

TAKING HOME LESSONS FROM THE 15TH INTERNATIONAL LEPROSY CONGRESS

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For the last 5 years, since the 14th Congress in Orlando, work on leprosy has been dominated by the continuation of what I would call the Great Chemotherapeutic Initiative, multiple drug therapy (MDT), in the context of the 1991 Resolution of the World Health Assembly on the "elimination of leprosy as a public health problem."

The rationale underlying this approach is that the clinical patient is the only reservoir of *Mycobacterium leprae* and the only source of infection for secondary cases. Therefore, by effectively treating these patients, transmission should be gradually reduced and ultimately interrupted. Incidence should thus, in the long term, be reduced to zero. MDT, as recommended by a WHO Study Group in 1981, has proven to be an effective treatment, with the major advantage that it prevents the emergence of drug-resistant strains of the bacillus. It should therefore be asked to do the job.

This strategy was made possible by the confluence of several orders of opportunity: not only the scientific opportunity (the natural history of the disease at the present state of knowledge), but also technological (MDT and the blister pack), political (commitment of the governments) and financial (support from a number of NGOs) opportunities.

Under the leadership of WHO, full use has been made of this unique window of opportunity. Objectives were defined in terms of targets (prevalence) and time-frames. Guidelines were developed. Efficient systems for the analysis of epidemiological trends and the monitoring of drug distribution were set into place. Imaginative and innovative approaches were devised in order to reinforce or supplement current leprosy control activities centered on MDT, such as the Leprosy Elimination Campaigns (LEC) and the Special Action Projects (SAPEL).

As made clear at the Congress, the elimination program as defined has proven

highly successful. Prevalence of registered cases has been considerably reduced worldwide, the elimination threshold of 1 per 10,000 population has already been attained in many countries. In a number of countries, however, including large ones, some leadtime should be given after the deadline of the year 2000 to allow for the full implementation of the program.

The ongoing elimination program also has an important added value: It helps developing capacity building and managerial skills at the country level, as shown through a large number of reports from national leprosy programs. It is also stirring community participation. It promotes a culture of partnership between all these parties concerned, that is, national governments, international organizations, nongovernmental organizations, as well as the constituency of the persons affected by the disease, referred to today as the stakeholders. In addition, for a large part due to the success of MDT, the stigmatization of the persons affected with leprosy has considerably diminished. These encouraging signs would have been unthinkable even 20 years ago.

In many countries, however, as reported at the Congress, in spite of the dramatic fall in prevalence, the number of newly detected cases reported each year does not show a marked decline. A number of operational reasons could be invoked to explain this apparent epidemiological paradox. All the same, it suggests that transmission might possibly be maintained at a level higher than expected. Could it be that the untreated or relapsing clinical patients do not constitute the sole source of transmission of the disease? To what extent could people with subclinical infection serve as a source of transmission? Would an extra-human reservoir of *M. leprae* exist and, in that case, what, where, and how does it operate?

These are questions that have resisted elucidation for ages. They nevertheless have important implications. Will transmis-

sion be maintained in some countries at a low level with no hope for further progress, at least for a while? Should we learn to live with leprosy as a rare disease, and concentrate on the prevention of disability in order to render it, in a way of speaking, "but a minimal skin inconvenience"? Should we be worried that, if large-scale MDT is stopped, incidence will resume? If so, what other strategy should already be envisaged and worked out to counteract this possible backlash?

It is too early to say. The next 5 years will provide a crucial test to vindicate the basic assumptions regarding transmission. Nevertheless, it is not too early to prepare for unpleasant surprises, however unlikely they may seem.

New investigative tools are being developed which may help to solve these issues. By comparing the gene sequences of *M. leprae* and *M. tuberculosis*, synthetic peptide skin tests can be designed that would identify individuals infected with or exposed to *M. leprae*. Actual proteins and products of genes have also been obtained from armadillos and tested for their immunogenicity. The prevalence of PGL-I antibodies has been correlated with the prevalence of clinical cases in endemic areas. Regarding the possible existence of an extra-human reservoir, using the polymerase chain reaction (PCR), DNA of *M. leprae* has been found in the water supply of rural communities that have a high prevalence of leprosy.

PCR is opening the door to the study of the epidemiology of leprosy infection. Hypotheses regarding an animal and/or environmental reservoir are becoming testable. In a large international cooperative research project conducted in a number of endemic countries, PCR is used to study the prevalence of subclinical infection, the risks associated with exposure to positive PCR individuals, the infection rates, the cell-mediated immunity in the nasal mucosa, and the role of the nose as the primary site and portal of entry for the bacillus. A pattern for the pathogenesis of early leprosy infection starts to emerge.

Although it may at times look as though new technologies are utilized to revisit old ideas, much can be expected from these studies in the years to come, and could have

significant implications to face possible setbacks and make room for the need to adjust the post-elimination control measures.

As a parenthesis, though this is perhaps not the right place, a word should be said on the importance of the *M. leprae* genome sequencing project, now close to its completion. It will in some way substitute for this long sought for and never attained goal of its cultivation *in vitro*. A number of epidemiologic as well as more fundamental research undreamed of until recently will become possible. Matches and mismatches between the genetic sequences of *M. leprae* and *M. tuberculosis* will offer new insights into the respective distastes or gustos of these microorganisms, as well as help in designing drugs, especially targeted for specific metabolic pathways. It could also lead to the engineering of a synthetic vaccine.

It is amazing to think that, while for a long time attempts were made, often with little success, to combine the field activities against leprosy and tuberculosis, the two bacilli will now be companions in the laboratory together with a panoply of other mycobacteria.

Having considered these current worries, and turning resolutely to the future, what is to be done?

It is obvious that a prevalence of 1 per 10,000 as the target of elimination, and the year 2000 as the deadline, are not goals *per se*. They are nothing but milestones on the way to having the "final word" against leprosy. I deliberately use the term "final word," because it is vague enough and precludes a firm definition. According to the epidemiological context of each country and its socioeconomic conditions, the aim could be to make leprosy a rare disease, ultimately eradicating it.

It should be clear for everybody that elimination programs should be continued after the year 2000 to achieve what should have been achieved by then. Conversely, it would be absurd to wait for the millennium to initiate, develop or expand needed activities not directly related to the program.

The question is: can we go along with the same objectives, the same strategy, the same methods, once the prevalence goals of elimination have been achieved. The answer, I think, is clearly "No." The program of elimination of leprosy as a public health

problem was and still is linked to the tremendous opportunity offered by chemotherapy, which has allowed us to strike a full-fledged blow, knocking out *M. leprae* inside the human reservoir. But there is more to leprosy than MDT, and more to the fight against leprosy than mere decimal digits. The next patients below 1 per 10,000 and all those that follow will still be patients in need of treatment. After populations have been efficiently dealt with, the individuals are still there.

This being said, what has definitely emerged from the Congress is a strong consensus that the future will be different. New challenges will need new approaches.

What will be different?

A preliminary remark to start with. Changes will not be achieved overnight. It will be a long process requiring patience, flexibility and determination. The key components as summarized by the Congress read as follows: a comprehensive patient-oriented approach, relevance to those affected, partnership, sustainability, and training.

What will be different though?

First, to the extent that the elimination program is successfully completed, and there is every chance that it will be, the epidemiological situation will show different patterns than at present.

Second, the political commitment is likely to evaporate as the elimination program becomes increasingly successful.

Third, the general evolution of society, together with reforms in the health sector, will bring with it threats as well as opportunities.

Let us start first with the changed epidemiological context. In low-endemic situations, that is, where the disease is becoming rare, patients will become harder to find. They could also show up at a later stage, with an increased risk to present impairment of some sort.

The activities will have to focus on sustained detection and early case finding. The surveillance of cured cases will become of major importance. With leprosy being in some way now defined as, and classified according to, "eligibility for a treatment of fixed duration," there has been some tendency toward complacency, i.e., a tendency to overlook follow up after completion of therapy. At times it looks as though patients

are not supposed to relapse. There is, however, a set of post-treatment complications, such as neuritis, eye lesions, problems associated with sensory loss and deformities, reactions, which need to be watched closely for several years after treatment has been stopped. Such surveillance is particularly important in view of the recently introduced shortening of MDT in multibacillary patients, possibly bringing with it an increased risk of relapse. This is one more reason for reinforcing surveillance, because the occurrence of small outbreaks or clusters of secondary cases cannot be excluded.

It should be kept in mind that low endemicity, however it is defined, refers to two contrasting situations: "natural low endemicity" on the one hand, in those areas where leprosy has been tailing off for many decades, and "induced low endemicity," engineered by the great chemotherapeutic initiative, on the other. One of the basic postulates of the MDT elimination program has been that by reaching low levels of prevalence, the transmission of the disease will automatically plug into the natural low endemicity dynamics, rendering further surveillance somewhat redundant. Such an assumption should now be revised in view of the persistence of relatively high detection rates. Incidentally, reports on the trends of leprosy in those areas where it has been on the way of disappearing for a long period of time are particularly valuable to test the validity of this postulate.

Secondly, priorities. There are so many health issues requiring attention and competing for resources that it would be naive to expect political commitment to be maintained at the present level while leprosy would have vanished as a public health problem. There are such things as challenge fatigue.

Many issues will still be facing the disease once elimination as a public health problem has been achieved. One should, therefore, strive to keep leprosy on the agenda even if, as one participant put it, no longer with capital letters. Just as high priority does not mean exclusivity, reduced priority should not be taken as absence of priority.

Among the issues for the future, no doubt the most important is the disablement leprosy causes among a large proportion of

the affected persons. Leprosy is said to be one of the four main causes of disability in the Third World. Statistics presented at the Congress were eloquent in this respect. It has even been proposed that early detection be defined as "detecting a case of leprosy before disability sets in."

As the number of patients detected lowers, the proportion of disabled among them could increase. There is a danger that stigmatization and exclusion would again set in, as is already suspected in some countries. Good programs for the prevention and management of disabilities should help in convincing governments and funding agencies that leprosy still constitutes a problem deserving careful attention.

Finally, leprosy activities in the years to come will likely have to be carried out in a context of accelerating reforms of the health sector, including increasing privatization of services.

In low-endemic situations, vertical programs are no longer effective or justified. There will be a need to dismantle vertical leprosy programs and shift to a policy of suspicion at the periphery, and referral to specialized levels for diagnosis and the management of complications. Detection and referral will have to be integrated into general health services, which supposes training and the capacitating of health workers. Private practitioners, and especially dermatologists, as well as the traditional sector whenever appropriate, should also be involved in referring suspect cases. Public awareness of the disease should be promoted. Self-help groups can be very useful in this respect. The importance of educating patients and families in recognizing the early symptoms of the disease cannot be overemphasized. In addition, quality of care will be essential to enhance the credibility of the program and to sustain the collaboration of the patients.

Thus, apart from surveillance for early detection and follow up, activities will have to concentrate on the prevention and management of deformities and disablement. There is an ongoing debate on the respective importance of cure and care. Would there be care or cure? Care after cure? Or would no more care be needed after cure? While it is true that the best way of preventing disabilities remains early diagnosis plus

MDT, the untreated patients of today are the mutilated ones of tomorrow, yet a large number of individuals survive and new ones will appear who are or will be victims of late detection or inappropriate treatment in the past. There is, therefore, no conflict between cure and care. One or the other may take precedence according to needs, resources and opportunities.

As mentioned by the participants, the social and economic integration of persons affected by leprosy is an important means for promoting human dignity, reducing stigma, increasing economic independence and efficiently using community resources. This must be a priority of leprosy programs along with cure and prevention of disabilities.

I was personally impressed by one concern that persisted all through the discussions: that people with impairments are not necessarily in need of rehabilitation. This is important. Concerned individuals are the only ones who should judge their degree of autonomy, self-dependence, and aspirations according to their own concepts of what is a satisfying life. Rehabilitation should never become a goal *per se*, no more than prevalence, institutional program, or even the leprosy image itself should.

It remains that life in all its fullness, that is, the integration and empowerment of persons affected by leprosy, goes through the prevention of disabilities, and the prevention of disabilities goes through research. Research on the pathogenesis of nerve lesions and the mechanisms of protective immunity for nerve damage should, therefore, be very high on the agenda of priorities. It was once said that eliminating leprosy as a public health problem will possibly be achieved before the epidemiology of its transmission is elucidated. I think that is correct. By contrast, large-scale prevention of deformities will certainly not be achieved as long as so little is known about their mechanism.

There is a great shortage of knowledge regarding the actual size of the disability problem in leprosy, its trends, its age and sex distribution, and its associated risk factors. A large cohort study is being carried out in Bangladesh, the results of which are expected to be the determinant for the planning of prevention and management of de-

formities. New insights are also opened by a molecular approach to characterizing the interaction between *M. leprae* and the peripheral nerves, which could throw light on a variety of questions, such as why does the bacillus target the nerve and how does it invade the Schwann cell, how often are the nerves infected at the latent stage or do they shelter bacilli responsible for later relapses. Such research could ultimately lead to more effective prevention in the future.

The relationship between the most abstruse pathological phenomenon and the daily life of persons affected by leprosy was well stated by one of the speakers: "If *Mycobacterium leprae* is denied entry to the

nerves, and effective chemotherapy kills the bacteria harbored in other sites, then the stigmatizing deformities associated with nerve damages in leprosy could be eliminated."

That would be elimination at its best.

Facing the new challenges, meeting the needs for change, grasping the opportunities, all require a spirit of partnership. At the Congress, it was referred to as an alliance of all parties concerned.

In this respect, the full participation of persons affected with leprosy at this 15th Congress reflects a major change of perspective as well as a message of encouragement for all of us.