As part of its 100th-anniversary celebration, the Pan American Health Organization has named 12 persons as "Public Health Heroes of the Americas" in recognition of their noteworthy contributions to public health in the Region of the Americas. Over the course of this year, the Revista Panamericana de Salud Pública/Pan American Journal of Public Health *will be carrying pieces written by or about these heroes.*

Como parte de la celebración de su Centenario, la Organización Panamericana de la Salud (OPS) ha distinguido con el título de Héroes de la Salud Pública a 12 personalidades que se han destacado por su valiosa contribución a la salud en el continente americano. A lo largo de este año, la Revista Panamericana de Salud Pública/Pan American Journal of Public Health *publicará una serie de escritos de los mismos galardonados o acerca de ellos.*

Fighting leprosy and other endemic diseases

Jacinto Convit[1]

An extraordinary event is taking place this year, with the Pan American Health Organization (PAHO) completing 100 years fighting for health in the Americas. As part of its Centenary celebration, PAHO is naming 12 persons—including myself—as "Public Health Heroes of the Americas" in recognition of exceptional contributions to public health in this Hemisphere. Below, I would like to mention some of the activities in which I have been involved as a health worker over the course of my life—and also some of the most important tasks that still need to be achieved.

In September 1938, when I graduated in medical sciences from the Central University of Venezuela, in Caracas, I became a resident on the staff of the Cabo Blanco Leprosy Hospital, where I had worked earlier when I had been a medical student.

The working conditions at the hospital, which at times had as many as 1 200 patients, were very uncertain. For leprosy patients, chaulmoogra oil was the treatment being used. The efficacy of this treatment had not been scientifically demonstrated, but the only other possibilities available were analgesics, including morphine, to relieve the strong pain due to the intense neuritis suffered by many patients.

With the discovery of sulfone (diaminodiphenyl sulfone, or DDS) in 1940, and its effect on *Mycobacterium leprae* as a competitive inhibitor of the dihydropteroate synthetase enzyme, and after the preliminary work done by Ernest Muir, I proceeded to use the drug to treat our hospitalized patients, with good results. During that time I was working with a group of medical students from the School of Medicine of the Central University of Venezuela who helped care for patients and assisted in the study of the disease. This work helped to change the leprosy control measures in Venezuela, replacing compulsory isolation with

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ambulatory treatment, since we had an effective treatment available with sulfone. In this way the patients did not lose the ties to their families, and neither did they acquire the status of "hospitalized patient" for the rest of their lives. This change also gave us the opportunity to treat a large number of patients who had remained in hiding due to their fear of mandatory hospitalization.

Also in the 1940s I studied dermatology at Columbia University, and I visited Brazil to observe the antileprosy campaign in that country, where there were about 30 000 patients kept in isolation in hospitals.

To implement ambulatory treatment in Venezuela we started training personnel who would take over fieldwork activities at the 24 regional public health dermatology services (PHDSs) throughout the country. These services were initially only in charge of treatment and control of leprosy, along with health education and the control of contacts of leprosy patients. The services later progressively increased their activities and added other diseases such as leishmaniasis and onchocerciasis. Initially, the leprosy control program was vertical, with supervision, administration, training, and technical guidelines coming from a central organization, the Division of Leprosy of the Ministry of Public Health and Social Welfare. The Division of Leprosy was later called the Department of Public Health Dermatology. In 1992 the regional PHDSs became part of the regional health units. For greater effectiveness in the control of the diseases involved, in 1971 we succeeded in having the Institute of Dermatology created. It is now known as the Institute of Biomedicine, due to the expansion in its activities to include other, nondermatologic diseases.

Since its creation in 1971 the Institute has brought together and integrated the activities of three major institutions: the Central University of Venezuela, the Ministry of Public Health and Social Welfare (today the Ministry of Health and Social Development), and the Dermatology Service of the J. M. Vargas Hospital, which is in Caracas. Over the last 31 years these institutions have functioned as a unified, flexible structure that gives priority to experimental innovations, with the formation of groups of researchers, professors, and supporting health personnel. Activities are carried out through a participatory process, which strengthens strategies to combat endemic diseases that include leprosy, leishmaniasis, onchocerciasis, mycoses, gastrointestinal diseases, parasitic diseases, allergies, tuberculosis in rural areas, and malnutrition. The Institute strives to generate knowledge through scientific research and to apply that knowledge in solving public health problems and extending its field activities.

Through the Institute, I have helped to form and develop an institution where research, education, and services are effectively integrated and where units in each of these areas serve the population sectors in Venezuela with the greatest needs, the highest poverty indices, and the lowest levels of development. Our Institute has been considered as a center of excellence in health and social development that can analyze public health problems in depth and present solutions to higher-level authorities.

I have been deeply interested in leprosy from the time I began working as a resident at the Cabo Blanco Leprosy Hospital. Initially, I mainly dedicated myself to transforming the control measures being practiced. The development of ambulatory treatment made it possible to treat over 14 000 patients as well as to control over 60 000 contacts of these patients. These dramatic changes in control measures transformed the Institute of Biomedicine into a training center for the directors of leprosy programs from other countries.

One of the most interesting aspects of ambulatory control was developing a vaccine that could be used both for immunotherapy and immunoprophylaxis of leprosy, formed by purified *M. leprae* obtained from highly infected armadillo tissue and mixed with live BCG. The initial use of this vaccine as immunotherapy in multibacillary forms of leprosy showed immunological changes in 85% of the patients. To investigate the preventive aspect, we carried

out a trial sponsored by the World Health Organization (WHO). However, due to problems related to the production of the vaccine in the laboratory contracted by WHO, our results were inconclusive. Nevertheless, other health personnel have obtained good immunoprophylaxis results with this product.

The difficulties and the high cost of using the armadillo as a source of *M. leprae* have limited the availability of this bacterium, given that it is still not possible to culture the bacterium in vitro.

In 1982 we initiated the control of leprosy through multidrug therapy in Venezuela, thanks to a WHO drug donation program. We now have a leprosy prevalence of 0.35 per 10 000 persons, meaning we have eliminated leprosy as a public health problem. Nevertheless, there are still five states in Venezuela where the prevalence is higher than the national average. In addition, the number of new cases per year has generally remained unchanged, and there was even a small increase last year. Therefore, on numerous occasions we have called for more intensive scientific research activities targeted mainly at obtaining a preventive vaccine for the disease.

Another disease that is endemic in the Americas, as well as Asia and Africa, is cutaneous leishmaniasis. I have studied clinical, immunological, and therapeutic aspects of this disease. We originally described the diffuse form of the illness and proposed a classification with two disease poles, with localized cutaneous leishmaniasis (LCL) as the benign pole and diffuse cutaneous leishmaniasis (DCL) as the malignant pole. Between those two poles is an intermediate area formed by the mucocutaneous and verrucous-cutaneous forms. Thus, from an immunological point of view, we defined a spectrum with well-determined characteristics: LCL, T helper type 1 (Th1) response, curable by immunotherapy or chemotherapy; DCL, T helper type 2 (Th2) response, characterized by an antigen-specific anergy and so far with no therapeutic solution; and the intermediate area, with aberrant types of responses due to the mixture of Th1 and Th2 responses. The LCL cure rate has been 93% with immunotherapy, chemotherapy, or even spontaneous cures. With DCL there has been almost complete therapy failure, with a very small number of cases being cured through the simultaneous application of both therapy procedures. In the intermediate area we have obtained positive therapy results with chemotherapy alone or in combination with immunotherapy, but only in a certain portion of the cases. These positive results can probably be explained by a predominantly Th1 response, with relapses or an absence of therapeutic effect when the Th2 response predominates. We are especially interested in these aspects of leishmaniasis treatment.

I will divide the studies we have done to develop a vaccine to prevent and treat cutaneous leishmaniasis into two stages. Both stages have been evidently influenced by the earlier work done to obtain a vaccine to prevent and treat leprosy.

In the first stage, the product we developed included heat-killed *Leishmania* promastigotes plus live BCG. The initial animal model used was guinea pigs infected with *L. enriettii*, where the vaccine showed a protective effect.

After having obtained the approval of the ethics committee of our Institute, the initial application of the vaccine for immunotherapy in human beings was done as a double-blind controlled randomized project, for which we had the help of PAHO. The results of this study were very positive, with a 93% cure rate for LCL immunotherapy, which was almost identical to the results obtained with the chemotherapy control group.

Given these results, we progressively increased the number of immunotherapy patients being treated throughout the country, with very good results. This is now the treatment of choice in our country. It does not produce the serious side effects induced by chemotherapy and so patients do not have to undergo extensive laboratory tests. This means that patients in rural areas, where

there are few clinical laboratories, can be treated with this therapy without problems. A cost-benefit study that we did showed that the cost of immunotherapy was less than 1/40 that of chemotherapy. We have treated 14 000 patients, with savings of over one million dollars per year. To assess the immunotherapy results with this new treatment, we asked PAHO to name an evaluation committee. The committee came to Venezuela in 1998 and corroborated our results. However, in an WHO evaluation of the results from the immunotherapy trials with this vaccine in areas endemic for leishmaniasis, it was shown that this vaccine does not protect against the disease.

In the second stage, we have been working with other researchers for more than a year on modifications to the vaccine that I described above. Our goal is to increase the vaccine's efficacy for immunotherapy and possibly to obtain an immunoprophylactic effect, since a preventive vaccine is considered the only possible way to eradicate this disease.

An interesting aspect of the proposed vaccine modifications is the use of various temperatures with the *Leishmania* parasite. Also of interest are the results that the modifications produce on the electrophoretic profile of parasite proteins. Death of the parasites is demonstrated by inoculation of parasites in BALB/c mice and trypan blue staining. These results will be published soon.

Between 1938 and 1960 I published, as the principal author or as a coauthor, 55 scientific papers in Venezuelan and international journals. These publications were on leprosy, leishmaniasis, Kaposi's sarcoma, and other dermatological diseases. Diffuse cutaneous leishmaniasis was described as a new syndrome, and on that basis we described a new classification for leishmaniasis, based on clinical, immunological, and parasitological aspects.

Between 1961 and 1980 I published papers mainly dedicated to leprosy control, leishmaniasis, and onchocerciasis, as well as the description of a new dermatological disease, erythema dyschromicum perstans.

Since 1981 I have published 105 scientific papers, mainly on leprosy and leishmaniasis vaccines and control. I have also contributed to the description of Hansen's disease in the armadillo.

In terms of academics, I achieved the status of full professor of the School of Medicine of the Central University of Venezuela in 1958. I have received 47 degrees and prizes given by institutions in Venezuela. I am an honorary professor of five Venezuelan universities. I received the National Prize in Medical Sciences, and I am a member of the National Academy of Medicine.

I have received 33 international prizes. Among these are: Principe de Asturias Prize (Príncipe de Asturias Foundation, Spain, 1987); "Health For All" Medal (PAHO, 1988); Abraham Horowitz Price (PAHO, 1988); International Prize for Science and Technology (Government of Mexico, 1990); Alfred Soper Prize (PAHO, 1991); Armand Frappier Medal (Canada, 1979); and Health Hero of the Americas (PAHO, to be awarded in Washington, D.C., in December 2002).

I was president of the International Leprosy Association and president of the International Journal of Leprosy Corporation for two terms, 1968–1972 and 1973–1978.

In looking back over the course of my life, I believe that the most important scientific advances due to my work have been the introduction of immunotherapy in Hansen's disease, the contribution to prevention of this disease through repeated BCG vaccination, and the development of immunotherapy for American cutaneous leishmaniasis. In all these activities, my fellow researchers and I have always been able to count on the full support of PAHO and WHO. In looking ahead, I believe that among the most important tasks that still need to be accomplished are the development of preventive vaccines for leprosy and leishmaniasis.