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LEPROSY RESEARCH IN LATIN AMERICA

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LEPROSY RESEARCH IN LATIN AMERICA*

Leprosy occurs in all countries and territories. The consequences in many families are devastating. The economic burden due to such variables as loss of productiveness, cost of diagnostic and medical services, support of patients and dependents has not been calculated.

The following examples illustrate the magnitude of the problem in a large, a medium-sized and a small country:

Brazil: 150,000 cases; 22,000 in leprosaria, 5,000 healthy children in preventoria, 700 physicians in leprosy work.

Venezuela: 15,000 cases; cost: 2.5% of annual health and hospital budget.

Surinam: 2,500 cases; 5,000 in leprosaria; cost: 9% of annual health budget.

Irrespective of investment, not enough is known to assure effective programs.

I. PRESENT KNOWLEDGE AND UNSOLVED PROBLEMS

The causative agent is the Mycobacterium leprae, the first microbe shown to cause disease in humans. In spite of progress in demonstrating the peculiarities of other related but "non-cultivated" species, M. leprae has not been cultivated in vitro. It does, however, proliferate slowly in the foot pad of mice.

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*Prepared for the Second Meeting of the PAHO Advisory Committee on Medical Research, 17-21 June 1963, by the late Dr. James Doull, Medical Director, and by Dr. John H. Hanks, Bacteriologist, Leonard Wood Memorial (American Leprosy Foundation).

The mode of transmission is presumed to be by direct and indirect transfer of leprosy bacilli into cuts and abrasions. In view of the hardiness of mycobacteria, the respiratory and gastro-intestinal routes cannot be ruled out.

The sources of infection are lepromatous and bacteriologically positive cases. Sources which have not been possible to evaluate are: (a) tuberculoid, reactional tuberculoid and indeterminate cases, and (b) clinically latent infections, especially in children.

On the matter of susceptibility, severe and persistent disease appeared in approximately 6%, milder and self-healing forms in about 24%, and approximately 70% appeared to be resistant in two populations where it may be assumed that 100% of persons were challenged by infection.

On the subject of factors limiting spread ("native" resistance), undated exposures to M. leprae and stronger stimulation by tubercle bacilli and/or related species and antigens increase resistance roughly in proportion to age and exposure, but too late to provide for control of the disease. In deliberate immunizations, some 3-6% of persons do not convert to the existing criterion of resistance (Mitsuda positivity).

In the treatment of leprosy, sulfone drugs, particularly diaminodiphenyl sulfone, are used almost universally. Beneficial results are achieved in nearly 100% of the patients. The action is bacteriostatic and slow, approximately 50% of bacteriologically positive patients becoming negative within three years. The great merit of sulfones is to delay emergence of "resistance", usually for seven or more years. Streptomycin and thiourea (CIBA 1906), though more expensive, are also effective. More efficient drugs are needed. The value of chemoprophylaxis remains to be demonstrated.

With respect to case-finding and control, administrative measures are rapidly being improved (see below).

Irrespective of investment, the facts summarized above indicate that greatly expanded research is necessary to define specific and more effective measures.

II. DEVELOPMENTS WHICH FAVOR PROGRESS

A. By-products of Consultations, April-May, 1963, Drs. Doull and Hanks.

1. Increased correspondence and cooperation with (and among) investigators in Latin America.
2. Several weeks of cooperative work by Dr. S. C. Chang, electron microscopist of the Leonard Wood Memorial, and Dr. T. Imaeda in the Instituto Venezolano de Investigaciones Científicas, Caracas, Venezuela.
3. Preparation by Dr. Doull of Kodachrome slides to be used in a regional teaching and training program in Venezuela, the Johns Hopkins School of Hygiene and elsewhere.

B. Forthcoming Meetings.

1. Study Group on Leprosy, Cuernavaca, Mexico, 4-10 August 1963, sponsored by PAHO.

2. Seminar on Leprosy, Cuernavaca, Mexico, 12-19 August 1963, sponsored by PAHO. In addition to an exchange of opinion and experiences on planning, programming and organization of leprosy control activities in Latin American countries, the major purposes of the seminar are: (a) to study administrative methods, (b) to seek improved definition and analysis of the leprosy problem, and (c) to choose and emphasize the best of current practices for case-finding, outpatient management, surveillance

and protection of contacts, future use of existing leprosaria, integration of leprosy work into general health services, and maximal utilization of personnel and facilities.

3. VIII International Congress on Leprology, Rio de Janeiro, 12-19 September 1963, sponsored by the International Leprosy Association and the Brazilian Government. Includes special round table discussions, reports by expert Panels to summarize the status and potentialities of the major aspects of leprosy work, and papers by members of the Congress.

4. Work Conference on the Serology of Leprosy, Ribeirão Preto, São Paulo, sponsored by PAHO and organized by Drs. José O. Almeida and Candido Silva of Brazil and Dr. J. H. Hanks of the Leonard Wood Memorial. Purpose: to review present work in Latin America and elsewhere, to attempt definition of priority problems and methods, and to improve communication and consultation among persons engaged in research in this field.

C. Training: PAHO Fellowships for Potential Directors of National and State Programs in Public Health and Leprosy (1963-1964).

1. A nine-month program at the Johns Hopkins School of Hygiene (organized by Dr. Hanks and committee), MPH course with special emphasis on:

a) Epidemiology and Public Health Administration, including analysis and assessment of problems and resources; mobilization of organizations and personnel, etc.

b) A course concerned with all disciplines which must be brought to bear on the study and managements of leprosy but not including clinical work.

2. Two to three month program of clinical and field training under the direction of Dr. J. Convit and associates, Division of Public Health Dermatology, Caracas, Venezuela. The Fellows will carry their new concepts

into an area where these may be re-examined in terms of an operational model. It is expected that their insight should be improved by familiarity with practical problems and with present efforts toward their solution.

III. STRATEGIC CONSIDERATIONS

The trend toward integration of leprosy into general health and medical services makes it mandatory to examine new horizons.

Tradition recognizes that tuberculosis is primarily an internal mycobacterial disease and that leprosy is more preponderantly external. This is small reason for a continued wastage of public health, clinical, social and laboratory investments by complete duplication of skills and facilities. Furthermore, a continued failure to recognize the common base-lines in essentially all avenues of research is a luxury which cannot be afforded, even by wealthy countries.

In short, improved study and management of leprosy needs three connections:

A. In Local Health Centers.

General dermatologic clinics for diagnosis, classification, ambulatory treatment, examination of contacts, etc.

B. Closer Association With Tuberculosis Services and Research.

1. The required laboratory facilities and skills are identical.

2. Radiology is an underdeveloped adjunct to the diagnosis of leprosy and fundamental to many aspects of physical rehabilitation.

3. The principles of chemotherapy are similar.

4. Administration: similar resources and methods are required for reporting, registries, follow-up, public health nursing, social work and psychologic and social rehabilitation.

5. Research:

a) Microbiology. Anonymous (perhaps identical?) mycobacteria are associated with both diseases. It is high time that students of the tubercle bacillus should be challenged with new problems in ecology, cultivation and bacterial physiology.

b) Immunology. There is a joint concern with principles involved in immunization and sensitization, both naturally or miscellaneous and deliberately specific. Pilot studies limited to the implications of cutaneous reactivities toward one agent, or to prophylactic immunization against one of these diseases, may be yielding 50% of the original investment.

c) Epidemiology. There is common interest in determining factors which influence the distributions of susceptibility and of infectious agents in populations, likewise in factors which lead to natural decline of prevalence or severity.

C. Psychological Connections.

Leprosy needs in particular to be associated with a disease which administrators and the public regard as "manageable". Problems related to leprosy are neither "strange" nor "different"; simply less well understood.

The modern-day student of tuberculosis begins to feel sympathy with "lame ducks". He should be placed in a position of realizing that society will require and respect his efforts for a long time to come. Otherwise, valuable resources will be lost to other interests. There is no point in letting the main spring of inspiration run down while big and challenging problems require developed imagination and skills.

IV. EXISTING RESEARCH POTENTIALS AND NEEDS

A previous report (RES 1/11) provides estimations of the character of the needs in the following directions:

1. Research (RES 1/11, pp. 8-11).

Two multi-country projects which are being sponsored by PAHO. One of these, the August Seminar in Cuernavaca, Mexico, has been summarized in this report.

One single-country project not in immediate need of external financial support. Cooperation between this project and the Leonard Wood Memorial has been mentioned.

Six single-country projects needing external financial support (see below).

2. Training (RES 1/11, pp. 11-13).

Training was considered in terms of: a) strengthening the full-time staff in several key institutions in which able research is being conducted, b) using these as nuclei for further training, and c) the exchange of students and investigators. The new PAHO fellowships are in support of the latter.

3. Physical Medicine (RES 1/11, p. 13).

There is urgent need for development in this field along the lines established by Dr. Paul Brand, Vellore, India. A rehabilitation center was suggested in Venezuela. Training was recommended for two orthopedic surgeons who are situated elsewhere.

Difficulties in Implementation of Projects Needing External Support

Last spring four groups of investigators in Latin America were encouraged to make application to NIH for partial support. The essence of these projects, evaluations by the PAHO Consultants, and results are shown in the Table.

Projects numbered 1 and 2 and 3 are in the hands of well-trained, thoroughly seasoned, well-known investigators.

Progress in Projects 1 and 2 has demonstrated imagination and assurance of success. The need is for logistic support.

Project 3 has no weak spots in the major proposal. Ancient theories and presumptive evidence of transmission of leprosy by biting insects deserve critical working over. Thought and tools in respect to the genetic proposition are considered inadequate. This project requires more organization and longer support than Brojects 1 and 2.

In Project 4 the need for more skill and confidence in long term maintenance of the proposed host cells may represent a weak spot. The Consultant requested is pre-eminent in this art. "Practicability" will be considered only by gamblers. However, the support requested is modest in comparison with the long-term investment in similar investigations by a small philanthropic organization.

V. GENERAL COMMENTS

In view of the fact that there are but few Latin American investigators who are working on leprosy, with limited local resources, external assistance is of even greater importance in this field of research than in other diseases which have attracted many investigators. This situation needs to be taken into consideration by granting agencies in assigning priorities to research proposals.

Priority Reference No.	Investigators (Amount in $)	Title and Summary of Projects	Evaluations by PAHO consultants 1/	2/	3/	4/	Result
#1 RES 1/11 p. 5 and Annex 1	R. G. Neves Lygia Andrade Candido Silva Inst. de Leprologia Rio de Janeiro Brazil ($8,907)	Direct Cytologic Study of the Skin in Leprosy (Use of exfoliative cytology to convert tedious pathology and inaccurate bacterial estimations into more meaningful indices of tissue reactivity and severity of disease. Without some such invention the necessary work related to leprosy is not likely to be accomplished).	4+	4+	4+	4+	Not Awarded.
#2 RES 1/11 p. 7	L. F. Bojalil J. Cerbon Unid.de Patologia Hosp. General, Mexico, D.F. ($12,070)	Biochemical and bacteriological properties of mycobacteria isolated from leprosy patients. (Ecology, identification and properties of mycobacteria from ulcers, leprosy patients and controls).	4+	4+	4+	4+	Not Awarded.
#3 RES 1/11 p. 6 and Annex 111	C. Sisirucá E. R. Bellabene J. Convit Div. of P. H. Dermatology Caracas, Venezuela ($33,678)	Study of Ecological Factors in Leprosy (By work in two areas to search for environmental factors related to the frequency and severity of leprosy, with a particular interest in arthropod vectors. Data also are to be obtained on parasitic infections, diet and tuberculin and Mitsuda reactivities).	3+	3+	4+	4+	Not Awarded.
#4 RES 1/11 p. 6 and Annex 11	M. P. Azevedo E. A. L. Wanderley Inst.de Pesquisas Leprologicas, São Paulo Brazil ($9,680)	Cultivation of M. leprae in human phagocytes. (Use of macrophages from Mitsuda negative persons and histiocytic tumors as host cells for possible in vitro growth of M. leprae).	2+	±	3+	4+	Not Awarded.

1/ Scientific merit; 2/ "practicality" of objectives; 3/ competency of investigators; 4/ stability of institution.