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PRESENT STATUS OF LEPROSY RESEARCH IN SEVERAL  
COUNTRIES OF SOUTH AMERICA

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PRESENT STATUS OF LEPROSY RESEARCH IN SOME COUNTRIES OF SOUTH AMERICA

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PRESENT STATUS OF LEPROSY RESEARCH IN SEVERAL COUNTRIES OF  
SOUTH AMERICA

Preamble

During February of 1968 the Pan-American Health Organization requested two special consultants<sup>1,2</sup> to visit with key representatives involved with leprosy work in Venezuela, Colombia, Peru, and Argentina.

In visiting each country, the consultants sought regional answers to the following questions with regard to leprosy:

1. What are the present qualitative and quantitative levels of basic research?
2. Who are the people doing this research?
3. What local agencies play the major promotional and supportive role for leprosy research?
4. What local conditions re administrative and social attitudes and what available facilities favor future expansion and/or development of leprosy research?

The modus operandi for this survey was as follows: The local PAHO offices were alerted prior to our arrival, and our first official visit was to the regional PAHO office. During this visit, arrangements were made for us to visit with selected individuals involved in the national leprosy endeavor.

In Venezuela and Colombia these schedules were well prepared and therefore

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we were reasonably satisfied that the greater majority of all people involved in leprosy research in both countries were visited. These schedules for interviews and visits in both Peru and Argentina were somewhat less than entirely satisfactory, and therefore probably a less than total cross-sectional picture of leprosy research efforts in these countries was obtained.

### Introduction

Initially, a general overview of the total extent of the leprosy problem is presented for each country visited.

The situation with regard to leprosy in Venezuela is summarized in Table I, below. The figures used in this table are approximate and should be regarded in a general way.

Table I  
1967 Leprosy Census of Venezuela

Total population of Venezuela	9,064,309
Total registered cases of leprosy	16,213
Prevalence of leprosy	1,228
Total no. of known leprosy contacts	21,343

The areas of highest incidence of leprosy in Venezuela are found in the west-central portion of this country where it borders Colombia, but the disease does occur throughout the entire country.

There are two major leprosaria in Venezuela--one located at La Guaira, and the other near the city of Maracaibo. Both hospitals, while adequate and well managed, are obsolete. There are plans for future construction of a new hospital for dermatologic diseases, and this facility when constructed will accommodate all leprosy patients in need of hospitalization.

The philosophy of providing primarily out-patient care for leprosy patients

is effectively practiced in Venezuela. Twenty-five dermatologic services, staffed by 22 full-time physicians and with the necessary lay auxiliary assistants, are distributed throughout the 20 Departments of Venezuela. These services provide routine treatments to the majority of leprosy patients as well as regular surveillance of local patient-contacts. Those few patients who require very special hospital treatments are referred to one or the other of the two hospital centers.

The lay auxiliary help for the dermatology services prior to assignment to a service are brought into the Caracas center and given training in leprosy control. Upon their assignment to a field service, they then function in a capacity similar to that of a field practical nurse.

The leprosy picture in Colombia was not made so clear to us as was the case in Venezuela. In Colombia, total, accurate, country-wide surveys remain to be performed. Most of the identified Colombian leprosy is found in the high altitude areas of the country. The impression that we gained is that this disease is of equal, if not greater, importance in Colombia as it is in Venezuela and that leprosy is considered a major public health problem.

There is only one very large leprosarium in Colombia. This was not visited, but from what we were told and observed in viewing a movie film, this hospital is obsolete and seriously overcrowded.

The true leprosy situation in Peru was even more difficult to assess accurately than it was in Colombia. At this time there is only a token leprosy control system active in Peru. To the extent that it is known, the Peruvians regard leprosy as mainly a disease of the high altitude Andean regions and the northeastern jungle area of the country.

In Argentina considerable time was spent in discussing the leprosy problem of this country, but no accurate, hard and fast statistics were obtained. We were informed that some 14,000 cases of leprosy were registered and that an

additional 6,000 were suspected to exist. In general, it would seem that leprosy patients are concentrated in the northwestern regions around Tucuman and in the suburban outskirts areas of Buenos Aires. However, no real, effective, total leprosy survey has been made to determine the actual prevalence of leprosy in this country. Essentially all treatment of leprosy is done either in the Hospital Muñiz (Infectious Diseases) located in Buenos Aires, or at the Tucuman center. All social and medical rehabilitation is centered at the Somers Hospital in Buenos Aires.

In discussions with Dr. E. Cappuro, assistant chief of Leprosy Campaign, and with his associates, one gets the general impression that with the exception of a very few people in Argentina, the rest of the professional population would prefer to forget about leprosy. For example, we learned that about 90% of the leprosy patients were treated by outpatient clinics and only 10% were treated in the hospital, but that 70% of the Ministry of Health budget was directed to the hospital while only 30% was appropriated for the clinics. Only 4 sanitary divisions with one dermatologist in charge of each, serves the entire country. Further, the leprosy program regrettably is not coordinated with other health programs, such as tuberculosis, etc.

The more significant and better quality research efforts in Argentina for the most part seem to be located outside of the immediate governmental structure. This statement is clarified, further, below, in the report on research in Argentina.

#### Leprosy Research in Venezuela

In Venezuela there is a significant quantity of both basic and clinical research being undertaken. Nearly all of this research is directly under the auspices of the Dermatology Division of the Ministry of Health, which is headed by Dr. Jacinto Convit. The geographic center for this research is divided between the Dermatologic Service of Vargas Hospital and those offices

and laboratories located within the nearby Dermatology headquarters building. Clinical applied research of the nature of chemotherapy trials, immunologic prophylaxis and testing of control administration does extend out into the service units outside of Caracas.

A second nidus of research is located at IVIC, where Dr. T. Imaeda is carrying out some histochemical and microanatomy research on Myco. species including leprae.

Basic Research Programs Directed by Dr. Convit

1. The patient-to-animal and animal-to-animal studies of leprosy transmission.

Golden hamsters have been used primarily for this work. Recently, however, in addition to ear inoculation of hamsters, Dr. Convit is now also performing foot-pad injections of mice after the method described by Shepard (CDC). This animal experimentation has been extensive, detailed, and continues to grow in magnitude. It is of generally excellent quality.

2. Antigenic relationships studies.

Dr. M. Ulrich, within Dr. Convit's organization, is undertaking immunologic studies of antigenic relationships between Myco. leprae and other possibly related microorganisms. Basically, this is an immunodiffusion study in which gel double diffusion precipitation techniques are used. This work is of high quality as far as it has been taken, but newer, more sensitive and more definitive techniques, and antigen purification studies should be added.

3. Dr. Campo-Aasen, in the Vargas Hospital laboratories, has just begun a histochemical enzyme study of tissue forms of mycobacteria. Dr. Campo-Aasen is well trained and very competent. Her intent is to comparatively study the phosphatases and nucleic acids from M. leprae, M. lepraemurium, and other species of mycobacteria, nocardia, and corynebacteria. This laboratory was just being established at the time of our visit and there was little by way of

experimental results for us to see. Dr. Campo, however, is well qualified for this study and the experimental design is good.

In addition to the basic research program carried out in the laboratories at the Dermatology Division and the Vargas Hospital, Dr. Convit is also using his field control organization to perform several promising, although relatively limited, clinical studies. In this effort Dr. Convit is especially well assisted by Dr. R. Albornoz. These clinical studies are as follow:

1. Homograft studies in lepromatous patients.

This is, as yet, not a fully developed study. Dr. Convit and his associates have performed pilot experiments to look at rejection rates of skin homografts in lepromatous leprosy patients. Preliminary observations strongly suggest that the time required before such grafts are rejected by the lepromatous patient is considerably longer than is the case with a normal subject. To date, no tuberculoid or cases other than lepromatous have been operated.

Even though no controlled study, as such, has been made to date, the results now available are intriguing. The hypothesis that lepromatous cases may have a R.E. system impairment or idiosyncrasy that could be demonstrated in prolonged homograft acceptance is imaginative and warrants follow-up. Not only might this study yield valuable leads useful for planning of future leprosy studies, but also might reveal significant information re the biologic mechanisms of tissue grafting.

2. Chemotherapy trials.

At the present time, no full scale chemotherapy trials are underway, although one limited pilot study of thalidomide in acute lepromatous reaction is being done. To date, Dr. Convit has tried thalidomide in 35 ENL cases (generalized reactions and some with acute neuritis manifestations) over the past 15 months.

Treatment of ENL patients begins at a dose level of 300 mg of thalidomide per day. Within 2 days generally the ENL reaction is under control. (Twelve days are required for comparable success using steroid therapy.) As the symptoms of ENL regress the thalidomide dose is gradually decreased. At this time it would appear that a dose level between 50-100 mg of thalidomide per day will control effectively this serious complication of lepromatous leprosy. Daily prolonged thalidomide therapy at the 100 mg per day level apparently produces no unfavorable side effects.

Because of the excellent administrative control program, Venezuela would be an ideal place to undertake new drug trials. Dr. Convit is interested, but while he awaits the building of the new hospital as well as his new Dermatology Research Center, he is primarily engaged in planning. There should be a bright future for clinical research in Venezuela.

The rehabilitation program in Venezuela is adequate but not yet impressive. The value of modern rehabilitation techniques and knowledge are thoroughly appreciated, however, and more extensive facilities for this activity are being planned for the new research building.

### 3. BCG prophylaxis of leprosy

Vaccination with BCG has been widely employed in this country. Approximately 679,000 have been vaccinated to date. The only area where this vaccination has not been used extensively is the Department of Apure. In this Department are located 150,000 - 200,000 people, and the estimated incidence of leprosy is 7 per 1000. Dr. Convit recognizes this as an area in which a study of BCG prophylaxis for lepromatous leprosy might be performed. The ways and means for performing this study are now under deliberation. Dr. Convit and Albornoz always examine records and watch for new cases and contacts who have received BCG in the recent past.

By way of information only, Dr. Convit did inform us that, to date, he

has seen no lepromatous leprosy in individuals who had received BCG vaccinations during the past 5 years. The numbers of individuals upon which this statement was based is, by his own acknowledgement, still relatively small.

#### Leprosy Research in Colombia

Basic leprosy research in Colombia is almost entirely due to the energies and efforts of Dr. Guillermo Muñoz-Rivas. Dr. Muñoz maintains a microbiology laboratory and staff in his private office building and it is here that most of the bacteriological work is done. (Except for a small \$1000 per year grant from WHO, Geneva, which terminates at the end of this year, Dr. Muñoz receives no financial assistance for his research.)

Dr. Muñoz has some additional laboratory space, personnel and animal facilities made available for his work by the Colombian N.I.H. Dr. Muñoz is himself, a volunteer researcher at this institute.

Dr. Muñoz is a very careful, thorough microbiologist, trained in Germany, and with a deep-seated enthusiasm for any research work (his own or others') which is concerned with the problem of leprosy. He views leprosy as one of the major public health problems of his country.

#### Basic Research Programs

Dr. Muñoz is very much concerned with the question of how leprosy is transmitted, and in past works has demonstrated that the Colombian native's home environment is amply seeded with various kinds of mycobacteria. He has shown that AFB can be isolated from pottery vessels, especially ollas used for storing water. These acid-fast organisms seem to proliferate in the wet mossy walls of the clay pottery. These ecological studies of acid-fast bacilli in the home environment of the leprosy patient are continuous in this laboratory.

In another study, Dr. Muñoz has isolated AFB from the intestinal tracts of fleas, flea larvae, and other insects commonly found in the dirt floors of

the rural sabana dwellings. In well controlled experiments Dr. Muñoz has shown that when AFB-free fleas are cultured on soil contaminated with AFB, that eventually the gastrointestinal tracts of the fleas and larvae come to contain cultivable AFB. Dr. Muñoz has further noticed that the pattern of flea bites on inhabitants of these dwellings are similar to the distribution patterns of leprosy lesions. The hypothesis that an insect vector may play a role in dissemination of Myco. leprae continues to be intriguing and warrants further study. The big question is: What are the AFB Dr. Muñoz isolates from soil, wet pottery, and fleas (insects)?

Dr. Muñoz also carries this line of investigation over to hamster inoculation studies. Dr. Muñoz' experiments are directed toward demonstrating that hamsters can be infected with Myco. leprae through intraperitoneal inoculations or with Myco. lepraemurium by the oral route. Further, this investigator is attempting to show that hamsters can become infected with Myco. leprae indirectly through host feeding of arthropod vectors. Similar successful experiments of indirect transmission of lepraemurium to hamsters have been published. Dr. Muñoz' animal experimentation is of high quality.

Another original line of investigation being studied by Dr. Muñoz is the examination of how in vitro culturing of BCG with graded amounts of lepromatous tissue seems to induce a mutational change in the resulting BCG cells. High concentration levels of macerated lepromatous tissues totally inhibit BCG growth, but as this concentration level is diluted, an inverse relationship between the amount of lepromatous tissue placed in each culture tube and the resulting yield of BCG cells becomes apparent. Such BCG cells upon inoculation into animals produce a disseminated systemic growth of apparently modified BCG throughout the tissues of the animals.

One of the immediate questions raised by this study and which remains to be answered is: Does something in the lepromatous tissue induce a true genetic

alteration in the BCG inoculum which grows up? To answer this question, special help is needed by Dr. Muñoz, and to our knowledge the level of sophistication required, both in terms of manpower and also equipment, does not exist in Colombia. Dr. Muñoz is, himself, well aware of this fact.

Dr. Muñoz is virtually alone in leprosy research in Colombia. He does what he can and has a backlog of ideas to be pursued in the future. He has trained some excellent technical help who are conscientious and dedicated. None of these, however, are capable of carrying on Dr. Muñoz' work independently should anything adverse happen to him. He is very anxious to have people trained and to train some himself, but the adverse financial situation for Dr. Muñoz again frustrates his sincere desires.

The only other supposedly research area located in Bogota is the Lleras Dermatology Clinic under the direction of Dr. Londono. This is a very busy, functional dermatology clinic with limited in-patient facilities. Leprosy patients are seen and treated at this clinic (40 new cases per month). Good quality medical diagnosis and treatment, including some surgical rehabilitation, are provided, but no real research, clinical or basic, is being undertaken.

#### Leprosy Research in Peru

In Peru no basic or clinical research was heard of or observed.

#### Research in Argentina

##### Basic Research Programs

The basic research programs in leprosy at this time in Argentina are not impressive. Even so, several isolated pockets of activity and a few identifiable people are working hard to solve some of the basic problems of leprosy and warrant citation in this report.

Within the government structure Dr. P. Arcury, located at and in charge of the Tucuman Leprosy Division, is undertaking basic and clinical studies to try to determine the significance of the true delayed hypersensitivity reaction

in the management and diagnosis of leprosy. This work is important to do, but Dr. Arcury, while extremely well motivated, is somewhat deficient in current basic immunologic knowledge as well as severely restricted in the time he can devote to this research. Both criticisms are understandable, since Dr. Arcury is in charge of the Tucuman Division and therefore has responsibility for the management of approximately 90% of the known leprosy patients in Argentina.

In addition, two other significant foci of basic research were identified in Argentina. An excellent program is being undertaken by and was described to us by Dr. Felix Wilkinson and his associate, Dr. Emilia Santa Baya. These investigators are studying the basic biology of acid-fast bacilli which are isolated by them from leprosy patients. The work is classical and relatively unimaginative but is of good quality.

Upon our return from Argentina Dr. Binford received a letter from Señora Fernandez, widow of Dr. J. M. M. Fernandez, who was out of town at the time we attempted to visit the Rosario group of investigators. From this letter it would appear that this center has been relatively quiescent since the demise of Dr. Fernandez who had been a world leader in leprosy research. However, our visit to Argentina apparently stimulated Mrs. Fernandez to organize available research talents in Rosario, and we are now informed that studies of the following types will be forthcoming from this center.

1. Dr. Rabaso will attempt to transfer immunological information by means of RNA injections. He has been working in this general area using rat sarcoma as a disease model. He now plans to parallel his past efforts with a leprosy situation. Nerve ganglion RNA from tuberculoid patients will be transferred to bacteriologically negative lepromatous patients.

2. Dr. Serial is now studying the behavior of mast cells in tissue changes in rodents immediately following infection with Myco. lepraemurium.

No major significant drug trial studies are now in progress in Argentina.

Dr. Jonquieres has reported some observations re high and low dose sulfone therapy but these remain solely clinical observations as opposed to planned drug studies with adequate placebo controls, etc. Dr. Jonquieres is similarly making observations on approximately 10 lepromatous ENL patients currently receiving thalidomide.

Considerable BCG is used in Argentina by the tuberculosis control program, but this division of the Ministry of Health functions independently of and apparently without any real communications with the leprosy program. No planned BCG leprosy prophylaxis studies are under way in Argentina.

The most impressive area of clinical activity in Argentina is the physical rehabilitation program guided by Drs. R. Manzi and A. Marzetti. Both of these men are very talented physical medicine men who approach their field with enthusiasm. Applied research and technique development is close to the surface of all phases of their efforts which range from very sophisticated tendon transplantation to patient education as an effective preventive measure against crippling injury. At the present time this rehabilitation clinic, located at the Sommers Hospital, is essentially the total rehabilitation program for this country. Patient access to rehabilitation is virtually impossible to achieve outside of the Buenos Aires and close-by suburban areas.

By and large, even though some excellently qualified men are available in Argentina for both basic and clinical research in leprosy, the total as a national product is relatively negligible.

#### Recommendations:

There is little doubt that leprosy is a major public health problem in South America. In many of the countries a significant portion of the total funds available for public health programs are expended on the leprosy program. At the present time, and with the exception of Venezuela, the funds that are available to the leprosy program are either not wisely used or are inadequate

or both. Whichever the reason, the overall effect is that leprosy continues to be a major and generally an uncontrolled public health problem.

In order to meet this problem head-on and accomplish a real reduction in its magnitude, several essential steps should be taken. These are:

1. The problem is actually international, and therefore the attack to the problem should be likewise. An international center for purposes of leprosy study, control, and training should be developed. The logical and even obvious site for this center should be Caracas, where there is now an impressive regional center. The highly effective organization which has been developed by Dr. Convit for the Ministry of Health in Venezuela could serve as the foundation for this hypothetical center. Identifiable high caliber scientists such as Dr. Muñoz (Colombia), Dr. **Arcury** (Argentina), and others could be recruited for the staff of this center.

2. Current national expenditures for leprosy are either inadequate or ineffectively used or both. Again, a demonstration of effective use of available funds has been demonstrated by Venezuela. This operational aspect could serve well as a model and as such be employed to good advantage through the mechanism of an international center which could be operated from an international fund.

3. It seems reasonable to hypothesize that such an international fund could be developed through combining resources such as a) annual contributions from member countries; and b) donated and/or solicited funds from foundations, and private institutions and industries.

4. Finally, while the problem has been viewed as one of South American identity in this report, it is actually one which could justifiably be regarded as hemispheric; therefore, the countries of the North American continent could be approached, also, for membership in this international center.

In conclusion, the leprosy situation can be summarized concisely:

1. Leprosy is a major problem over a large area of the Western hemisphere and particularly in South America.

2. Current national expenditures for leprosy treatment, control, and research are not producing any identifiable reduction in the problem; hence, something else must be done.

3. There are identifiable people scattered throughout the area who have both the will and the ability to participate in an effective leprosy control program.

4. In at least one large problem area there is now an effective program, e.g., Venezuela.

5. We need to bring together all talents and available means into one international center where both commodities can be employed with greatest impact.

6. We suggest that Venezuela should be the location for creating such an international center.

7. Ideally, all countries of the Western hemisphere should participate both professionally and financially.

8. Financial participation could be adjusted proportionally to the magnitude of the leprosy problem in the home state.

9. Effort should be made to solicit non-governmental subsidy of this center from interested foundations, industries, and private individuals.

All necessary component parts for the above machinery now exist. All that is now needed is an engineer to perform the assembly.