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**WHO EXPERT COMMITTEE  
ON LEPROSY**

**Third Report**

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## WHO EXPERT COMMITTEE ON LEPROSY

Geneva, 27 July - 2 August 1965

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## CONTENTS

	Page
1. Leprosy control . . . . .	5
1.1 Epidemiology . . . . .	5
1.2 Diagnosis for use in field projects . . . . .	6
1.3 Classification for use in field projects . . . . .	6
1.4 Chemotherapy . . . . .	7
1.5 Control . . . . .	10
1.5.1 Medical measures . . . . .	11
1.5.2 Training . . . . .	14
1.5.3 Health education . . . . .	17
1.5.4 Rehabilitation . . . . .	17
1.5.5 Social measures . . . . .	18
1.5.6 Legislation . . . . .	18
1.5.7 Administrative measures . . . . .	19
1.6 Role of voluntary bodies in national leprosy programmes	24
2. Research . . . . .	25
2.1 Microbiology . . . . .	25
2.1.1 Transmission to animals . . . . .	25
2.1.2 Biological significance of solid-staining <i>M. leprae</i>	26
2.1.3 Infections in cell cultures . . . . .	26
2.2 Immunology . . . . .	27
2.2.1 The Mitsuda reaction . . . . .	27
2.2.2 Serological studies . . . . .	27
2.2.3 Reactional states . . . . .	28
2.2.4 Prophylaxis by BCG . . . . .	28
2.3 Pathology . . . . .	28
2.3.1 Practical applications . . . . .	28
2.3.2 Neuropathology . . . . .	28
2.3.3 Electron microscopy . . . . .	29
2.4 Epidemiology . . . . .	29
2.5 Diagnosis . . . . .	30
2.6 Chemotherapy . . . . .	30
2.6.1 General . . . . .	30
2.6.2 Problems related to treatment with DDS . . . . .	31
2.6.3 Prevention and treatment of reactors . . . . .	31
2.7 Chemoprophylaxis . . . . .	31



# WHO EXPERT COMMITTEE ON LEPROSY

## Third Report

The WHO Expert Committee on Leprosy met in Geneva from 27 July to 2 August 1965.

Dr P. Dorolle, Deputy Director-General, on behalf of the Director-General, welcomed the members of the Committee.

The Committee elected Dr J. H. Hanks Chairman, Dr Dharmendra Vice-Chairman, and Dr R. J. W. Rees Rapporteur.

### 1. LEPROSY CONTROL

#### 1.1 Epidemiology

Recent and past evidence continue to support the universally accepted assumption that leprosy is caused by *Mycobacterium leprae*, that the sources of infection are exclusively human cases discharging bacilli, and that transmission occurs by direct or indirect contact.

Lepromatous cases constitute the principal, though not necessarily the only, source of infection. The attack rate for household contacts of lepromatous cases is six to eight times higher than in non-contacts; that for contacts of tuberculoid cases is less than twice that for non-contacts.

The continued maintenance of high prevalence rates in hyperendemic areas where tuberculoid-type leprosy constitutes as much as 90 % of the total cases may be attributed, at least in part, to the usually undetermined proportion becoming "open" during periods of reaction.

Exposure to known cases cannot be established in an appreciable proportion of leprosy infections, even in young children, in part because of the long incubation period. Undetected cases with inconspicuous lesions may account for some untraceable infections.

Leprosy may occur in all races and at any age. It is thought that the age at which leprosy is contracted depends primarily upon opportunities for exposure.

The preponderance of lepromatous cases in males, especially after adolescence, may be due to greater susceptibility rather than to greater exposure or to a longer duration of the disease in males compared to females.

Although the disease is not highly infectious, and although most individuals are resistant, the attack rate in contacts of lepromatous cases can be considerable, especially among children. Most secondary cases, however, are tuberculoid and of minimal extent, and often heal spontaneously.

Reactivity to lepromin increases rapidly with age, from negativity in infancy to almost universal positivity after adolescence in endemic areas, and is associated with relative resistance. It is hoped that the prophylactic value of BCG, with the associated induction of lepromin reactivity, may be established by the two controlled trials now under way in Uganda and Burma.

### **1.2 Diagnosis for use in field projects**

Diagnosis of leprosy is based mainly on clinical grounds.

The detection of impairment of sensation and the thickening of cutaneous nerves and nerve trunks are most important elements in the diagnosis. Bacteriological examination of skin and nasal smears is useful for confirming the diagnosis and is essential for determining the infectivity of the patient. In doubtful cases, the histamine and anhidrosis tests may be helpful.

Diagnosis can be made by paramedical personnel but, as far as possible, it should be confirmed by a medical officer.

### **1.3 Classification for use in field projects**

In spite of repeated efforts, it has not yet been possible to produce a single system for the classification of leprosy. For practical purposes, there are two systems to be considered: the Madrid and the Indian classifications. Although complete unanimity has not been achieved, there are no serious basic differences between these two systems. Efforts should be made to appreciate the two points of view and to concentrate on the areas of agreement rather than on those of disagreement.

The main difference is regarding the flat, well-defined patches with loss of sensation. According to the Madrid classification, these lesions belong to the tuberculoid type and are labelled as "macular tuberculoid". According to the Indian classification, these lesions form a distinctive clinical entity apart from the tuberculoid and have been allotted a separate place, under the designation "maculo-anaesthetic". Nonetheless, in the Indian classification, the relationship of maculo-anaesthetic to raised tuberculoid lesions is recognized by placing them in the "non-lepromatous" type.

Until agreement is reached, and while the use of two systems is continued, at least two things should be done to avoid or minimize confusion. First, as already stated, it should be clearly recognized that the macular tuberculoid lesions of the Madrid classification and the maculo-anaesthetic

lesions of the Indian classification refer to the same form of the disease. Secondly, for the purpose of special investigations, and for collecting data for subsequent analysis, macular tuberculoid (Madrid) or maculo-anaesthetic (Indian) lesions should be listed separately from the other components of the tuberculoid type, in the case of the Madrid classification, or of the non-lepromatous type, in the case of the Indian classification. This is essential because of the differences between the so-called macular tuberculoid variety and the other components of the tuberculoid type regarding such matters as the extent of nerve involvement and consequent deformities, the evolution and course of the disease, and the response to treatment. With attention to this small matter of detail, data could be collected from various countries that would be comparable even without making any change in the classification that is being followed at present in any particular country.

For practical purposes, in the majority of field projects, the cases of borderline leprosy should be included in the lepromatous type.

The classification of pure neural cases presents many difficulties, even with the help of the lepromin test and histopathological examination of nerves. Biopsy, however, is not recommended and, in any case, it is not possible under field conditions. Bacteriological examination is generally negative, though positive findings have sometimes been reported. Again, for practical purposes, patients with positive findings should be considered as lepromatous, and those with negative findings as tuberculoid.

Therefore, in field projects, cases should be classified as lepromatous, tuberculoid<sup>1</sup> or indeterminate leprosy. In tuberculoid cases, the presence of reaction should be recorded.

In addition, from the control point of view, the cases should be classified either as infectious (open) or non-infectious (closed) on the basis of bacteriological results by the routine "slit-and-scrape" method of examination. All lepromatous cases, and the non-lepromatous cases found bacteriologically positive, should be considered as infectious (open); in the latter category, however, this status may be only temporary.

#### 1.4 Chemotherapy

The introduction of sulfone drugs marked a great advance in the treatment of leprosy. Other chemotherapeutic agents have since been tried, but none has proved to be as effective as the sulfones. Therefore, sulfone administration continues to be the basic treatment. For field projects, the parent sulfone, diaphenylsulfone (4,4'-diamino-diphenylsulfone, DDS), is the drug of choice.

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<sup>1</sup> According to the Indian classification, the tuberculoid type is designated as "non-lepromatous" and includes both maculo-anaesthetic and tuberculoid lesions.

Sulfone therapy is effective in all types of leprosy. In order to obtain good results, it is essential to start it at the earliest possible stage of the disease and to maintain it regularly for a sufficient period.

Early sulfone treatment usually prevents the evolution of the indeterminate form of leprosy to the lepromatous type, as well as disabilities and deformities subsequently requiring rehabilitation. Treatment at this stage usually arrests the disease in a shorter period than when it is initiated later, although sulfone therapy is also effective in more advanced cases.

In tuberculoid cases, the disease is usually arrested by sulfone treatment; relapses in such cases are rare and have little epidemiological significance. In lepromatous and borderline leprosy, regression of lesions and bacteriological negativity are achieved in the majority of cases, thus reducing infectivity.

Limitations of sulfone therapy are recognized to be: slow action, intolerance in certain cases, and the possibility of relapse, mainly in lepromatous leprosy.

It has to be stressed that chemotherapy constitutes only a part, although a very important part, of the treatment of leprosy. Other measures, such as physiotherapy, care of hands, feet and eyes, are also important.

(a) *Routine treatment.* In field projects, oral administration of the sulfones is the method of choice because of its simplicity and because it is as effective as parenteral administration. Parenteral administration of a repository preparation of DDS may be used, however, in order to increase the intervals between administration to once weekly or once in two weeks.

For oral administration, the total weekly dose can be given once per day for six days of the week or, preferably, twice a week or even once a week.

For parenteral administration, special repository preparations of DDS are available in a suspension in oil or water with aluminium monostearate.

The maximal total weekly dose of DDS for an adult of about 60 kg should not exceed 600 mg, and the dose for children should be correspondingly lower. There are indications that even smaller doses may be equally effective.

Treatment must be started with a much smaller dose than the maximum suggested above, and the dose should be gradually, and cautiously, increased until the maximal dose is reached. In some patients, especially in field projects, the maximum may have to be kept at 400 mg per week.

The starting weekly dose may be in the range of about 50-60 mg, 25 mg twice a week or 10 mg daily for 6 days a week. The increase in dose should be very gradual, and the maximum should be reached in about 4 to 6 months.

Treatment with DDS should be suspended on the appearance of signs of "reaction". Suspension should continue until all signs of reaction subside and for about 1 or 2 weeks thereafter. DDS treatment should then be resumed with a dose smaller than that used at the time of appearance of reaction, and the increase in dose should be even more gradual than that suggested above. It may not be advisable to increase the dose beyond the level at which the reaction appeared.

A small proportion of cases, especially the lepromatous, may not be able to tolerate even the small doses indicated earlier. In such cases, an attempt should be made to build up tolerance, starting with minute doses; otherwise an alternative drug may have to be used. Such cases should be treated by a medical officer.

Fortunately, the question of drug resistance to DDS is not an important one. The possibility of development of drug resistance has been reported recently, but only in a negligible proportion of the cases under treatment.

(b) *Alternative drugs to DDS.* It has been the experience of most leprosy workers that a patient found to be intolerant to DDS is generally intolerant to other anti-leprosy drugs. However, an attempt has to be made to treat such patients with an alternative drug. For this purpose, the drug to be recommended is thiambutosine 1-(*p*-butoxyphenyl)-3-(*p*-dimethylamino-phenyl)-2-thiourea, DPT. For oral administration, DPT must be given twice daily, but a repository preparation in arachis oil is now available that can be given parenterally once a week.

By the oral route, a start is made with 0.5 g (1 tablet) daily, and the dose is gradually increased to 1.5 g. By the parenteral route (intramuscular, deep into the gluteal region), a start is made with 1.0 ml (200 mg), and the dose is gradually increased to 5 ml (1 g) once a week. The drug is well tolerated by both the oral and the parenteral routes.

Treatment with DPT should not be continued beyond 2 years, since its activity diminishes, probably on account of the development of drug resistance in the patient.

(c) *Treatment of reaction.* With the appearance of signs of reaction, the anti-leprosy treatment should be suspended. The patient should be put to bed and given symptomatic treatment for fever, pain etc. with anti-pyretics and analgesics. In mild cases, this treatment may suffice.

In cases not responding to these measures, some special treatment should be given. For this purpose antimonial and antimalarial drugs (such as chloroquin) may be effective.

In more serious cases, it may be necessary to administer prednisolone or one of its analogues. To begin with, the dose of prednisolone should be about 20 mg per day, and the dose of the analogue should be correspondingly lower. The dose at this level should generally be maintained for

a few days, then gradually reduced; it is important that steroid treatment should not be stopped suddenly. It should be borne in mind that the corticosteroids do not constitute a treatment for leprosy but are of value during acute reactional conditions and in avoiding permanent sequelae.

The corticosteroids are particularly indicated in acute iritis and neuritis, where their systemic use should be supplemented by topical application or by perineural injection, respectively.

In cases with acute neuritis, with oedema of the nerve and swelling of the parts supplied by the nerve, drug treatment should be supplemented by resting the affected limb in order to prevent serious and irreversible complications and sequelae. For this purpose, either a simple splint of a plaster cast should be applied.

### 1.5 Control

Measures of control have been established, taking into account existing knowledge of epidemiology, immunology and pathology and the progress in therapy. The continuous progress in these fields has necessarily imposed new directions and policies on leprosy control.

The control of leprosy must be practical, economical and flexible. It should be adapted to the conditions of each country or area and to available resources.

Recognizing the impossibility, in many areas, of overcoming all difficulties at the present time, a system of priorities should be adopted according to local conditions.

Countries with limited budgets, only a few physicians, and facing other serious problems, should treat first of all the lepromatous and other infectious cases and the indeterminate lepromin negatives.<sup>1</sup> They should keep child household contacts, especially of infectious cases, under surveillance and try to help patients in the prevention of disabilities. Means and personnel should be concentrated on the infectious cases and their contacts, particularly children.

At the other extreme, countries with adequate budgets and good leprosy services, whether or not integrated in the public health services, should diagnose and treat as early as possible *all* patients, maintain surveillance of *all* contacts, prevent disabilities, rehabilitate *all* patients with deformities, and examine certain population groups, in particular, children.

(a) *Priority in the treatment of leprosy patients.* If it is not possible to treat all patients, priority must be given to open cases. It is obvious that if a tuberculoid patient comes to a treatment centre he will be examined

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<sup>1</sup> In countries that are unable to perform the lepromin test, all indeterminate cases should also receive first priority.

and treated. In field work, however, a doctor or an auxiliary worker must not occupy himself with tuberculoid cases if this means leaving the lepromatous patients without attention.

(b) *Priority in the surveillance of contacts.* Even in the better leprosy projects, usually not more than 30% or 40% of contacts are examined regularly. Therefore, for preference, contacts of lepromatous and other infectious cases, and household contacts under fifteen years old should be examined. Contacts of non-infectious cases should be examined when the index case is registered and subsequently when they wish to come for examination.<sup>1</sup>

(c) *Priority in the follow-up of patients.* Priority should be given to the follow-up of infectious patients who are irregular in treatment. Even in the best-organized leprosy service, there are many "out-of-control"<sup>2</sup> patients (10% or more). Leprosy services should trace *all* contagious cases. Personnel should not spend time going after a tuberculoid case when lepromatous patients are not under control or while hundreds of child household contacts of lepromatous cases remain to be examined.

#### 1.5.1 *Medical measures*

Leprosy control has been chiefly based on the use of chemotherapy. Regular and prolonged treatment with sulfones causes a reduction in infectiousness, which subsequently should reduce the incidence of the disease. Up to now, the minimum proportion of open cases to be treated in order to obtain a significant reduction in incidence is not known. Long-term trials designed with this aim should be undertaken in pilot projects. As a tentative proposal, while awaiting the results of such studies, it is suggested that leprosy-control projects should treat regularly at least 75% of the estimated open or infectious cases, to whom first priority must be given. This objective should be reached *in each operational area* within a period that could tentatively be fixed at around five years.

On the other hand, the limitations of chemotherapy in leprosy are known, especially in the treatment of lepromatous cases. Special emphasis should therefore be placed on early diagnosis and early treatment. The prevention of leprosy has also received particular attention. BCG and chemoprophylaxis trials are going on and might provide additional weapons for the control of leprosy.

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<sup>1</sup> It has been suggested that, if possible, the lepromin test be performed, thus reducing by 70% or 80% the amount of work in the surveillance of contacts, because surveillance could then be limited to the lepromin negatives.

<sup>2</sup> "Out of control", "absentee", "lost sight of", and other terms have been used for registered patients who have not been under control for two or more years.

(a) *Case-finding*.<sup>1</sup> The choice of case-finding methods should be related to the prevalence rate in the country, region or focus in which leprosy control is to be carried out.

It is difficult to determine when leprosy starts to be an important public health problem and when it should be considered hyperendemic. As a tentative proposal it is accepted that, when the prevalence rate of known cases is around one per thousand or higher, leprosy should be considered an important public health problem. In countries, areas or foci with a prevalence rate about ten per thousand or more, leprosy should be considered hyperendemic. However, the occurrence of even a few cases of leprosy constitutes a health problem. Lepromatous rates should also be taken into account in the assessment of the problem. In view of the findings of the WHO Leprosy Advisory Team in Africa, America and Asia, it is estimated that the prevalence rate in the majority of countries would be at least double the known rate.

In areas of low endemicity, the most effective and practical case-finding methods are the examination of household contacts of infectious cases, especially children, and of persons reported to be suspected cases. When the rate is about one per thousand or higher, additional case-finding methods should be employed such as examination of schoolchildren, military recruits and other selected groups. Mass surveys are recommended only for hyperendemic areas.

Contacts of "open" cases should be examined annually for five years, excluding those who have already been exposed for five or more years.

(b) *Out-patient care*. Out-patient care of leprosy patients should be conducted from health centres that also deal with the general health of the community. Mobile units are required, as an interim measure, until these health centres are able to give an adequate service.

Out-patient treatment is to be preferred, since it is better to reduce the infectiousness of many than to abolish that of only a few. It is also more acceptable to the patient and considerably more economical; in-patient treatment is calculated to cost at least ten times as much *per capita* as that of out-patients and, furthermore, the hospitalized patient's ability to maintain himself and his family is grossly curtailed.

Oral treatment with DDS is advised but, in some situations, repository injections may be preferable. In areas in which injectable DDS is given by mobile units, oral treatment may be advisable during farming and rainy seasons.

Although the quantity of tablets given to patients at any one time depends upon local circumstances and may eventually have to be sufficient

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<sup>1</sup> This section and sections *b*, *c* and *d* following represent, to a great extent, the conclusions and recommendations (to be published) of the WHO First Western Pacific Regional Seminar on Leprosy Control (Manila, 1965).

for three months, it is important to gain the patient's co-operation gradually before entrusting him with a three-month supply. A simple urine test for detecting DDS in the urine can be used to check DDS intake.<sup>1</sup>

The Committee agrees with the criterion established at the WHO Inter-regional Leprosy Conference, Tokyo, 1958, in that a patient taking at least 75% of his prescribed medication is considered to be under "regular" treatment.

The major problem in out-patient care is to ensure regularity of treatment. Irregularity of treatment is attributable in part to inefficiency or indifference of health personnel. On the other hand, ignorance, disinterest or disability may deter the patient from attending regularly. It follows that the education of all concerned is the best method of solving this problem.

It is strongly recommended that the prevention and treatment of deformities should start in the field. Of prime importance is the systematic instruction of each patient on the protection of hands, feet and eyes. Other practical measures applicable are simple physiotherapeutic exercises, plaster casting, splinting, the use of preventive and therapeutic footwear, and provision of devices for protecting the hands.

Mobile leprosy units should be equipped, also, to supply simple treatment for other conditions and should co-operate with other branches of the health services.

The co-operation of private practitioners in the treatment of leprosy patients is to be encouraged. Other responsible persons, such as school teachers and local government officials, should be encouraged to assist in the administration of treatment.

(c) *In-patient care.* The role of sanatoria should be limited to the treatment of cases with acute lepra reactions and other complications, to surgery and physical rehabilitation, and to serving as centres for research and training. In countries with adequate 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 reduce infectiousness. It is not necessary to obtain bacteriological negativity prior to discharge. The sooner a patient can be discharged, the better.

As stated in the Eighth International Congress of Leprology (1963),<sup>2</sup> "efforts at hospitalization should not be permitted to drain the budget

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<sup>1</sup> Strips or circles of filter paper are soaked in *p*-dimethylaminobenzaldehyde (Ehrlich's reagent used for detecting urobilinogen) and allowed to dry. A drop of urine is placed on the test-paper and allowed to react for one minute. A yellow colour is given by sulfones and sulfonamides.

<sup>2</sup> In : *Proceedings of the Eighth International Congress of Leprology, Rio de Janeiro, 1963 (Final Reports of the Technical Panels Approved by the Plenary Session of September 20th)*, Rio de Janeiro, 1963, p. 39.

and the efficiency of out-patient treatment centres, which form the core of leprosy control ”.

Leprosy patients needing temporary hospitalization for acute complications of leprosy or intercurrent diseases should be admitted to general hospitals. Patients needing attention for special reasons, such as maternity and reconstructive surgery, should also receive the same consideration.

Patients discharged from sanatoria should be assimilated into the general population and encouraged not to congregate in special “ villages ”. Permanently disabled patients needing nursing care may need special provision. This may be accomplished by setting aside a section of the sanatoria or facilities detached from the sanatoria.

(d) *Protection of the healthy population, with special reference to contacts and children.* In view of the general acceptance of the public-health approach to the control of leprosy, of the progress in therapy, and of the risk of psychological trauma to child and mother, the separation of infants from infectious parents should be limited to special cases. When separation is necessary, infants should be sent to relatives, foster homes or institutions for general child care. There is no need for special institutions for children of leprosy patients. Separation should be as short as possible.

The value of BCG vaccination and chemoprophylaxis in the prevention of leprosy is under study and is considered in section 2.2.2.

#### 1.5.2 *Training*

The best programme of leprosy control, no matter how large the budget allocated to it, may be ruined if staff training is not adequate. Training must be a planned and organized activity designed to fulfil its aim for each type of personnel assigned to leprosy work.

As stated in the WHO First Western Pacific Regional Seminar on Leprosy Control (Manila, 1965),<sup>1</sup> the duration and content of the courses should be related to the functions of the trainees and the needs, resources and cultural background of each country.

##### 1.5.2.1 *Training of medical personnel, general practitioners and medical students*

The characteristics and duration of courses for medical officers would be related to the nature of their functions.

(a) *Medical personnel to be assigned to leprosy work.* Courses on leprosy should be organized, giving special emphasis to clinical aspects, diagnosis, treatment, epidemiology and control; these courses should be complemented by field work. Physicians should also be trained to apply

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<sup>1</sup> To be published.

simple physiotherapeutic methods and to teach patients how to prevent disabilities. Full-time courses are preferable. Courses for dermatologists and public health officers can be shorter than those for lay personnel.

(b) *Senior medical staff in leprosy work.* Medical officers in charge of out-patient treatment centres should have adequate knowledge of epidemiology; a short course of epidemiology would enable them to deal efficiently with data and its interpretation.

Senior staff should also have refresher courses in dermatology and a knowledge of public health. Training in public health is essential for physicians assigned to administrative posts in leprosy control.

Advanced training could also be provided in selected institutions or control projects, or in international courses organized by WHO.

(c) *Health service physicians.* Courses should be shorter than those for leprologists and deal with the practical aspects of leprosy control, diagnosis, treatment and epidemiology. Further training should be given to the same staff after they have demonstrated willingness to co-operate.

(d) *General practitioners.* In order not to interfere with their private practice, part-time courses should be organized, giving emphasis to clinical aspects, diagnosis and treatment of the disease.

(e) *Undergraduate training.* Special priority should be given to teaching leprology to medical students. It is of the utmost importance to give adequate and proper instruction to the future physicians. In order to teach students adequately, the department of dermatology in conjunction with the department of preventive medicine, should admit leprosy patients, so that the students can learn how to diagnose and treat leprosy and how to follow up patients; at the same time, they would make surveillance of the contacts of these patients.

(f) *Staff in leprosy research.* Facilities should be provided for research training of the staff in other institutions, in the same or in other countries. Research should be considered important, not only for improving leprosy control measures, but also for allowing better training of senior staff and of personnel to be assigned to leprosy work.

Training should not stop at the end of a course: the senior staff should take advantage of every opportunity to impart their knowledge to the younger physicians and auxiliary personnel.

#### 1.5.2.2 *Training of auxiliary personnel*

Courses for auxiliary personnel should be programmed according to the nature of their functions. When leprosy control is conducted mainly by auxiliary personnel, training should be longer and more complete. It should be essentially practical, with emphasis on control measures, clinical aspects, diagnosis and treatment, including dressings, application of

simple physiotherapeutic methods in the field and prevention of disabilities.

Training of health service auxiliary personnel should follow the same lines, but courses would be shorter.

#### 1.5.2.3 *Training of voluntary collaborators*

Teachers, civil administrative personnel and other responsible people may co-operate in administering drugs to patients, in keeping them under regular treatment, and in stimulating the examination of contacts and of suspected cases and in health education. The type and duration of training provided for those people would be determined by the existing facilities, the cultural background of these voluntary collaborators and the activities to be carried out by them. For some of them, teaching would be reduced to explanations, given by doctors or health personnel during their visits, concerning the administration of antileprosy drugs and the reactions and side-effects that should determine interruption of treatment.

#### 1.5.2.4 *Training centres*

Training may be given in out-patient treatment centres and/or in sanatoria with adequate facilities for teaching, demonstration of patients and a laboratory, at least for bacteriological examination.

Co-operation among countries has proved useful and should be strengthened to make use of their training centres, research institutes and qualified staff.

Medical or public health schools can also be important centres for undergraduate and post-graduate training and for staff assigned to leprosy research. For this, close co-operation with the leprosy service is important. In developing countries, leprosy is not the only health problem; others may be more important and have higher priority. Therefore, medical schools should give students a public health outlook, so that the future physicians will be able to take care of the patient without forgetting the rest of his family and the society of which he is a fundamental unit. Teaching in medical schools should be kept at the highest possible level and, at the same time, place special emphasis on the study of diseases and health problems that are more common in the region or country. Students should have the opportunity to observe and apply preventive measures to individuals, families and population as part of their clinical training.

#### 1.5.2.5 *Evaluation of training*

Questionnaires completed by participants in the courses may give an indication of how to improve training. The follow-up of their activities in the field will show whether the training has influenced the quality and quantity of work.

### 1.5.3 *Health education*

Since health education is an important duty of all health workers, they should be given special training for this purpose. Health education should be based on known scientific facts presented in their proper perspective. As stated by the Committee on Education and Social Aspects, Eighth International Congress of Leprology, "Our educational objective should be to evolve in the public at large, the patients and their families, a reasoned attitude towards leprosy which neither exaggerates the dangers nor minimizes it".<sup>1</sup>

Health education in leprosy should be conducted in conjunction with that of other diseases. The first consideration is to enlist the interest and assistance of public health educators. An adequate budgetary provision for health education should be made.

Prejudice and indifference are harmful to leprosy control programmes. As recommended by the WHO First Western Pacific Regional Seminar on Leprosy Control (Manila, 1965),<sup>2</sup> investigation into the causes of prejudice against leprosy should be conducted in different countries, with a view to developing better methodology for overcoming it.

### 1.5.4 *Rehabilitation*

As pointed out at the Eighth International Congress of Leprology, if rehabilitation is to be really effective, it must be initiated as soon as the disease is diagnosed.<sup>1</sup> Early diagnosis and treatment are therefore of the utmost importance.

The main difficulty in rehabilitation is the public prejudice against the disease. Health education is essential, and measures tending to increase the stigma should be avoided. Periods of isolation in sanatoria should be reduced to the minimum, and special villages or colonies for inactive cases or cases released from control should be discouraged.

Vocational training should be available in leprosy institutions. Out-patients may also need vocational training; such training must avoid further dislocation of the patient. Centres training those disabled by other causes should be open to those disabled by leprosy.

As stated in the WHO First Western Pacific Regional Seminar on Leprosy Control (Manila, 1965): "Patients with readjustment problems should receive aid from official and private organizations for social welfare and from experts in relevant fields. International organizations should co-operate in the study of these problems."<sup>2</sup>

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<sup>1</sup> In: *Proceedings of the Eighth International Congress of Leprology, Rio de Janeiro, 1963 (Final Reports of the Technical Panels Approved by the Plenary Session of September 20th)*, Rio de Janeiro, 1963, pp. 71, 79, 90.

<sup>2</sup> Report to be published.

Priority should be given to the prevention of disabilities by simple methods that can be applied in the field; doctors and paramedical personnel engaged in leprosy work should be given adequate training; principles of rehabilitation should be incorporated in leprosy control as routine work; simple forms of physiotherapy should be available to the patients in the field.

Surgical and orthopaedic services for leprosy rehabilitation should be integrated with other rehabilitation programmes in general hospitals and clinics. General rehabilitation services should include facilities for leprosy patients.

The Committee endorses the resolution of the Eighth International Congress of Leprology (Rio de Janeiro, 1963) that: "in every antileprosy campaign the doctors and paramedical workers should be trained to look for danger signs in hands and feet and eyes, and should give advice and simple treatment to prevent deformity and blindness."<sup>1</sup> Therefore the Committee is in favour of the establishment of training centres for rehabilitation, integrated into leprosy control programmes, provided that first priority is given to the above aim.

International organizations also should co-operate in training national staffs in reconstructive surgery in countries in which leprosy-control programmes have reached a satisfactory level. However, as stated in the report of the WHO First Western Pacific Regional Seminar on Leprosy Control (Manila, 1965): "Funds for leprosy control should not be diverted for the provision of reconstructive surgery."<sup>2</sup> It should not be forgotten that the aim of leprosy control is to prevent disabilities by early diagnosis and treatment, rather than have to correct them.

The Committee emphasized the importance of producing a simple and practical classification of disabilities for use in field projects.

#### 1.5.5 *Social measures*

Governments should provide social assistance to leprosy patients and their families, according to existing facilities, in the same way as it is given to other disabled persons.

#### 1.5.6 *Legislation*

The legal measures applicable to communicable diseases should also be applied to leprosy. No special legislation is considered necessary.

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<sup>1</sup> In: *Proceedings of the Eighth International Congress of Leprology, Rio de Janeiro, 1963 (Final Reports of the Technical Panels Approved by the Plenary Session of the September 20th)*, Rio de Janeiro, pp. 79, 90.

<sup>2</sup> Report to be published.

### 1.5.7 *Administrative measures*

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 planning, programming and organization of health programmes should also be applied to leprosy control.<sup>1</sup>

#### 1.5.7.1 *Planning*

The following requirements are essential for the proper planning of leprosy control programmes.

As accurate a knowledge as possible of the magnitude of the problem : prevalence, and distribution of leprosy ; clinical patterns of the disease ; and frequency of disabilities. In addition, the following information is necessary : (i) geographical description of the area of operations, climate, social and economic standards, communications, etc. ; (ii) relevant information about the population and its distribution ; (iii) the health situation in the area, mortality rates, morbidity rates of the most prevalent diseases, nutritional status, housing, environmental sanitations, etc.

The ideal method of obtaining basic epidemiological information for planning leprosy control is by means of random sampling surveys in the area of operations. Usually, this is not possible because of the high cost involved ; as an alternative, information readily available in the countries may be used. Limited surveys of selected groups of population may give useful information.

(a) *Resources*. An appraisal of available resources is indispensable for planning. This should include :

Budget (for the country in general, for health and for leprosy work),

General structure of health services in the country and coverage of populations including,

- (i) facilities for medical assistance at different levels (hospitals dispensaries, rural health centres and sub-centres, etc.),
- (ii) mobile units — number and functions, and
- (iii) laboratory facilities, especially at local level.

Leprosy service personnel

- (i) number of doctors (full-time and part-time) ;
- (ii) number and kind of para-medical personnel ;

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<sup>1</sup> Pan American Sanitary Bureau/WHO Regional Office for the Americas (1963) *Seminario sobre lepra : documentos de trabajo, conclusiones y recomendaciones, Cuernavaca, Mexico, 1963*, Washington (*Publicaciones científicas* No. 85).

- (iii) number of social workers ;
- (iv) administrative personnel ;
- (v) others (drivers, porters, etc.).

Facilities for medical assistance to leprosy patients :

- (i) number and capacity of sanatoria ;
- (ii) dispensaries ;
- (iii) skin clinics ;
- (iv) mobile units ;
- (v) laboratory facilities.

Other possible resources :

- (i) number of general practitioners working in the area
- (ii) voluntary agencies and their activities

Training facilities — medical and public health schools, nursing schools, postgraduate courses. etc.

(b) *Collection of data, recording and reporting.* A suitable system for collecting and recording data is indispensable for planning, programming, control of the development of the programme, analysis of final results, and evaluation. This information is also necessary to improve knowledge of the epidemiology of leprosy and the efficiency of preventive and treatment techniques.

It is recognized that available information about the leprosy problem in the majority of countries is poor or unsatisfactory. On the other hand, owing to lack of uniformity in the definition of terms and concepts, data obtained from different countries, and even in different areas of the same country, are hardly comparable ; consequently, they have little epidemiological value.

In order to obtain comparable data, the recording system should be improved and standardized as far as technical information is concerned. A standard report for use at local, national and international level is highly desirable.

(c) *Terminology.* Current terminology in dermatology and epidemiology should be adopted in leprosy work, as well as the classification of leprosy, terminology and definitions accepted by international meetings of experts.

In different countries, different terms are used for indicating that the disease has been arrested and that treatment is no longer required. These terms include words like subsided, inactive and arrested. For administrative purposes, the operational definitions of "inactive" case and "released from control" ("*rayé de contrôle*", "*alta definitiva*") are

proposed, accepting the criteria established in the WHO First Western Pacific Regional Seminar on Leprosy Control (Manila, 1965):

A leprosy patient without any sign of clinical activity and with negative bacteriological examinations should be considered as an "inactive" case. Once inactivity is achieved full treatment should be continued for varying periods of time before the patient is "released from control". These periods should be one and a half years for tuberculoid, three years for indeterminate, and five years for lepromatous and borderline cases.<sup>1</sup>

#### 1.5.7.2 *Programming*

Programming comprises two main subjects: definition of objectives and establishment of time-tables.

(a) *Objectives*. Objectives should be well defined in terms of quantity, areas and time. They should be realistic, i.e. feasible with available resources and useful, the achievement of the objectives being sufficient to protect the majority of the population exposed to the risk of infection.

The difficulties of establishing quantitatively defined objectives are recognized. Nevertheless, attempts should be made to define quantitatively the objectives of leprosy control programmes even if they merely express the amount and quality of services to be given to the population for a unit of time, so that current and final evaluation may be possible.

Long-term epidemiological studies are required for predicting the trend of the disease, the development of better methods for control and to determine the quantitative expression of the benefit derived from leprosy control programmes.

(b) *Time-tables*. Once the objectives of the programme have been quantitatively defined, in order to accomplish them in the scheduled time, a number of actions (clinical examinations, bacteriological examinations, visits to patients, etc.) must be performed in each unit of time (day, week or month). This detailed schedule or time-table is the basis for the control of the development of the programme and should be designed and incorporated in the plan of operations.

All leprosy control activities such as case-finding, follow-up of the cases, treatment, surveillance of contacts, training of personnel and health education activities, should be reflected in the time-table according to the three main elements involved in the programme: i.e., quantitatively defined objectives, work standards of personnel and equipment, and period of time.

(c) *Organization*. It was concluded at the WHO/PASB seminar on leprosy in 1963 that "Since health is an indivisible whole, leprosy control programmes should be included within the structure of the general health

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<sup>1</sup> Report to be published.

services.”<sup>1</sup> This position has been endorsed by the WHO First Western Pacific Seminar on Leprosy Control (Manila, 1965).<sup>2</sup>

Because of the usual limitations in personnel and equipment, it is difficult or even impossible for leprosy services alone to face, on a permanent basis, the overload of work resulting from the accumulation of patients in the attack phase of the campaigns in endemic areas. Therefore, active co-operation with general health services at different levels and the progressive integration of leprosy control into health centres at local level, as and when possible, are of the utmost importance.

At local level, this co-operation should be attempted from the very beginning of the campaign. For this purpose, personnel of health centres should receive adequate training in leprosy, and personnel of leprosy services in communicable diseases control and in public health.

The role of the leprologist in leprosy control campaigns is mainly to give technical advice and guidance and to train personnel. Executive functions in the field should be performed by properly trained public health doctors and paramedical personnel. The co-operation of general practitioners working in the area is also very important.

According to the conclusions of the WHO Study Group on Integration of Mass Campaigns against Specific Diseases into General Health Services,<sup>3</sup> mass campaigns against leprosy are useful and even indispensable in countries of high endemicity that do not yet have satisfactory general health services. However, such programmes must be considered as temporary expedients, and the ultimate goal must be the establishment of a permanent system of general health services.

In countries with leprosy campaigns and concurrently existing general health services, their progressive convergence and ultimate merging must be sought in order to comply with the accepted view that all problems and programmes in the health field are so interdependent that they must be considered together. The need for integration, however, must not lead to precipitate action that may cause the possible loss of benefits gained so laboriously. The transfer of duties to the general health services must be preceded by a careful study of the situation using the pilot survey and trial to obtain the necessary facts and experience.<sup>3</sup>

#### 1.5.7.3 *Evaluation*

Evaluation is not merely an assessment of results but a continuous procedure that begins at a very early stage of the project and covers all

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<sup>1</sup> Pan American Sanitary Bureau/WHO Regional Office for the Americas (1963) *Seminario sobre lepra : documentos de trabajo, conclusiones y recomendaciones, Cuernavaca, Mexico, 1963*, Washington (*Publicaciones cientificas* No. 85), p. 36 (translated).

<sup>2</sup> Report to be published.

<sup>3</sup> *Wld Hlth Org. techn. Rep. Ser.*, 1965, 294

different stages of the programmes, i.e., planning, programming and execution. There are two main types of evaluation.

(a) Current evaluation during the development of the programme. This allows control of the efficiency of the administrative set-up, personnel, equipment and operational methods, and the way in which objectives are being accomplished in the scheduled time, so that the persons responsible for the programme may have exact knowledge of its development and, if advisable, take pertinent action in good time.

(b) Final evaluation : Determination of the extent to which the objectives of the programme have been accomplished and whether these achievements have served the purpose of the programme by reducing, for the community, the risk of contracting leprosy.

Several prerequisites are indispensable in making possible the evaluation of the programmes : relevant baseline information, objectives quantitatively defined and measurement indicators.

As far as leprosy is concerned, the best possible indicator would be the annual incidence rate but, taking into account the difficulties in obtaining reliable information about incidence, the six following indicators are suggested for evaluation : (i) prevalence rate ; (ii) rate of cases registered yearly ; (iii) specific prevalence rates in selected groups of population (contacts, schoolchildren, soldiers, etc.) ; (iv) proportion and rates of the different forms of leprosy ; (v) proportion of bacteriologically negative cases among lepromatous patients under treatment ; (vi) proportion of cases released from control, according to the classification of the form of the disease in the individual patient.

In general it may be said that evaluation should be the constant task of all technical personnel and a routine activity in periodical reports.

#### 1.5.7.4 *Pilot or demonstration areas for leprosy control*

The experience gained in recent years has confirmed the usefulness of the recommendations given in the second report of the WHO Expert Committee on Leprosy<sup>1</sup> concerning pilot projects aimed at improving the methodology and adapting operational methods to local conditions. Leprosy campaigns should always start with a pilot project. Countries in which a leprosy campaign is under way should also have a pilot project or demonstration area. The areas will serve :

(a) to study operational methods, the development of a suitable recording system, and the integration of the leprosy control project into the general health service,

(b) to study the nature, extent and rhythm, etc. of treatment,

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<sup>1</sup> *Wld Hlth Org. techn. Rep. Ser.*, 1960, 189

- (c) to study means for protecting child contacts against leprosy, and
- (d) to give practical training in leprosy control.

Where resources are available the project would also serve :

- (e) to undertake epidemiological, sociological, administrative and field research according to the recommendations to be found in the corresponding sections of this report.

The operational area should be selected with the five following factors : (i) estimated prevalence and patterns of the disease, (ii) population density, (iii) communication facilities and routes, (iv) pre-existing health centres and availability of competent local health personnel and, (v) ecological conditions.

Collection, classification and study of existing data on the leprosy problem in the operational area should be made in order to establish the approximate prevalence and to assess the characteristics of the endemic. Additional information mentioned above under *Planning* (section 1.5.7.1) is necessary.

A map of the operational area should be prepared, showing the situation of all villages, road communications, number of inhabitants in each village (if possible, child and adult population), situation of health centres and leprosy institutions, number of known patients and form of the disease in each village.

In areas of high endemicity, a survey of the population should be carried out in order to make a complete census of leprosy cases, with relevant clinical, bacteriological and epidemiological data.

Periodical assessment of the project should be carried out.

Expansion of leprosy control to other areas of the country should not be attempted until operational methods have been tested and adapted to local conditions in the pilot areas, and the necessary resources, adequately trained personnel, and equipment are available. Premature expansion can ruin good leprosy control projects.

### **1.6 The role of voluntary bodies in national leprosy programmes**

Leprosy attracts voluntary and charitable organizations in increasing numbers. Great benefit for patients has been derived from the activities of most of these organizations, and their efforts are appreciated. Their activities should always be developed in line with present concepts of leprosy control and should complement the action of governments.

Voluntary organizations could also co-operate in leprosy control in the field, provided that the personnel have the necessary training and qualifications. These activities should be in accord with government schemes and under the control and supervision of the health authorities, in order to eli-

minate competition and duplication and to avoid gaps in the over-all programme.

Taking into consideration the great importance of research in the field of leprosy, the Committee recommends that voluntary organizations should be asked to contribute to research programmes.

## 2. RESEARCH

Every aspect of leprosy control that has been discussed in this report has illustrated the need for intensified research in operational methods, field work, sociological aspects, clinical problems and the basic sciences.

It is particularly important that, in order to attract the assistance of experts in the basic sciences and allied disciplines, leprosy research be conducted in general centres of research throughout the world. It is no less important that both governments and international organizations should foster training and research in countries where leprosy is endemic.

Some of the more important research objectives are considered below.

### 2.1 Microbiology

Fundamental progress has been made in three areas: transmissible infections in animals; morphological features that predict the infectiousness of leprosy bacilli; and evidence that *M. leprae* can be propagated in cell cultures.

#### 2.1.1 *Transmission to animals*

The most important advance has come about through a concerted effort to establish infections in animals and the infection in the foot-pads of mice, first reported in 1960, has been the most widely confirmed and exploited.

Although 6-8 months are required for 100- to 1000-fold increases in bacilli, and the maximal yields are limited to the order of  $10^6$  bacilli per foot-pad, the usefulness of these infections in leprosy research has been clearly established.

(a) The characteristic infection by non-cultivable mycobacteria has been induced by well over 100 strains of *M. leprae* from Africa, Asia and the Americas, and from patients with lepromatous, borderline and reactional tuberculoid leprosy. DDS-resistant strains have been obtained from a small proportion of patients whose infection had not been controlled by that drug. Lepromin prepared from animal foot-pads produces skin reactions corresponding to those induced by the classical Mitsuda-type lepromin.

(b) It is particularly significant that nerve involvement characterizes these infections with *M. leprae*, but not other mycobacteria, in the ears and foot-pads of mice and hamsters, thus providing an experimental tool for the investigation of neuropathology and neurophysiology.

(c) Two new fields of investigation have been opened by demonstrations that foot-pad infections are inhibited by anti-leprosy drugs and also by prior BCG vaccination.

(d) The suppression of the immune response in mice by means of thymectomy and irradiation has enhanced multiplication of *M. leprae*, indicating that immunization during infection is one factor that limits the experimental infections. This provides a possibility for improving the yields of bacilli. The reliable preservation of *M. leprae* by refrigeration means that experimental work can be conducted in laboratories and pharmaceutical establishments throughout the world.

(e) The demonstration that the infectiousness of *M. leprae* for the foot-pad is proportional to the number of solid-staining bacilli clearly suggests the importance of these forms as an index of the infectiousness of patients.

#### 2.1.2 *Biological significance of solid-staining M. leprae*

Because *M. leprae* has not been cultured, indirect methods have been sought for determining its viability or infectiousness. *M. lepraemurium* was chosen as the model because "viability", measured as infectivity, could be checked in the experimental animal. Early studies using electron microscopy and the inoculation of animals showed that increasing proportions of degenerate forms of *M. lepraemurium* were associated with decreased infectivity. The appearance of these degenerate forms under the electron microscope resembled that of dead *Escherichia coli*, the death of which had been confirmed by plate counts. The next step was the demonstration that degenerate forms of *M. lepraemurium* were stained irregularly by the routine Ziehl-Neelson method. It was thus established that only bacilli showing uniform or solid-staining with carbol-fuchsin were likely to be healthy or infective. It was reasonable to expect that this analogy could be extended to *M. leprae*, and this expectation has now been confirmed by the foot-pad infection in mice. Thus, the proportion of solid-staining bacilli (known as the morphological index) determined, where possible, on not less than 100 organisms from routine Ziehl-Neelson stained skin or nasal smears, offers a measure of the response to chemotherapy and of the infectiousness of patients.

#### 2.1.3 *Infections in cell cultures*

Two groups of investigators have reported limited proliferation of *M. leprae* in mouse monocytes and rat and human fibroblasts. This event

is of the greatest significance to many necessary lines of work. Since it is known that the intracellular growth of fastidious mycobacteria depends in part upon ingredients in the extra-cellular medium, work on cell culture systems should contribute information fundamental to progress on the problem of mass cultivation.

## 2.2 Immunology

Developments in the field of immunology are handicapped by the lack of mass cultures of *M. leprae* as a source of homologous skin-test reagents and of antigens for immunization or for serological work.

### 2.2.1 *The Mitsuda reaction*

The significance of the Mitsuda reaction has been related to the rates at which tissue cells can digest heat-killed *M. leprae*. Because many studies suggest a correlation between Mitsuda reactivity and resistance to leprosy, it is urged that research with lepromins of the present Mitsuda-Hayashi-Wade type be pursued in the five following directions :

(a) The standardization of bacillary concentrations in lepromin at the level of 160 million acid-fast bacilli per ml.

(b) The significance of the 1+ grade of reactions as read in accordance with the criteria recommended by WHO<sup>1</sup> and by international congresses of leprology. The optimal time of reading should also be investigated.

(c) The possibility of reducing non-specific reactions and of extending available supplies of lepromin by means of new reading scales adjusted to the use of lepromins diluted in saline and in oil adjuvants.

(d) The unexplained causes of increased Mitsuda reactivity with advancing age.

(e) The permanence of positive reactions induced by BCG or other mycobacterial antigens.

### 2.2.2 *Serological studies*

A most widely confirmed observation is that lepromatous patients produce antibodies that react with mycobacterial polysaccharides, and that significant levels of these antibodies do not occur in tuberculoid patients. There is a great need for data regarding antibodies against proteins. The present evidence of circulating antigen and of antigen-antibody complexes in lepromatous patients requires further study along the lines suggested during the Work Conference on Serology of Leprosy.<sup>2</sup>

<sup>1</sup> *Wld Hlth Org. techn. Rep. Ser.*, 1960, **189**.

<sup>2</sup> *Work Conference of the Serology of Leprosy : Report of Meeting on 19 September, 1963* (Rio de Janeiro) Pan American Sanitary Bureau/WHO Regional Office for the Americas, Washington (ref. : RES 63.3)

### 2.2.3 *Reactional states*

Reactional states in leprosy are responsible for many of the severe complications. Clinically, the manifestations may resemble those seen in Arthus- and Schwartzman-type reactions. An important question is whether these are largely reactions to *M. leprae* or whether there is an important component of auto-immunity. With techniques now available, such questions could be studied in some detail. The finding that there is increased complement fixation between normal tissues and sera obtained during reactional states has opened up one avenue of investigation of auto-immune phenomena that is not dependent upon antigens obtained from *M. leprae*.

### 2.2.4 *Prophylaxis by BCG*

The epidemiological characteristics of leprosy indicate the need for protective measures applicable to entire populations in endemic areas.

BCG vaccination may accelerate the conversion of the lepromin test in children. It appears, however, that there is a group of poor or slow responders whose lepromin conversion cannot be elicited by BCG or other agents. The value of BCG vaccination in the control of leprosy should be determined in field trials.

Two large and well controlled trials are now under way. The first, in Uganda, was initiated in 1960 and is now being supported by the Medical Research Council of Great Britain. The second BCG trial, undertaken by WHO in Burma in 1964, is in an area with a higher proportion of lepromatous leprosy. These two trials, therefore, are complementary. It is hoped that the results may give a useful assessment of the value of BCG for the prevention of leprosy.

## 2.3 **Pathology**

### 2.3.1 *Practical applications*

The usefulness of histological examinations in leprosy has been improved by combining assessments of the area of cellular infiltration with the concentration of acid-fast bacilli to yield a histological index that is more instructive than the classical bacteriological index. Inclusion of data on the proportion of solid-staining bacilli should further enhance the value of histological examinations.

### 2.3.2 *Neuropathology*

The special predilection of *M. leprae* for peripheral nerves creates disabilities that handicap many patients. It is important that basic studies be carried out by applying the techniques available for studying nerve and

muscle functions. It appears that leprosy bacilli do not enter nerve fibres directly but do so by infecting activated Schwann's cells. The latter ingest neural debris, foreign particles and mycobacteria, including *M. leprae*. Schwann's cells are most actively phagocytic during nerve degeneration and regeneration. Since there is a constant physiological turnover of cutaneous nerves, some Schwann's cells are always in an active phase and capable of phagocytosing *M. leprae*. Recent experiments on leprosy patients have shown that activated Schwann's cells ingest heat-killed *M. leprae* more readily than heat-killed *M. lepraemurium*. Since nerves become involved during experimental human leprosy infections in the foot-pads of mice or ears of hamsters, it should now be possible to study neuropathology in experimental models.

### 2.3.3 *Electron microscopy*

Electron microscopy provides a useful method for studying the host-bacillus relationship at the intra-cellular level. Such studies are providing more precise knowledge of the host-bacillus inter-reaction in different types of leprosy. Similar studies are essential for investigating nerve involvement in leprosy, particularly since Schwann's cells can be identified only by the presence of a basement membrane.

## 2.4 **Epidemiology**

A number of puzzling features of leprosy require further epidemiological investigation in different parts of the world.

Tuberculoid cases may become bacteriologically positive during periods of reaction. Comparative studies should be made, in different geographical areas, of the occurrence of such reactional episodes in order to assess the role of tuberculoid cases in the spread of the disease.

Some consideration might be given to the possibility that symptomless but presumably infectious individuals exist. The existence of sub-clinical leprosy infections should be verified by more field studies. Such studies should include the investigation of the relative frequency of nonclinical leprosy in individuals who are not contacts of persons with clinical leprosy as well as those who are. The presence of *M. leprae* in suspected individuals might be detected by the injection of material from them into the foot-pads of mice. This technique should be useful in other studies as well.

Combined field and laboratory studies are required to verify the possible arthropod transmission in leprosy.

The nature and causes of natural reactivity to lepromin may be further clarified by a study of the reactivity of different groups of children comparable in sex and age but living in widely divergent environments. Such a study should include the testing of their reactivity to other antigens.

There is no available evidence at present that a dietary deficiency predisposes to leprosy. Comparisons should be made, by those competent in such matters, of possible differences or deficiencies of diet between areas of high prevalence and of low prevalence, preferably in the same geographical area. The possible influence of climatic conditions might be considered for investigation.

Susceptibility and resistance to leprosy may have a significant genetic component. Studies should be carried out on patients with lepromatous and tuberculoid leprosy, testing for a wide range of genetically controlled determinants (enzyme deficiencies, blood groups, salivary factors, taste, and colour vision, etc.). Such a study should include healthy persons, contacts and non-contacts, in relation to their lepromin reactivity. Studies should also be made of the possible occurrence of familial tendencies towards either tuberculoid or lepromatous leprosy, the occurrence, clinical type, and course of leprosy in identical twins as compared to non-identical twins, and also of lepromin reactivity on a genetic basis.

The minimum proportion of infectious cases to be treated in order to achieve a significant reduction in the prevalence and incidence of leprosy still remains to be determined. Long-term trials with this aim in mind should be undertaken in pilot projects.

## 2.5 Diagnosis

The presence of acid-fast bacilli in small numbers in the skin and nose of healthy contacts of leprosy patients has been reported from a few centres. The significance of the findings is, however, not clear. It would be desirable to undertake further studies of the matter, provided methods are available for the identification of the acid-fast bacilli found in the contacts. The possible usefulness of the mouse foot-pad method should be investigated.

## 2.6 Chemotherapy

### 2.6.1 General

Therapeutic trials should be conducted using the standards recommended by WHO for controlled clinical trials in leprosy.<sup>1</sup>

It is suggested that the mouse foot-pad infection be utilized for: (a) screening new anti-leprosy drugs, (b) detecting drug-resistant strains of *M. leprae* and (c) testing the infectivity of *M. leprae* during treatment.

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<sup>1</sup> Unpublished document WHO/PA/97.60

### 2.6.2 *Problems related to treatment with DDS*

In particular, studies should be conducted on the five following facets of these problems :

(a) to determine the minimum effective dose : (i) relationship between blood levels of the drug and the clinical and bacteriological results ; (ii) relationship between the concentration of the drug in the blood and the tissues ;

(b) to determine the maximum effective dosage spacing obtainable by the parenteral administration of repository preparations of DDS and to find the most suitable vehicle for such preparations ;

(c) to study the value of this drug in preventing or limiting nerve involvement ;

(d) to determine the duration of treatment required after arrest of the disease in patients with lepromatous leprosy ; and

(e) to compare, during treatment, the proportion of solid-staining bacilli (morphological index) obtained from nasal washings and from skin lesions.

### 2.6.3 *Prevention and treatment of reactions*

(a) To find drugs that will reduce the frequency, severity and sequelae of reactions.

(b) To discover which corticosteroid preparation is the most effective and has the least side effects.

## 2.7 **Chemoprophylaxis**

The Committee noted with interest the well-planned investigation on the prophylactic value of DDS against leprosy that is in progress at the Central Leprosy Teaching and Research Institute, Chingleput, India.

The preliminary results are highly significant and suggest the value of chemoprophylaxis in the prevention of leprosy. The study should be continued so that a definite conclusion can be reached. If its effectiveness is established, it would be necessary to plan further studies to determine the optimum dose and the length of time for which preventive treatment would be required. In addition, practical methods of applying chemoprophylaxis in the field should be developed.

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