Elimination of Leprosy as a Public Health Problem*

The global burden of leprosy

Leprosy occurs in significant numbers in 87 countries or territories of Asia, Africa, and Latin America. Estimates for 1993 indicate that a global total of 3.1 million cases, of which approximately 2.3 million were on treatment registers by mid-1993. About 600,000 new cases are being detected annually and 2400 million people live in countries with a leprosy prevalence of more than 1 per 10,000. In all, between 2 and 3 million individuals are visibly disabled as a result of leprosy.

Of all the communicable diseases, leprosy is most important for its potential to cause permanent and progressive physical disability. In addition, the disease and its visible disabilities in particular, contribute to intense social stigma and the social discrimination of patients. It is estimated that the expected healthy years of life lost is about 6.3 years per patient. Disability adjusted life years (DALY) lost globally due to leprosy is estimated to be about 1 million per year.

Ten years of MDT

Until 1980 dapsone, through domiciliary treatment of patients, was able to contribute to a degree of success in leprosy control in well-organized programs. However, the resistance of *Mycobacterium leprae* to dapsone became widespread, making treatment increasingly ineffective. In addition, the long-term and often life-long treatment required with the drug led to poor patient compliance and ineffective disease control in general. This period of failure and frustration changed dramatically with the introduction of greatly improved treatment through the application of combinations of drugs, known as multidrug therapy (MDT), the standard regimens of which were first recommended by a World Health Organization (WHO) Study Group in 1981.

The recommendations on MDT received enthusiastic support from leprosy-endemic countries, donor agencies and professional bodies alike. The increasing acceptability of MDT among national health services and leprosy patients themselves is due to: a) the fixed, and relatively short duration of treatment; b) increased acceptance and compliance to treatment by patients; c) the low level of toxicity and treatment-related side effects; d) the very low relapse rates following completion of treatment (mean cumulative risk of 1% over 9 years of follow up); e) a significant reduction in the frequency and severity of erythema nodosum leprosum (ENL) reactions; and f) the absence of treatment failures attributable to drug resistance.

The introduction of MDT also has contributed to other improvements in the organization of leprosy control. Some of these indirect benefits have been substantial in those countries starting with poor leprosy control activities. For instance, reviewing leprosy registers and deleting inactive cases have contributed considerably to case-load reductions in certain countries. In several others it was possible to implement MDT, even where the basic health services were not so very well organized.

Although MDT does not have any direct impact on deformities in those patients who are already deformed, it has contributed substantially to the prevention of deformities through early self-reporting and early cure. With the increasing application of MDT and the large number of patients being discharged from registers, some programs are increasing their focus on deformed patients, whether under treatment or already cured.

Following its widespread introduction in the 1980s, leprosy prevalence has been greatly reduced. By the middle of 1993 (10 years after its introduction) about 4.2 million patients had been cured with MDT and the global prevalence had been reduced by about 57%.

Opportunities and possibilities for eliminating leprosy

The WHO recommendation on MDT is recognized today as a major technological improvement in leprosy control. In the ab-

* Based on state-of-the-art lecture presented at the XIV International Leprosy Congress on 1 September 1994, Orlando, Florida, U.S.A.

sence of any primary preventive approach to date, such as an effective vaccine, MDT remains the sheet anchor of leprosy control. Because the leprosy patient is the only epidemiologically significant reservoir of infection, there is every hope that through early diagnosis and effective treatment, the transmission of the disease could virtually be stopped over a period of time.

Experience in several countries in the past 10 years or so has demonstrated convincingly that in well-organized leprosy control programs it is possible to reduce the prevalence of registered cases up to tenfold within a period of 5 years.

In several countries MDT has provided governments with the opportunity to increase the priority given to leprosy control and to strengthen their political commitment for leprosy. MDT also has made possible the strengthening of health services for leprosy control in many countries. Its cost-effectiveness and the results obtained have also contributed to increased resources, including those from bilateral international agencies as well as nongovernmental organizations (NGOs) both national and international, in a number of leprosy-endemic countries.

World Health Assembly's resolution on elimination of leprosy

Because of the optimism that developed as a result of MDT, the Forty-fourth World Health Assembly (WHA), which met in May 1991, adopted a resolution to eliminate leprosy as a public health problem by the year 2000, and defined elimination as attaining a level of prevalence below 1 case per 10,000 population. This resolution declared WHO's commitment to attaining global elimination, and urged countries to increase their political commitment toward the leprosy elimination goal.

By establishing a target for the year 2000, the World Health Assembly drew attention to the effectiveness of the available treatment technology, the need for leprosy-endemic countries and donor agencies to stop regarding leprosy as a permanent problem and to redouble their efforts toward controlling the disease, and to accept leprosy as simply another health problem with a clear solution.

Clarifications on elimination of leprosy

What is elimination? The term "elimination of leprosy as a public health problem" clearly defines elimination as attaining a prevalence below 1 case per 10,000 population. It is obvious that elimination is not total eradication of the disease. We are willing to accept a small residual problem in the hope that, when such low levels are reached, the transmission of infection will be so minimal that the disease will eventually die out. Although the WHA resolution refers to global elimination, it is implicit that it should also occur at regional and national levels, and ultimately at the local levels.

Perceived concerns about elimination. Some people are concerned that MDT is not showing any visible impact on the incidence of leprosy as reflected in case-detection figures. This is partly true because in some countries the number of new cases detected annually remain constant, despite MDT implementation, for quite some time. This is because it is only recently that its coverage is 50% or more.

In the early years of MDT implementation, some countries saw an increase in the number of new cases detected annually: this was due to a revitalization and expansion of the program which attracted new patients who would otherwise not report to the health services. However, there are several programs which are noticing a significant but steady decline in the number of new cases detected annually. It is likely that after an initial increase or static period others will also notice a declining trend as MDT is implemented more widely for a longer period of time.

The second important concern seems to be that the call for elimination may undermine the capacity of some agencies to raise funds. It is not clear if this is actually happening or if it is merely a fear. In any case this concern can be addressed by adequately informing the donor community of the situation.

Strategy for global elimination

Following the adoption of the WHA resolution, strategies to attain elimination have been discussed at national and regional levels, and based on these WHO has developed

a global strategy for the elimination of leprosy as a public health problem. A global strategy is essential if the envisaged goal is to be achieved. The time-limited nature of the goal warrants constant review of the progress being made and the application of flexible approaches, particularly in areas where special problems are faced.

Elimination aims at reducing prevalence below 1 case per 10,000. Thus a major focus, at least in the early years, is to reach all prevalent cases with MDT and to cure them. By continuously reducing the source of infection, it is expected that transmission of the disease will be significantly reduced over a period of time.

Leprosy is a disease with a very uneven distribution among and within countries. The development of health services and their capacity to implement disease control vary widely in the different leprosy-endemic countries. The elimination strategy will have to take into account such variations and be adaptable to suit specific needs.

The uneven distribution of leprosy among countries is very striking globally. Based on 1993 data, it is seen that just one country, India, contributes to 55% of all estimated cases in the world; six countries, namely Bangladesh, Brazil, India, Indonesia, Myanmar and Nigeria, together contribute to 80%; and 94% of all registered cases in the world is accounted for by the top 25 leprosy-endemic countries. The gap between estimated and registered cases shows variations among countries, and is particularly large in those with no organized case-detection activities.

Delivery of leprosy control services also varies considerably. A small number of high-endemic countries and some dependent upon external support have special vertical programs while in a large majority leprosy control is delivered through integrated services, although most of them have specialized supervisory and referral services.

The approaches essential for achieving elimination are the detection of patients and their treatment with MDT. Disability prevention and rehabilitation are also important, although not directly related to the elimination goal.

Stratification, target-setting and working toward the targets are essential aspects of the elimination strategy. Capacity building, preparation of action plans and resource mobilization will be the other important elements of the strategy.

If the intensification of leprosy control activities through MDT continues as anticipated, the expectations are that the figures for estimated prevalence, registered prevalence, estimated incidence and case-detection will approximate each other nearer the year 2000.

Stratification. In terms of stratification, the following will be the most important factors to be considered: a) size and intensity of the problem: registered prevalence—absolute number and rate; estimated prevalence—absolute number and rate; annual case-detection—absolute number and rate; and estimated incidence—absolute number and rate. b) delivery of leprosy control services: MDT coverage—current and cumulative rates; accessibility and type of health services; and social factors, including community awareness, that enable early detection of cases. Resource allocation and priority setting at regional and global levels, and development of strategies and target setting at country level could be based on the above considerations.

From the national point of view, the strategy will have to take into account registered prevalence and cumulative MDT coverage, the gap between estimated and registered cases, the existence or not of inactive cases in the registers, the proportion of disabilities among new cases as an indirect marker of delayed diagnosis, and health service accessibility and social factors.

A stratification based on the most significant epidemiological and operational indicators helps for setting priorities. For example, four strata can be used for categorizing countries. If in the top stratum the turnover is optimal and patients are diagnosed, treated and cured in a short period of time, this is likely to lead to elimination early. When the prevalence/incidence ratio is high and MDT coverage is poor, elimination will not be achieved without substantially intensifying control activities.

Target setting. The elimination strategy calls for the setting up of intermediate targets and their constant monitoring. Short-term target-setting will relate mainly to disease reduction through cure of patients with MDT and the consequent reduction in prev-

alence, while target-setting for the latter phases of MDT implementation will, in addition, be aimed at disease reduction in the occurrence of new cases through reduction in transmission of infection. While prevalence reduction is directly proportional to the number of patients treated, incidence reduction will depend upon treating all or nearly all patients, particularly of the multibacillary (MB) types, and the duration of maintenance of high coverage with MDT, to allow for occurrence of cases infected prior to its introduction.

Activities aimed at elimination of leprosy at country level

For the elimination strategy to be effective it needs to be simple enough to be widely implemented and flexible enough to adapt to the rapidly changing needs of the disease and disease control. Existing plans should be adapted and phased in order to take into account the time frame defined for elimination. The activities can be grouped broadly as preparatory activities, core activities and evaluating activities.

Preparatory activities include preparation of a plan of action for the elimination of leprosy, mobilization of resources, strengthening of health services and training. Plans of action should include intermediate targets and how they are expected to be achieved. The elimination strategy does not envisage an endless activity but rather a substantial investment limited to a specific period of time. This calls for the mobilization of additional resources, additional to regular sources. Strengthening of health services to ensure implementation of leprosy control is important and should be based on integrated peripheral health service provided it is supported for supervision, referral, training and evaluation from the intermediate level. The intensive nature of MDT implementation calls for special task-oriented training to peripheral health workers. Management training for program managers at different levels is also essential to ensure success.

Core activities include case-detection, review of treatment registers, MDT implementation, treatment compliance and completion, disability prevention and management, and community participation. Case-detection should aim at discovering hidden cases not reporting to health services because of social stigma, as well as identifying early cases not recognized by the individual and the community. It will be necessary to maintain a high level of sensitivity to suspect leprosy; however, a high level of specificity will be required to confirm the diagnosis of leprosy, especially where the prevalence is becoming very low. Information on registered cases in countries with large prevalence rates and low MDT coverage will need to be checked for accuracy to find out whether or not the cases actually exist and whether or not the patients have active disease requiring MDT. The implementation of MDT is central to the elimination strategy. The initial aim is to reach all registered cases, and to cover all new cases as and when identified. Logistics for drug supply and treatment delivery through a flexible approach are important aspects of MDT implementation. Treatment compliance is essential if MDT is to be successful and most patients who start MDT should complete their treatment within the required period. Although MDT is central to the elimination strategy, disability prevention and management are also quite important and these activities, employing simple cost-effective approaches, should be incorporated into routine leprosy control activities. Community participation should be an integral part of all efforts toward the elimination of leprosy.

Evaluating activities include both program monitoring and evaluation as well as epidemiological surveillance. Program monitoring and evaluation is an essential activity for measuring the progress toward specific targets as well as identifying problems needing specific local solutions. Epidemiological surveillance should be carried out through information collected routinely as well as through special investigations. Such surveillance is also important to predict future trends. Surveillance through sentinel centers is also likely to be a useful method.

Implementation of elimination strategy

The basic strategy of stratification and targeting applies to all levels—global, regional, national and subnational. At the global level, the top 25 countries contributing to 95% of all leprosy cases will be the major

target. Even among these, certain countries with very large case-loads and high incidence will need intensive efforts if elimination is to be achieved. While reducing prevalence will be directly proportional to MDT efforts, reducing incidence will be dependent upon other additional factors. Thus, countries which have an annual incidence rate of less than 1 case per 10,000 population and a prevalence rate of several times that figure will, by administering MDT to all the existing leprosy cases, achieve the elimination goal much earlier and more easily than countries which have annual incidence rates substantially higher than 1 per 10,000 population.

Additional resource needs

The elimination strategy envisages substantial additional resources up to the year 2000. Major costs will revolve around MDT and carrying out other activities, including case-detection, training, supervision, referral, and monitoring and evaluation, the cost for which varies greatly according to prevalence and health service development in different countries. Assuming that between 1993 and 2000 about 6.5 million patients will have been treated with MDT, the estimated additional costs would amount to about US$420 million (including US$140 million for drug costs).

Potential problems

It is clear that the treatment technology for leprosy through MDT is working very well with very high cure rates and very low rates of relapse. So far, there has been no significant problem with drug resistance. However, with the increasing use of MDT by different sectors, and some employing injudicious drug combinations, drug resistance may emerge as a problem in the future, and better and newer MDT may become necessary. Currently, more than one new combination of drugs is already under clinical trial, providing optimism that better MDT regimens capable of dealing with drug resistance problems and of reducing the period of treatment will become available in the future.

Although MDT has contributed to a rapid reduction in prevalence, its positive impact on case-detection and incidence has been limited and in many areas not easily visible, at least during the first 5 years of its implementation. This appears to be due largely to the long incubation period of leprosy as well as operational factors such as vigorous case-finding activities. However, it is expected that over a period of 5–10 years of implementation, MDT will have an impact on incidence rates. This is already seen in a small number of countries. However, it is not clear yet as to how strong the impact will be, particularly in areas where the current intensity of the disease is very high. If the impact in such countries is not sufficiently strong, it may be that the elimination goal will not be attained by the year 2000 in a very small number of countries and an additional 5–10 years to attain that goal may be needed.

MDT has no direct impact on disability since disability prevention primarily depends upon early case-finding. Pre-existing nerve damage and deformities among new patients cannot be reversed by MDT itself. Among patients who have been cured through chemotherapy, significant numbers of those with residual deformities will persist well into the next century.

The application of MDT requires a minimum level of health service organization not always found in many leprosy-endemic areas. Despite MDT being quite a robust technology for treatment, many patients are not able to benefit from it because of the inaccessibility of health service facilities. MDT coverage beyond 80%–90% will be relatively difficult in view of the problems relating to patients living in inaccessible areas and to patients not complying with regular treatment.

Irrespective of political commitment and availability of resources, the situation is likely to be relatively more difficult in countries starting with a larger base of prevalence than in countries starting with a smaller base, warranting even more vigorous efforts.

Research needs

The most important area for research will continue to be the development of better treatment for affected individuals with existing and new drugs. The impact of HIV infection on the individual patient and the epidemiology of the disease also will need close monitoring although thus far HIV infection does not appear to have any adverse

effects on the leprosy situation. In addition, studies to monitor post-treatment relapses, development of resistance to existing and new drugs, including studies to improve drug-delivery systems and patient compliance, will be important. Tools to identify subclinical infection of sufficient sensitivity and specificity will need to be developed in order to facilitate epidemiological monitoring of the disease in the community.

The evaluation of immunoprophylactic efficacy of candidate antileprosy vaccines in field trials will have to continue, along with research relevant to the development of second-generation vaccines although any antileprosy vaccine, when developed, is likely to be used only in restricted situations. Studies addressing the significant issue of nerve and tissue damage need further support. The highest priority will remain with health services research or operational studies directly beneficial to the control programs.

Post-elimination issues

As the goal nears, tools and methods for monitoring and evaluating very low prevalence situations will be important in order to certify whether or not elimination levels have been achieved. Furthermore, since elimination is not eradication, different strategies will have to be developed to deal with the very small number of incident cases and the backlog of already deformed individuals. Maintaining skills and facilities for diagnosing and treating leprosy will be particularly important. While its resurgence after reaching very low levels is not expected to be a significant problem, it is important to maintain epidemiological surveillance.

Need for a partnership approach to eliminating leprosy

Eliminating leprosy as a public health problem calls for coordinated efforts by all interested parties, keeping in mind the specific mandates of the various agencies interested in leprosy control, the amount and nature of the resources available to them, their relative advantage and their special interests. Ongoing coordination efforts should be further strengthened so that the resources available are utilized optimally.

Leprosy programs which lack resources are being supported by the international community, and particularly by agencies such as the Sasakawa Foundation and international NGOs such as the International Federation of Anti-Leprosy Associations (ILEP). ILEP members have already committed themselves to providing "MDT for All" by the year 2000.

Conclusions

Given the available and anticipated technologies and strategies for leprosy control, given the political will that has been generated in recent years, and given the opportunities to raise resources through various mechanisms, the attainment of eliminating leprosy as a public health problem by the year 2000—in spite of difficulties foreseen in a small number of countries—should be considered as a real possibility. However, the attainment of the goal will not come easily, and it really calls for the vigorous and coordinated efforts of all concerned.

It is clear that there is still an immense amount of work to be done if this elimination target is to be achieved by the year 2000. It can be achieved provided that further, substantial, intensified efforts are made, both in terms of action and mobilization of adequate resources. Such intensification is important, particularly during the next few years. For the leprosy-endemic countries, it is an important opportunity to solve a major public health problem, and it cannot be missed.

—Dr. S. K. Noordeen

Chief, Leprosy Program
World Health Organization
Geneva, Switzerland