INTERNATIONAL JOURNAL OF LEPROSY

Volume 41, Number 3
Printed in the U.S.A.

INTERNATIONAL JOURNAL OF LEPROSY

And Other Mycobacterial Diseases

VOLUME 41, NUMBER 3 JULY-SEPTEMBER, 1973

Advances in Leprosy Control in the Last 100 Years

L. M. Bechelli[1]

Though marked by continuous local wars and two world wars, considerable scientific and technological progress was achieved in the last 100 years, culminating with man walking on the moon and exploring outer space. In medicine, when Hansen described the etiologic agent of leprosy in 1874, great microbiological discoveries were in process and the preparation of vaccines and/or sera for the treatment of several diseases was the natural consequence of these achievements. Several decades later sulfonamides and antibiotics were introduced for the therapy of many diseases, with dramatic results in some of them and allowing successful campaigns such as that for yaws.

In leprosy, unfortunately, progress was not so dramatic though there were substantial advances in experimental transmission, epidemiology, pathology, genetics, immunologic understanding, classification of leprosy, and clinical management including therapy with sulfones, treatment of lepra-reaction with steroids and thalidomide. Nevertheless, *M. leprae* has not yet been cultivated and a specific vaccine has not been prepared, nor is a very effective drug yet available. Also, more knowledge is required about the epidemiology as well as other aspects of leprosy. These developments and deficiencies have affected the development of control projects, since the control of leprosy, like that of any infectious disease, depends on knowledge of epidemiology, facilities for diagnosis and on availability of very effective therapeutic and/or preventive agents. Progress in these and other fields may cause, and has already determined, great changes in control methods and for this reason we shall consider advances in leprosy control in the past 100 years in the light of scientific achievements during this period, beginning with the findings of Hansen.

Understanding of leprosy when Hansen described the leprosy bacillus and impact of the discovery on the control measures. Isolation. Up to 1874, control was essentially based on the isolation of leprosy patients. Since the most remote times leprosy had been considered as a contagious disease and by segregation of patients, very often in the most inhuman way, attempts were made to avoid its spread in the population. In the 18th century and also for half of the 19th, many workers regarded leprosy as a hereditary disease (Danielssen and Boeck ([23]), among others). Zambaco-Pacha ([94]) was one of the most enthusiastic advocates of this hypothesis and considered compulsory notification and segregation to be entirely unnecessary. Besides holding the concept of hereditary transmission of the disease, he believed that the hereditary

[1] L. M. Bechelli, M.D., Professor of Dermatology, Faculty of Medicine, Ribeirão Prêto, University of São Paulo, Brazil.

influences also influenced susceptibility to the disease.

Danielssen and Boeck admitted that leprosy was a hereditary disease in the great majority of cases, while in some individuals it seemed to appear spontaneously. Once acquired, leprosy would be transmitted by a hereditary mechanism. In their opinion only the isolation of patients could prevent the spread of the disease, because segregation would impede hereditary transmission and prevent patients from originating a sickly generation.

After the studies of Hansen [36, 37, 38], which climaxed with the description of the leprosy bacillus in 1874, and later of Neisser [52], confirming the hypothesis of its importance as the causative agent of leprosy, the contagiousness of leprosy was accepted [34].

Hansen's discovery introduced an important element in the diagnosis of lepromatous leprosy, as emphasized by Leloir [48], "It has been demonstrated that the leproma always has an enormous number of microorganisms and that none of the skin diseases present a microorganism with similar characteristics. From the diagnostic point of view it does not matter if the bacillus is or not the cause of the disease. . ."

It should be pointed out that specialists were aware of the basic element essential for the differential diagnosis of leprosy and took into account the same clinical elements considered today for the detection of the disease. In the diagnosis of nonlepromatous cases, they knew that it would be difficult to find *M. leprae* in smears and remarked that the anamnesis, antecedents, signs of the disease and evolution were to them the most important elements in the diagnosis. As a matter of fact, this was made possible by the classical studies of Danielssen and Boeck [23], Leloir [48] and Hansen and Looft [39]. These authors described the disease with great accuracy and detail, drawing attention to the elements that would be most important for diagnosis.

With regard to treatment, Leloir in 1886 stated that in most cases leprosy is incurable. However, it seemed that very rare cases would recover, most often with mutilations and blindness. In these cases the physician could not claim the merit of therapeutic cure because there was no specific treatment available for leprosy. Empirical treatment with mercury, potassium iodide, arsenic, antimony, phosphorus, potassium bromide, bismuth, creosote, phenylic acid, chaulmoogra oil and others had failed; this was also Danielssen and Boeck's opinion.

Danielssen thus indicated to Leloir, "I have used all the medicaments considered effective in the treatment of leprosy, from the iodides to chaulmoogra, gurjum, creosote, etc., etc. . . . Often I had some hopes but I finally was convinced that I had to repeat to myself, I do not know any medicament that cures leprosy" [48].

Serum therapy of leprosy was attempted [Carrasquilla [16], Buzzi [15], Dehio [25], Thompson [83] and others] as well as treatment with vaccines from supposed cultures of *M. leprae* [Rost [63]] or extracted from *Streptothrix leproides* obtained from the cultivation of material from lepromas [Deycke [26], Kupfer [46], Rodriguez [62], Brinckeroff and Wayson [11], Rashid [61], and others].

The findings of Hansen did not cause change in the technical policy of leprosy control. In the absence of an effective drug, isolation continued as the essential measure to prevent spread of the disease. In fact, in the I International Conference on Leprosy in 1897, Hansen [quoted by Darier [24]] reported the results obtained in Norway with isolation. He noted that, in 1856, there were 2,833 cases and at that time institutions for inpatients were established. Subsequently, the number of cases decreased progressively by extinction and by diminution of "new" cases, and this proportionately to the severity of the control measure and to the proportion of patients who were hospitalized. In 1895 there were only 321 cases. Isolation was not obligatory in the beginning, but it was made more stringent by the 1885 law which obliged patients to be isolated in their homes and if this was not done they would be isolated in leprosy institutions.

The I International Leprosy Congress (34) made recommendations to governments regarding control measures to be

adopted and Hansen's point of view was reflected in the final conclusions:

1. In all countries with foci of leprosy or where the disease is widely spread, isolation is the best way to prevent the dissemination of the disease.
2. Obligatory notification, surveillance and isolation, as practiced in Norway, should be recommended to all countries in which the municipalities are autonomous and have a sufficient number of doctors. . . .

It is interesting to note Darier's ([24]) remark in his report regarding the Berlin Conference: "Other endemics . . . require defense and preventive measures; the way is open for an international agreement to organize their control." He seems to have anticipated the need for an international organization, such as the World Health Organization, to coordinate cooperative efforts in the control of diseases.

The subsequent II International Leprosy Conference in Bergen ([95]), endorsed the conclusions of the Berlin Conference and added:

1. In view of the successful results obtained in Germany, Iceland, Norway and Sweden it is desirable that other countries with leprosy should proceed to isolate their patients.
2. It is desirable that leprosy patients should not be permitted to follow certain occupations which are particularly dangerous with respect to the contagion of disease.
3. In every country and in all cases, strict isolation of leprous beggars and vagrants is necessary.
4. It is desirable to separate healthy children from their affected parents as soon as possible and to keep them under surveillance. [Later this recommendation led to the creation of preventoria for children.]
5. An examination should be made from time to time of those who have lived with leprosy patients, by a competent physician.
6. The clinical study of leprosy induces the belief that it is not incurable. [A correct statement, confirmed later by the observation of self-healing cases.] We do not at present possess a certain remedy. It is desirable, therefore, to continue the search for a specific remedy. [The need for research had already been recognized.]

The III Leprosy Conference in Strasbourg ([84]) also supported the previous principles of leprosy control (isolation), and adopted the following recommendations:

1. In countries where leprosy is slightly spreading, isolation as practiced in Norway, in a hospital, or if possible, at home is recommended.
2. In the endemic foci isolation is required:
   a) this isolation should be humane and should leave the patient in the proximity of his family, if this is compatible with an effective treatment;
   b) if the patients are indigents, nomads or vagrants, and, in general, if patients cannot be isolated at home, isolation in a hospital is required and the most efficient treatment will be carried out in hospital, sanatorium or agricultural colony, according to the circumstances and countries.
3. Populations should be informed that leprosy is a contagious disease.

The importance of isolation was admitted by most leprologists and reflected in the reports of the above conferences. However, some authors held that other factors in addition to isolation might have played a role in the results claimed. Lie ([50]) believed that isolation and surveillance of patients had played a considerable role in the decrease of leprosy in Norway following 1856. But this decrease must also be regarded in the light of the great progress the country had made during that time in all respects, not least in hygiene and sanitation. The trend of leprosy in Norway and in some other countries was also analyzed in detail by Rabello ([59]) and by Rotberg and Leser ([69]). The latter two authors considered the possible importance of improvement of environmental and health conditions and of health education of the population.

After analyzing the role of isolation in the control of leprosy in the Middle Ages and in recent times (Norway, Germany and other countries), Bechelli and Quagliato ([7]) stated that because of the following, isolation alone could not have controlled leprosy within a few decades: 1) Only advanced cases, recognized as leprosy patients, had probably been isolated; early lepromatous cases or those with only diffuse infiltration of the skin most probably had not been diagnosed. These bacillary cases continued to live in the community and only several years later, with the progress of their disease, would they have been segregated. The early lepromatous cases

are exactly those that may offer greater risk to the population because they are unrecognized as such. The advanced lepromatous cases are "naturally" isolated by friends and sometimes even by relatives. 2) Every patient that was isolated had lived with a certain number of persons: 3% to 5% and, in some countries, up to 12% of these contacts are prone to eventually develop leprosy. These cases, even in present control projects, very often are not detected at the time that they become infectious. Thus, other persons are exposed to *M. leprae* and may develop the disease later, establishing a kind of vicious circle. 3) The infectious cases that escaped from or left hospitals could have exposed to *M. leprae* a certain number of persons. 4) No effective drugs were available before the sulfones. Even now, with sulfones and other drugs, a long period is required to attain inactivity of infectious cases, and the possibility of relapses is high, helping to maintain the load of infectiousness at a certain level.

Thus, from these early experiences in leprosy control it is evident that several coordinated measures should be taken at the same time. Additional factors such as the socio-economic situation, education, hygiene and housing would play a role in the control of the disease.

Studies with lepromin. Better knowledge of forms of leprosy, their evolution and epidemiological importance. Influence on the control measures. Taking into account the results of the lepromin reaction, Mitsuda [51] and Hayashi [40] clearly pointed out the low resistance of lepromatous patients in contrast with nonlepromatous cases and the majority of the healthy individuals. The prognostic value of the lepromin test was also established by these authors. These findings were confirmed mainly by Rotberg [64, 65, 66], Dharmendra and Chatterjee [28] and the Committee on Immunology [21] at the VII International Congress of Leprology in Tokyo, which stated that, "The use of the lepromin reaction as an index of the degree of resistance to leprosy infection is constantly increasing. It offers a useful element in respect of prognosis and classification of cases of leprosy and consequently its use in practice is recommended." In the Second Report of the WHO Expert Committee on Leprosy [89], it was stated, "The lepromin reaction is of established value as a test of the reactivity of the individual to the leprosy bacillus; it provides a criterion in the classification of cases and an indication of the prognosis of the patient and of the relative resistance of contacts."

The lepromin test has made possible great progress in the understanding and practice of pathology, epidemiology, prognosis, classification and control in leprosy.

The knowledge of forms of leprosy gradually improved. The attention to tuberculoid leprosy was intially drawn by Jadassohn [44] and later tuberculoid cases were reported by many authors. Wade [85] described the reaction in the tuberculoid leprosy and also [Wade and Rodriguez [86]] the borderline (dimorphous) leprosy. Among other elements, the bacterial positivity in these patients had to be taken into account for control purposes. In the IV International Congress of Leprology [35] the tuberculoid leprosy was admitted to the classification, but inside the "neural" type with the "neuromacular lesions" and on the "pure neuritic" cases. The "cutaneous" form of the Manila classification [49] became the lepromatous type.

Gradually the contrast between the lepromatous and tuberculoid types became clearer and Rabello [60] classified them as the "polar forms" of the disease. The indeterminate group of leprosy was deeply studied by Souza Lima and Alayon [77].

The epidemiological aspects related to each form of the disease were studied mainly in the Philippines by Doull, Guinto, Rodriguez and others, and it appeared that lepromatous patients (and also borderline) were the main source of infection.

The spontaneous disappearance of tuberculoid and some other lesions was also observed in untreated cases or in the absence of an active treatment, because sulfones had not yet been used in the therapy of leprosy. The most impressive reports, even if they appeared later, are those of Lara and Nolasco [47] and Dharmendra [27]. In the Lara and Nolasco study, 77% of

early childhood cases were free of lesions before adult life. According to Dharmendra, at the Silver Jubilee Children's Clinic, Madras, where 644 nonlepromatous child cases were followed for periods varying from 1 to 20 years without any treatment being given to them, spontaneous arrest of the disease was seen in about 65%; in over 55% of maculoanesthetic, over 78% of minor tuberculoid and over 88% of major tuberculoid cases. Souza Campos ([75]) also made an important contribution to the study of tuberculoid leprosy in children and its spontaneous regression.

In the light of all these studies the isolation of tuberculoid and indeterminate cases was no longer considered necessary. This represented a considerable progress from the human and economic point of view, because thousands of patients could have outpatient care and be released from control without being isolated, thus reducing the expenses in institutions for inpatients.

In fact in the Cairo Congress ([35]) a recommendation on this particular point was made and also concerning the detection of leprosy cases: 1) isolation of open cases in special institutions or at home; 2) ambulatory treatment of cases with bacterial negativity.

With regard to methods for detection of cases, examination and surveillance of contacts, it was recommended that there be periodic examination of schoolchildren and notification of cases, as well as dispensaries for diagnosis.

School surveys were recommended as a method of case finding, which has been very useful in highly endemic areas, as shown mainly by Noussitou ([55, 56]). The dispensaries also deserved a special position and complemented the previous recommendations of conferences concerning institutions for inpatient care and preventoria for children of leprosy patients.

This tripod became a classic *sine qua non* in any leprosy project during this period. Certain of these approaches, later discarded, had been suggested and recommended because of the limited state of understanding of leprosy and absence of effective agents of cure and prevention.

The Committee on Epidemiology and Control ([17]) of the V International Congress of Leprology in Havana, confirmed that, "A leprosarium is a place for isolation of a) infectious patients, and b) noninfectious patients for social, economic and other reasons." The same committee stated that, "Dispensaries or outpatient clinics are of fundamental importance for the control of leprosy." Great emphasis was given to the description of their functions, reflecting their increasing importance. Their functions were delineated as: "1) finding of cases and segregation of infectious ones; 2) epidemiological investigations; 3) selection of cases for isolation; 4) control of treatment of nonisolated cases, including those paroled from leprosaria; 5) control of suspected infectious cases; 6) control of absconders; 7) removal to preventoria of children of infectious parents when necessary; 8) sanitary education, and 9) disposal of cases for final discharge."

The control of contacts, it was noted, should be carried out in accordance with modern concepts, with special reference to the lepromin reaction. On that basis, contacts should be divided into two groups: lepromin-negative and lepromin-positive. Contacts with negative and weakly-positive reaction should be given special attention.

With regard to "preventoria" it is interesting to note the concessions made to children who presented signs of the disease in these institutions. "Modern clinical and immunological concepts of leprosy indicate that children with the bacteriologically-negative tuberculoid and indeterminate forms may be permitted to remain in the preventorium; likewise lepromin-positive children paroled from leprosaria. It is recommended, however, that this concession be granted only in institutions where medical control is regular and efficient." Before the developments in understanding of the broader immunopathologic spectrum of leprosy as noted above, children with tuberculoid and indeterminate lesions could not stay in preventoria.

The Committee also made important general recommendations for the control of the disease and considered at length different aspects of health education. The following essential points should be brought out: "1)

to avoid the use of the word 'leper' and other undesirable terms; 2) to correct the present error of public opinion that leprosy is a Biblical scourge and that the patient is cursed. This error brings stigma and injury to the patient, makes him conceal the disease and even prevents him from seeking medical assistance. and increases the danger to the public; 3) we deprecate all publicity in newspapers, magazines, novels, movies, etc., and all other situations in which leprosy and the patient are dramatized, when the presentation does not agree with modern knowledge. . . ."

The last portion of these pronouncements indicates the great interest in protecting the leprosy patient and reducing the stigma attached to the disease. Similar preoccupation was shown by the Committee concerning the use of the words "leprosy" and "leper." It was agreed: "1) that the use of the term 'leper' in designation of the patient with leprosy be abandoned, and the person suffering from the disease be designated 'leprosy patient'; 2) that the use of any term, in whatever language, which designates a 'person suffering from leprosy' and to which unpleasant associations are attached, should be discouraged. However the use of the name 'leprosy' should be retained as the scientific designation for the disease. Active steps should be taken to explain fully to the general public its real nature; 3) that if the regional popular use of any less specific terms in substitution for the scientific name 'leprosy' enables the public to understand more fully and clearly the advances that have been made in the understanding, diagnosis and treatment of the disease, such terms may be used as suitable opportunity offers; but it would be unwise to adopt such terms to conceal the true nature of the disease."

Finally, it should be pointed out that sulfone usage on a large scale began about 1946 and its impact on control measures had not been fully appreciated by the time of the Havana Congress.

Sulfones and their impact on leprosy control. In a paper published in 1943, Faget *et al* [32] indicated that they had begun the experimental treatment of leprosy with Promin two years earlier and felt that this drug was a therapeutic agent worthy of further trials. These were undertaken all over the world and especially by Souza Lima and collaborators [76, 78, 79, 80] in hundreds of inpatients and also in patients treated in dispensaries.

The Committee on Therapy of the Havana Congress [22] stated, "Existing evidence shows that these drugs (of the sulfone group) are of great value in lepromatous leprosy, and many workers are of the opinion that they offer the best available therapy in this condition. Their use in cases of that type is therefore recommended. . . . It is the opinion of the Congress that the sulfones are the present drugs of election for the treatment of leprosy." No special reference had been made to the treatment of indeterminate (I) leprosy. Bechelli [1, 73] in 1947 and Souza Lima [76] in 1948, drew attention to the need of trying sulfones in the treatment of indeterminate patients, especially those nonreactors to lepromin in whom the disease might evolve into lepromatous leprosy. If sulfones could stop this progression this would represent an important contribution to the control of leprosy. Souza Lima [76] reported that indeterminate cases under treatment did not evolve into lepromatous leprosy. Bechelli [2] compared the results of treatment of indeterminate cases with chaulmoogra oil and with sulfones. Forty patients with negative or doubtful reactions to lepromin, treated with sulfones did not evolve into lepromatous leprosy in a period of one to four years, while 44.8% also nonreactors but treated with chaulmoogra [65], did progress to lepromatous leprosy. In the group of lepromin reactors, none of the 253 patients treated with chaulmoogra oil or of the 53 treated with sulfones evolved into the lepromatous form.

The International Congresses of Leprology [96, 98, 99] and the WHO Expert Committees on Leprosy [88, 89, 90, 91] recognized that sulfones are the drug of choice for the treatment of leprosy. Of these, the parent sulfone (dapsone) has the widest application because of its effectiveness, simplicity of administration and low cost. However, it was 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 at the VIII International Congress of Leprology ([99]). Because of the long treatment period required for lepromatous patients, a large proportion of them became irregular in their treatment maintenance. To this must be added the high proportion of inactive lepromatous patients who reactivate (relapse) [Erikson ([31]), Price ([57]), Khazizov ([45]), Quagliato *et al* ([58]), Noordeen ([54]), Jacobson and Trautman ([43])]. The above explains the maintenance of leprosy endemicity for many decades.

In spite of their shortcomings, sulfones had a great impact on the technical policies of leprosy control; probably the greatest since Hansen's discovery. More and more patients were treated in dispensaries or outpatient clinics, and lepromatous patients left sanatoria with bacterial negativity. Thus, the role of sanatoria greatly decreased, while early diagnosis and chemotherapy in the dispensaries became the most important method of leprosy control, supported by health education and relevant measures. There was a shift from inpatient to outpatient care, and patients that continued in sanatoria, mainly due to social atrophy due to institutionalization, constituted a heavy burden on the budgets of leprosy projects.

Compulsory isolation was finally recommended to be abolished at the PASB/PAHO Panamerican Seminar on Leprosy Control ([70]). The inconveniences of compulsory isolation, as stressed by this seminar, are also applicable to inpatient care at the present. These were noted to be:

1. Hiding of numerous patients who are afraid of being isolated. This makes it more difficult to control those with whom he associates.
2. High cost to the public treasury, resulting in the dissipation, without benefit for the control of the disease, of funds that might be of better use in the development of more rational and efficient methods for fighting leprosy.
3. Disintegration and stigmatization of the family itself, making its social readjustment more difficult.
4. Unfair and inhuman discrimination of a category of patients, who then are regarded as outcasts, which makes it impossible to reintegrate them into society.
5. Perpetuation of popular prejudices.

This seminar also stressed that the basis of any campaign against leprosy is the effective control of all sources of contagion by the treatment of all cases and the control of all contacts. Hospitalization should be restricted to the cases for which there are special medical or social indications.

In addition to the above mentioned inconveniences, the Committee on Epidemiology and Control ([19]) noted, "From the epidemiologic point of view *it is more important to reduce infectiousness in many patients than to eliminate infectiousness in a few.*"

"The role of sanatoria should be limited to the treatment of cases with acute lepra reaction and other complications, to surgery and physical rehabilitation and to serving as centers for research and training. In countries with existing facilities, the most infectious cases may also be admitted to sanatoria on a voluntary basis. The period of hospitalization, however, should be temporary and only sufficient to effect clinical regression or to reduce infectiousness. It is not necessary to obtain bacteriological negativity prior to discharge. The sooner a patient can be discharged the better" ([90]).

It is important to interpret this statement on the basis of the recommendation of the Committee on Epidemiology and Control ([100]), endorsed by the above WHO Committee, ". . . efforts at hospitalization should not be permitted to drain the budget and the efficiency of outpatient treatment centers, which form the core of leprosy control."

With a few exceptions, the shift from inpatient to outpatient care became widely accepted and efforts were made to reduce to a minimum the number of patients in institutions. Preventoria also lost their functions mainly because isolation of infectious cases was no longer required. Thus, from the control tripod—sanatoria, preventoria and dispensaries—only the latter remained. It is now accepted that its functions should be gradually and progressively handed over to the general health services (see below). Therefore, in the course of 100

years from isolation as practically the only measure of leprosy control, there was an expansion of the control measures to be carried out by sanatoria, preventoria and dispensaries; later, only dispensaries were considered as in fact required and now, with the integrated approach, the general health services should gradually be in charge of their relevant activities.

In view of the shortcomings of sulfones, several drugs were tried or are under study in the therapy of leprosy (clofazimine, acedapsone, long acting sufonamides, thiambutosine, rifampicin). The favorable results in the treatment of lepra reaction with thalidomide ([72]), confirmed by many authors, deserves special attention. The WHO Expert Committee on Leprosy ([91]), taking into account the reports of possible toxic effects on the central and peripheral nervous systems and the well-known teratogenic effects of thalidomide, recommended that for the present this remedy be used only for strictly investigative purposes under proper conditions of observation and control.

Shift from vertical, specific campaigns to integrated control activities. With the present facilities it is almost impossible for a leprosy service alone to control the disease in endemic areas because of the usually limited resources. Even if better means were available for controlling the disease, the cooperation of health services would be desirable and necessary. As experience has shown for some diseases, no lasting control is possible without the active cooperation of a capable health service. WHO has for some time been recommending this cooperation as well as the gradual and progressive integration of leprosy services into public health services ([4, 70, 71, 87, 88, 89, 90, 91]). The principle of integration of leprosy control activities into the general health services is widely accepted although the difficulties in achieving this are fully recognized.

Attention should be drawn to risk of a hasty integration, which may lead to the failure and/or the disintegration of the leprosy control program perhaps for many years, with serious consequences for the population at risk. "Full integration will be attained only as a result of a long drawn out process, and for this reason countries should be encouraged to take the first step as early as practicable . . ." ([91]).

Controlled trials on the prevention of leprosy by BCG vaccination. The possibility of using BCG as a preventive agent in leprosy, first suggested by Fernandez ([33]) was for many years investigated by determining the effect of the vaccine on the lepromin reaction. Even without controlled trials, vaccination with BCG was recommended by the Committee of Control at the VI International Congress of Leprology in Madrid ([97]) for the protection of contacts and as a part of leprosy control projects. In contrast to this at the same congress, the Committee on Immunology required further studies to determine the real value of BCG in the prevention of leprosy. At the VII International Congress of Leprology the Committee on Epidemiology and Control ([19]) stated, "Although such studies are under way in several countries and although some preliminary reports have been published, evidence regarding the value of BCG in the prevention of leprosy is still insufficient to warrant its general use. The recommendation of the VI International Congress of Leprology is therefore modified in this document." Field studies were undertaken in Uganda ([12, 13, 14]), New Guinea ([68, 69]) and Burma ([6]).

Thus far the findings in the three trials are strikingly different. The difference is mainly related to the incidence of the disease in vaccinated and unvaccinated children, degree of protection, and age group in which BCG action was apparent or not. The study of the evolution of the disease, possible prevention of lepromatous leprosy and of other parameters is essential to determine the meaning of a reduction in incidence in vaccinated children (mainly related to T cases), effect on appearance of early and benign cases of leprosy, and its possible impact on the trend of the disease. It is hoped that further data from these trials may lead to the formulation of definite conclusions regarding the preventive value of BCG vaccine against leprosy. This protective role should be considered not only in relation to hyperendemic areas but also

for those areas in which the degree of endemicity is relatively low or which have different ecological situations and different socio-economic and cultural patterns.

Controlled trials on chemoprophylaxis. Two controlled trials with dapsone have been undertaken, one in Chingleput, India ([29, 30, 53]), and the other in Culion, Philippines, by Dr. Lara. The WHO Expert Committee on Leprosy ([91]) which analyzed the findings from both trials, noted that the results of the two controlled trials were rather similar, with an estimated reduction of 52.5% in Chingleput and 44.5% in Culion, attributable to chemoprophylaxis. This subject is still under study to determine the optimum dose and the length of time that preventive treatment should be given.

If further investigations confirm the above findings, and if the protection continues after chemophrophylaxis is stopped, prevention of child household contacts of infectious cases should be tried. It is not likely that chemoprophylaxis with present drugs would be feasible for all contacts and the total population in highly endemic foci, especially since irregularity of treatment is very frequent even among leprosy patients.

Management, training, health education, priorities, rehabilitation and evaluation. One of the main problems in leprosy control is that of administration and operation in order to make the best possible use of available means and resources. Leprosy being a public health problem, the general principles of public health administration regarding formulation (planning and programming) and organization should also be applied to leprosy control ([41, 42, 71]).

The Committee on Leprosy Control ([97, 100]) and the WHO Expert Committee on Leprosy ([90, 91]) gave special emphasis to training, health education, research, including operational research, and epidemiological models.

Rehabilitation of leprosy patients was considered especially at the WHO meeting in Vellore, India ([93]), and at the VII and VIII International Congresses of Leprology. It became evident that the surest and cheapest rehabilitation is to prevent physical disability and social and vocational dislocations by early diagnosis and early treatment. Thus, rehabilitation must begin as soon as the disease is diagnosed. The importance of education in the prevention of disabilities was strongly emphasized by Brand ([10]).

In addition, as recommended by the VII International Congress of Leprology and endorsed by the WHO Expert Committee on Leprosy ([90]), ". . . in every antileprosy campaign the doctors and paramedical workers would be trained to look for danger signs in hands, feet and eyes, and should give advice and simple treatment to prevent deformity and blindness." At the same congress, the Panel on Physical Rehabilitation stated, "While this panel seeks to encourage every leprosy worker to participate in the preventive aspects of deformity, it must strongly discourage attempts at reconstructive surgery by medical officers who have no special training, who have to work in centers where aseptic conditions are doubtful, and who are not assisted by trained physiotherapeutic help in the preparation and reeducation of their patients."

According to Bechelli and Walter ([8]), in countries with limited resources the use of funds for the creation of special surgical units for the rehabilitation of leprosy patients does not serve the primary objective of leprosy control. In countries with greater resources, it is desirable to undertake such rehabilitation in general rehabilitation centers, surgical and orthopedic services, including university hospitals. In fact, the WHO First Western Pacific Regional Seminar on Leprosy Control ([92]) recommended that, "Funds for leprosy control should not be diverted for the provision of reconstructive surgery." In addition, the Expert Committee on Leprosy ([90]) emphasized that, "It should not be forgotten that the aim of leprosy control is to prevent disabilities by early diagnosis and treatment, rather than to have to correct them."

Recognizing the impossibility, in many areas, of overcoming present difficulties, a system of priorities ([3, 4, 90]) was proposed and should be adopted, based on the limitation of each area and according to local conditions. These priorities concern the

treatment and follow-up of infectious and indeterminate patients, and the surveillance of contacts of infectious cases.

The importance of evaluation of leprosy control projects has been greatly emphasized in the last ten years and many measurement indicators have been suggested for operational and epidemiological assessments.

Impact of present control measures on the trend of the diseases. Theoretically the existing methods should lead to the control of leprosy, provided they are thoroughly and correctly applied and that favorable conditions exist in which to do so, including full cooperation of the population and of all concerned. In countries or areas where the above conditions are attained, it can be expected that the incidence of the disease will gradually decrease and, subsequently, the prevalence. And if, accordingly, early indeterminate patients are detected and treated regularly, the number of lepromatous cases become fewer and fewer.

However, many factors may influence the application of the control measures and delay or decrease the impact of these measures on the trend of the disease. Among these are the socio-economic, political and hygienic conditions as well as cultural patterns and the health infrastruture in leprosy endemic areas, together with factors related directly to the disease. Thus, results of the control projects are not spectacular from the epidemiological point of view and indeed cannot be so in a disease with the characteristics of leprosy as combatted only with limited tools. An analysis of the situation in many countries and of the relevant factors, with a reference to epidemiological models, was recently made in an editorial published by this JOURNAL (5) and for the sake of brevity it is not repeated here. The present impression and the pattern suggested by an epidemiological 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 with a rise in the standard of living and education at all levels of the population. 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 these prospects can only be improved by intensifying research. Only research can furnish the elements capable of controlling leprosy even in unfavorable local conditions, such as was possible in the yaws campaigns.

REFERENCES

1. BECHELLI, L. M. Posicão dos doentes de forma tuberculóide e incaracterística (inflamatória simples) na profilaxia da lepra. Rev. Brasil. Leprol. **15** (1947) 251-260.
2. BECHELLI, L. M. Experiência com a sulfonoterapia. Arq. Mineiros Leprol. **12** (1952) 286-294.
3. BECHELLI, L. M. A review of present-day concepts of leprosy control with special reference to the role of the local health services. Unpublished working paper WHO WP/RC14/TD5, 1963.
4. BECHELLI, L. M. Leprosy control. First WHO Western Pacific Regional Seminar on Leprosy Control, 1965 and Acta Leprol. **38-39** (1970) 111-127.
5. BECHELLI, L. M. WHO experience in the therapeutic control of leprosy. Internat. J. Leprosy **39** (1971) 885-889
6. BECHELLI, L. M., GALLEGO GARBAJOSA, UEMURA, K., ENGLER, V., MARTÍNEZ DOMÍNGUEZ, V., PAREDES, L., SUNDARESAN, T., KOCH, G. and MATEJKA, M. BCG vaccination of children against leprosy. Bull. WHO **42** (1970) 235-281.
7. BECHELLI, L. M. and QUAGLIATO, R. A importância do isolamento hospitalar dos doentes contagiantes na profilaxia da lepra. *In:* Conferencia Panamericana de lepra, No. 2, Rio de Janeiro, 1946. Rio de Janeiro, 1946, Vol. 3, pp 243-275.
8. BECHELLI, L. M. and WALTER, J. Assessment of the importance of reconstructive surgery in the control of leprosy from the public health point of view. Acta Leprol. **45** (1971) 5-29.
9. BEURMANN. Traitment de la lèpre. Ann. Derm. Syph. **10** (1909) 596.
10. BRAND, P. W. The value of surgical and physiotherapeutic measure in leprosy. Leprosy in India **27** (1955) 86-88.
11. BRINCKERHOGF, W. R. and WAYSON, J. T. A report upon the treatment of six cases of leprosy with Nastin (Deycke). Lepra Bibliot. Intern. **11** (1910) 291-295.

12. Brown, J. A. K. and Stone, M. B. BCG vaccination of children against leprosy: first results of a trial in Uganda. Brit. Med. J. **1** (1966) 7-13.
13. Brown, J. A. K., Stone, M. M. and Sutherland, I. BCG vaccination of children against leprosy in Uganda: results at end of second follow-up. Brit. Med. J. **1** (1968) 24-27.
14. Brown, J. A. K., Stone, M. M. and Sutherland, I. Trial of BCG vaccination against leprosy in Uganda. Leprosy Rev. **40** (1969) 3-7.
15. Buzzi, F. Vorläufige Mittheilung über einen mit Carrasquilla'schem. Serum behandelten Fall. Deuts. Med. Woch. **42** (1897) 672.
16. Carrasquilla, J. D. A serumtherapia da lepra. Brasil Medico **10** (1896) 78-80.
17. Committee on Epidemiology and Control. Report. *In:* Memoria del V Congreso International de la Lepra, Habana, 1948. Habana, 1949, pp 84-91.
18. Comision de Epidemiologia y Profilaxis. Informe. *In:* Memoria del VI Congreso Internacional de Leprologia, Madrid, 1953. Madrid, 1953, pp 105-112.
19. Committee on Epidemiology and Control. Technical resolutions. *In:* Transactions of the VII International Congress of Leprology, Tokyo, 1958. Tokyo, Tofu Kyokai, 1959, pp 473-482.
20. Comision de Inmunologia. Informe del comite de inmunologia. *In:* Memoria del VI Congreso Internacional de Leprologia, Madrid, 1953. Madrid, 1953, pp 96-104.
21. Committee on Immunology. The lepromin reaction. *In:* Transactions of the VII International Congress of Leprology, Tokyo, 1958. Tokyo, Tofu Kyokai, 1959, pp 463-466.
22. Committee on Therapy. Report. *In:* Memoria del V Congreso International de Lepra, Habana, 1948. Habana, 1949, pp 66-69.
23. Danielssen, D. C. and Boeck, W. Traité de la spédalskhed. Paris, Baillière, 1848, pp 81-100, 147-176, 334-346.
24. Darier, J. Conférence Internationale de la Lèpre, Berlin, 1897: (2e. article) compte rendu destravaux. Ann. Derm. Syph. **8** (1897) 1149-1163.
25. Dehio-Dorpat. Zur Serumtherapie der Lepra. St. Petersburg Med. Wochenschr. **4, 5** (1898) apud Monatshef. Prak. Derm. **28** (1899) 211.
26. Deycke, F. A lecture on a specific treatment of leprosy. Brit. Med. J. **1** (1908) 802-806.
27. Dharmendra. Personal communication, 1964.
28. Dharmendra and Chatterjee, K. R. Prognostic value of the lepromin test in contacts of leprosy cases. Leprosy in India **27** (1955) 149-152.
29. Dharmendra, Mohamed Ali, P., Noordeen, S. K. and Ramanujam, K. Prophylactic value of DDS against leprosy —an interim report. Leprosy in India **37** (1965) 447-467.
30. Dharmendra, Noordeen, S. K. and Ramanujam, K. Prophylactic value of DDS against leprosy—a further report. Leprosy in India **39** (1967) 100-106.
31. Erickson, P. T. Relapse following apparent arrest of leprosy by sulfone therapy. Public Health **65** (1950) 1147-1157 apud Internat. J. Leprosy **19** (1951) 63-74.
32. Faget, G. H., Pogge, R. C., Jahansen, F. A., Dinan, J. F., Prejean, B. M. and Eccles, C. G. The promin treatment of leprosy. A progress report. Public Health **58** (1943) 1729-1741.
33. Fernandez, J. M. M. Estudio comparativo de la reaction de Mitsuda con las reacciones tuberculinicas. Rev. Argent. Derm **32** (1939) 425-453.
34. First International Leprosy Conference, Berlin, 1897. *In:* Thibierge (81).
35. Fourth International Congress on Leprology, Cairo, 1938. Reports of meetings. Internat. J. Leprosy **6** (1938) 377-424.
36. Hansen, G. A. Norsk. Med. Arch. **1** (1868) 3; apud Souza Araujo, H. C. O bacilo da lepra. Folha Medica **17** (1936) 419-420.
37. Hansen, G. A. Spedalskhedens arsager. [Causes of leprosy.] Norsk Mag. Laegevidenskaben **4** (1874) 76-79.
38. Hansen, G. A. The bacillus of leprosy. Quart. J. Microb. Sci. **20** (1880) 92-102.
39. Hansen, G. A. and Looft, C. *Leprosy in its Clinical and Pathological Aspects.* London: Simpkin, Marshall, Hamilton, Kent, 1895, pp 5-86.
40. Hayashi, F. Mitsuda's skin reaction in leprosy. Internat. J. Leprosy **1** (1933) 31-38.
41. Huerta, R. S. and Pereda, E. O. Algunas ideas sobre planificación programación y organización en las actividades de salud. Unpublished document, WHO/PASB Seminar, Cuernavaca, 1963 (a).

42. Huerta, R. S. and Pereda, E. O. Ejemplo teorico del calculo de una tabla de operaciones de um programa de control de lepra. Unpublished document. WHO/PASB Seminar, Cuernavaca, 1963 (b).
43. Jacobson, R. R. and Trautman, J. R. The treatment of leprosy with the sulfones. Internat. J. Leprosy **39** (1971) 726-737.
44. Jadassohn, J. Lésions tuberculoides de la peau dans la lèpre non tubéreuse. Ann. Derm. (1898) 435; apud Ann. Derm. Syph. **10** (1899) 429-430.
45. Khazizov, E. I. K boprosu o bacterioskopičeskikh retsidibakh u ambulatorno lečasikhsi bol'nykh leproi. Voprosy Leprol. Derm. **2** (1964) 99-102.
46. Kupfer, A. Ein Beitrag zur Behandlung der Lepra mit Chaulmoograöl und Nastin. Lepra Bibliot. Intern. **8** (1908) 144-151.
47. Lara, C. B. and Nolasco, J. O. Self-healing, or abortive and residual forms of childhood leprosy and their probable significance. Internat. J. Leprosy **24** (1956) 245-263).
48. Leloir, H. Traité pratique et théorique de la lèpre. Paris, Progrès Medical, 1886, pp 9-226.
49. Leonard Wood Memorial Conference on Leprosy, Manila, 1931. Report. Philippine J. Sci. **44** (1931) 449-480.
50. Lie, H. P. Why is leprosy decreasing in Norway. Internat. J. Leprosy **1** (1933) 205-216. Reprint.
51. Mitsuda, K. Les lépreux maculo-nerveaux, d'une part, les tubéreux, d'autre part, se comportent différemment a la suite d'une inoculation d'émulsion de tubercule lépreux. *In:* Conférence Internationale de la Lèpre, No. 3, Strasbourg, 1923. Communications et debats. Paris, Baillière, 1924, pp 219-220.
52. Neisser, A. and Souza Araujo, H. C. Bacilo da lepra. Folha Medica **17** (1936) 419-420.
53. Noordeen, S. K. Chemoprophylaxis in leprosy. Leprosy in India **41** (1969) 227-254.
54. Noordeen, S. K. Relapse in lepromatous leprosy. Leprosy Rev. **42** (1971) 43-48.
55. Noussitou, F. M. School surveys in Burma. *In:* Congreso Internacional de Leprologia, No. 8, Rio de Janeiro, 1963. Anais. Rio de Janeiro, 1963, vol. 3, pp 11-21.
56. Noussitou, F. M. School surveys in leprosy control campaigns. Acta Leprol. **20-21** (1965) 47-61.
57. Price, R. B. Relapse of leprosy in American Samoa. Amer. J. Trop. Med. Hyg. **8** (1959) 358-363; apud Internat. J. Leprosy **27** (1959) 396.
58. Quagliato, R., Bechelli, L. M. and Marques, R. M. Bacterial negativity and reactivation (relapse) of lepromatous outpatients under sulfone treatment. Internat. J. Leprosy **38** (1970) 250-263.
59. Rabello, F. E. Segregação e isolamento na prophylaxia da lepra. Folha Medica **14** (1933) 1-33. Reprint.
60. Rabello, F. E. A. Questões em discussão sôbre a classificação das formas da lepra. Arq. de Higiene **8** (1938) 59-76.
61. Rashid, F. "Nastin" in the treatment of leprosy. Brit. Med. J. **2** (1909) 1343.
62. Rodriguez. The treatment of leprosy by means of Nastin injections. The Therapists **19** (1909) 73.
63. Rost, E. R. Further notes on the treatment of leprosy by injections of leprolin. Lepra Bibliot. Intern. **5** (1905) 268-273.
64. Rotberg, A. Some aspects of immunity in leprosy and their importance in epidemiology, pathogenesis and classification of forms of the disease. Rev. Brasil. Leprol. **5** (1937) Spec. No., pp 45-97.
65. Rotberg, A. Valor prognóstico da lepromino-reação de Mitsuda. Rev. Brasil. Leprol. **12** (1944) 367-377.
66. Rotberg, A. Fator "N" de resistência à lepra e relações com a reatividade lepromínica e tuberculínica. Rev. Brasil. Leprol. **25** (1957) 85-106.
67. Rotberg, A. and Leser, W. Radicação e erradicação de focos lepra: estudo analítico e crítico. *In:* Simposio Sôbre Profilaxia da Lepra, Rio de Janeiro, 1964. Rio de Janeiro, Ass. Brasil. Leprol., 1964, pp 129-145.
68. Russell, D. A., Scott, G. C. and Wigley, S. C. BCG and prophylaxis—the Karimui trial. *In:* International Leprosy Congress, No. 9, London, 1968. Abstracts of papers. London, 1968.
69. Scott, G. C., Wigley, S. G. and Russell, D. A. The Karimui trial of BCG. 2. Tuberculin reactions in a leprosy-endemic but tuberculosis-free population. Internat. J. Leprosy **34** (1966) 139-146.
70. Seminário sobre el Control de la Lepra, Belo Horizonte, 1958. Washington, Oficina Sanit. Panamer., 1959. Reprinted from Bol. Ofic. Sanit. Panamer. **45** (1958) 469-556.

71. Seminario sobre Lepre, Cuernavaca, 1963. Washington, Organizacion Panamer. de la Salud, 1963, p. 37. Publicaciones Científicas, n. 85.
72. SHESKIN, J. Thalidomide in the treatment of lepra reactions. Clin. Pharmacol. Ther. **6** (1965) 303-306.
73. Sociedade Paulista de Leprologia. Sessão ordinária, 142., 21-4-1947. Rev. Brasil. Leprol. **15** (1947) 123-126.
74. SOUZA ARAUJO, H. C. O bacilo da lepra. Folha Medica **17** (1936) 419-420.
75. SOUZA CAMPOS, N. Aspects cliniques de la lèpre tuberculoide chez l'enfant. Rev. Brasil. Leprol. **5** (1937) 99-128.
76. SOUZA LIMA, L. Importância da sulfonoterapia nos dispensários e resultados. Rev. Brasil. Leprol. **18** (1950) 24-32.
77. SOUZA LIMA, L. and ALAYON, F. L. Sôbre a signuficacao patológica das lesoes incaracteristicas (maculares simples). Sao Paulo, Dep. Profil. Lepra, 1941, p 302.
78. SOUZA LIMA, L. and CERQUEIRA, G. C. Tratamento experimental da lepra pelas diamino-di-fenil-sulfonas. *In:* Conferéncia Panamericana de Lepra, No. 2, Rio de Janeiro, 1946. Rio de Janeiro, 1946, vol. 2, pp 9-76.
79. SOUZA LIMA, L., CERQUEIRA, G., MAURANO, F. VALENTE, E., RODRIGUES, D., AMENDOLA, F. and GUIDA, H. A. Resultados atuais da sulfonoterapia no Santório Padre Bento. Rev. Brasil. Leprol. **16** (1948) 75-85.
80. SOUZA LIMA, L., CERQUEIRA, A. G. C., VALENTE, E. C., GUIDA, A. H., MAURANO, F., RODRIGUES, D. and AMENDOLA, F., Estado atual da sulfonoterapia no Sanatório Padre Bento. *In:* Congreso International de la Lepra, No. 5, Habana, 1948. Memoria, Habana, 1949, pp 120-127.
81. THIBIERGE, G. La Conférence Internationale de la Lèpre. Ann. Derm. Syph. **8** (1897) 1031-1034.
82. THIBIERGE, G. La prophylaxie de la lèpre dans les pays où elle n'est pas endémique. *In:* Internationalen Wissenschaftlichen Lepra Conferenz, No. 1, Berlin, 1897. Mittbeilungen und Verhandlungen. Berlin, A Hirschwald, 1898, vol. 3, pp 452-459.
83. THOMPSON, J. Serum treatment of leprosy. Lepra Bibliot. Intern. **1** (1900) 140.
84. Troisième Conferénce Internationale de la Lèpre, Strasbourg, 1923. Communications et debats. Paris, Baillière, 1924, p 507.
85. WADE, H. W. Tuberculoid changes in leprosy. II. Lepra reaction in tuberculoid leprosy. Internat. J. Leprosy **2** (1934) 279-292.
86. WADE, H. W. and RODRIGUEZ, J. N. Borderline tuberculoid leprosy. Internat. J. Leprosy **8** (1940) 307-331.
87. WHO AFRO Seminar on Leprosy, Kampala, 1970. WHO document.
88. WHO Expert Committee on Leprosy: first report. Wld. Hlth. Org. Tech. Rep. Ser. **71** (1953) 31 pp.
89. WHO Expert Committee on Leprosy: second report. Wld. Hlth. Org. Tech. Rep. Ser. **189** (1960) 27 pp.
90. WHO Expert Committee on Leprosy. Wld. Hlth. Org. Tech. Rep. Ser. **319** (1966) 31 pp.
91. WHO Expert Committee on Leprosy: fourth report. Wld. Hlth. Org. Tech. Rep. Ser. **459** (1970) 31 pp.
92. WHO First Western Pacific Seminar on Leprosy Control, Manila, 1965. WHO unpublished document,
93. WHO Scientific meeting on rehabilitation in leprosy, Vellore, India, 1960. Report. Wld. Hlth. Org. Tech. Rep. Ser. **221** (1961) 37 pp.
94. ZAMBACO-PACHA, D. A. La lèpre a travers les siècles et les contrées. Anthologie. Paris, Masson Ed., 1914, pp 664-748.
95. Internationale Wissenschaftliche Lepra-Konferenz, Bergen, 1909. Mitteilungen und Verhandlungen. Leipzig, 1910, vol. 3, pp 418-419.
96. VI Internat. Cong. Lepr., Madrid, 1953. Committee on Therapy. Memoria del VI Cong. Internat. Lepr., Madrid, 1953, pp 87-91.
97. *Ibid.* Committee on Epidemiology and Control, pp 109-112.
98. VII Internat. Cong. Lepr., Tokyo, 1958. Committee on Therapy. Trans. of VII Internat. Cong. Lepr., Tokyo, Tofu Kyokai, 1959, pp 466-473.
99. VIII Internat. Cong. Lepr., Rio de Janeiro, 1963. Panel on Therapy. Final Reports of the Technical Panels, Rio de Janeiro, 1963, pp 18-22.
100. *Ibid.* Panel on Epidemiology and Leprosy Control, pp 23-46.