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LEPROSY

by

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and

Gerald P. Walsh, Ph.D.

March 1991

VBC Tropical Disease Paper No. 10

Other papers in the VBC series include:

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The blue square shows the rod-shaped bacilli, Mycobacterium leprae, *that cause leprosy. The other symbols depict essential components of tropical disease control: the environment, communities and research.*

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Table of Contents

Executive Summary 1

1. Introduction 2

   a. Transmission and inoculation period 2
   b. Clinical leprosy 3
   c. Immunity 4
   d. Agent 5
   e. Reservoirs 5

2. Distribution and Severity 7

   a. Populations affected 9
   b. Endemic and epidemic disease 9
   c. Child survival 9
   d. Economic impact 10

3. Control Measures 11

   a. Diagnosis 11
   b. Chemotherapy 11
   c. Vaccination 12
   d. Constraints to control 13

      Case detection 13
      Treatment 13
      Health care delivery 14

4. Current Research 16

   a. Diagnosis 16
   b. Chemotherapy 16
   c. Vaccine Development 17

5. Leprosy from the A.I.D. Perspective 18

   a. The Horizon 18
   b. Priorities for future action 18

6. Selected References 20

Maps

Map 1. Registered Leprosy Cases Worldwide 8

Annexes

Annex 1. Registered Leprosy Cases, 1985 26

Executive Summary

Leprosy is a chronic infection caused by *Mycobacterium leprae*, an acid-fast, rod-shaped bacterium. Approximately 1.6 billion people live in areas of the world where leprosy is an important public health problem and an estimated 10 to 12 million people have leprosy. More than half of the patients live in Africa (approximately 4 million) and India (approximately 3.8 million).

The disease affects cooler parts of the body, particularly the skin, mucous membrane of the upper respiratory tract, testes, eyes and segments of peripheral nerves. The inflammatory response to invasion of the peripheral nerves by *M. leprae* often leads to loss of sensation and paralysis, which cause deformity and mutilation.

The exact mode of transmission is not known. Many authorities still believe that transmission by prolonged skin-to-skin contact is important. However, many experts consider transmission via secretions of the upper respiratory tract the most likely mode. Transplacental transmission is also thought to occur. Armadillos, chimpanzees and monkeys have been implicated as reservoirs of the disease. The incubation period is prolonged and variable, but usually ranges from two to five years.

Recent trials of multidrug therapy (MDT), a combination of the anti-leprosy drugs dapsone, rifampicin and clofazimine, have demonstrated a drastic reduction in prevalence, suggesting that it might be possible to interrupt transmission. During the past five years, the number of registered patients declined for the first time in the history of leprosy control, largely because of the release of people who had successfully completed MDT treatment in field trials.

The goal of the World Health Organization's Immunology of Leprosy Program (IMMLEP) is development of a vaccine and methods of detecting subclinical infections. Vaccination trials of the bacillus Calmette Guerin (BCG) vaccine in Uganda, Mali, Burma, Papua New Guinea and Venezuela have shown varied protective effects, ranging from a high of 80 percent in Uganda to a low of 20 percent in Burma.

Early detection and effective treatment of leprosy can prevent disability and deformity. Case detection is severely handicapped by the social stigma associated with leprosy and results in registration of less than half of all cases. Case detection efforts must be supported by health education to dispel myths about leprosy, emphasize the importance of early diagnosis, teach people to recognize the early symptoms, and inform them about where to seek diagnosis and treatment.

1. Introduction

Leprosy, or Hansen's Disease, is a chronic infection caused by *Mycobacterium leprae*. It affects the cooler parts of the body, particularly the skin, mucous membranes of the upper respiratory tract, testes, eyes and segments of peripheral nerves. If left untreated, leprosy can result in deformity and disability. It is among the most feared and least understood of all infectious diseases. Many leprosy patients are ostracized and stigmatized for life, even after effective treatment, because of myths and prejudices about the disease.

Although the origins of leprosy are obscure, written records from India around 600 B.C. describe a skin disease that was probably leprosy. From India, the disease may have spread to China and Japan. Other records suggest that there was leprosy in China several millennia B.C. The disease was introduced into Europe by the armies of Alexander the Great.

Leprosy reached peak prevalence in Europe by the 14th century, but declined dramatically for reasons that are poorly understood. Some authorities attribute this decline to the plague epidemics of the Middle Ages. The deaths of many leprosy patients from plague, combined with improved standards of nutrition, hygiene and housing, probably contributed to the reduced prevalence of the disease.

The introduction of leprosy into the Americas is attributed to Spanish and Portuguese explorations into Central and South America and to the importation of African slaves. The French brought leprosy to Canada, and migration of French-speaking Canadians to Louisiana in the 18th century established a small focus that persists today.

Leprosy affects 10 to 12 million people, most of whom live in tropical and subtropical regions in developing countries.

a. Transmission and Inoculation period

The exact mode of transmission of leprosy is not known. Many authorities still believe that transmission by prolonged skin-to-skin contact is important. Others consider transmission via secretions of the upper respiratory tract the most likely mode. When an infected person sneezes, leprosy bacilli are discharged on droplets or dust particles, which can be inhaled by healthy

persons. Transplacental transmission of leprosy is also possible. *M. leprae* are occasionally demonstrated in human placentas.

Reports of naturally acquired leprosy in armadillos, a chimpanzee and two mangabey monkeys indicate that animal reservoirs of the disease are possible. Although experimental animals can be infected by insects that have been fed on infected people, the epidemiologic patterns of leprosy do not suggest that the disease is transmitted by a vector.

The spread of leprosy depends on the dissemination of *M. leprae* in a susceptible population. The prevailing theory has been that an individual becomes infected after repeated exposures, but many consider a single exposure under optimal conditions sufficient to contract leprosy.

The incubation period of the disease is prolonged and variable, but usually ranges from two to five years. A notable exception may be in infants in endemic areas. A report by the Leprosy Registry at the Armed Forces Institute of Pathology (AFIP) describes leprosy in 49 infants. Only half of these infants had mothers who had leprosy or a history of leprosy. The youngest infant was 2 1/2 months old at diagnosis.

b. Clinical leprosy

Leprosy is a single disease with a spectrum of manifestations that largely depend on the cell-mediated immune response (CMI) of the patient to *M. leprae*. At one extreme, patients with polar tuberculoid leprosy mount a strong CMI response to *M. leprae*. These patients have one or a few randomly distributed skin lesions. In tuberculoid leprosy, bacilli are scarce in the lesions. The primary symptom is loss of sensation.

At the other extreme, patients with polar lepromatous leprosy have no immune response to *M. leprae* and develop widely disseminated disease with spreading lesions and often severe nerve damage. Without treatment, the cooler parts of the body become massively infiltrated. For example, testicular function may be markedly reduced, causing sterility, or the cartilage and bone of the nose destroyed, causing nasal collapse. These patients shed large numbers of bacilli in their nasal secretions or from open ulcers in the skin, which are thought to be common sources of bacilli for leprosy transmission.

There is a third category called borderline leprosy. In this form, the disease possesses characteristics of both polar forms and the CMI response to *M. leprae* is intermediate between the two extremes. Patients with symptoms similar to the tuberculoid type are classified as borderline-tuberculoid and those with symptoms more like those of lepromatous leprosy are classified as borderline-lepromatous. Patients with the polar forms tend to be stable, while those in the borderline area tend to have potentially dangerous reversal reactions that may result in shifts across the spectrum.

Most disability and deformity caused by leprosy is a result of *M. leprae* invading the peripheral nerves, which maintain skin sensation and muscle movement. The ensuing inflammatory response can lead to loss of skin sensation and paralysis. The cornea may lose sensation and the eyelid muscles may become paralyzed, which can cause blindness.

Blindness and other disabilities caused by leprosy can be prevented through early diagnosis, treatment and patient education. For example, infections leading to ulceration of the foot are a common problem among leprosy patients. Most of these ulcers would heal with proper rest and care, but often a patient does not realize the severity of the infection because he cannot feel the pain. If he continues to walk without protection, severe tissue damage and eventually bone loss can result.

The very early form of the disease, called indeterminate (I) leprosy, usually begins with a single lesion containing a few *M. leprae*. Fifty percent or more of patients with indeterminate leprosy heal without treatment, but in others the disease develops into one of the established forms of leprosy described above. Without therapy, the course of the disease depends on the level of CMI the patient is capable of mounting.

In establishing therapeutic regimens, the World Health Organization (WHO) has divided leprosy patients into two categories: 1) multibacillary, or those with moderate or large numbers of bacilli; and 2) paucibacillary, or those with few bacilli.

c. Immunity

Immunity is a key element in understanding the development of leprosy in an infected person. *M. leprae* causes disease by its

ability to survive and multiply in macrophages. If macrophages are able to kill and destroy the bacilli soon after ingestion, there is little or no disease. If macrophages are incapable of destroying the bacilli, the widely disseminated multibacillary form of the disease develops.

There is abundant evidence that CMI to *M. leprae* is markedly suppressed in lepromatous patients. Skin test responses to some other antigens are sometimes depressed, but the depression is most profound to antigens of *M. leprae.* Suppression becomes less and less pronounced as the type of disease approaches the tuberculoid end of the spectrum of forms of leprosy.

d. Agent

The acid-fast bacillus *M. leprae* was discovered and designated as the agent of leprosy by G. Armauer Hansen in 1873 in Bergen, Norway. Hansen consistently demonstrated this bacillus in excised lepromatous nodules of patients with lepromatous leprosy. His observations were a landmark in microbiology because *M. leprae* was the first bacterium shown to cause chronic disease in humans.

M. leprae is a bacillus, or rod-shaped bacterium, 0.3 to 0.5 microns wide by up to 7 microns long. It has never been cultivated *in vitro*, so its identification depends on criteria other than those routinely used for cultivable mycobacteria. Cultivation of *M. leprae* is essential to gaining an understanding of the metabolic pathways of *M. leprae* and developing new chemotherapeutic agents. Much progress has been made in understanding the *in vitro* metabolism of *M. leprae* and there is considerable optimism that the organism will be cultivated for laboratory studies in the not too distant future.

In experimental animals, *M. leprae* has a generation time of 12 1/2 days. The long doubling time of the organism may be partially responsible for the prolonged incubation period of the disease.

e. Reservoirs

Traditionally, leprosy has been considered a disease confined to humans. The recent discoveries of naturally-acquired leprosy

in three species of wild animals, however, have demonstrated that there are animal reservoirs of leprosy.

Naturally acquired leprosy has been reported in 150 armadillos in Louisiana and Texas, or about 4.6 percent of the wild armadillos caught in these states. Although one early study reported no association between armadillo contact and the disease in humans, more recent studies have implicated a history of contact with armadillos in seven leprosy patients from Texas and several others from Louisiana. A case control study of leprosy in Mexican residents of Los Angeles concluded that direct and indirect exposure to armadillos was a significant risk factor in the development of leprosy in male patients.

Most people contract the disease through contact with leprosy patients, but epidemiologic data do not support the once common belief that this is the only way to contract leprosy. Approximately two-thirds of the native-born leprosy patients in the United States are inhabitants of Louisiana and Texas. These are the only states where the majority of leprosy patients belong to the indigenous population and, interestingly, the two states where large numbers of armadillos have naturally-acquired leprosy.

Naturally acquired leprosy has also been reported in a chimpanzee from Sierra Leone and two mangabey monkeys from Nigeria. Surveys are needed to determine the prevalence of natural leprosy in nonhuman primates and possibly other animals in the wild. Experimental studies have shown that several species of primates, particularly African green monkeys and rhesus monkeys, are susceptible to leprosy. Their role in the epidemiology of human leprosy must be ascertained.

2. Distribution and Severity

The number of registered leprosy patients in the world doubled between 1966 and 1985, from 2.8 million to 5.3 million. Since then, it has dropped to about 4.5 million, largely because of the release of more than 800,000 patients who had successfully completed multidrug therapy (MDT) regimens in field trials. However, it is estimated that there are one to two undetected patients for each registered patient because of inadequate health care delivery in most endemic areas and the social stigma associated with the disease. The numbers of registered leprosy cases in selected countries are listed in Table 1 in the annex.

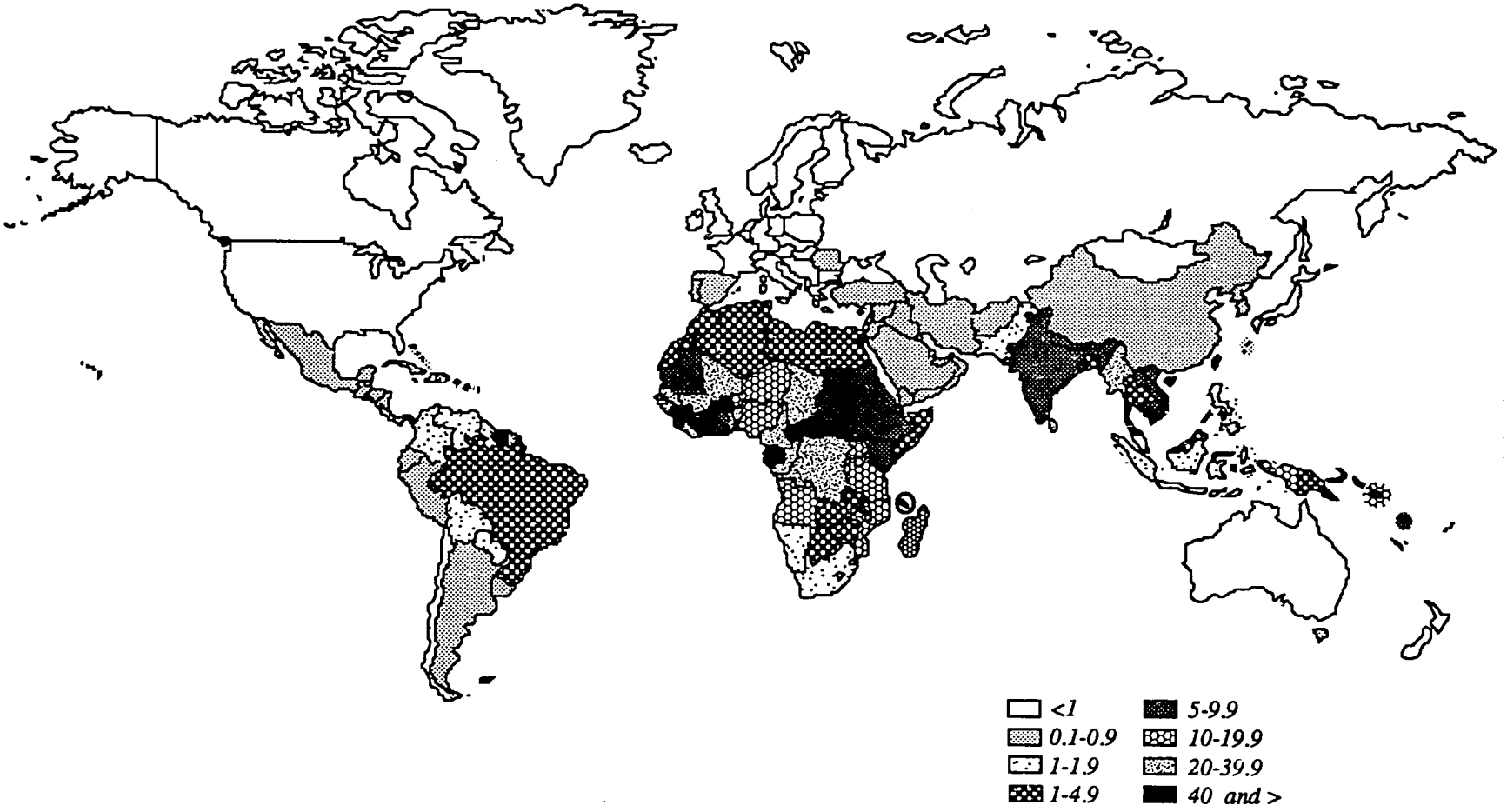
Approximately 1.6 billion people live in areas of the world where leprosy is an important public health problem, with a prevalence of one case per thousand people.

The distribution of the estimated 10 to 12 million leprosy cases in the world is shown in Map 1. More than half of the cases are in Africa (approximately 4 million) and India (approximately 3.8 million). There are 5,000 to 6,000 known patients in the United States. Most are in immigrants, but a few indigenous cases are detected each year from the Gulf Coast states and Hawaii.

Geographic, ethnic and socioeconomic factors may influence the spread of the disease. The number of multibacillary patients and the opportunities for exposure in a given area contribute to the spread of infection. Ethnic background also appears to play a role. For example, in some Asian populations, 50 percent or more of the leprosy patients have the more severe lepromatous disease, compared to approximately five to 10 percent of African patients. The role that nutritional factors may play in the spread of leprosy is unknown. Genetic factors may enhance susceptibility to leprosy, but evidence for a decisive role for genetic factors has not been established.

Improved living conditions undoubtedly helped prevent the spread of leprosy. In spite of the absence of effective chemotherapy, the prevalence of leprosy sharply declined in Europe after the Middle Ages. This reduction was particularly apparent when and where improved housing and public health practices began to be implemented.

Map 1. Registered Leprosy Cases, 1985



Prepared by the Vector Biology and Control Project
Source Map: World Health Organization, 1985

The abundance of inadequate housing and poor public health practices in areas where leprosy is now highly prevalent also supports this theory.

a. Populations affected

There are many suggestions in the literature that leprosy may be more a rural than an urban disease, but supporting evidence is sparse. Interpretation of data is further confused by the tendency for leprosy patients in many countries to migrate to cities to seek medical care and escape the social ostracism they are more likely to suffer in a rural setting.

b. Endemic and epidemic disease

Leprosy is usually considered an endemic disease, but occasionally there are focal epidemics. An epidemic on the island of Nauru in the Pacific started in 1912 when the disease was introduced into the population by a patient from the nearby Gilbert Islands. There were four known patients in 1920, but by 1924, following an epidemic of influenza, at least 24 percent of the population of 1,200 were known to have the disease. The number of leprosy cases started to decline in 1927 and by 1981, less than one percent of the population had active leprosy. There have been less dramatic epidemics in New Guinea and Nigeria and, more recently, in Amazonia in Brazil.

c. Child survival

In highly endemic areas, there is a clear peak incidence at 10 to 14 years of age. Early detection and treatment can prevent progressive disease, mutilation and deformity.

The assumption that children are more susceptible to leprosy than adults, however, may be more apparent than real. Congenitally susceptible individuals may be selected out early in life and children may have greater exposure to infected individuals. In adults, leprosy is more common in males than in females (2:1), but in children the sex ratio is approximately 1:1.

Leprosy is not a cause of child mortality, except perhaps occasionally in untreated children with lepromatous leprosy. In adults,

leprosy is rarely an immediate cause of death, but population studies in India and other countries have found that mortality rates are three to four times greater among lepromatous patients than in the general population.

d. Economic impact

Approximately 30 percent of registered leprosy patients suffer from deformities and disabilities and about 250,000 people may be blind as a result of leprosy. It is difficult to measure the impact of leprosy on economic productivity in endemic areas, particularly because only about half of all leprosy cases are reported. It is clear, however, that preventable disabilities severely limit the productivity of many people with leprosy.

A recent study in the state of Tamil Nadu indicates that eliminating the deformity caused by leprosy would have a strong impact on productivity in India. Extrapolation of the study results to all of India's 645,000 leprosy patients with deformity suggests that eliminating deformity would increase productivity by $130 million a year.

3. Control Measures

For centuries, leprosy control consisted of segregation of patients in in hospitals or colonies known as leprosaria. Effective treatment was not available, and because of the stigma associated with what was considered a loathsome affliction, segregation often improved the socioeconomic status of leprosy patients. Although isolating patients may have had a minor effect on reducing incidence rates in some instances, any favorable result was offset by the social ostracism nurtured by such a practice.

a. Diagnosis

Early detection of leprosy is crucial to preventing disability and deformity, but diagnosis can be difficult because the disease appears in so many different forms. The definitive diagnostic signs of leprosy are reduction or loss of feeling in skin lesions, enlargement and tenderness of peripheral nerves, and the presence of acid-fast bacilli in a skin smear.

Skin-smear results are used to confirm leprosy diagnosis, classify the disease and monitor the effectiveness of chemotherapy. Skin smears are usually taken from at least one ear lobe and from the most active edges of two to four skin lesions. Accurate interpretation of smears depends on the skill of health workers and laboratory technicians and the condition of microscopes and other laboratory equipment.

b. Chemotherapy

Leprosy control changed dramatically after the discovery and use of sulfones to treat the disease in the early 1940s. Clinicians finally had an effective treatment. Therapy with diaminodiphenylsulfone (dapsone or DDS), an inexpensive, stable drug with minimal side effects, provided an alternative to segregation. The WHO promoted the concept that leprosy transmission could be interrupted by reducing and eventually eliminating the reservoir of the disease through DDS therapy of multibacillary patients.

Dapsone undoubtedly reduced the proportion of patients who became mutilated, and, where assiduously administered, also re-

duced the incidence of leprosy. It must be noted, however, that during this era socioeconomic conditions improved and extensive bacillus Calmette Guerin (BCG) vaccination programs were carried out in some endemic geographic areas. These factors probably contributed to reducing the incidence of leprosy.

Approximately 20 years after the introduction of the DDS, the first patients with DDS resistance appeared. Today, the extent of DDS resistance in many endemic areas is as high as 50 percent in newly diagnosed patients. The WHO discourages, even countermands, DDS monotherapy and urges that all newly diagnosed patients receive multidrug therapy (MDT), composed of various regimens of DDS, rifampicin and clofazimine, or one of the thioamides.

MDT was introduced as a dapsone monotherapy replacement by WHO's Special Programme for Research and Training in Tropical Diseases (TDR) in 1982. Unlike monotherapy with DDS, which must be administered throughout the life of a patient, MDT involves a much shorter drug regimen. Six months of treatment are required for the milder form of leprosy (paucibacillary) and two years' treatment for the multibacillary form. Recent MDT clinical trials have demonstrated a drastic reduction in prevalence, suggesting that it might be possible to interrupt transmission.

Chemoprophylaxis of household contacts has been effective in reducing incidence when carefully applied, but it is not widely practiced because of the danger of inducing drug resistance in people with subclinical infections, who may have minimal motivation for regular treatment. Inadequate chemoprophylaxis also may delay onset of disease instead of eradicating minimal or early disease.

c. Vaccination

The quest for a specific vaccine has been a high priority in leprosy research during the past decade. Because a specific vaccine against *M. leprae* is not yet available, there have been numerous studies to assess the protective effect of BCG, a vaccine that is used to protect people against tuberculosis.

Prospective BCG vaccination trials for leprosy in Uganda, Burma, Mali and Papua New Guinea have been well evaluated and widely publicized. The protective effect of BCG against leprosy in

these studies varied from a high of 80 percent in Uganda to a low of 20 percent in Burma. The protective effect in New Guinea was approximately 46 percent. The differences in the results of these trials seem to reflect genuine variations in the efficacy of BCG in different areas, but the reasons for these variations remain obscure.

After the discovery of the nine-banded armadillo's susceptibility to leprosy, sufficient quantities of *M. leprae* were available from the infected tissues of armadillos to undertake development of a specific anti-leprosy vaccine. The WHO Immunology of Leprosy Program (IMMLEP) was initiated in 1984 to develop a vaccine against leprosy and methods for detecting subclinical infection.

d. Constraints to control

The main shortcomings in leprosy control are the result of 1) inadequate methods of case detection; 2) inappropriate treatment; 3) inadequate infrastructures for health care delivery and 4) lack of an effective anti-leprosy vaccine.

Case detection

Early detection and effective treatment of leprosy can prevent disability and deformity, but current case detection methods result in the registration of less than half of all leprosy cases.

A variety of active methods have been used for early case identification and registration, including screening schoolchildren, job-site screening and rapid surveys combined with general health examinations. Most cases, however, are identified through self-reporting, referral and notification. This passive detection is severely handicapped by the social stigma associated with leprosy, which makes many people reluctant to seek treatment. Case detection must be supported by health education to dispel myths about leprosy, emphasize the importance of early identification, teach people to recognize the early symptoms of the disease, and inform them about where to seek diagnosis and treatment.

Treatment

Many leprosy patients are still treated with DDS therapy. The WHO recommended the use of MDT to treat multibacillary patients 10 years ago, but less than half of all registered leprosy patients have been put on MDT.

Few countries have established effective delivery systems for combination therapy. Funding and operational capability are the major obstacles to implementation. In the early stages of MDT programs, additional funding is required to train personnel in the use of therapeutic regimens. However, it is anticipated that more effective treatment programs will sharply reduce the number of patients, thus reducing expenditures. Moreover, although the initial cost of MDT is more expensive than DDS treatment, the treatment regimens are shorter and more cost-effective.

Health care delivery

Integration of leprosy care into primary health care delivery systems will further reduce costs and extend treatment coverage. This will require targeted programs for training general health care personnel in leprosy diagnosis and treatment and for improving supervision and program management. Patients on MDT must be monitored carefully to promote compliance and avoid interruption of treatment. WHO recommends that, if possible, paucibacillary patients and their household contacts be kept under surveillance for at least two years and multibacillary patients and their contacts for five years.

The success of any leprosy control program depends on the ability of developing countries to train and supervise paramedical and auxiliary personnel. WHO awarded more than 300 fellowships for training in leprosy control to developing country personnel between 1960 and 1974. Unfortunately, by 1976, the awards had fallen to six a year.

Well-organized formal courses on leprosy control are offered at regional training and research centers in Venezuela, Ethiopia, Senegal, Liberia, India and the Philippines. The American Leprosy Missions, the Leprosy Mission International, the German Leprosy Relief Organization, the Damien Foundation and the Leonard Wood Memorial are a few of the voluntary agencies that have provided major support for training and field programs. These activities are generally coordinated through WHO and the International Federation of Antileprosy Associations (ILEP). Regional workshops are held regularly, but it is important that financial assistance be provided for public health staff of leprosy-endemic countries to attend these important training sessions.

Most endemic countries need long-term plans for leprosy control personnel requirements and trained teachers to imple-

ment such plans. The cooperation of WHO and other voluntary agencies in developing long-term plans would be invaluable. On the other hand, every effort must be made to increase the involvement of local government agencies. Providing career opportunities for personnel in leprosy work would attract competent, highly motivated individuals to the field.

Progress in many leprosy programs has been disappointing, primarily because of a failure to accurately define the magnitude of the problem and provide realistic estimates of the human and financial resources necessary to attain program objectives. Expanded use of MDT may eventually lead to the control of leprosy, but an effective vaccine is the most obvious solution to these constraints.

4. Current Research

a. Diagnosis

Early diagnosis and the detection of subclinical infection are active areas of research. Specific immunodiagnostic tests are required to detect infection and, if possible, the risk of disease. Several studies indicate that specific antibodies can be detected in nearly all multibacillary patients early in the disease. These antibodies are being used in an effort to develop specific immunodiagnostic tests for leprosy. They also will be used to determine whether the antigens against which they are directed are capable of inducing cell-mediated immune responses.

Widespread use of immunodiagnostic techniques could greatly enhance leprosy control and prevent the serious effects of the disease, but much more data are needed to establish the usefulness of these serologic methods in early diagnosis. Several long-term programs to assess these methods are in progress.

Skin test antigens are being developed, but the use of these antigens as diagnostic reagents does not appear promising.

b. Chemotherapy

One of the primary goals of current leprosy research is to assess the efficacy of MDT in patients with multibacillary disease. Trials evaluating the effect of MDT on both multibacillary and paucibacillary leprosy are in progress in many countries. Operational research is also being conducted to determine the efficacy of even shorter MDT regimens.

Recent studies demonstrate that MDT can greatly reduce the prevalence of leprosy. In Malawi, for example, the number of cases was reduced from more than 13,500 to about 3,500 in 1987 and 1,895 in 1989. Continued use of MDT has the potential for interrupting transmission in Malawi.

A.I.D.'s Office of Health supported a five-year MDT study conducted by the AmeriCares Foundation and the Institute of Biomedicine in Caracas from 1985 to 1990. More than 55 percent of

the registered leprosy patients in Venezuela participated in this study. By July 1990, 60 percent of all participants had been released from treatment as cured and no relapses had been reported. In Area I, where the pilot phase of the study began in 1985, 2,253 people received supervised MDT and 70 percent of them were released from treatment. In Area II, 3,305 patients were treated and 51 percent were released from treatment. The compliance rate for the study was 87.8 percent.

In addition to evaluating different regimens of established anti-leprosy drugs, some agencies are supporting efforts to develop new anti-leprosy drugs. Betalactam antibiotics, aminoglycosides, quinolones, rifampin analogs and others are being assessed. Emphasis must be placed on assaying the efficacy of new drugs or drug regimens in animals that develop lepromatous leprosy. The nine-banded armadillo is the only immunologically-intact species that regularly develops lepromatous leprosy after inoculation with *M. leprae*. Unfortunately, no experimental chemotherapy studies have been reported using this animal model.

c. Vaccine Development

Leprosy vaccines have two potential uses: immunoprophylaxis and immunotherapy. Immunoprophylaxis studies are designed to protect people at risk. Studies of immunotherapy in combination with chemotherapy are intended to stimulate the cell-mediated immune response of lepromatous patients, resulting in the rapid elimination of *M. leprae* from their tissues.

Vaccines combining heat-killed *M. leprae* with BCG have recently been developed and are being field tested in Malawi and Venezuela. It is hoped that this vaccine combination will induce a strong immune response in patients who previously had little or no response.

5. Leprosy from the A.I.D. Perspective

Leprosy remains a serious problem in many A.I.D.-assisted countries. Current A.I.D. health sector emphasis on child survival de-emphasizes leprosy as a priority disease for the Agency. However, A.I.D. has had a tradition of supporting research in detection, treatment and vaccine development through TDR and other WHO divisions. Most recently, A.I.D.'s Office of Health supported a five-year MDT study by the Venezuelan leprosy control program, the Pan American Health Organization and the AmeriCares Foundation.

a. The Horizon

The next 10 years will bring many technological advances in immunodiagnosis and treatment. The promising results of recent MDT trials indicate that it is theoretically possible to interrupt leprosy transmission. Leprosy control and treatment programs will be integrated into primary health care systems. Through its support of WHO's efforts, the Agency can continue to play a major role in leprosy control in the future.

b. Priorities for future action

- Operational research in treatment, including expansion of the evaluation of MDT.
- Development of animal models for experimental chemotherapy and vaccine studies and cultivation of *M. leprae in vitro* to enable scientists to do the detailed metabolic studies that would point the way to developing antimicrobial agents.
- Control in high-risk populations through early detection and effective treatment. Early detection can be facilitated by improving the training of health care delivery personnel in the diagnosis of leprosy and effective surveillance of MDT. Laboratory and field research on serologic techniques for the early detection of leprosy are of high priority.
- Development of an effective vaccine against *M. leprae*.

- Integration with primary health care systems and community participation. Such integration requires large-scale programs to train health care personnel in the management of leprosy. Effective community participation will occur only if the community is well-informed about the disease.

- Operational research in diagnosis, including expanded studies to detect subclinical infections in inhabitants of leprosy-endemic areas.

- Epidemiologic studies to determine the role of sooty mangabey monkeys, other nonhuman primate species, and wild armadillos as reservoirs of *M. leprae*.

6. Selected References

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Annex 1

Table 1. Number of Registered Patients and Prevalence of Leprosy

Country	Population ($x10^3$)	No. of Registered Cases	Year	Prevalence Rate Per 1,000
		AFRICA		
Angola	9,481	4,046	1988	0.43
Burkina Faso	8,684	13,312	1988	1.53
Burundi	5,359	75	1989	0.01
Cameroon	10,633	12,302	1988	1.16
Cape Verde	352	491	1989	1.39
C.A.R.	2,879	7,096	1988	2.46
Chad	5,428	10,651	1988	1.96
Comoros	435	83	1987	0.19
Congo	2,269	6,416	1989	2.83
Ethiopia	44,727	31,753	1988	0.71
Equatorial Guinea	420	47	1987	0.11
Gambia	812	440	1988	0.54
Ghana	13,900	7,773	1989	0.56
Guinea	6,541	15,818	1988	2.42
Guinea Bissau	945	1,179	1988	1.25
Kenya	23,100	3,188	1988	0.14
Lesotho	1,676	78	1988	0.05
Liberia	2,400	4,589	1988	1.91
Madagascar	10,723	19,210	1988	1.79
Malawi	9,270	1,895	1989	0.20

Source: Leprosy Epidemiological Bulletin No. 5, July 1990. WHO Collaborating Centre for the Epidemiology of Leprosy. Prepared by E. Declercq and M.F. Lechat.

Table 1 (cont.)

Country	Population ($x10^3$)	No. of Registered Cases	Year	Prevalence Rate Per 1,000
		AFRICA		
Mali	8,824	22,121	1988	2.51
Namibia	1,500	26	1989	0.02
Niger	6,688	6,279	1988	0.94
Nigeria	105,471	193,715	1988	1.84
Rwanda	712	70	1989	0.10
Sao Tome	114	4	1987	0.04
Senegal	6,978	11,554	1988	1.66
Seychelles	66	41	1987	0.62
Sierra Leone	3,969	1,680	1989	0.42
South Africa	36,470	962	1988	0.03
Swaziland	680	42	1988	0.06
Tanzania	25,397	9,305	1988	0.37
Togo	3,247	3,987	1988	1.23
Uganda	17,189	23,000	1988	1.34
Zaire	34,650	14,740	1988	0.43
Zambia	7,851	7,469	1988	0.95
Zimbabwe	7,967	369	1989	0.05

Table 1 (cont.)

Country	Population ($x10^3$)	No. of Registered Cases	Year	Prevalence Rate Per 1,000
		AMERICAS		
Argentina	32,425	9,809	1989	0.30
Belize	180	0	1988	0.00
Bolivia	6,918	1,706	1987	0.25
Brazil	144,427	256,979	1988	1.78
Colombia	29,789	17,839	1988	0.60
Costa Rica	2,866	389	1989	0.14
Cuba	10,405	5,806	1988	0.56
Dominican Rep.	7,012	1,098	1989	0.16
Ecuador	10,204	1,047	1988	0.10
El Salvador	4,934	6	1987	0.001
Guatemala	8,680	278	1986	0.03
Guyana	1,006	120	1988	0.12
Haiti	6,263	558	1985	0.09
Honduras	4,717	82	1989	0.02
Jamaica	2,392	20	1989	0.01
Panama	2,227	102	1987	0.05
Paraguay	4,157	3,056	1989	0.74
Peru	21,255	1,604	1988	0.08
Uruguay	2,788	279	1987	0.10
Venezuela	19,246	4,158	1989	0.22

Table 1 (cont.)

Country	Population ($x10^3$)	No. of Registered Cases	Year	Prevalence Rate Per 1,000
		SOUTHEAST ASIA		
Bangladesh	112,539	21,191	1989	0.19
Burma	37,614	253,285	1985	6.73
China	1,103,983	68,666	1988	0.06
India	820,000	2,692,927	1989	3.25
Indonesia	175,630	121,512	1988	0.69
Nepal	18,234	25,361	1989	1.39
Sri Lanka	16,832	2,416	1989	0.14
Thailand	55,537	16,663	1989	0.30
USSR	283,682	2,689	1988	0.01
		EASTERN MEDITERRANEAN		
Afghanistan	15,090	1,680	1988	0.11
Cyprus	684	102	1988	0.15
Djibouti	383	70	1978	0.18
Egypt	51,453	10,196	1989	0.20
Iran	53,126	13,761	1988	0.26
Iraq	17,656	500	1980	0.03
Jordan	2,897	20	1987	0.01
Lebanon	2,827	45	1984	0.02
Oman	1,377	651	1989	0.47

Table 1. (cont.)

Country	Population ($x10^3$)	No. of Registered Cases	Year	Prevalence Rate Per 1,000
EASTERN MEDITERRANEAN (cont.)				
Pakistan	114,939	16,226	1987	0.14
Saudi Arabia	13,070	76	1987	0.01
Somalia	7,106	746	1988	0.10
Sudan	23,797	51,716	1988	2.17
Tunisia	7,809	145	1987	0.02
Yemen	769,911	2,379	1989	0.24
WESTERN PACIFIC				
Fiji	7[illegible]2	204	1988	0.27
Korea	42,621	21,707	1988	0.51
Laos	3,846	3,019	1988	0.79
Papua New Guinea	3,661	5,188	1989	1.42
Philippines	60,097	23,999	1989	0.40
Thailand	55,537	16,663	1989	0.30
Vietnam	59,872	38,219	1988	0.64

Table 1 (cont.)

Country	Population ($x10^3$)	No. of Registered Cases	Year	Prevalence Rate Per 1,000
		EUROPE		
Greece	10,593	19	1989	0.002
Israel	4,442	203	1989	0.05
Italy	57,265	540	1980	0.01
Morocco	20,420	3,485	1981	0.17
Portugal	10,246	1,168	1989	0.11
Spain	39,053	5,055	1984	0.13
Turkey	53,213	3,466	1989	0.07