JOHN BLAIR

LEPROSY

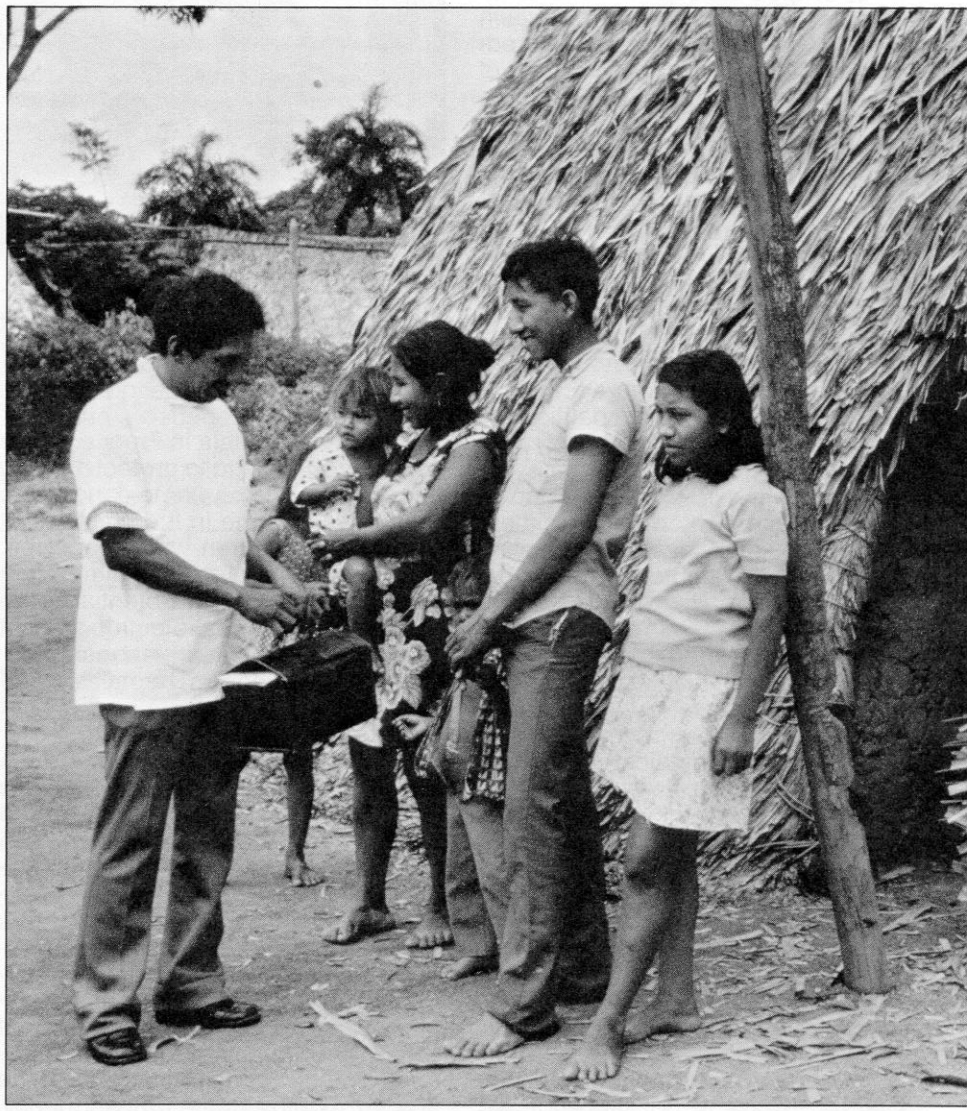
GUARDING AGAINST THE ANCIENT ENEMY

Healthy Americans and Europeans will volunteer by the hundreds this year to receive shots containing killed leprosy bacilli. The immunization experiment and the simultaneous work to develop new drug treatments for patients already affected by the disease mark major advances against one of humanity's most persistent enemies.

As the volunteers in the international research effort recognize, leprosy, also known as Hansen's disease, is not something that vanished with the Middle Ages. The untreated disease, caused by the tuberculosis-like bacterium *M. leprae*, damages the nerves and often causes disfigurement. It may affect as many as 15 million people. Estimates that 3.5 million Indians, almost 300 000 Brazilians, and one in 40 citizens of Zaire have the infection demonstrate the endemic situation in the Third World. World Health Organization (WHO) authorities assert that less than half, and perhaps as few as one-third of the people with the disease receive the drug treatments that arrest the sickness and render it noncommunicable. Almost as alarming is evidence that *M. leprae* has begun to develop resistance to the cheapest medication, dapsone (4,4'-diamino-diphenyl sulfone, or DDS).

The spectre of drug resistance (occuring in 40 percent of Mali's new cases of leprosy), as well as the fact that most people do not come in for initial treatment until long after they have reached the infectious stage, makes immunization the ideal method for complete control. Because the only known reservoir for transmitting leprosy to a human is another human, the vaccination weapon against the disease seems especially appropriate. With such a tool, it eventually might be possible to eliminate the sickness from the face of the Earth, just as WHO did during the last decade with smallpox.

Until recently, scientists could not cultivate *M. leprae*, the basic component of a vaccine, outside the body. Discovered in 1873, the bacterium was the first such organism ever to be identified as a cause of human disease. But 109 years later, researchers have not been able to make it multiply in a test tube. Yet John H. Hanks, who has kept a form of rat leprosy alive *in vitro* since 1979, is optimistic that his techniques can be refined to grow *M. leprae* as well. Although it may take considerable time to achieve such a laboratory victory, Hanks and his colleagues at Johns Hopkins University Tropical Medicine Center, in Baltimore, U.S.A., say they are already halfway there.



A second option for producing the bacterium is to grow it in a laboratory animal that can be sacrificed, but it took until 1971 to find an animal capable of producing the microbes in quantity: the armadillo. Nine special farms with over 300 animals have been created since Waldemar F. Kirchheimer and Eleanor E. Storrs first observed *M. leprae* in their experimentally inoculated armadillos. Today, the laboratory armadillos are being harvested for their abundant bacterial crops.

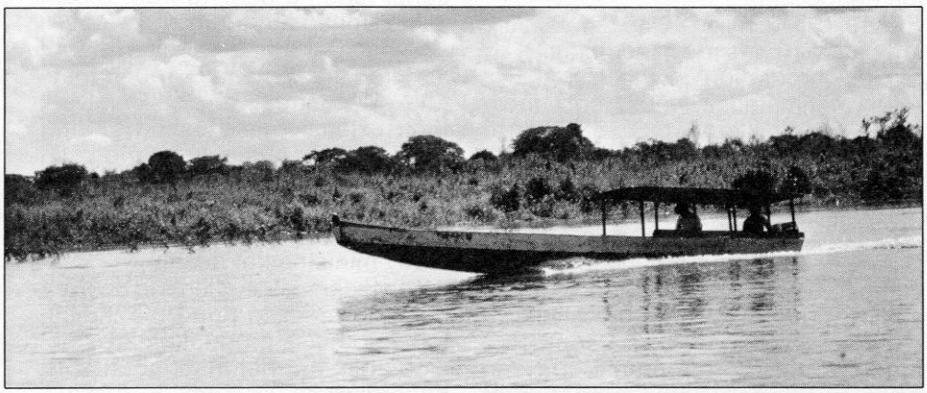
According to Barry Bloom, coordinator of WHO's leprosy immunization program (IMMLEP), the highly susceptible animals generate 100 to 1000 times more microbes per gram than human tissue. He points out that in humans the organisms are restricted to the cooler skin regions, but in the low-temperature, weakly immune armadillos, the body invasion is total within three years. "Ten billion bacilli can be obtained from a single gram of liver tissue," Bloom declares. "Enough for possibly 1000 to 10 000 doses of vaccine."

Last year biochemists at the British National Institute for Medical Research used U.S. material to produce a killed-*M. leprae* vaccine free of armadillo tissue contaminants. The purified vaccine's protective power

has since been proven in animal tests by Kirchheimer at the U.S. Public Health Service Hospital in Carville, Louisiana, Charles Shepard at the Center for Disease Control in Atlanta, Georgia, and Bloom at New York's Albert Einstein Medical College. The human trials, which will begin within the next few months, will be aimed at finding the vaccine's optimal dosage and its effectiveness over time, as well as spotting any potential side effects. Bloom asserts that the worst side effect that a volunteer might have is a sore arm.

One of the vaccines that WHO will consider for trials in endemic countries within the next three years will be such a combined preparation. Bloom cites the experiences of Venezuelan Jacinto Convit, director of the National Institute of Dermatology in Caracas' Pan American Center for Research and Training in Leprosy and Tropical Diseases. Convit inoculated patients suffering from lepromatous leprosy with a mixture of tuberculosis vaccine and killed-*M. leprae* bacilli. Not only did the volunteers develop immunity and thus recover from their severe form of the disease, but they did so without drugs or nerve damage. Convit wants to use his therapeutic medication as a preventive vaccine. He has already used purified *M. leprae* to create a skin test that identifies persons who should receive such a vaccine.

Some leprosy vaccines show promise. But bringing immunization services to remote areas, here in Venezuela, may be difficult.



Research makes progress in the prevention and treatment of leprosy, but public ignorance and fear are aspects of the disease for which no scientific working group has a ready solution

Although Europe has not had a substantial outbreak of leprosy since one in Norway in the 1850s, and the United States currently has only several thousand persons under treatment for the disease, the selection of the two regions for the first trials sidetracks any possible charge that Third World people are being used in unproven experiments.

The tests on either side of the Atlantic should also provide valuable additional data. All the Europeans have received the tuberculosis vaccine BCG. The Americans have not. In bacterial terms, leprosy is closely related to tuberculosis. Some experts even speculate that the disease lost its epidemic hold on Europe only when the faster-acting tuberculosis bacilli killed off people that would have been susceptible to leprosy. Specialists will be watching closely for differences in the skin tests of the TB-immunized Europeans and their American counterparts.

Most immunologists do not expect the *M. leprae* vaccine alone to wipe out live bacilli in a person who already has a subclinical infection. At best they hope the inoculations would give such individuals enough immunity so that if the disease eventually manifests itself, it will be the less severe tuberculoid variety that is readily treatable with drugs, or even self-healing. The *M. leprae* vaccine combined with BCG vaccine, however, might knock out the slowly incubating leprosy bacilli in such individuals and keep them disease-free.

Although Convit has submitted plans to WHO for an inoculation campaign in the endemic areas of Venezuela, the logistics of a pilot field trial are awesome. Family members and acquaintances of patients, who have a sixfold higher risk of the disease, could be vaccinated for control studies. But because of the slow incubation period of the disease, systematic checkups would have to be conducted for 10 to 15 years. Health authorities will have to be alert for the slightest variation in vaccine results. For example, if the vaccine proves more effective among people inoculated in childhood than among those immunized as adults, it could be important for future efforts.

A mass general vaccination campaign involving hundreds of thousands, perhaps millions, of people could then be launched.

Robert C. Hastings, chief of the U.S. National Hansen's Disease Center pharmacological division, points out that the vaccination effort must be "sustained," noting that in many areas of the world paralytic polio is still extremely common 20 or more years after a cheap, safe, and essentially permanent vaccine has been made available. He adds, "A massive program of public health education, mobilization, delivery and follow-up will be required."

Plans for distributing and testing leprosy vaccine — an activity that would have been inconceivable only a few years ago — are at the top of the IMMLEP agenda. Convit, with Venezuelan government approval, may be the first to venture into the mass vaccination field. Another of the WHO's task forces has meanwhile moved to improve the chemotherapy of patients. Regimens have been developed that use drug combinations to help the small minority of sufferers whose infection cannot be suppressed by any one medication. Studies of dapsone resistance, along with efforts to develop new drugs, are under way. The creation of analogs of clofazimine, thalidomide, and cycloserine are being given the highest priority.

Another field trial that is especially important to persons with Hansen's disease concerns the withdrawal of chemotherapy from persons who have received two years of intensive treatment with multiple anti-leprosy drugs. If the relapse rate is low (no greater than one percent per year) hundreds of thousands of persons who show no clinical sign of *M. leprae* could be released from the obligations of regular medication.

Public ignorance and fear of leprosy are aspects of the disease for which no scientific working group has a ready solution. Although at least 90 percent of the population is apparently immune to the sickness, and only a small percentage of those who are susceptible could ever come down with active symptoms of the disease, the stigma is still there. Bloom calls this feeling "a disease of the mind" that "affects the lives, psychology, socialization, as well as the health of the people."

Brazilian scientist Dr Abraham Rotberg argues for the substitution of the term "Hansen's disease" for leprosy. He says that renaming the sickness after the Norwegian discoverer of the bacilli would "dissociate the disease from centuries of ignorance, infamy, and prejudice."

Bloom, however, thinks that the stigma will disappear only when people realize that the disease can be prevented and cured. Progress toward that goal in the last 10 years has, in his words, been "extraordinary." "Immunology, biochemistry, and combined chemotheraphy all are contributing new data to the effort. WHO put all the information together through its network of cooperation. It couldn't be done alone in England, the United States, Venezuela, Ethiopia, or India. All are pulling together and sharing material. It doesn't happen often in science, but it is happening." □

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