INTERNATIONAL JOURNAL OF LEPROSY
and Other Mycobacterial Diseases
OFFICIAL ORGAN OF THE INTERNATIONAL LEPROSY ASSOCIATION
Publication Office: 1200 - 18th St., N.W., Washington, D. C.

VOLUME 41, NUMBER 1 JANUARY-MARCH, 1973

EDITORIAL

Editorials are written by members of the Editorial Board, and occasionally by guest editorial writers at the invitation of the Editor, and opinions expressed are those of the writers.

Editorial by Dr. Jacinto Convit
President of the International Leprosy Association

Our present concepts of leprosy naturally fall into two aspects, namely the ideas prevailing prior to the discovery of its bacterial etiology by the Norwegian physician Gerhard Armauer Hansen, in 1873, and those that developed subsequently and led to our present understanding of the disease as a congenital incapacity of the so-called macrophages to destroy and digest the particular intracellular parasite. The term "leprosy," which has carried with it a certain stigma from time immemorial, is as far as possible avoided at present and "hanseniasis" or Hansen's disease" is current. Nonetheless, in medical science lepra is still the official international name of the disease. Unfortunately the evasive term "hanseniasis" to most minds calls for an explanation and when it is identified with traditional leprosy it is apt to impress the mind more poignantly than would be the case when the disease is called by its current name. Rather than change the name, it might be better to deprive it by educational measures of the stigma that is associated with it in the popular mind. It would be difficult to eradicate a name that has been in public use for more than two thousand years. At the same time, the terms *Aussatz* in German and *Spedalskhed* in the Scandinavian languages carry with them the same stigma as "lepra" in the languages of Latin origin. The same is the case with the current names used for the disease in many other vernaculars.

The literature about leprosy in Hebrew, Greek and Latin goes back to a very remote antiquity. The Hebrew term *saraath*—literally uncleanliness—comprised undoubtedly more than one dreaded and disfiguring form of dermatitis and early in history it went into Greek as *lepra*. In most cases, however, there is little doubt about its identity with leprosy as it is known clinically today, at least in its lepromatous form. Still, the ancients distinguished between "lepra magna" and "lepra minor," and it is quite possible that these terms referred to the two polar types of the disease, lepromatous and tuberculoid. Nevertheless, "lepra minor" might have included other more or less benign skin diseases.

In our modern recognition of the forms of leprosy, we follow the classification established by the Latin American leprologist, Francisco Eduardo Accioli Rabello, who distinguished as polar the lepromatous and the tuberculoid forms. The general adop-

tion of this classification has been of the greatest importance in dealing internationally with the problems of leprosy.

Lauro de Souza Lima has defined the form uncharacteristic, which was later called the indeterminate, as an initial lesion, dynamic in its activity and tending to become transformed into one of the other forms of the disease.

Wade subsequently introduced the term "borderline" to distinguish a form with an ample spectrum of characteristics, that gives it a position intermediate between the two polar types.

Recently, D. S. Ridley has defined the immunopathology of the borderline form as an expression of the variable immunological responses within that spectrum.

Although C. Y. Chang has cultivated the bacillus of rat leprosy (*Mycobacterium lepraemurium*) in the macrophages of the mouse and Rees has done the same in the fibroblasts of the rat, that bacillus does not multiply outside living cells. As for the bacillus of human leprosy (*Mycobacterium leprae*), it has never shown any significant increase *in vitro*, neither within nor without living cells. It is for all intents and purposes an obligatory parasite in living animal tissue.

Ever since the discovery of the bacillus in 1873, various investigators have attempted to cultivate the bacillus, but the results have been the multiplication of some wild mycobacterial contaminant or mutant that did not possess the full characteristics of *Mycobacterium leprae*. Recently, however, Shepard has successfully cultivated it in the foot pads of mice. This has been the first transmission of the disease to a nonhuman host. Rees working in England, has done the same in the foot pad of the thymectomized and irradiated mouse producing a much greater multiplication of the bacillus at various distances from the site of the inoculation. To make it easier, Binford has modified the technic of Rees by protecting one of the legs of the mouse during the irradiation so as to eliminate the need for transfusion of syngenic bone marrow.

A recent interesting development has been the inoculation by Kirchheimer and Storrs, of the armadillo with bacilli from human leprous lesions. They produced in that animal a generalized mycobacterial disease with the characteristics of human leprosy. This is apparently the first successful transmission of lepromatous leprosy to such an animal with the conservation of its immunopathological characteristics. This fact will undoubtedly make the armadillo an animal of primary importance in our future investigations of the disease.

Leprosy as a disease is not inherited, but the lack of defense against it is due to congenital incapacity of the macrophages of the skin to destroy the bacilli after they have ingested them.

During the last ten years it has been demonstrated by immunological research in leprosy, that the phenomena of hypersensitivity of the delayed type, as well as those of resistance to *Mycobacterium leprae*, depend on the interaction of two types of cells, namely the lymphocyte and the macrophage. Of these, the former has been considered as the site for the production of the so-called transfer factor, which enables the macrophage to destroy the bacillus. It is quite possible that the congenital lack of it in some individuals is at the root of the intracellular mechanism that makes leprosy possible. Should it be possible to isolate that factor from persons highly resistant to the disease, or from some other as yet unidentified protozoan, we should have a weapon of great possibilities against leprosy.

In view of this concept some attempts have been made to treat the disease with the injection of lymphoid cells from tuberculoid patients or from contacts that have a strongly positive lepromin reaction. Still there is another possibility to be considered, namely the specific involvement of the lymphocyte, which would make the infection of the macrophage a secondary phenomenon. However, we must not overlook the possibility that both types of cells are initially and simultaneously involved. If so, the situation would be still more complicated.

Leprosy should be considered as another public health problem, the solution of which should be included within the mod-

ern planning concepts, which have rendered such good results in other areas of medicine.

As a communicable disease, leprosy represents a low risk for the general population, but undoubtedly it does represent a risk for the small percentage of the population which is highly susceptible. These are the characteristics that condition its endemicity, with a low morbidity as the general rule.

During the last decade, an important effort has been made in basic research on leprosy. The first important result of these activities has been the international adoption of Rabello's classification. Subsequently, a number of investigators in various countries have made important contributions to the study of the disease. These efforts have been due to the growing interest that has risen regarding leprosy as a model for resarch in the felds of microbiology, immunology and biochemistry. Due to this, several investigators, who have been doing basic research in these fields, have dedicated part of their time and effort to trying to clarify the numerous unknowns that the disease still presents.

In a manner similar to the use of tuberculin in connection with tuberculosis we have in lepromin, also called the Mitsuda test, a means of determining natural resistance or congenital susceptibility to leprosy. The antigen, which is administered intradermally in doses of 0.1 cc, consists of an aqueous suspension of boiled leprosy bacilli to which phenol has been added in a quantity of 0.4% as a preservative. The larger tissue particles that accompany the preparation are removed by straining it through a piece of gauze. Resistance to leprosy is indicated by the appearance of a hard nodule at the site of administration in the fourth week after applying the test. A negative reaction is a strong sign of leprous susceptibility. Fortunately, about 90% of humans react positively. All new cases of lepromatous leprosy appear among the negative reactors.

Geographically, leprosy is common in the countries of Africa and Asia. In both continents the patients are counted by the million. In Latin America it is common in Brazil, Argentina, the Guayanas, Venezuela, Colombia, Central America and Mexico, but all these countries are making strong efforts to control and ultimately to eradicate it—a formidable task when we consider the scattered, often migratory populations of the very extensive regions involved.

Leprosy was formerly considered as an incurable disease. In the late twenties of this century the use of chaulmoogra oil, which has been used in India almost from time immemorial, was introduced. For more than 20 years it was the only known medication that gave the physicians and their patients hope, although a frail one, of arresting and ultimately eliminating the leprous lesions. However, the very slow effect of the oil during years of treatment and the frequent states of reaction with serious relapses were the concern and often the despair of physicians as well as patients.

The first use of a modern drug in the treatment of leprosy was made by H. Faget at Carville, Louisiana, who successfully treated the lepromatous form of the disease with a sulphone derivative known by the commercial name of Promanide. Faget used it in intravenous injections with very good results in a group of lepromatous patients.

We owe to R. G. Cochrane, working in India, the introduction of sulphone treatment in leprosy. The product he used with encouraging results from 1928 and onward was diaminodiphenyl sulphone, now generally known as DDS. The use of that drug had become a standard practice by 1950, and the use of chaulmoogra oil became sporadic and exceptional, often at the request of the patients themselves.

With the use of sulphone the practitioner can expect in the course of a year a substantial improvement in leprous lesions and may entertain a certain confidence that continued treatment will bring about bacteriological negativity in the great majority of his cases. Still, there are patients who do not respond to sulphone. They represent a therapeutic problem and an incentive for experimental treatment with recent new drugs. As a general principle, any drug of

proved benefit in tuberculosis is given a trial in sulphone-resistant cases of lepromatous leprosy. Among the newer drugs now being tried out are clofazimine and rifampicine, which have both shown possibilities in the treatment of the disease.

Our present approach to leprosy treatment and control is purely chemotherapeutic as the only products at our disposal are artificial chemicals of proved antileprotic effect by their direct action on the bacilli after being taken up by the infected macrophages of the skin. It is to be hoped that the near future will see a real biological approach to the problem with successful efforts to isolate, perhaps even to synthesize the natural factor that is at the root of natural resistance to the disease in the vast majority of mankind. It would be natural to solicit the cooperation of eminent leaders in the major biological research centers of the world.

The isolation of leprosy as a disease separate from other clinical entities has been due to prejudice and false interpretations, which have developed not only in the general population, but also within the medical profession. These negative aspects have tended to keep this disease outside the general scientific progress, which has had so favorable an influence in other areas of public health.

In conclusion I can only emphasize once more, as I have done so often in the past, that leprosy should be shorn of the superstitions and prejudices that have accompanied it in the public mind and that it should be regarded simply as a mycobacterial disease susceptible to treatment in the vast majority of cases and of very low danger to the "general" public.

We are preparing to commemorate this year in Bergen the centenary of the discovery of the leprosy bacillus by Gerhard Armauer Hansen, who lived and carried on his work in that city; a center for nine centuries, second only to Oslo, in the intellectual and commerical life of Norway and the birthplace of the author Ludvig Holberg, the composer Edward Grieg and the musician Ole Bull, all three internationally well-known.

It is a fortunate incident that the year of the centenary coincides with the Tenth International Congress of Leprosy held for that reason in Hansen's native city. That important event will give leprosy workers from all parts of the world an opportunity to know and appreciate the environment in which Hansen worked and exchange experience with each other in regard to current problems in leprosy.