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PROGRESS REPORT FROM THE PAHO/WHO INTERNATIONAL CENTER FOR TRAINING AND RESEARCH IN LEPROSY AND RELATED DISEASES

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The PAHO International Center for Training and Research in Leprosy and Related Diseases (CIALEA) was inaugurated at the Instituto Nacional de Dermatología, in Caracas, on June 11, 1973.

Figure 1 shows the structure of the Center. Photographs 1,2,3 show some aspects of the various departments.

The Center has the following objectives and purposes:

A. Development of scientific research of a multidisciplinary nature, oriented towards solving public health problems such as: leprosy, leishmaniasis, onchocerciasis, mycoses, etc.

B. Develop effective administrative methods for the control of leprosy and related diseases in a system coordinated with or integrated within general public health programs, including:

1. Recollection, analysis and utilization of epidemiological data.
2. Improvement of methods for the early diagnosis of leprosy and related diseases, and consequently, of the discovery of new cases.
3. Prevention and treatment of disabilities produced by leprosy, through the application of simple techniques, as part of the general care being given to patients.

C. Provide qualified practical training for medical and paramedical personnel who are intended to work in control programs and evaluate the efficacy of training programs.

D. Prepare and distribute specialized technical information (in Spanish).

E. Use the existing facilities for field and laboratory research in

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selected aspects of leprosy and related diseases which might be used in control programs.

F. Development of a field demonstration area in Aragua State.

G. Promote the development of other Centers in other countries of the American Continent.

Scientific Research.

The fact that within the Instituto we have a clinical out-patient department, as well as various laboratories with specialized personnel and the fact that there is a close relationship with the Dermatology Department of the Vargas Hospital and the Department of Clinical Dermatology of the Vargas Medical School of Universidad Central de Venezuela, and also a close connection with the Department of Public Health Dermatology of the Ministry of Health, make it possible for the Center to use in-patient facilities of the Vargas Hospital and to have access to the clinical material of the Public Health Dermatology Departments distributed all over the country.

All these facilities make possible the development of applied research projects of multidisciplinary characteristics.

A series of research projects are under way, in relation to subjects such as the experimental transmission of leprosy and various aspects of the immunology, biochemistry and microbiology of leprosy and related diseases. Among the most interesting of these projects, we would like to mention the following:

1. Experimental transmission of human leprosy to the armadillo Dasypus sabanicola. A colony of 96 armadillos has been developed, 44 of which were inoculated with M. leprae of human origin, at a concentration

which varied between 10^7 and 10^8 bacilli per ml. Each animal was injected with 0.5 to 1 ml, intradermally or endovenously. The first inoculation lesions in one animal were seen at 8 months. At the moment, 33% of the animals have shown inoculation lesions. Passage from animal to animal has been done in 28 animals.

Up to now, 4 animals have developed systemic lesions, with involvement of the skin, subcutis, lymph nodes, lungs, liver, spleen, muscles, testes and central nervous system.

This infection differs from the human infection, in that it shows lung, hepatic cell and central nervous system lesions. Photographs 4, 5, 6 show the D. sabanicola, as well as some aspects of the experimental lesions it develops.

The transmission of leprosy to the D. sabanicola, as well as its introduction as a laboratory animal due to its small size (maximum weight 1.7 kg) and its ease of handling, opens a wide field of possibilities for the utilization of this animal for other types of experimental research, even though there is still the problem of its breeding in captivity to be solved.

2. Preparation of an antigen obtained from the supernatant of a suspension of human or armadillo M. leprae, sonicated or non-sonicated.[1] The suspension is prepared at a concentration of 160×10^6 bacteria per ml, then centrifuged, and the supernatant filtered, to obtain a bacteria-free material. The antigen is then obtained by precipitating this material with 80% ammonium sulphate. This antigen showed high specificity in intradermal tests, in a comparative study done between endemic leprotic rural foci in Venezuela and rural areas of Chile[2]

(country non-endemic for leprosy). (Tables 1, 2, 3).

At present, we are working on the fractionation, by column chromatrography, of the precipitate obtained with ammonium sulphate, with the aim of isolating the specific fraction.

Considering the very large amounts of M. leprae that can be obtained through the experimental transmission, in armadillos of the genus Dasypus, we will have the amount of antigen needed for epidemiological investigation and control of contacts, through both the 48-hour Fernandez reaction and the 30-day Mitsuda test.

Apart from these projects, we have shown the identity of M. leprae from armadillo lesions with M. leprae from human lesions, using techniques developed in our laboratories, such as the competency test (Photographs 7, 8), the loss of acid-resistance through the pyridine test (Photograph 9), we have also done a study in which we have compared antigen of human origin with antigen from armadillo origin, through the 48-hour Fernandez test and the 30-day Mitsuda test.[3]

We have also shown that macrophages of lepromatous leprosy patients can be activated by adjuvants (BCG) and the capacity of this activated macrophage to destroy M. leprae. (Photograph 10).[4]

All these studies, and others, were presented in 21 scientific publications in various journals.

Personnel training.

1. Courses:

a). III International Seminar on the Histopathology of Leprosy. Caracas, November 20, 21, 22, 1.973. This Seminar was attended by 12

participants from Argentina, Brasil, Costa Rica, Ecuador, Mexico and Venezuela.

b). IV International Seminar on the Histopathology and Immunology of Leprosy and Related Diseases. Caracas, December 2-6, 1.974. This Seminar was attended by 13 participants from Brasil, Barbados, Costa Rica, Cuba, French Guyana, Haití, Perú and Dominican Republic.

c). Workshop on Histopathological Techniques for Histopathology Technicians. This Seminar was attended by 31 Histopathology Technicians from various Universities and Hospitals in the Venezuela.

2. Fellows.

We received 7 fellows who came to observe administrative and control systems from Colombia, Costa Rica, Curacao, St. Lucía, Frech Guyana and Cuba.

Production of audio-visual material.

The Section for Production of Audio-Visual Material was created, for self-teaching in medical education. The production of some educational units on clinical, immunological and leprosy rehabilitation aspects was started.

For this Section, we have hired an Engineer specialized in audio-visual methods, and two Medical Artists. We hope that during this year we may obtain the collaboration of a specialist in Medical Education, who has been offered to us by the German Leprosy Relief Association (Deutsches Aussatzigen-Hilfswerk).

The plans for the development of this Section are directed towards using the material it prepares, first at the Vargas Medical School of the Universidad

Central de Venezuela and, later on, orient its activities towards other Latin-American countries.

Short-term consultants.

We had the opportunity of welcoming 12 short-term consultants in the areas of Administration, Microbiology, Education, Biochemistry, Rehabilitation, etc.

Plans for 1.975.

The plans for 1.975 include the following:

In relation to scientific research, continue the study of the experimental infection of armadillos D. sabanicola with M. leprae; complete the study on the purification of an antigen for the 48-hour Fernandez reaction; study the basic immunological characteristics of the armadillo; culture of cells from various organs of D. sabanicola, with the purpose of infecting them with M. leprae, epidemiological studies directed to detect those persons who are susceptible to develop leprosy.

In relation to Leishmaniasis and Mycosis, study further aspects of cellular immunology in these diseases.

We are also planning to develop operational research in the Aragua area, in relation to the epidemiological study of extradomiciliary infection with M. leprae.

In relation with training of personnel, we will continue with the courses on the Immunopathology of Leprosy, as well as the development of a Seminar for Heads of Anti-leprosy Campaigns of various countries of the American Continent and the training of fellows from various countries, in administrative techniques for anti-leprosy programs and their progressive integration within the General

Public Health Services.

Finally, we are extremely interested in organizing at the Center, in coordination with other public health departments of the country, a clinic which could be called "Sexually Transmitted Diseases" (STD), where we could establish, apart from the venereal diseases program, methods for early cancer detection and for birth control.

If this project could be developed, it would mean that the Center would act as a catalytic agent in this respect, towards the transformation in this direction of the present Venereology Departments.

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3.- Convit, J. and M.E. Pinardi. Leprosy: confirmation in the Armadillo. Science, 184: 1191-1192, 1974.

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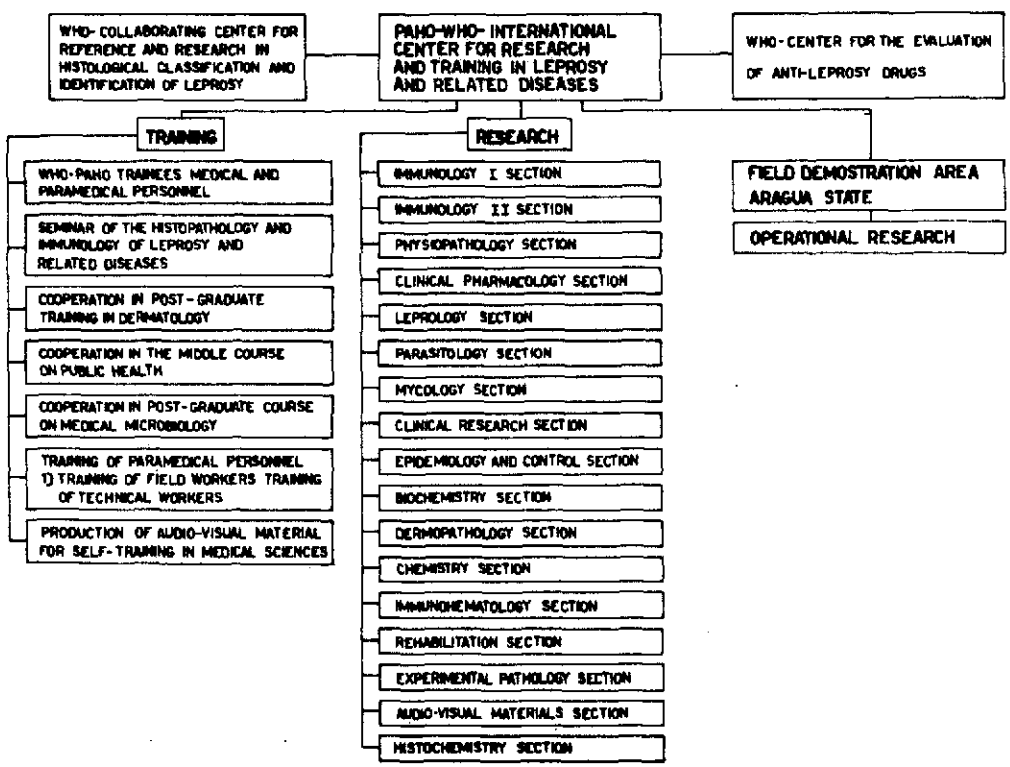

WHO- COLLABORATING CENTER FOR REFERENCE AND RESEARCH IN HISTOLOGICAL CLASSIFICATION AND IDENTIFICATION OF LEPROSY
PAHO-WHO- INTERNATIONAL CENTER FOR RESEARCH AND TRAINING IN LEPROSY AND RELATED DISEASES
WHO-CENTER FOR THE EVALUATION OF ANTI-LEPROSY DRUGS
TRAINING
WHO-PAHO TRAINEES MEDICAL AND PARAMEDICAL PERSONNEL
SEMINAR OF THE HISTOPATHOLOGY AND IMMUNOLOGY OF LEPROSY AND RELATED DISEASES
COOPERATION IN POST-GRADUATE TRAINING IN DERMATOLOGY
COOPERATION IN THE MIDDLE COURSE ON PUBLIC HEALTH
COOPERATION IN POST-GRADUATE COURSE ON MEDICAL MICROBIOLOGY
TRAINING OF PARAMEDICAL PERSONNEL 1) TRAINING OF FIELD WORKERS TRAINING OF TECHNICAL WORKERS
PRODUCTION OF AUDIO-VISUAL MATERIAL FOR SELF-TRAINING IN MEDICAL SCIENCES
RESEARCH
IMMUNOLOGY I SECTION
IMMUNOLOGY II SECTION
PHYSIOPATHOLOGY SECTION
CLINICAL PHARMACOLOGY SECTION
LEPROLOGY SECTION
PARASITOLOGY SECTION
MYCOLOGY SECTION
CLINICAL RESEARCH SECTION
EPIDEMIOLOGY AND CONTROL SECTION
BIOCHEMISTRY SECTION
DERMOPATHOLOGY SECTION
CHEMISTRY SECTION
IMMUNOHEMATOLOGY SECTION
REHABILITATION SECTION
EXPERIMENTAL PATHOLOGY SECTION
AUDIO-VISUAL MATERIALS SECTION
HISTOCHEMISTRY SECTION
FIELD DEMOSTRATION AREA ARAGUA STATE
OPERATIONAL RESEARCH

Figure 1.

TABLE 1
PERCENTAGE OF POSITIVITY AN CHILDREN AND ADULTS ACCORDING TO THE AREA AND THE TEST CHILE AND VENEZUELA

Test	Children			Adults		
	Chile	El Corozo	El Tesoro	Chile	El Corozo	El Tesoro
Mitsuda (30 d.)	92.0	99.1	97.7	94.1	100.0	99.1
Fernández (48 h.)	3.5	24.3	43.5	3.7	45.4	44.7
PPD	9.3	17.1	39.7	28.2	36.4	36.8

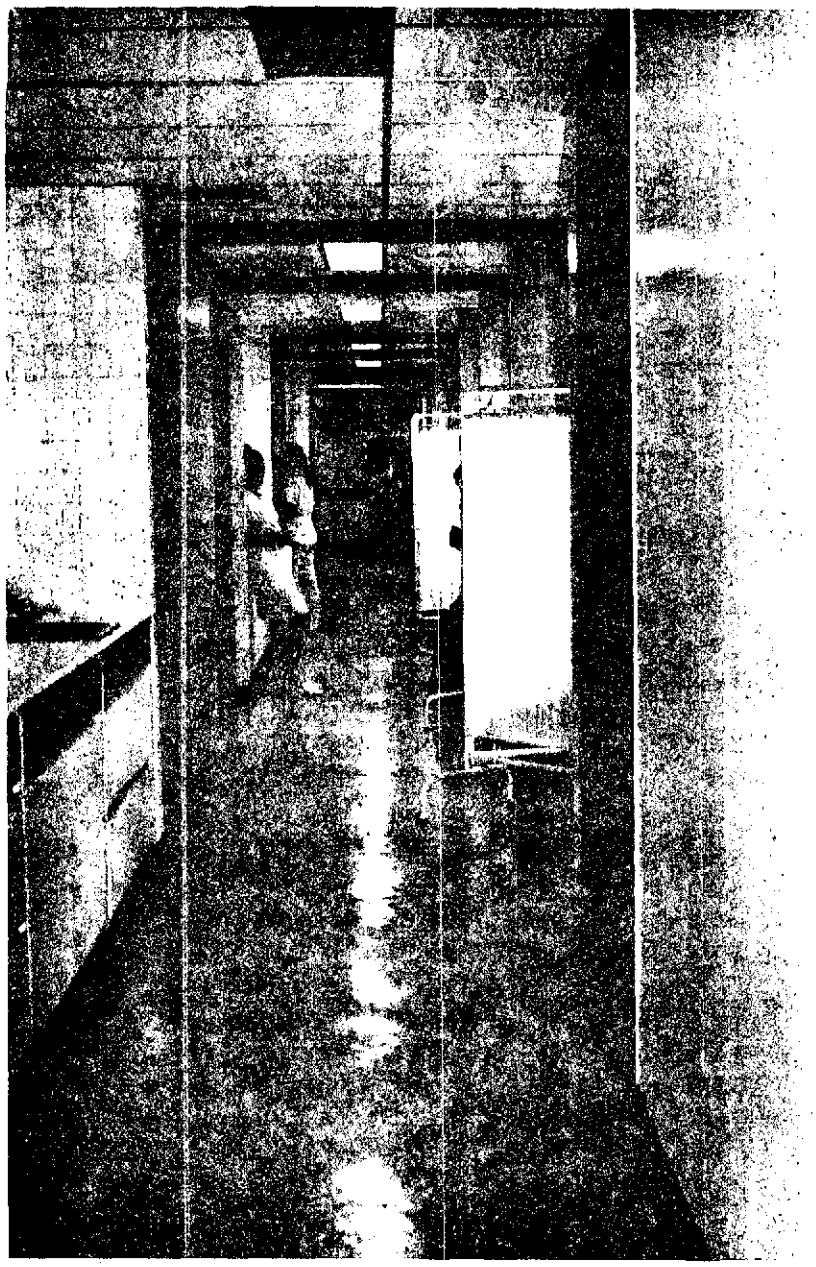
TABLE 2
RESULTS OF THE TEST FOR STATISTICAL SIGNIFICANCE OF THE DIFFERENCES BETWEEN PERCENTAGES OF POSITIVITY IN CHILDREN, ACCORDING TO AREA AND TEST BEING STUDIED. CHILE AND VENEZUELA

Test	Children		
	Chile – El Corozo	Chile – El Tesoro	El Corozo – El Tesoro
Mitsuda (30 days)	SIGNIFICANT	SIGNIFICANT	NON-SIGNIFICANT
Fernández (48 h.)	HIGHLY SIGNIFICANT	HIGHLY SIGNIFICANT	HIGHLY SIGNIFICANT
PPD	SIGNIFICANT	HIGHLY SIGNIFICANT	HIGHLY SIGNIFICANT

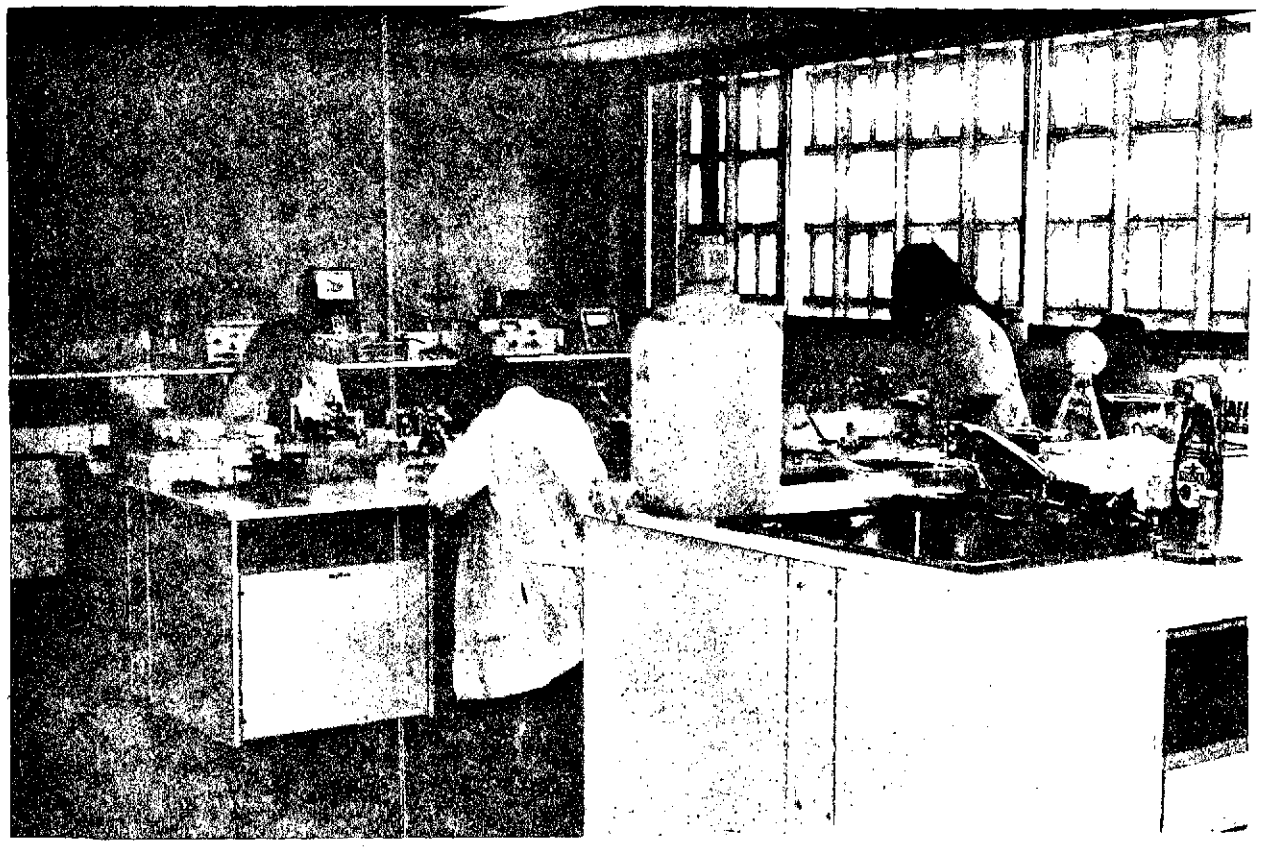
TABLE 3

RESULTS OF THE TEST FOR STATISTICAL SIGNIFICANCE OF THE DIFFERENCES BETWEEN PERCENTAGES OF POSITIVITY IN CHILDREN ACCORDING TO AREA AND TEST BEING STUDIED. CHILE AND VENEZUELA

Test	Adults		
	Chile - El Corozo	Chile El Tesoro	El Corozo - El Tesoro
Mitsuda (30 days)	SIGNIFICANT	SIGNIFICANT	NOT SIGNIFICANT
Fernández (48 h.)	HIGHLY SIGNIFICANT	HIGHLY SIGNIFICANT	NOT SIGNIFICANT
PPD	NOT SIGNIFICANT	NOT SIGNIFICANT	NOT SIGNIFICANT

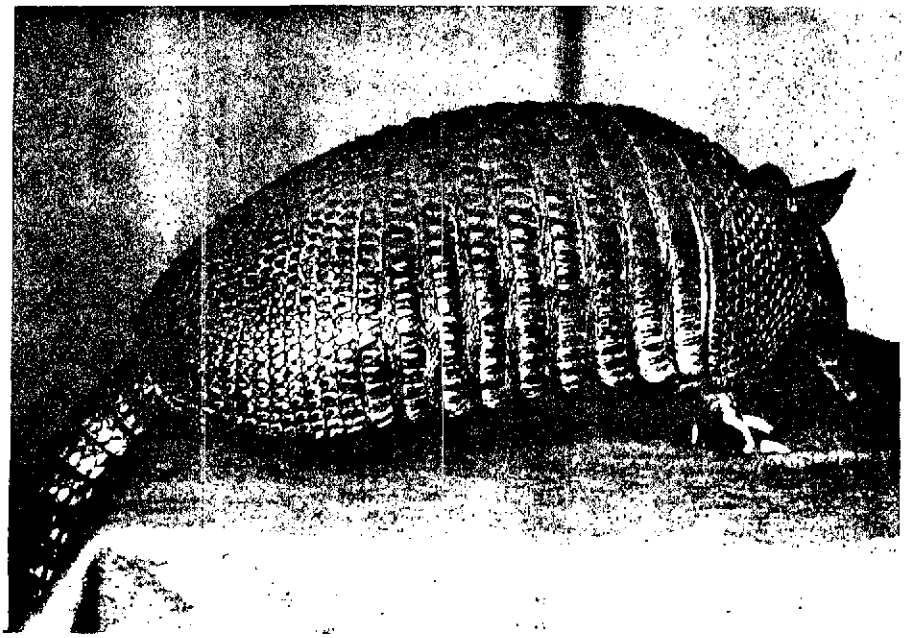


Photograph 1. Outpatient clinic.

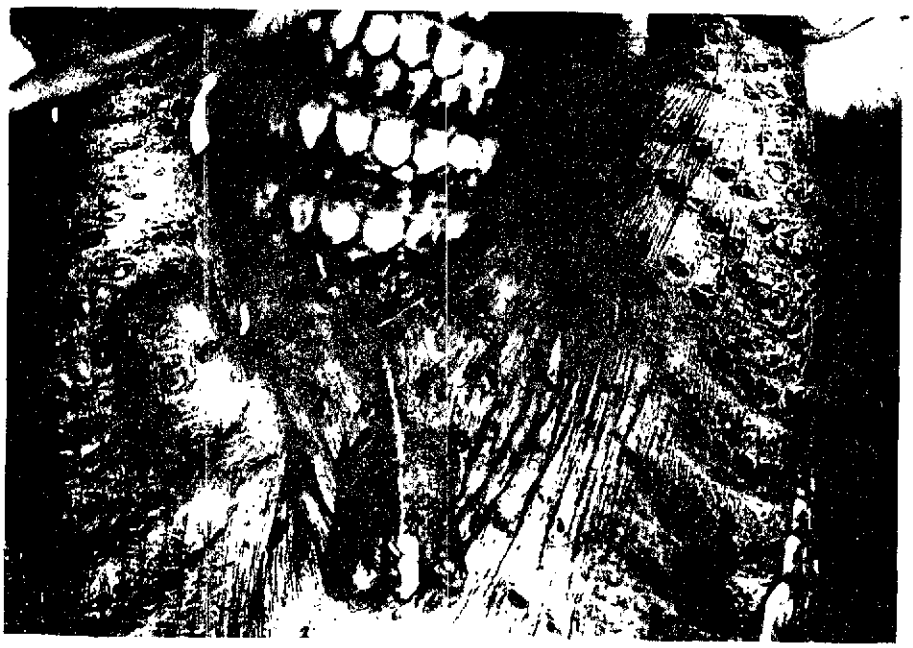


Photograph 2. Immunology Laboratory.

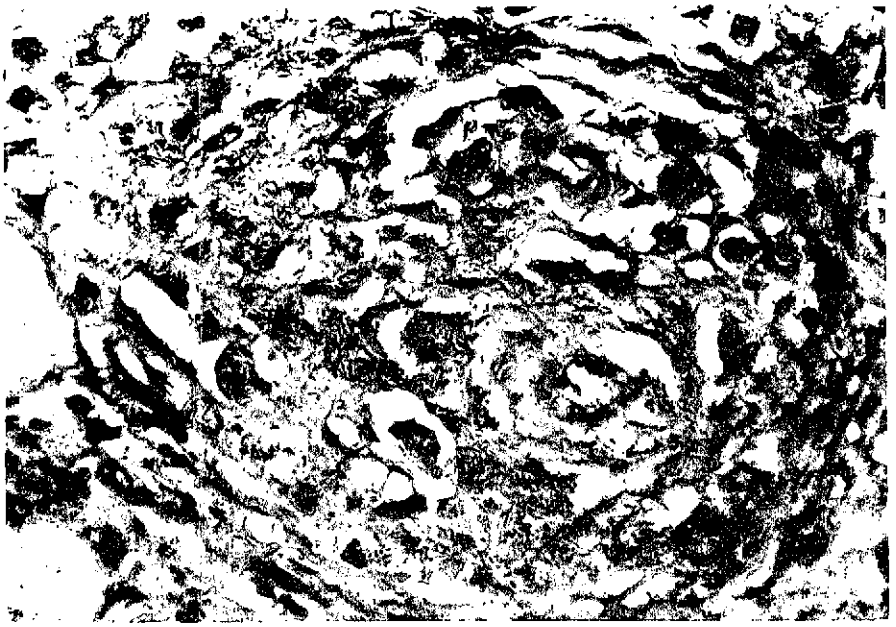
Photograph 3. A view of the Rehabilitation Section.



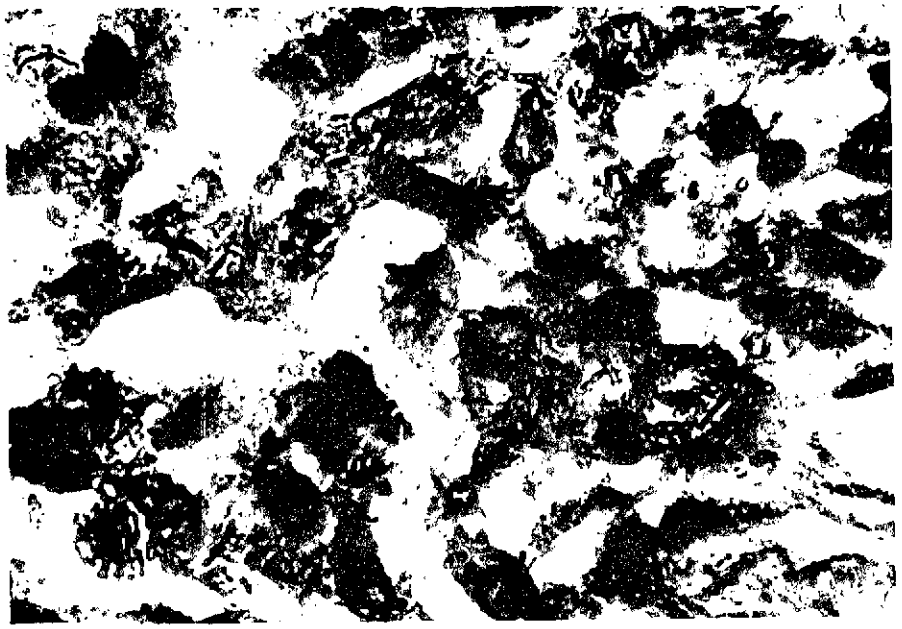
Photograph 4. D. sabanicola



Photograph 5. D. sabanicola showing metastatic nodules on back legs two years after inoculation with M. leprae of human origin.

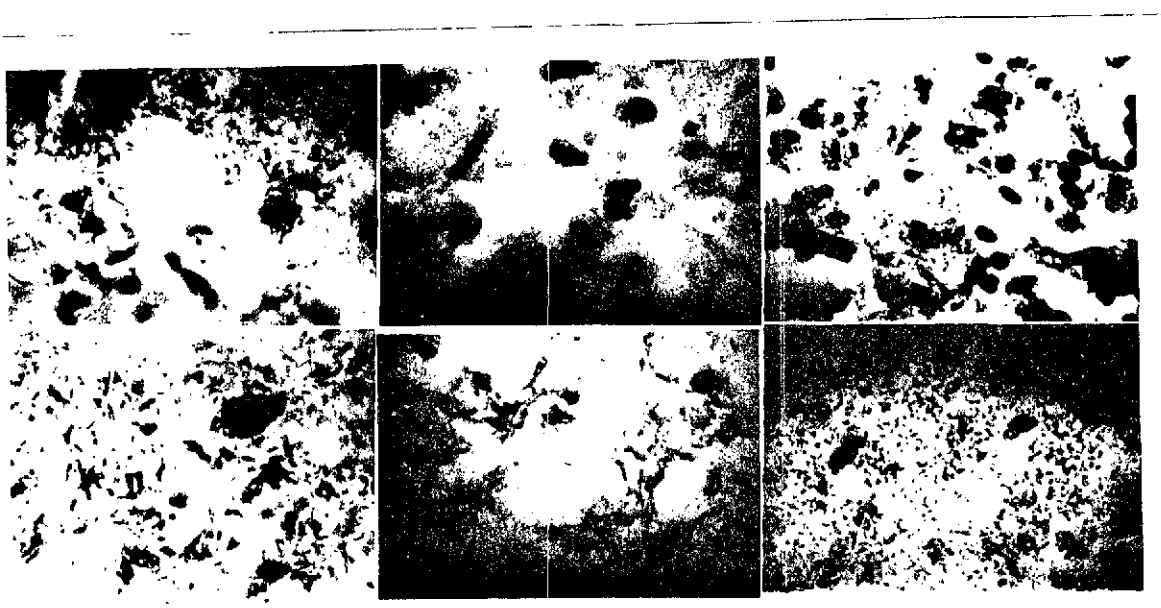


Photograph 6. Subcutaneous leproma showing large accumulations of bacilli within macrophages.



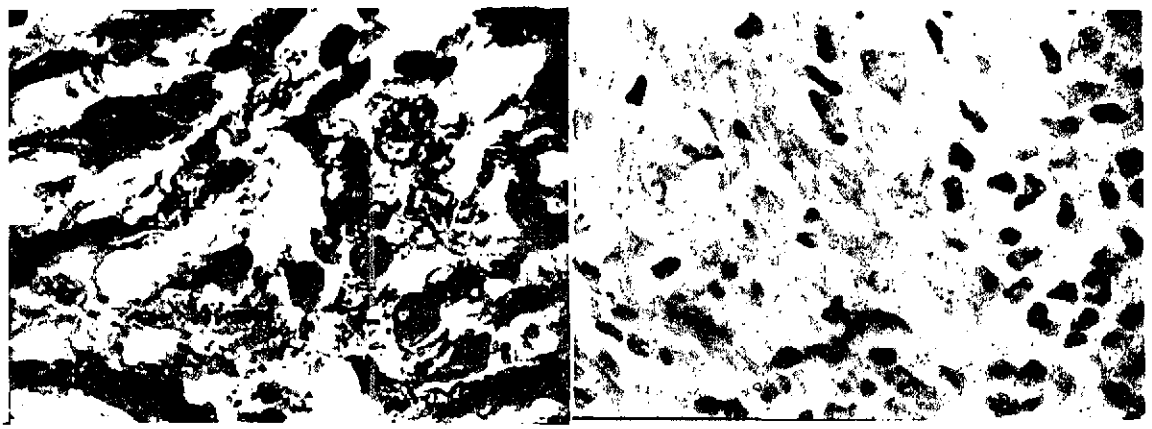
Photograph 7. Negative competency test in a lepromatous patient, using M. leprae from an armadillo. Observe the large number of bacilli within macrophages.

Photograph 8. Positive test of competency performed with M. lepraemurium in a lepromatous patient, showing the absence of bacilli within macrophages.



Photograph 9. Left side: M. leprae of human origin, above, and from the armadillo, below. In the center: loss of acidfastness after treatment with pyridine.

Right side: Gram stain, which is positive after treatment with pyridine.



Photograph 10. Left side: lepromatous macrophages filled with M. leprae (CCB test negative).

Right side: lepromatous macrophages activated by BCG, showing destruction of M. leprae. Fite-Faraco stain, 100 X.