

EDITORIALS

WHO Experience in the Therapeutic Control of Leprosy*

In appraising the impact of antileprosy drugs on the trend of the disease, it is not possible to dissociate entirely the influence of therapy from the other measures of leprosy control or from socio-economic and other factors which may influence the endemic.

The value of antileprosy drugs and their impact on leprosy control. In a report prepared by Convit and other investigators,¹ some of them from research centers cooperating in WHO trials with antileprosy drugs, it was stated that: "None of the drugs used in the last five years has proved to be more effective than sulfones and the opinion expressed by the Panel on Therapy at the VIII International Congress of Leprology must still be considered valid. The Panel

stated that no single drug seems to be outstanding in its action, or likely to supplant dapsone on the grounds of therapeutic efficacy, cost or ease of administration. . . . dapsone is still the drug of choice for general use in active leprosy."

The WHO Expert Committee on Leprosy, held in Geneva in June 1970,² was of the opinion that oral administration of DDS continues to be the most practical method for mass campaigns in leprosy, and considered valid the opinion expressed by the Panel of Therapy at the VII International Congress of Leprology,³ and the WHO Expert Committee on Leprosy (1966).⁴

From experience gained in several centers almost 100% of lepromatous patients under very close supervision and regularly

* Guest editorial. Paper given at the Primera Reunion Leprológica del Cono Sud, Buenos Aires, 15-17 August 1970. Published in a special number of *Leprologia* (1970).

¹ Convit, J., Browne, S. G., Languillon, J., Petit, J. H. S., Ramanujam, K., Sagher, F., Sheskin, J., Souza Lima, L. de, Tarabini, G., Tolentino, J. G., Waters, M. F. R., Bechelli, L. M. and Martinez Dominguez, V. Therapy of leprosy. *Bull. Wld Hlth Org.* 42 (1970) 667-672.

² WHO Expert Committee on Leprosy (1970) *Wld Hlth Org. techn. Rep. Ser.* 459.

³ VIII International Congress of Leprology (1963). Final reports of the Technical Panels approved by the Plenary Session of 20 September 1963. Panel on Therapy, Rio de Janeiro, the Organizing Committee of the VIII International Congress of Leprology, p. 18.

⁴ WHO Expert Committee on Leprosy (1966) *Wld Hlth Org. techn. Rep. Ser.* 319.

treated may attain bacterial negativity after ten years of sulfone therapy; for incipient lepromatous cases about 90% may be inactive ("arrested") after five years. Theoretically, in a leprosy control project with excellent case-finding and case-holding the load of infectiousness may be significantly reduced in a relatively short time. However, it has been recognized that the main shortcoming of dapsone is its slow effect (clinical, bacteriologic, and histologic) in the severe forms of leprosy as noted by the Panel on Therapy in Rio de Janeiro (1963).⁵

Because of the long treatment period required for lepromatous patients, a large proportion of them become irregular in their treatment maintenance (70% after three years in a great number of countries) and some even completely escape from control. To this must be added the high proportion of inactive lepromatous cases mainly under irregular treatment who reactivate (relapse). This was shown by Quagliato *et al*.⁶ The data they presented are important from the epidemiological and administrative points of view and confirm the great length of time required for achieving bacterial negativity especially in the most advanced lepromatous cases. Almost all L1 cases (91%) achieve bacterial negativity by the end of five years; similar results were observed in L3 only after 9.5 years or more. This is aggravated by the occurrence of bacterial reactivation despite treatment (especially if irregular) after five years or as much as ten or more years, even if inactivity may again be achieved in a relatively short period. The persistence of "open" cases for so many years explains the maintenance of leprosy endemicity for many decades.

Socio-economic, political, and hygienic situation in leprosy endemic areas; health infrastructure. The socio-economic, health and educational status does not reach the desired level in most areas where leprosy is endemic. There is a shortage of doctors in

many countries and many doctors are not interested in working in leprosy control projects. In one area with 500,000 registered leprosy cases only five doctors were available for supervision of the paramedical staff. Salaries are not considered high enough to encourage staff to devote themselves fully to their work. Thus, doctors prefer to work in other health sectors or to have a private practice. Indeed, first rate work is usually not possible unless personnel work full-time and receive adequate salaries. Furthermore, leprosy campaigns have been hampered by the appointment of personnel, even in supervisory posts, who lacked the necessary technical qualifications. Political instability has also been detrimental to the normal development of the health program.

In several countries leprosy has a low position in the scale of priority in relation to other diseases. In fact, even where leprosy is highly prevalent in certain areas or countries, the health services have to deal with other urgent and serious diseases of much higher prevalence and/or mortality rate.

The health infrastructure is poor in many countries and adequate in only a few; consequently, the contribution of health units to leprosy control has been limited or unsatisfactory. A contributing factor is the fact that not enough time is devoted to the teaching of leprology in most medical schools.

Funds available are very often limited and full advantage of resources often is not taken because of inadequate planning and programming. With active case-finding an accumulation of leprosy cases will take place and the known prevalence rate will increase significantly year by year during a variable period because:

- a) leprosy is a disease of chronic evolution,
- b) there is an increase in the number of newly detected cases,
- c) years elapse before a patient can be released from control,
- d) the mortality from leprosy has been greatly reduced by the use of sulfones.

The detection of new cases, each one

⁵ Op cit.

⁶ Quagliato, R., Bechelli, L. M. and Marques, A. L. V. (1970). Bacterial negativity and reactivation (relapse) of lepromatous outpatients under sulfone treatment. *Internat. J. Leprosy* **38** (1970) 250-263.

necessitating the surveillance of about four contacts, increases the volume of work and the total expenditure for drugs, doctors, auxiliary personnel, outpatient clinics, equipment, etc., which most governments can ill afford. Nor is the health service—directly or indirectly—able to control all patients and to carry on surveillance of all contacts in extensive areas with large populations, because of lack of personnel and facilities.

Governments working on limited budgets gradually realize that the leprosy program may be a burden and that results are not achieved as quickly as with some other diseases. It is difficult or impossible to increase leprosy budgets proportionately and the speed of work is thus reduced, to the great detriment of the development of the general program.

Other factors, related directly to leprosy, may influence control.

- a) The incubation period, usually long, makes the discovery of new cases difficult, especially those not infected at home.
- b) Every contagious case has been in close contact with a certain number of persons. About 3% to 5% or even more (12% in some areas) of these contacts may acquire leprosy in a three to five year period. If untreated many of these new patients may develop the lepromatous type of the disease and establish a new chain of infection, which is subsequently extended to include further people. Open cases no longer under control and the relapsed infectious cases may also create new foci.
- c) Prejudice against leprosy exists practically all over the world, being much stronger in certain countries or areas.
- d) The tendency towards migration and urbanization has greatly increased the risk of spread of leprosy.

With due permission from Dr. Rotberg, Director, Divisao de Hansenologia e Dermatologia, Sao Paulo, Brazil, we may mention that in the State of Sao Paulo, with roughly 35,000 cases under control, the staff has to keep about 140,000 contacts under surveillance. Of the 1800 new cases regis-

tered in Sao Paulo each year, 20% (about 360) have been detected among known contacts. Therefore, 80% of the cases are detected in the general population (about 17,500,000 inhabitants). It is clear that the relevant staff cannot give complete coverage to the whole population; even with the collaboration of health units this would be impossible. Consequently, over 50% of the newly registered cases are lepromatous. The staff can detect incipient cases in contacts but cannot detect them in the general population. It is obvious that with the relatively low prevalence rate of leprosy in the State of Sao Paulo, a mass survey could not be considered. This example gives an idea of the difficulties in controlling leprosy in the above state and similar areas of Latin America where endemics have the same characteristics. The fact that a great proportion of cases are not detected early enough, when they have indeterminate leprosy, constitutes a major obstacle in the control of the disease in these and also other areas of the world.

WHO/UNICEF assisted programs on leprosy control. WHO gives technical assistance to countries through permanent advisers, consultants, regional advisers and headquarters staff in Geneva. Following WHO's lead, in the seminar organized by the Regional Office for the Americas and the Pan American Sanitary Bureau, abolishment of compulsory isolation of leprosy patients was recommended. Isolation in special hospitals would be restricted to certain cases where there was a special medical or social reason. These recommendations were confirmed in Tokyo and led to the expansion of leprosy projects in developing countries.

On the other hand, recognizing the impossibility in many areas of overcoming all difficulties at present, a system of priority for treatment of indeterminate and infectious cases, and surveillance of the contacts of the latter, was recommended according to local conditions (Bechelli (1965)⁷ and Expert Committee on Leprosy, 1966).⁸

⁷ Bechelli, L. M. (1965) First Regional Seminar on Leprosy Control, Manila; (1970, *Acta Leprologica*, No. 38-39, 111-127).

⁸ *Op cit.*

These are some of the initiatives in leprosy control taken by WHO with the collaboration of its panel of experts on leprosy.

Case-finding is satisfactory in the majority of countries and excellent in some of them. In one, the detection of a case of leprosy plus one year's treatment and follow-up costs only three dollars, in contrast to a few countries where the cost is several hundred dollars. Because of the slow action of antileprosy drugs and the long duration of treatment, it has been difficult for most of the countries to keep patients under regular treatment over long periods. The number of cases out of control is frequently high, even in some countries with an apparently satisfactory leprosy program. Taking into account the number of patients who have become bacterially negative, those in whom the degree of positivity has been much reduced and the high percentage in whom the nasal smears have become inactive, it may be stated that infectiousness of the disease has been reduced in leprosy control projects assisted by UNICEF and WHO. The number of cases released from control is high, mainly in African countries where the proportion of tuberculoid cases is higher than in other areas of the world.

In some areas where long-term programs are in progress, the rate of newly registered cases seems to maintain the same level or to decline slightly. However, it is known that several factors, economic, political, and others, may influence the speed of case-finding. Therefore, great caution is required in interpreting these results. In some countries or areas the proportion of lepromatous cases among the yearly detected cases is decreasing and only a few are detected even in mass surveys, indicating the efficiency of case-finding.

Results of the control projects are not spectacular from the epidemiological point of view, and indeed can not be so in a disease with such characteristics and combated only with limited tools.

On the whole, substantial progress has been made; striking in several projects. Adult and child populations, especially the latter, are benefiting from these campaigns by the reduction of infectiousness. Health

has been given to leprosy patients. Early diagnosis and treatment have prevented the development of serious forms of the disease. Control projects have, therefore, brought about an increase in man power which will contribute to raising the economic level and standard of living essential to the control of communicable diseases. The impact of these control programs on the suffering and distress of patients and their families cannot be measured but in view of the foregoing it can nevertheless be said that from this aspect also the projects have brought benefit.

In order to appraise the epidemiological impact of the projects on the disease it is interesting to consider the level of infectiousness in areas with active control projects and the trend of prevalence rates. The findings of the WHO Leprosy Epidemiological Team in random sample surveys in several countries (Africa, Asia, and America) are of great interest: they showed that the proportion of lepromatous cases with bacterial positivity ("regularly" or irregularly treated with dapsone) varied from 33% to 70% with an average of 54% for all countries surveyed.⁹

With regard to the trend of prevalence rates, from the data of Barros¹⁰ concerning the State of Sao Paulo, Brazil, approximately the same level has been kept since 1940. In addition, the proportion of newly detected lepromatous cases is still around 50% each year.

The impact of control measures on the trend of the disease can be predicted by using epidemiologic models. These are being developed in WHO by the Health Statistical Methodology Unit (Mr. K. Uemura and Mr. T. Sundaresan) and the Leprosy Unit (Drs. L. M. Bechelli and V. Martinez Dominguez). We are initially dealing with data of a highly endemic area where the prevalence rate is over 30 per

⁹ Bechelli, L. M. and Martinez Dominguez V. (1970). Maintenance of leprosy endemicity and bacterial positivity of lepromatous patients under treatment with sulfones. International Leprosy Colloquium, Forschungsinstitut Borstel, August 26-27, 1970, Summaries, Abstract No. 40, p. 70.

¹⁰ Barros, J. M. de (1968). Considerações sobre 40 anos de combate à endemia de lepra no Estado de Sao Paulo. Bol. Serv. nac. Lepra (Rio de J.), 27 (1/2) 5-10.

1000. Later, areas of low prevalence (1-2 per 1000) will also be considered. Several simulations have been made in the model, to forecast the trend of the endemic if no control measures are applied, if only 30% and 50% of the patients are treated, and if all of them (100%) receive treatment regularly. These studies are in progress and, with reservation, some preliminary information is given here to stimulate thoughts on the subject. With present antileprosy drugs and socio-economic and hygienic conditions, regular treatment of only 30% to 50% of cases does not seem to affect to a great degree the trend of the prevalence rate. When 100% of cases are regularly treated, a few decades would be required to obtain a great reduction in the prevalence rates, but many decades would still have to elapse before these rates were reduced to almost zero.

This preliminary information, concerning an area with a prevalence rate over 30 per 1000, does not necessarily apply to Latin American countries and others with prevalence rates of one or two per 1000 and differing epidemiologically. Epidemiologic models

should also be developed for these countries, taking into account the relevant parameters. However, the preliminary information obtained in the highly endemic area appears to be confirmed by the trend of prevalence in the State of Sao Paulo (Brazil) already mentioned. It should be remembered that with arsenicals, bismuth and lately with long-acting penicillin, syphilis has not been eradicated in the course of half a century.

The pattern suggested by the model for a highly endemic area may change substantially if a breakthrough is found in the control of leprosy by the discovery of a very effective drug and/or of an immunizing agent, and also with improved socio-economic conditions. At present, with the drugs available the prospects of controlling leprosy in a few decades are not favorable for most areas of the world, and the prospect can only be improved by intensifying research.

—DR. L. M. BECHELLI
*Chief Medical Officer, Leprosy
Division of Communicable Diseases,
WHO, Geneva*