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LEPROSY RESEARCH

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The progress report on research in leprosy upto March 1979 was presented at the Fifth Session of the South-East Asia Advisory Committee on Medical Research (document SEA/ACMR/79.1/7.2.8). This report therefore relates to the activities in continuation thereof upto the period 31 March 1980.

The 32nd World Health Assembly noted that leprosy is still a major public health and social problem in several countries and requested the Director-General to continue to mobilize resources from extrabudgetary sources both for the leprosy control programme and for the UNDP/World Bank/WHO Special Programme for Research and Training in Tropical Diseases (TDR), particularly for epidemiological surveys and chemotherapeutic trials and to promote relevant research for the development of new drugs as well as in the field of immunology with the objective of producing a vaccine for prophylaxis.

A WHO Medical Officer (Leprosy) has been reassigned to the Regional Office since January 1980 in order, among other things, to promote and co-ordinate research in leprosy in the countries of this Region. Leprosy research is expanding rapidly both under the regional research programme and under TDR. Pressing problems have been recognized whose applied aspects need prompt consideration. The foremost among these are inadequacies in case-finding, case-holding and release from control of inactive cases. Equally important is the problem of persistence of infection and DDS-resistance. Plans are underway to organize an inter-country consultative meeting in the Regional Office from 2 to 7 June 1980 which will bring together the workers actually engaged in leprosy research and control to consider these problems and to assist in formulating a co-ordinated regional approach to their solution. The

main objectives of the meeting are:

- (1) To review the current status of leprosy control and research, and specifically, the implications of DDS resistance and the available knowledge on multi-drug therapy regimens.
- (2) To formulate criteria for provision of multiple drug therapy in the field and to suggest feasible regimens within the means of the countries and the available knowledge on the subject.
- (3) To review draft protocols on (a) operational studies on methods of improved case-finding and case-holding, and release of inactive cases from control, and (b) multi-drug therapy regimens.
- (4) To outline strategies for implementation of research on above topics.

Leprosy research projects supported by SEARO are enclosed as Annex I, and those supported under TDR are attached as Annex II.

In Burma, support is being provided for the conduct of Rifampicin Trial to assess the effectiveness of chemotherapy with Rifampicin in controlling leprosy.

In India, the Central Leprosy Teaching and Research Institute has been undertaking THELEP multicentre drug trials for quite some time. In 1978, a Standardization Workshop for the TDR/THELEP Multicentre Drug Trials was organized there for those medical officers, statisticians, nurses and other personnel who had direct responsibility for the day-to-day management of the trials, to enable them to be trained in the methods and procedures to be used in the THELEP drug trials. In November-December 1979, a THELEP Mouse Foot Pad Standardization and Application Workshop was held at Chingleput. The purpose of the Workshop was two-fold: (1) to teach the mouse foot-pad methods for cultivation of M. leprae, and (2) to teach the application of the technique for research in leprosy. The emphasis was on (a) on intensive practical work in the standardization of the mouse foot-pad technique, and (b) in the promotion of its use in leprosy research and control activities.

In India, a new SIDA-funded leprosy project for multidrug trials is

being started in Purulia and Wardha. This will be an intensified programme involving a closed, supervised treatment with more effective drugs like Rifampicin and Clofazimine in these two districts on pilot basis. The agreement for implementation of this project between SIDA and the Government of India was signed in 1979; in accordance with this agreement, SIDA will supply the drugs direct to Government of India and funds to cover the local costs will be supplied through WHO.

In Indonesia, possibilities are being explored for conducting a dapsone resistance survey as well as clinical trials in the chemotherapy of leprosy under the TDR.

In Thailand, WHO is providing support for an Evaluation Project of Integrated Leprosy Control Services in Uthai Thani Province. A WHO consultant has been assigned to assist in the planning stage, to assess and evaluate the survey operations of the epidemiology survey, and to design parameters for further analysis of epidemiological and operational survey.

In Bangladesh, research is being supported by WHO on "An Epidemiology Study of Dapsone Resistant Leprosy" and it is proposed to strengthen the Institute of Post-Graduate Medicine and Research, Dacca for undertaking leprosy research under the TDR.

As will be seen from the foregoing, regional research in leprosy is complementary to that supported by the TDR.

1. Title of the Project : Rifampicin Trial in Burma

Country: Burma

Name and Address of the Institution

Leprosy Control Division, Department of Health, Rangoon, Burma

Principal Investigator

Dr U Maung Maung Gyi, Regional Leprosy Officer

Starting Date and Duration: 1975 - ten years

Problem and Aim of the Research Study

A mass survey of leprosy in the designated areas was conducted during 1975 and 1976. Coding and analysis of data of the survey has been completed. In spite of the concentrated programme, the annual incidence of new cases from the trial area has remained constant throughout the period of study. This implies that infectious cases are still present and contact-tracing suggests that most new cases have closer than average contact with an "Index case" (lepromatous or borderline) under treatment. It is therefore likely that the treatment being received by these patients is inadequate to render them non-infectious. In order to deal with this situation, a Rifampicin Trial has been started in Mandalay, Burma in 1975.

The aim of the study is to give supplementary treatment to registered lepromatous and borderline patients, sufficiently supervised as to give the maximum chance of rendering and maintaining them non-infectious for a period of five years by a fully supervised chemotherapy with rifampicin; to monitor them for the degree of infectivity and for regularity of drug-taking, and to assess the effect of this programme by its impact on the annual incidence of new cases of leprosy in the study area.

Method

Subsequently during the years 1977 to 1978, all multibacillary cases received four-week course of 600 mg. RFM and dapsone daily, to be followed up with dapsone alone in full dosages and DADDS injection every two months. All newly detected bacteriologically positive cases in the trial area from 1978 onwards will receive a single supervised dose of 1500 mg of RFM followed up with dapsone alone in full dosages and DADDS injection every two months. Until end of November 1979, a total of 388 bacteriologically positive cases received RFM treatment (278 received the four-week course and 110 received the single dose). The above given population and case data include a control group (Shwebo district) comprising the 1976-1977 mass survey of 25,000 population, 498 total leprosy cases, 130 of which are borderline and lepromatous patients. Incidence rates, subsequent to the RFM/dapsone treatment, are being monitored. Random samples of urine are collected

once a year from RFM-treated cases as well as from bacteriologically positive cases serving as controls (Shwebo) and analysed for urine dapsone to monitor regularity of dapsone intake. In addition, mouse foot pad tests are done for suspected dapsone-resistant cases (a total of twelve experiments have been set up until end of November 1979).

Results so far

Results may be available after 10 years, in view of the long incubation periods of lepromatous and borderline leprosy.

Significance of the study

New and important data are collected from the Rifampicin trial which it is hoped will assist in acquiring new knowledge of the use of RFM on a fairly large scale. The data produced by the trial will provide information not only with regard to improved treatment of individual patients but also on the possible reduction of secondary cases, i.e., on the incidence of leprosy in this population in which leprosy is highly endemic. The results of this study with its comprehensive statistical background, are expected to have a wide implication for leprosy control also outside of Burma.

Publications, if any

Reports of the WHO Short-Term Consultants, as follows:-

SEA/Lep/61	Assignment Report on Leprosy Control in Burma, June-July 1976	Dr J.M.H. Pearson
SEA/Lep/62	Assignment Report on Leprosy Control in Burma, February-March 1977	Dr J.M.H. Pearson
SEA/Lep/63	Assignment Report on Leprosy Control in Burma, June-July 1977	Dr J.M.H. Pearson
SEA/Lep/66	A report on the BCG Rifampicin Trial in Burma, February-March 1978	Dr J.M.H. Pearson
SEA/Lep/68	Assignment Report on Rifampicin Trial in Leprosy Control in Burma, February-March 1979	Dr J.M.H. Pearson

Source and Quantum of WHO funds

Project BUR MBD 003	\$ 62614	-	1976
Project BUR PHC 001.02	\$ 25273	-	1977
	\$ 63117	-	1978
	\$ 86107	-	1979
Project ICP RPD 002	\$ 35000	-	1978
	\$ 3620	-	1979

Any other information of relevance AND future activities

In view of the long incubation period of lepromatous and borderline leprosy, it is planned, subject to availability of funds, to follow up this population for a period of at least ten years.

2. Title of the Project: Purchase of Armadillos for leprosy research

Country : India

Name and Address of the Institution

Indian Council of Medical Research, New Delhi

Principal Investigator

The Director-General, Indian Council of Medical Research, New Delhi
The Director, Central Leprosy Training and Research Institute,
Chingleput

The Director, Schieffelin Leprosy Research Training Centre, Karigiri

Starting Date and Duration : 1978

Problem and aim of the research study

Several institutions in India such as the Central Leprosy Training and Research Institute, Chingleput; Schieffelin Leprosy Research Training Centre, Karigiri are engaged in leprosy research under the auspices of the Indian Council of Medical Research.

The aim is to establish an armadillo colony for leprosy research aimed at the development of an effective vaccine for leprosy (import of 50 armadillos).

Method

Armadillo is the animal model so far known for the successful growth of lepra bacillus. Research is being conducted at various institutions under the auspices of ICMR in relation to the development of a leprosy vaccine using animal model. Armadillos will be imported by WHO for use in research in leprosy.

The institutions will provide for the maintenance of armadillo colony, necessary manpower and laboratory facilities for leprosy research.

Results

Results may be available after a number of years.

Significance of the Study

If it is possible to grow lepra bacillus in armadillo, it will be a big step forward towards development of a vaccine against leprosy.

Publications, if any: to be decided at a later date.

Source and Quantum of Funds:

Project ICP RPD 002 \$4,500 1978

Any other information of relevance: None

3. Title of the Project : Mycobacteria of the Sri Lanka Environment

Country : Sri Lanka

Name and Address of the Institution

Department of Microbiology, Faculty of Medicine, University of Sri Lanka
Peradeniya Campus, Peradeniya

Principal Investigator

Dr M.R.M. Pinto, Resident Physician, General Hospital, Kandy

Starting Date and Duration

1979 - five years.

Problem and aim of the research study

Primary work done in the field shows that the vast majority of isolates from environment are rapid growers. It also suggests that M. leprae is more closely related, antigenically, to rapid growing mycobacteria than to slow-growing species.

The study aims at isolation and characterization of members of the genus Mycobacterium from environmental sources (soil, water, etc.) and at determination of their antigenic composition. The study will also investigate the role of these strains in immunity to tuberculosis and leprosy which are of low prevalence in Sri Lanka in comparison to the neighbouring countries.

Method

The methods of isolation will be the standard procedures. The antigenic characteristics will be studied by standard immunological methods such as agar gel diffusion, immunoelectrophoresis, etc. Pathogenicity tests will be done on pure strains of laboratory animals. Drug sensitivity tests in vitro will be done on the strains.

WHO will supply equipment, reagents, chemicals as requested in the project proposals only for the first year, thereafter the Institute will continue the study on its own. The institution will provide skilled manpower, laboratory facilities, operating costs, etc.

Results

Results may be available after a number of years.

Significance of the Study

The study will enable understanding the cause of low prevalence of leprosy in Sri Lanka by identifying different mycobacteria present in the environment which might have effect on low prevalence. After that, some of these mycobacteria may be tested as immunizing agents.

Publications, if any: may be decided at a later date.

Source and Quantum of Funds

Project ICP RPD 002 \$8,500 - 1979

Any other information of relevance

None.

4. Title of the Project: Immuno-Epidemiological Studies in Leprosy

Country: India

Name and Address of the Institution

Central Leprosy Training and Research Institute, Chingleput

Principal Investigator

Deputy Director (Epidemiology)

Starting Date and Duration: 1980 - a number of years

Problem and aim of the study

To study sub-clinical infection and its relationship to occurrence of overt diseases; to study the occurrence of subclinical infection in various categories of population such as contacts, etc., and to study variations in occurrence of subclinical infection over a period of time.

One of the serious handicaps in the study of epidemiology of leprosy is the lack of reliable information on the occurrence of sub-clinical infection in leprosy.

Method

This immunological study will be carried out in a leprosy endemic area of about 70000 population in two phases. In phase I, survey of the characteristics of the study population will be done and additional information on the type of leprosy, bacteriological state, etc., will be collected. In phase II, collection of blood samples will be done for serological studies and serological tests will be carried out.

Results

May be available after a number of years.

Significance of the Study

This is a very important study and is expected to throw light on epidemiological aspects of leprosy. It is important to carry it out as new tools become available for detection of sub-clinical infection.

Publications, if any : to be decided at a later date.

Any other information of relevance

Awaiting Government of India's clearance, before WHO decides on the quantum of funds.

5. Title of the Project: Survey of secondary dapsone resistance in a part of South India

Country : India

Name and Address of the Institution

Central Leprosy Training and Research Institute, Chingleput

Principal Investigator

Deputy-Director (Epidemiology)

Starting Date and Duration 1980 - a number of years

Problem and aim of the research study

Purpose of the study is to measure the prevalence of secondary dapsone resistance in Trivellore Taluk of S. India and to study factors associated with dapsone resistance.

Method

All lepromatous leprosy patients from one leprosy control unit and the patients who were registered for treatment five years earlier and are still under treatment will be clinically and bacteriologically assessed. Patients who have a BI of at least 3 by Ridley Scale will be biopsied with their consent for mouse inoculation.

The Institute will provide laboratory and institutional facilities, skilled manpower, expert services and other operating costs.

Results

Results may be available after a number of years.

Significance of the study

The need for improved therapy in leprosy is closely related to the evaluation of the importance of dapsone resistance in different geographic areas.

Publications, if any: to be decided at a later date

Any other information of relevance

Awaiting Government of India's clearance, before WHO decides on the quantum of funds.

HQ/TDR-SUPPORTED RESEARCH STUDIES IN SEAR

1. Survey of dapsone resistant leprosy in Myingyan township in Central Burma
 - Department of Health, Ministry of Health, Rangoon
 - \$ 32,400 in 1980
 - Dr U Kyaw Lwin, Deputy Director (Leprosy Control)
 - THELEP: Research on Chemotherapy of leprosy
2. Systems Analysis approach to leprosy control
 - Directorate of Health Services, Ministry of Health (Anti-Leprosy Control Project), Rangoon
 - \$ 3,000 in 1977, \$ 15,962 in 1971-1976
 - Dr U Kyaw Lwin, Deputy Director EPID
 - Leprosy Research
3. Laboratory procedures for screen anti-leprosy drugs
 - Department of Biochemistry, All-India Institute of Medical Sciences, New Delhi-110016
 - \$ 25,500 in 1980, \$ 12,500 in 1979, \$ 5,000 in 1977
 - Dr Indira Nath
 - THELEP: Research on Chemotherapy of leprosy
4. Study of cell-mediated immune reaction in neural (T) leprosy cases (nerve damage mechanism)
 - Department of Biochemistry, All-India Institute of Medical Sciences
 - \$ 2,494 in 1976
 - Dr Indira Nath
 - IMMLEP: Research on immunology of leprosy
5. Feasibility of selected cultivable strains of mycobacteria as immunizing agents against leprosy
 - Department of Biochemistry, All-India Institute of Medical Sciences
 - \$ 6,750 in 1978 (suppl.)
 - Dr G.P. Talwar
 - IMMLEP: Research on immunology of leprosy
6. Immunotaxonomy of *M. leprae*
 - Department of Biochemistry, All-India Institute of Medical Sciences
 - \$ 4,000 in 1978, \$ 8,100 in 1977
 - Professor G.P. Talwar
 - IMMLEP: Research on immunology of leprosy
7. Taxonomy of *M. leprae*
 - Department of Biochemistry, All-India Institute of Medical Sciences, New Delhi, India
 - \$ 14,000 in 1979
 - Dr G.P. Talwar, Professor and Head
 - IMMLEP: Research on Immunology of Leprosy

8. Survey of secondary dapsone resistance in a part of South India
 - Central Leprosy Training and Research Institute, Chingleput
 - \$ 5,800 in 1980
 - Dr S.K. Noordeen
 - IMMLEP: Research on Chemotherapy in Leprosy

9. Chemoprophylaxis of leprosy
 - Central Leprosy Teaching and Research Institute, Chingleput, Tamil Nadu, India
 - \$ 4,000 in 1978, \$ 4,000 in 1977, \$ 3,750 in 1976, \$ 50,350 in 1962-1975
 - Deputy Director Epidemiology
 - Leprosy Research

10. Development of a reliable chemoprophylaxis against leprosy
 - Central Leprosy Teaching and Research Institute, Chingleput
 - \$ 4,000 in 1979
 - Deputy Director Epidemiology
 - Leprosy Research

11. Prevalence of secondary dapsone resistance among patients in Gudiyatham Taluk and its yearly incidence among patients from the same area in the next four years
 - Schieffeling Leprosy Research and Training Centre, Karigiri, Tamil Nadu, India
 - \$ 10,700 in 1980, \$ 7,300 in 1978
 - De E.P. Fritschi, Superintendent and Consultant Surgeon
 - THELEP: Research on Chemotherapy of leprosy

12. DDS induced peripheral neuropathy during *M. leprae* infection as studies in the mouse model
 - Foundation for Medical Research, Bombay
 - \$ 5,100 in 1980
 - Dr N.H. Antia
 - THELEP: Research on Chemotherapy of leprosy

13. Study of bacterial load and viability of *M. leprae* in human nerves
 - The Foundation for Medical Research, Bombay
 - \$ 3,000 in 1979
 - Dr N.H. Antia
 - THELEP: Research on Chemotherapy of leprosy

14. In vitro interaction between macrophage, lymphocytes and M. leprae
 - The Foundation for Medical Research, Bombay
 - \$ 3,500 in 1979
 - Dr N.H. Antia
 - THELEP: Research on Chemotherapy of leprosy

15. Susceptibility of normal mice and T900R mice to M. leprae
 - Norman Institute of Pathology, Christian Medical College and Hospital, Vellore
 - \$ 10,000 in 1979
 - Dr C.K. Job
 - THELEP: Research on Chemotherapy of leprosy

16. Longitudinal studies of circulating immune complexes in leprosy
 - Clinical Immunology Laboratory, Department of Pathology, Ramathibodi Hospital, Bangkok, Thailand
 - \$ 5,500 in 1980
 - THELEP: Research on Chemotherapy of leprosy

17. Immunology of leprosy (HLS antigens in leprosy)
 - Division of Blood Banking and Immunohaematology, Department of Pathology, Faculty of Medicine, Ramathibodi Hospital, Bangkok, Thailand
 - \$ 4,000 in 1979, \$ 2,000 in 1978, \$ 2,000 in 1977, \$ 2,000 in 1976
\$ 6,000 in 1976-1978
 - Dr Pimol Chiewsilp, Chief of the Blood Bank
 - Leprosy Research