coverage of all registered cases. Moreover, on a global level, patients are diagnosed at an earlier stage of the disease (⁴).

Implementation of MDT has contributed to the dramatic reduction of the number of patients registered for treatment and, as a consequence, the case-holding workload of the health staff. However, the number of new cases detected globally has changed very little over the years, demonstrating the need to sustain leprosy services.

3 How may leprosy control activities be best sustained?

3.1 Integration of leprosy control within the general health services

Disease control can be defined as reduction of the incidence and prevalence of the disease, and of the morbidity and mortality resulting from the disease to a locally acceptable level as a result of deliberate efforts. Continued intervention is required to maintain the reduction (⁵).

The strategy to achieve control of leprosy consists of four major elements:

- early case detection;
- adequate chemotherapy (MDT);
- prevention of leprosy related impairments, and
- rehabilitation.

Implementation of this strategy ideally requires readily accessible, efficient and sustainable health services that cover the population fully, and are accepted by the community and the patients. This strategy implies that leprosy control activities should be implemented by the general health services. Several integrated programs have shown that leprosy control can be effectively implemented by the general health services (⁶⁻¹³)*.

0.0 Basic requirements for sustaining effective integrated leprosy services:

- The government should be committed to sustained leprosy control activities, and there should be a national policy on leprosy control.
- A prerequisite for integration is the existence of an adequately functioning general health service infrastructure (¹⁴). Where this does not exist, the vertical program should be continued for the time being.
- The change from a vertical to an integrated program is far from easy. The process must be carefully planned, and must be appropriate to the local situation. If the process is hurried and staff and patients are not properly prepared, the quality of patient care and the confidence of patients in the services, as well as their willingness to cooperate, will deteriorate. If the process is too slow, it is likely to fail by default (⁶).
- The process of integration must be introduced step-by-step (phasing in place, time and activities) (^{6, 7}). Important steps toward realizing this change are sensitization

* A number of articles describing experiences with integration are currently in press, and will appear in a special number of *Leprosy Review* devoted to this topic.

of administrators and health authorities, and sensitization and training of general health staff and former vertical staff⁽¹⁴⁾.

- Training should be based on clearly defined job descriptions for all categories of workers who have leprosy related tasks.
- Regardless of the level of endemicity in a country, a well-functioning central unit, usually housed in the Ministry of Health, is necessary. The central unit should be responsible for advocacy, policy formulation, technical guidance, technical training, planning, monitoring and evaluation. Moreover, countries should coordinate national and international donor support.
- An uninterrupted supply of anti-leprosy drugs must be guaranteed.
- Most vertical programs have detailed recording and reporting systems. With integration, however, these systems must be simplified to allow for appropriate data collection by peripheral, multipurpose health workers. The numbers of forms, reports or registers should be reduced to the minimum, and be incorporated into an already existing general health management information system. Only data directly linked to decision-making should be routinely collected.
- The private for-profit health sector will play an increasing role in the provision of leprosy services. This may pose problems, such as treatment by non-standard regimens, incomplete treatment, inadequate instructions to patients and the consequent risk of drug resistance, and increased incidence of disability. National strategies should therefore clearly define the role of the private sector, including training and quality control.
- Non-governmental organizations supporting leprosy control continue to be important partners with governments in integrated leprosy control programs. If donors wish to ensure the establishment of sustainable leprosy services, they must work with and strengthen the national general health services system.
- In integrating leprosy control into general health services, equity and quality of care for leprosy patients should be assured. This implies that the services for leprosy patients (including diagnosis, treatment, rehabilitation, *etc.*) should provide the same level of quality (not less, but also not more) as do the services for other health problems.
- In order to establish sustainable services, broad ownership of the strategy must be assured, both within the specific leprosy organizations and, equally important, outside⁽¹⁵⁾. It is important that the various agencies involved in leprosy control collaborate and coordinate their activities, in order to increase their effectiveness.

3.3 Referral services and specialized support

Integration means that day-to-day patient management, recording and reporting will become the responsibilities of general health staff. However, integration does not mean that specialized elements need disappear from the health service. On the contrary, specialized components must be available within the general health service at the central and intermediate levels for planning and evaluation, provision of training, technical supervision, advice, referral services (including those at hospitals) and research. Depending upon local conditions (*e.g.*, the incidence and prevalence of leprosy; the availability and level of training of various categories of health staff), each country or region must decide at which level of the health system such specialized support should be available, and whether this should be combined with specialized components for other diseases.

0.0 Combined vertical control programs

Combination of several vertical control programs, such as those for leprosy and tuberculosis, is not the same as integration within the general health services. Combination of two vertical programs into a single vertical program increases cost-effectiveness, because supervision, training, and patient management for both diseases can be implemented by the same personnel, thus reducing the costs of salaries, transport and facilities. The same advantages apply to integration, but with integration the gains are greater. In addition, a combined vertical program is subject to most of the limitations of a vertical leprosy program. Therefore, integration of leprosy control within the general health services is preferable to combination with another vertical program. (¹⁶).

1.0 Leprosy control in areas of low endemicity

In situations in which case-detection rates are low, a focused approach is appropriate, whereby services are provided mainly in selected general health facilities in the area in which leprosy still occurs. The skills of health workers will mainly be limited to suspecting leprosy (¹⁷). Referral centers should verify the diagnosis and start the treatment of the patient. Continuation of treatment could be delegated to the peripheral health facility serving the community in which the patient resides. The community should be informed, and the general health staff of the peripheral health facility should be trained in diagnostic skills and case management.

2.0 Health sector reforms

Because leprosy control is implemented within the health sector of a country, the services provided are highly dependent on changes in this sector. In many countries over the past several years, the health sector has been dominated by so-called health sector reforms (HSR), which have become the umbrella, under which a wide variety of changes and developments in the health sector have been brought together (^{18, 19}). HSRs have profound consequences for disease control programs, such as leprosy control. However, the strategy of HSR is consistent with that of leprosy control, because integration is also a

central element of the strategy of most HSRs. On the other hand, the drive of health sector reforms to decentralize decision-making and financing may have an impact on the sustainability of leprosy services: because leprosy is a relatively rare disease, district health authorities may reallocate resources to more pressing health problems⁽¹⁵⁾. This constitutes a challenge for national leprosy control programs and leprosy NGOs, which, in order to be effective, must appreciate the relative importance of leprosy and the need for appropriate control strategies. The resources devoted to leprosy must be in balance with those required for other, often much more serious, public health problems.

Recommendations

In order to guarantee sustainable leprosy services, leprosy control programs should be integrated within the general health services. The process of change from a vertical to an integrated program should be carefully planned, and must be adapted to the local situation. A prerequisite for integration is the existence of an adequately functioning general health service infrastructure. Timely training of general health staff and former vertical leprosy staff is important; it should be based on clearly defined job descriptions for all categories of workers who will have leprosy-related tasks. An uninterrupted supply of anti-leprosy drugs must be guaranteed. Recording and reporting of data must be simplified to allow for appropriate data collection by peripheral, multipurpose health workers.

Where case-detection rates are low, a focused approach is appropriate, whereby services are provided mainly in selected general health facilities in the areas in which leprosy still occurs. The skills of health workers will be limited mainly to suspecting leprosy. Referral facilities should confirm the diagnosis and begin treatment. Continuation of treatment could be delegated to the peripheral health facility serving the community in which the patient resides. The resources devoted to leprosy must be in balance with those required for other, often much more serious, public health problems.

1 How can appropriate and effective training be developed for all grades of staff involved in leprosy control?

Health-related activities should be undertaken by adequately trained workers at the most peripheral level of the health service as possible. In most leprosy endemic countries these are usually paramedical workers. Paramedical general health care providers play a central role in delivering cost-effective health interventions; they are easier to employ in rural areas, and usually communicate better with the patients. These workers must be adequately trained for their tasks, well-supervised, provided with logistical support, and linked with well-functioning district health services for referral.

Depending on the patient load, a tailor-made leprosy-control strategy will have substantial consequences for the specific level of expertise required. In areas of high endemicity, peripheral general health staff should be capable of diagnosing and treating leprosy under the technical supervision of specialized workers who are stationed at the intermediate level. This category of specialized staff will usually have responsibility for

diseases in addition to leprosy. In settings of low endemicity, the ability to suspect leprosy and refer the patient to a health unit capable of diagnosis and initiation of treatment is the most important skill required for peripheral general health workers. Continuation of treatment is another task that can be implemented at the most peripheral level. In areas with small patient loads, management of nerve damage will have to be concentrated in health facilities serving a larger population -- *e.g.*, a district hospital responsible for a population of 200,000-500,000. The centers that treat complications of leprosy and provide rehabilitative surgical services will be even more centralized.

Training programs should be both formal and informal, applying appropriate methods, including interactive learning and contact with patients, and should be based on the tasks assigned to the specific category of workers. In addition to the degree of endemicity of leprosy, the distribution of tasks will depend upon other local conditions, such as health service coverage, availability and level of education of the different categories of staff, *etc.*

The crucial problem is that a larger number of staff will have to be trained (also because of the high turn-over of staff), whereas, at the same time, it is obvious that some of them may never see a single patient. As the number of contacts between health workers and leprosy patients diminishes, fewer staff members will attain skills in case management and leprosy control. In terms of cost-effectiveness, the frequency, duration and the cost of training must be adapted to this situation.

Specific courses on leprosy for general health workers are not cost-effective in areas of low endemicity. Therefore, incorporating leprosy control into the curricula of medical faculties and paramedical schools (*e.g.*, as part of the instruction in dermatology and communicable diseases) is essential for both the successful operation of leprosy control as an integral part of the general health services, and sustaining leprosy expertise within the health services (²⁰). Courses dealing specifically with leprosy may still be required for supervisors and training of trainers.

Each leprosy-endemic country should have at least one center of expertise for management of the complicated patients and training of specialized staff. This need not be a special leprosy hospital, but may well be an adequately equipped general (university) hospital (¹⁷).

General health staff with responsibilities for leprosy-related activities should preferably be trained in their own country. Because of increasing integration of leprosy control programs, the need for international training for leprosy will decrease, except for the training of highly specialized experts in management of leprosy control, clinical leprosy, reconstructive surgery, *etc.* At the international level, some centers of excellence should be maintained for the training of leprosy specialists in the various disciplines and research. Such institutions could diversify according to local capacity and needs (²¹).

Donor agencies could play a supportive role in the production and distribution of appropriate health learning materials.

Technical supervision is an essential element in human resource management and development, and remains a cornerstone of integrated leprosy control programs. Technical supervision implies continuous guidance, support and on-the-job training. This motivates staff and prevents loss of skills. The contents of the on-the-job training should be consistent with the contents of the national manual and the formal training courses. Identifying strong and weak spots in the supervised institution and its staff members, listening to feedback and trying to remove obstacles are important tools with which to enhance the program.

Recommendation

Training of staff involved in leprosy control should be based on the tasks assigned to the specific category of workers. In addition to the degree of endemicity of leprosy, the distribution of tasks will depend upon other local conditions, such as health service coverage, and the availability and level of education of the different categories of staff. Leprosy should be included into the curricula of medical faculties and paramedical schools.

2 What is the evidence that IEC interventions can change the knowledge, attitudes and behavior of the public with regard to leprosy-especially with regard to self-reporting, reduction of stigma and compliance? Which methods are most cost-effective?

Information, education and communication (IEC) is defined as a set of activities based on the process of communication and learning that is designed to improve the health behavior of the populace. In the case of leprosy, IEC activities aim to dispel the social stigma of leprosy, and to seek the participation of the community in facilitating early self-reporting⁽²²⁾. IEC messages focus on the cause of leprosy, early signs and symptoms, the need for treatment in order to be cured, the availability of free drugs at the nearest general health facilities, and that disability can be prevented. An equally important part of IEC activities is education of the patients and their relatives regarding compliance with treatment, prevention of disability and self-care.

Many different IEC methods are used for public education, and there is not a clear consensus as to which are the most effective:

- talks to communities, community leaders, *etc.*;
- radio and TV messages;
- street dramas, puppet shows, posters, and pamphlets;
- talks at schools, clinics, *etc.*;

Is it realistic to expect that massive spreading of information will eventually change people's attitudes and behavior with regard to leprosy? There is evidence that educational approaches, especially participatory approaches, result in increased knowledge, change of behavior and reduction of stigma (²³⁻²⁵). It has also been reported that mass-media campaigns using dynamic and entertaining media messages have an impact in shifting attitudes (²⁶). Successful health education depends on using a few messages of proven benefit, repeatedly and in many forums (²⁷). The BBC media campaign in India in 2000 contributed strongly to reduction of the stigma and to early self-reporting of patients (²⁸). However, other reports suggest that IEC activities were much less effective than had been expected (^{29, 30}). Moreover, increased knowledge of leprosy does not always generate a positive change of attitude towards patients or earlier self-reporting (³¹⁻³⁴). Therefore, studies should be carried out to evaluate the impact of IEC activities, and to identify the methods that are most cost-effective under different conditions.

Stigma continues to exist at various levels in many countries. The isolation of vertical leprosy control programs may encourage rejection of sufferers from the disease, whereas integration of leprosy control into the general health services may have a positive educational effect on the community towards reduction of the stigma.

Recommendation

There is evidence that IEC activities, especially participatory approaches, result in increased knowledge, change of behavior and reduction of stigma. Studies should be carried out to identify the methods that are most cost-effective under different conditions.

Whenever IEC is planned, the following issues should be considered:

- MDT services delivered by well-trained staff should be available in the area before IEC activities can be implemented;
- because the leprosy problem is decreasing, a trade-off must be made in each country between the magnitude of the problem and the inputs required for raising public awareness. Combination of IEC for leprosy with IEC for other diseases is more cost-effective and, moreover, does not set leprosy apart from other health problems;
- cooperation with other sectors such as the Ministry of Education or the Ministry of Information. A concerted approach will gain in efficiency and effectiveness;
- inclusion of IEC techniques in training curricula for all levels of staff. Health workers must be taught communication skills with the aim of establishing effective communication with the patient, his family and his neighbors;

- inclusion of guidelines on IEC in the national manual, and development of simple and practical instruction manuals to be used in the field. This will strongly facilitate effective IEC;
- application of the WHO communications tool box. This is useful for developing local IEC materials ⁽³⁵⁾;
- IEC activities should consist of the most appropriate mix of various elements (*e.g.*, personal selling, advocacy, advertising, printed materials, community mobilization, point-of-service promotion). The use of individual elements will depend upon available resources, both financial and managerial, as well as the specific audience or behavioral outcome that is being elicited ⁽³⁶⁾.

3 Special initiatives

In 1995, WHO introduced Leprosy Elimination Campaigns (LECs) and Special Action Projects for the Elimination of Leprosy (SAPEL) as special initiatives to accelerate progress towards the elimination of leprosy as a public health problem.

6.1 What role can LECs play in promoting sustainable services?

The main objective of LECs is to detect leprosy patients who have remained undetected, and to cure them with MDT. LECs are indicated in areas with a perceived large number of “hidden” patients. The major elements of LECs are training of general health staff, community education, passive case-finding and treatment. LECs are intended to be one-time activities, enabling every peripheral health center to provide MDT services ⁽³⁷⁾. LECs have been widely implemented in different ways, and have increased public and professional awareness regarding leprosy and its treatment. Hundreds of thousands of patients have been detected and placed on MDT during LECs ⁽³⁸⁾. Also, in some countries, LECs have contributed to the integration process ^(39,40).

However, a number of risks are involved. Especially if LECs are modified to include active case-finding surveys, as has been done in many countries, they may harm the development of effective and sustainable leprosy services ⁽⁴¹⁾. Those suspected of leprosy are directed to report to campaign teams, sometimes at makeshift venues such as huts or schools ⁽⁴⁰⁾, supporting the misconception that leprosy is a disease apart from other diseases, which must be diagnosed and treated by special services. It harms the people’s confidence in the general health staff, which is essential for self-reporting of new cases, compliance with treatment and early reporting of NFI.

Case-detection may decrease temporarily during the first years after an LEC, as will the prevalence, once the patients found in the course of the LEC have completed their treatment. The backlog may gradually build up again, after which case-detection and prevalence may increase. Repeated LECs might prevent this development ⁽⁴²⁾. However, accessibility, compliance with treatment, monitoring, drug supply, and prevention of

disabilities can be more effectively realized by permanently available general health services than by repeated, short-term campaigns (⁴¹).

Integration of leprosy services within the general health system, including the establishment of supervision, monitoring and uninterrupted drug supply, is the best strategy to bring sustainable services closer to the patients. In conformity with their original aims, LECs can be a valuable element of this strategy. In order to establish effective leprosy services, case-finding in LECs must be based on self-reporting to the general health staff, and should include the diagnosis and management of nerve function impairment (^{41, 43}).

Recommendation

LECs should be implemented as an element of the process of integration. In order to establish effective integrated leprosy services, case-finding in LECs must be based on self-reporting to the general health staff, and should include the diagnosis and management of NFI.

6.2 What can be done if there is no health care infrastructure?

WHO designed Special Action Projects (SAPEL) to address unavailability of MDT services among special population groups living in difficult-to-access or under-served areas, including ethnic minorities, nomads, refugees, *etc.* The basic approach of SAPEL was the development of innovative, situation-specific strategies for diagnosis and delivery of MDT, including capacity building of local health workers or volunteers, and promotion of community awareness and participation. Linkages of WHO with other partners, including NGOs, in the planning and implementation of activities have been encouraged, with a view to replicating the strategies in other under-served populations. By the end of 2001, of 92 approved projects in 30 countries, 73 had been completed, and approximately 12,500 patients had been reached in a target population of 33 million. The identified solutions included flexible MDT delivery to border-crossing nomads by heads of clans, reduction of defaulting among slum dwellers by involvement and training of private practitioners, support of military personnel in areas of insecurity, *etc.*, (³).

Many SAPEL projects can be conceived of as health systems research projects, in which a problem is identified and a specific solution defined and tested. Although the number of cases detected is relatively small, the SAPEL initiative has been valuable in demonstrating how countries may identify approaches to expand leprosy services to under-served populations. These activities should be combined, wherever possible, with other special initiatives to address other health problems.

Recommendation

In leprosy endemic areas in which there is no health infrastructure, innovative, situation-specific strategies for diagnosis and delivery of MDT should be developed. This kind of activity should be part of the overall framework of the integrated leprosy services.

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