MEMORANDUM SETTING OUT THE BRITISH EMPIRE LEPROSY RELIEF ASSOCIATION'S RESEARCH PROJECT IN EAST AFRICA*

by

R. G. COCHRANE.

The advances in the therapy of leprosy have opened up the way towards a better understanding of the disease. Now that it has been demonstrated that leprosy is amenable to treatment interest has been created in the search for more efficient, more rapid, and more certain remedies for the "cure" of a disease which has baffled the Medical Profession for decades, if not centuries.

The advances in Chemotherapy place at the disposal of the Medical Profession new and powerful drugs, but if we are to avail ourselves of the opportunity the new age of chemotherapy has placed in our hands, an essential pre-requisite is a better understanding of the disease.

There are research stations in Britain and the Empire for Tuberculosis, for Malaria, for Trypanosomiasis, and many other conditions, but, despite the fact that of the estimated five to ten million victims of leprosy more than half are probably citizens of the Empire and Commonwealth, there is no comprehensive research and training centre.

There are centres which undertake research—e.g. Calcutta, Uzuakoli, Sungei Buloh—but these are either limited in their scope or activities. For example, Calcutta is handicapped by having no adequate In-patients institution; Uzuakoli is chiefly a therapeutic unit and has few or no facilities for clinical photography and histo-

* This Memorandum was accepted by the Medical Committee of the British Empire Leprosy Relief Association at their meeting on 25th July, 1952. The Committee issued a directive that research in Epidemiology, Immunology and Therapy should first be undertaken, leaving other aspects of the programme for later consideration.

pathology. Sungei Buloh is in an area of political uncertainty, and, therefore, personnel problems arisè.

FUNCTIONS OF THE BRITISH EMPIRE LEPROSY RELIEF ASSOCIATION

Apart from informing the general public of the need for leprosy relief, the British Empire Leprosy Relief Association's main function is to advise Governments and other bodies as to the most efficient way of bringing leprosy under control in the Empire and Commonwealth. If this is to be done adequately, and if the Association's opinions are to be of value, and not second-hand, a Research Station is an absolute necessity. It is quite true that research in leprosy must never be conducted in a water-tight compartment, but the research worker must be in touch with scientists in allied fields, and, therefore, a research station should be within reasonable reach of Medical Research Institutions. Because one of B.E.L.R.A.'s functions is to stimulate pioneer and pilot experiments in leprosy, it is vital that this organisation, in co-operation with the Colonial Governments, should contemplate establishing a Research Unit. The objectives of this Research Unit should be—

I. Research in all practical aspects of leprosy, with a view to
   (1) Acquiring a better understanding of the disease.
   (2) Assessing critically new Chemotherapeutic remedies.
   (3) Investigating speedier and more effective methods of control.
   (4) Studying ways and means of preventing and alleviating deformities.

II. The establishment of a Central Training Institution where workers would receive a comprehensive training in leprosy.

I. RESEARCH IN ALL PRACTICAL ASPECTS OF LEPROSY.

(1) I stress the point " practical aspects " because while basic research is essential it must have a practical objective and lead to a better understanding of the disease, and not just result in information of academic and theoretical interest. Nevertheless, an adequate appreciation of the time needed for fundamental research must be present, and the research worker must not be expected to produce results of significant practical importance every year; neither must his work be solely judged on this criterion. A better understanding of leprosy will ultimately influence the practical policies of treatment and control, but years of research may be necessary before its practical application can be appreciated. In discussing research work in these terms I shall consider the following subjects, which need special attention.

a. Epidemiology.
b. Histopathology.
c. Bacteriology.
d. Immunology.
e. Animal Inoculation.

a. EPIDEMIOLOGY.

While much epidemiological research is highly technical and only of practical application over a very prolonged period, nevertheless it is quite true to say that we know little or nothing about the factors which cause leprosy to increase under natural conditions. Detailed epidemiological investigations apart from a limited area in the Philippines, in Brazil, and in certain parts of India and Nigeria, have received very little attention, particularly on a long term basis. It may not be correct, for instance, to state that solely because sulphone therapy has been given on a wide scale, leprosy has been controlled within certain areas. Nevertheless it may be said that leprosy control has been greatly assisted through the discovery of the sulphones, and has given confidence to workers in discharging patients. To investigate all the factors of decline or increase of leprosy, and to be able to judge the stage of the epidemic in any given area, would be of utmost practical importance, and would save unnecessary expenditure in areas where all the evidence available indicated that leprosy was on the decline.

b. HISTOPATHOLOGY.

While it may be said that the study of the detailed histopathological process in leprosy is an item of basic research more of academic than practical importance, nevertheless, if we are to understand the factors which influence the healing of the disease, either spontaneously or by means of chemotherapeutic agents, the more knowledge we have of the reactions of the dermal tissues—favourable or unfavourable—to invasion by the *M. leprae*, the greater will be our understanding of the processes necessary in chemotherapy, and the better will we be able critically to assess therapeutic results. Further, the recent suggestive work of the Bombay workers indicates that the answer to the development of leprosy may be found in the skin, and it appears that the *M. leprae* invade the nerve plexuses of the skin first, and spread from these structures. This work, and the investigation of the presence of bacilli in the dermis of contacts of open cases is of great importance, but to confirm these observations needs patient, meticulous, and prolonged study of a large number of smears and sections from contacts.

As a result of the more detailed study of histopathology the classification of leprosy is being better understood. Classification

of disease can hardly be considered of academic importance only, for without a proper appreciation of this, it is difficult to explain the various clinical and immunological anomalies which are seen in leprosy. The complete elucidation of the protean clinical manifestations of leprosy will only be achieved by a detailed long-term study of the histopathology of the skin in leprosy.

I believe that therapy should be combined with the study of skin changes during resolution of the disease under treatment. If this were done more, and compared with resolution or extension of the disease in untreated cases, fewer premature claims for success would be made, and a more accurate assessment of the benefits of therapy would be available. The question of relapses, and the nature and viability of the granular forms of the *M. leprae*, entails not only detailed histological studies, but observation over a number of years.

While certain histopathological techniques—e.g. the study of nerve changes, the exact position of the *M. leprae* within the nerve, the nature and mode of spread along the nerve—*need special methods and knowledge*, a research station with good clinical records can always enlist the help of specialist workers and send material to these workers for their comment and *guidance in future research*. Only detailed methods of histopathological research will answer a number of problems which have arisen in the new and successful therapy of leprosy with the sulphone group of drugs.

c. BACTERIOLOGY.

I am aware that research in the bacteriology of leprosy is not only extremely difficult, but, up to now, has been extraordinarily barren of results. Nevertheless recent work, indicating the importance of nerve tissue in the evolution and development and spread of leprosy, opens up new lines of research, and a fresh approach to cultivation in vitro of *M. leprae* and animal inoculation. Advances in chemotherapy of leprosy are very seriously handicapped because of the lack of success in culturing *M. leprae*, and the failure to infect animals with leprosy. If these disadvantages could be overcome, a more detailed study of the metabolism of *M. leprae*, could be undertaken, and our trial of drugs might be less confined to those which have been shown to be effective in tuberculosis. Admittedly this may require complicated and costly apparatus, but, now there are possibilities of despatching material by the freeze-dry technique, lines of development in the culture of the *M. leprae*, which are suggested by the research on other aspects of the disease, could be followed up by sending the material to well-equipped laboratories in this country. No part of East Africa is

more than 24 hours by air from Great Britain, and by the new Comet service Entebbe in East Africa is but twelve hours from London.

d. IMMUNOLOGY.

The detailed immunological study of leprosy is again a long-term project. The work of the South American and French workers in B.C.G. vaccination and the lepromin test is most interesting, and should be followed up on a long-term basis. There seems to be considerable evidence that in children, and possibly also in adults, a lepromin negative reaction is converted into a positive after B.C.G. vaccination. The importance of this in child contacts is obvious, but finally to assess (a) whether this reaction is actually accompanied by increased resistance to *M. leprae*, and (b) whether any tissue immunity which may be established is permanent, needs detailed and careful observation of persons in an endemic area for many years. To clear up these and cognate questions epidemiological investigation will be necessary in an easily accessible area where leprosy is highly endemic. The research unit contemplated in E. Africa would be a most suitable centre from which to carry out a long-term research project of this nature.

e. ANIMAL INOCULATION.

One of the greatest handicaps to a better understanding of the life history of *M. leprae* is the lack of a suitable experimental animal. With the lead which recent work has given on the importance of the nerves in leprosy, and the work on cortisone and ACTH on inhibiting healing processes, an entirely new avenue of animal experimentation has opened up. A research station in East Africa, where large animals—e.g. monkeys—are more readily available, might contribute significantly to our knowledge in this respect.

In this connection, it may be said that an endeavour is being made to secure the help of research workers in this country. This would be of great value to such a research station as is contemplated, because workers in a research station in East Africa could be kept in constant touch with experienced research workers in the ancillary fields of bacteriology, including experimental pathology.

(2) CRITICAL ASSESSMENT OF NEW CHEMOTHERAPEUTIC REMEDIES.

The first requirement in assessing chemotherapeutic remedies is a knowledge of how they act on the *M. leprae.* Therefore, if we are to have a clear understanding of the way chemotherapeutic remedies and antibiotics act in leprosy, such phenomena as the following need fuller elucidation, (a) erythema nodosum, (b) changes in the morphology of *M. leprae,* (c) reservoirs, e.g. nerves,

which may continue to harbour *M. leprae*, and from which they may spread and cause relapse. This aspect of research would, therefore, be an important item in the research programme of such an institution as is envisaged by B.E.L.R.A.

Because of the increasing number of chemotherapeutic and antibiotic drugs being advocated against mycobacterial disease, it is essential to have a fully equipped research unit. I am of opinion that much money would be saved and unnecessary suffering, through the creation of exaggerated hopes, would be avoided, if all new drugs could first be tried in such a station. Admittedly, there are several institutions in which therapeutic trials can be undertaken, but there are special advantages when they take place in a centre where there are facilities for controlled comparisons, histopathological examinations, and the keeping of photographic and other records.

Initial chemotherapeutic trials could also be advantageously undertaken, for these can be combined with detailed biochemical estimations. In this way much information could be collated as to the method of the action of drugs on *M. leprae*, and their actual or potential toxic properties.

(3) INVESTIGATION OF SPEEDIER AND MORE EFFECTIVE METHODS OF CONTROL.

The place of treatment, particularly sulphone therapy, in the control of leprosy, is a subject which demands close investigation. As already stated, there are so many factors influencing the stage of the " epidemic " of leprosy, not only in a given country, but in a particular area of the same country, that only the most general conclusions can be reached as to the effect of a given therapeutic remedy on the control of the disease. Therefore, it would be of utmost value to plan a long-term experiment in a suitable area, with adequate controls, on the influence of effective anti-leprosy drugs on the spread and control of leprosy. Such a project would involve preliminary detailed survey, and periodic resurveys. Statements on the control of leprosy by means of therapy are sometimes made on insufficient data.

(4) STUDY OF WAYS AND MEANS OF PREVENTING AND ALLEVIATING DEFORMITIES.

One of the most serious problems in leprosy is the question of deformity which is such a frequent end result of the disease. It is true that the more widespread the use of sulphones, the less likely are the unfortunate sequelae of leprosy to be seen. Nevertheless, as the problem of deformity due to paralysis and paresis of muscles is likely to continue to be serious for many years, investigation

into the methods of preventing or alleviating these conditions deserves high priority in our planning. Admittedly, if one is contemplating orthopaedic and physiotherapeutic measures, an institution in which there is already a general research unit would be ideal for this purpose, and, therefore, in all planning the claims for orthopaedic and physiotherapeutic investigation should be considered.

II. A CENTRAL TRAINING INSTITUTION.

A thorough training in leprosy is as essential as teaching in tuberculosis. It is a great handicap for young doctors, who become initially interested in leprosy, not to be given facilities to acquire a basic knowledge of this speciality before assuming responsibility for an institution, and, as is frequently the case, also for leprosy prevention in the area around the leprosy colony.

Outside Calcutta there are no set courses of leprosy instruction. If a young medical man is not only to offer for leprosy, but to remain in this work, it is essential that he be given a training for at least three months. Recruits, particularly medical men, for leprosy work are lamentably few, and I believe this is largely due to the fact that there is little opportunity given to young men to appreciate the fact that leprosy is a most interesting speciality, and one which gives ample scope for their talents.

ORGANISATION OF UNIT.

It is proposed to place this unit under the charge of an experienced Leprologist, Dr. Ross Innes, who would have under him:—

(1) A fully trained laboratory technician.
(2) A biochemist.
(3) A secretary (clerical) to the unit.
(4) Junior clerks and junior technicians.

In so far as the Member Governments of the East Africa High Commission would be associated with B.E.L.R.A., reports of the working of the unit would be sent not only to the Secretary of the Medical Committee of B.E.L.R.A., but also to the Colonial Office and to the Director of Medical Services in the three Territories. This would be of inestimable value to the work, and would relate leprosy to other research projects already in existence in East Africa.

COST OF UNIT.

Detailed plans remain to be worked out when the site is chosen and general principles of organisation have been drafted. It is, however, estimated that the capital cost would be in the neighbourhood of £30,000 and the recurrent cost £8,000. B.E.L.R.A. could

see its way to providing £8,000 to £10,000 for the capital cost, leaving some £20,000 to £22,000 to be raised. The recurrent cost would, we hope, be met by B.E.L.R.A. in co-operation with the East Africa High Commission and its constituent Governments.

The question of future recruitment of other Senior Staff may be raised, as the Leprosy Research Worker contemplated is a very senior Officer. I am of opinion, and I have reason for this statement, that once this research station is under way, it would not be difficult to secure a keen but younger person to assist Dr. Ross Innes.

Leprosy has entered the field of practical medicine, and the stage is now set, not only to correlate and investigate the importance of certain relatively simple facts*—e.g. the part diet plays in influencing the development and spread of leprosy in a given area, the importance of tribal and other customs, etc.—but to undertake detailed research into the pathology, treatment and control of leprosy. Not only should our increasing knowledge of chemotherapeutic agencies be used to combat this disease, but, in addition, as a result of a better understanding of the disease, suffering, particularly that due to deformities and paralysis, should be prevented, and leprosy at last cease to be the terror it is in many of Her Majesty's Dominions and the Commonwealth at large.

ROBERT G. COCHRANE,

May, 1952. *Medical Secretary.*

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* In this connection attention should be drawn to the Report of the late Professor McSwiney on the importance of relatively simple observations and facts and their bearing on disease in East African Medical Research, 1935-36.