Leprosy: Steps Along the Journey of Eradication

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Leprosy, or Hansen's disease, is a chronic, infectious disease caused by the *Mycobacterium leprae*, which has been associated throughout its history with extreme prejudice, fear, and revulsion. Through the passage of time, the disease has spread globally to affect nearly all regions of the earth. It remains one of the leading causes of deformity and physical disability from a communicable disease, affecting millions of individuals worldwide, despite evidence that suggests more than 95% of the world's population has natural resistance to development of the disease.[1,2]

In addition to the disease's physical effects, patients historically have suffered severe social stigma and ostracism from their families, communities, and even health professionals to such an overwhelming extent that leprosy has been known as "the death before death" since ancient times.[3] Although much remains unknown about the disease transmission and pathogenesis, tremendous advances have occurred in the understanding and treatment of the disease. In the past two decades, the marked success of combined efforts from the World Health Organization (WHO), local governments, health professionals, and nongovernmental organizations (NGOs) in identifying patients with leprosy and providing effective treatment to them has resulted in an almost 90% reduction in the global prevalence of leprosy.[1] This statistic has generated substantial hope that success can be achieved in alleviating the effects that this ancient disease has had on millions of patients and raising the possibility that the disease can be eliminated in the near future.

ORIGINS AND SPREAD OF THE DISEASE

There has been substantial debate as to whether leprosy originated in ancient Eastern Africa or India centuries ago; however, the origins will likely never be known with any degree of certainty. Early written records giving clinical descrip-

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tions generally accepted as being true leprosy date from 600 BC to possibly as early as 1400 BC in India, where a disease called *Kushta* was distinguished from *vitiligo*.[4] Chinese documents from about 500 BC that mention skin lesions, numbness, and loss of eyebrows attest to the spread of the disease eastward to China and subsequently to Japan.[5] The disease was thought to have spread to the Middle East and westward to Greece by conquering armies or traders. The return of Alexander the Great's armies from the India campaign of 327–325 BC is noted as a likely event for the spread of the disease, particularly when coupled with the contemporaneous mention by Greek physicians of a novel disease called *elephantiasis Graecorum*.[4,6] The disease may have originally been spread around the Mediterranean basin and to Western Europe by the Romans, and its spread then may have intensified during the Crusades.[3,5]

There appeared to be rampant spread followed by an unexplained decline of the disease throughout much of Europe during the Middle Ages (1000–1400 AD), as evidenced by the presence of hundreds of "Lazar houses" (a special colony for people with a repulsive disease—frequently administered by religious orders) to house diseased individuals during this period. The prevalence of the disease during this period cannot be readily ascertained due to likely misdiagnosis and misclassification of large numbers of inhabitants; however, characteristic findings of leprosy in the skeletal remains of residents (e.g., *facies leprosa*—erosion of the anterior nasal spine, erosion of maxillary alveolar processes, and perforation of the hard palate) suggest that true leprosy was indeed quite common during this period.[5,6] The factors involved in the near self-elimination of the disease in Europe remain unknown. Possible explanations have been offered, such as the rise in standards of living, the widespread death of the most vulnerable population due to the black plague, or perhaps cross-reactive protective immunity from the parallel increase in tuberculosis during medieval times.

European explorers and the slave trade likely introduced leprosy to Western Africa and the Western Hemisphere within the past 500 years. A comparative genomics study evaluating rare single-nucleotide polymorphisms of leprosy supports the historical evidence of transmission of the disease through successive migrations of populations, as well as the migration of the disease from the Far East to the Pacific Islands as recently as the 19th century.[7]

By the mid-1980s, the global burden of disease was estimated at about 10 million to 12 million patients, with 122 countries reporting endemic cases of leprosy to WHO. Of note, the disease burden was unevenly concentrated, with the majority of the cases (>90%) occurring in the developing world, showing marked variation in prevalence rates from <1 case per 10,000 population to >500 cases per 10,000 population.[8]

CULTURAL ATTITUDES TOWARD LEPROSY

Due to the potential severe deformities and disfigurement associated with untreated disease, there has been a history of fear, stigma, and revulsion toward victims afflicted with leprosy throughout time and across cultures.[3,9] Since ancient times, there has been a link between leprosy and sin. In Jewish tradition and in the regions of ancient Mesopotamia, there is an association between chronic skin disease and ceremonial uncleanliness requiring ritual purification and quarantine. Shintoism in Japan uses the same word for both leprosy and sin.[4] China linked the concept of personal guilt to the presence of repulsive skin diseases. Leprosy as the embodiment of evil forces also comes from the theory of *feng shui*, which held that individuals with leprosy needed to be buried alive to prevent spread of the disease to other members of the family and community.[3] In ancient Benin, the darkest forces of nature were considered the source of the disease that was given to its victims as a punishment.[9] And Hindu belief was that the disease was contracted as a form of divine punishment.[10]

Of historical impact, much of the stigma associated with the Western view of leprosy likely stemmed from an erroneous translation of Biblical passages in Leviticus by scholars from Alexandria around the third century BC. The scholars translated the Hebrew term regarding unclean acts or conditions from the Hebrew term *tsara'ath*, associated with chronic skin conditions as previously mentioned, into the Greek word *lepra*, which was a word used by Greek physicians for a scaly skin condition as well as describing bark and flakes.[4] Although much evidence today suggests that Hansen's disease, or true leprosy, is not the condition of concern in Leviticus and other biblical passages, the connection of the word *lepra* to leprosy was a major influence in Western attitudes about the victims of the disease being unclean and the subsequent shunning and isolation of the victims from the rest of society in a leprosarium.[3,11] In medieval times, leper masses were held in which diseased people were declared officially dead as far as the church and society were concerned, and were banished and forced to wear distinctive clothing and announce their presence with bells or clappers.[5]

Unfortunately, social stigma, alienation, and violence against sufferers of leprosy are attitudes that have continued through the ages up to the 20th century and

that still exist today. Feeny gives a number of examples of persecution within the past century. In the U.S., a man was left alone to die of exposure and starvation in a cattle truck; in China in 1937, 80 victims with leprosy, including women and children, were shot and thrown into a lime pit; and in Korea in 1957, a mob beat 10 patients from a leprosarium to death.[3] Stigmatizing attitudes have even been incorporated into modern law, as demonstrated in India where the Motor Vehicles Act of 1939 forbade the granting of drivers' licenses to leprosy sufferers and, until recently, the Indian Christian, Muslim, and Hindu marriage acts included leprosy as grounds for divorce.[10]

ADVANCES IN THE UNDERSTANDING AND TREATMENT OF LEPROSY

One of the first advances away from the age of superstition into the modern scientific era occurred in response to the last endemic wave of leprosy in Europe, which peaked in Norway in the mid-1800s, when approximately 3,000 cases were reported.[5] As a result of detailed investigation of the disease's characteristics, Dr. Daniel Danielssen and Dr. Carl Boeck published a groundbreaking book, *Om Spedalskhed* (*On Leprosy*), in 1847. The book is recognized as the first authoritative publication clearly distinguishing leprosy from other infectious diseases affecting the skin, such as syphilis, psoriasis, and scurvy, and describing the two main forms of true leprosy with illustrations. In 1873, Dr. Danielssen's son-in-law, Dr. Gerhard Armauer Hansen, was the first to identify the causative agent of leprosy, *Mycobacterium leprae* (*M. leprae*), when he discovered multiple rod-shaped bacilli while examining a patient's nasal biopsy specimen under a microscope.[3–5] Even though Hansen's discovery was the first bacteria identified as a human pathogen, attempts to develop standard bacteriologic or cell cultures remain unsuccessful to this day.

Prior to the age of antibiotics, leprosy was treated with chaulmoogra oil, an extraction from the seeds of *Hydnocarpus wightiana*, with some limited success.[4,12,13] The modern era of leprosy treatment started in the 1940s, when Dr. Guy Faget of the National Hansen's Disease Center (renamed the Gillis W. Long Hansen's Disease Center in the 1980s) in Carville, Louisiana, was able to show remarkable benefits of sulfone therapy (Promin) in treating the disease. This discovery was heralded as "the miracle of Carville" and marked the onset of the first real hope that what was now called Hansen's disease (HD) could be successfully treated and "cured."[5] In the late 1940s, further work on limiting the toxicity of treatment led to the use of dapsone, the parent compound of Promin, which was broadly used as long-term monotherapy until the onset of drug resistance was noted in the 1970s.[4]

In the 1960s, there was a growing appreciation that the broad spectrum of clinical responses to infection was due to variations in the cellular immune response of the individuals infected with HD. Building on the concept of the immunopathologic spectrum of the disease put forth by Dr. Olaf Skinsnes of the University of Hawaii School of Medicine, Dr. Dennis Ridley of the Hospital for Tropical Diseases in London and Dr. William Jopling of Jordan Hospital, Surrey, England, helped to unify clinical practice and develop a practical system to classify the clinical, histopathologic, and immunologic findings associated with the diversity of disease presentation.[2,14] At one end of the disease spectrum, called polar tuberculoid disease (TT), patients have a relatively well-developed cell-mediated immune response and delayed hypersensitivity. TT patients present with a single, well-demarcated skin lesion exhibiting loss of sensation to heat and touch. Biopsies of these skin lesions show a well-formed granulomatous inflammatory response and rare acid-fast bacilli within the granuloma and affected peripheral nerve.

At the other end of the spectrum, polar lepromatous (LL) patients exhibit poor T-cell immunity and appear unable to mount an effective immune response to *M. leprae* despite the presence of a marked increase in circulating antibodies. LL patients present with numerous, poorly demarcated skin lesions that exhibit sensory loss and, upon biopsy, reveal a disorganized immune response with large numbers of bacilli within macrophages and nerve tissue.

The vast majority of HD patients fall into borderline categories—between these two polar extremes—with classifications of borderline tuberculoid, borderline borderline, and borderline lepromatous forms of the disease, and are considered to have an unstable immunologic response with periods of increasing immune effectiveness (upgrading) and decreasing cellular immune response (downgrading) as the disease progresses.[2,15] In recent years, WHO further simplified this classification into paucibacillary (having five or fewer skin lesions) and multibacillary (having greater than five skin lesions) disease states—roughly correlating to the effectiveness of cellular immunity and corresponding bacterial load—in an effort to simplify and standardize clinical diagnosis and operational treatment regimens globally.

Research into additional therapies and treatments was tremendously accelerated by the discovery in 1960 by Dr. Charles Shepard of the Communicable Disease Center (now the Centers for Disease Control

and Prevention) that *M. leprae* could be cultivated in the footpads of mice.[5,15] The further discovery in 1968 by Dr. Eleanor Storrs and Dr. Waldemar Kirchheimer of the Gulf South Research Institute in New Iberia, Lousiana, that the nine-banded armadillo was also susceptible to disseminated HD enabled the harvesting of substantial quantities of the bacteria to bolster vaccine trials and other HD research efforts.[2,5,15] Further studies by Richard J. Rees of the National Institute for Medical Research in London on athymic mice led to enhanced multiplication of the bacillus and greatly advanced the study of the physiology and genetics of the organism.[2,5,15] In the absence of viable standard bacteriologic and cell-culture media, which persists to the present, the importance of this pioneering work in increasing the availability of viable bacilli to support today's ongoing genomic and proteomic HD research is immeasurable.

Emergence of resistance to dapsone

The initial enthusiasm for conquering HD was dampened by the emergence of treatment relapses and drug resistance to dapsone in the 1970s of up to 19% of patients.[16] In response, WHO supported the establishment of the Special Program for Research and Training in Tropical Diseases in 1976 to evaluate effective responses to dapsone resistance and promote the development of vaccines.[15,17] In 1982, WHO recommended the use of multidrug therapy (MDT) protocols combining rifampin, clofazamine, and dapsone in the treatment of HD. Paucibacillary patients were to be treated for six months and multibacillary patients were to be treated for 12–24 months.[15] The response to MDT treatment was very gratifying, with a relapse rate of <1% for multibacillary disease and slightly >1% for paucibacillary disease. The renewed hope that the disease could be controlled led to a World Health Assembly announcement in 1991 of a goal to "eliminate leprosy as a public health problem," defined as reducing the global prevalence of HD to <1 case per 10,000 population by the year 2000.[16]

Epidemiology—gaps in knowledge

To accurately assess the challenges in meeting WHO's elimination goal, one needs to be aware of the remaining gaps in knowledge about the epidemiology and treatment of HD. Despite the tremendous advances reviewed in this article, much remains unknown about the source, transmission, susceptibility, and pathogenesis of the disease.

M. leprae is slow-growing, with a doubling time of 11 to 13 days. It is an obligate, intracellular parasite that grows best at 27°–30°C, which is consistent with the characteristic major target organs of the disease in humans as the skin, peripheral nerves, nasal mucosa, upper respiratory tract, and eyes. The natural reservoir of the disease is thought to be humans, with an average period of incubation of three to five years. The disease has been discovered in wild armadillos in the southern United States and has been reported in three species of nonhuman primates (chimpanzees, cynomolgus macaques, and sooty mangabey monkeys), but these are not thought to be significant sources for human disease. The mechanism of transmission is not well known; however, the ulcerated nasal mucosa of multibacillary patients can yield more than 10 million viable bacilli per day, which is supportive of transmission via respiratory droplet spread.[8] Additionally, organisms have been found to survive for up to nine days outside of the human host under tropical conditions, raising the possibility of contact spread through broken skin. The possibility of the disease being spread through insect vectors also cannot be definitively excluded.[8]

Much also remains unknown about disease susceptibility and the pathogenesis of the disease. More than 95% of people have innate resistance to development of the disease after an exposure. Of those who do develop an infection after the three- to five-year incubation period, a substantial number of these patients will heal spontaneously. The factors that lead to variations in cellular immune response seen in paucibacillary disease vs. multibacillary disease are not completely understood, but there is emerging evidence that a substantial number of genetic factors play an important role in modulating the host immune response.[2,12]

The hallmark of HD is the unique ability of *M. leprae* to survive within the Schwann cells of peripheral nerves as well as within macrophages. The bacterium itself is of very low virulence and is essentially nontoxic to tissues. However, the infected nerves and surrounding tissues can be damaged as the host mounts an immune response to bacterial antigens. Two types of immune reactions are seen in HD. Type 1, or "reversal reaction," is a delayed-type hypersensitivity reaction; Type 2, *erythema nodosum leprosum*, is thought to be an immune complex disorder. The factors that trigger these immune responses are not well understood, and the reactions can occur during the natural course of untreated disease, during antimicrobial therapy, or after completion of antimicrobial "cure" of the infection. If the reactions are not medically managed appropriately, the patient will experience permanent sensory, motor, and/or autonomic peripheral or other nerve damage, which may result in severe disability (e.g., claw hands, claw toes, and/or foot drop). Secondary infections and disfiguring injuries due to loss of sensation in the

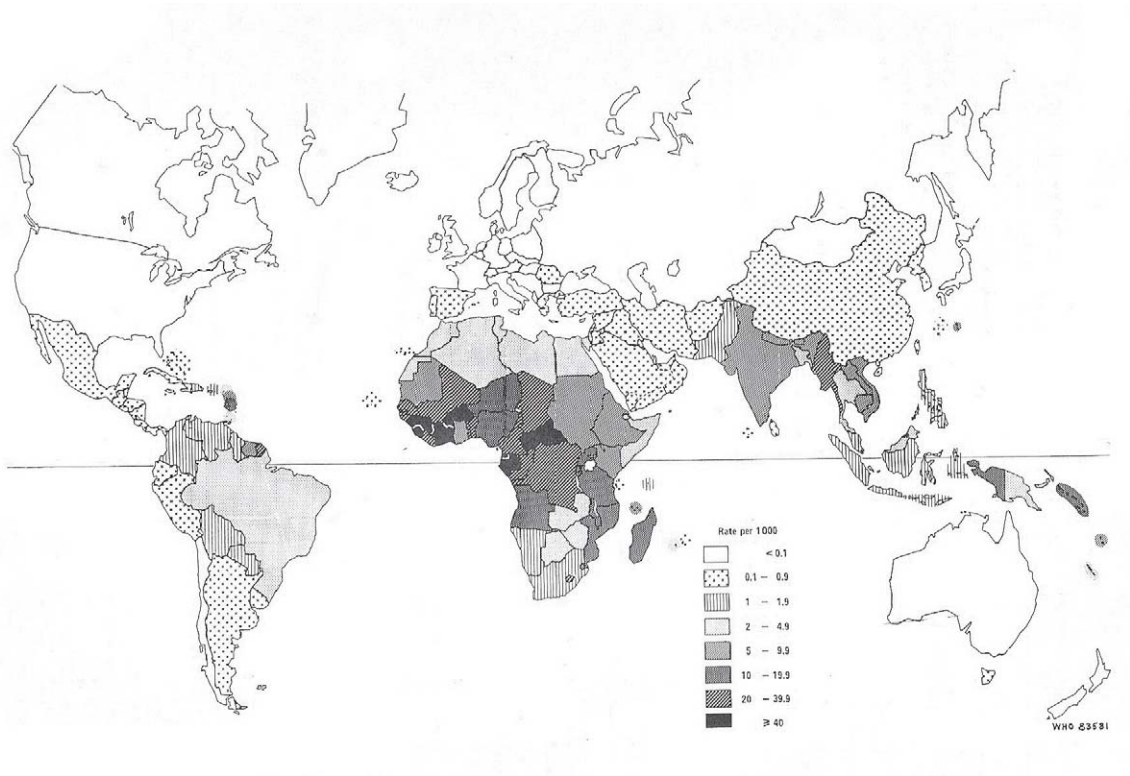
affected areas can further compound physical disabilities and have marked social consequences related to stigma, in addition to impairing patients' abilities to earn a living and care for themselves.

Another significant gap in knowledge is the lack of a simple and effective screening test to identify individuals or populations with subclinical disease or asymptomatic infections. Promising technologies in the form of detecting *M. leprae* through polymerase chain reaction or with measuring antibodies to phenolic glycolipid-1 are on the horizon.[2,15] However, in the absence of effective screening tools, the early treatment of disease depends primarily on either self-identification by the patient or a high index of suspicion by the clinician when evaluating a patient with a skin lesion associated with sensory loss.

Results of WHO's MDT programs

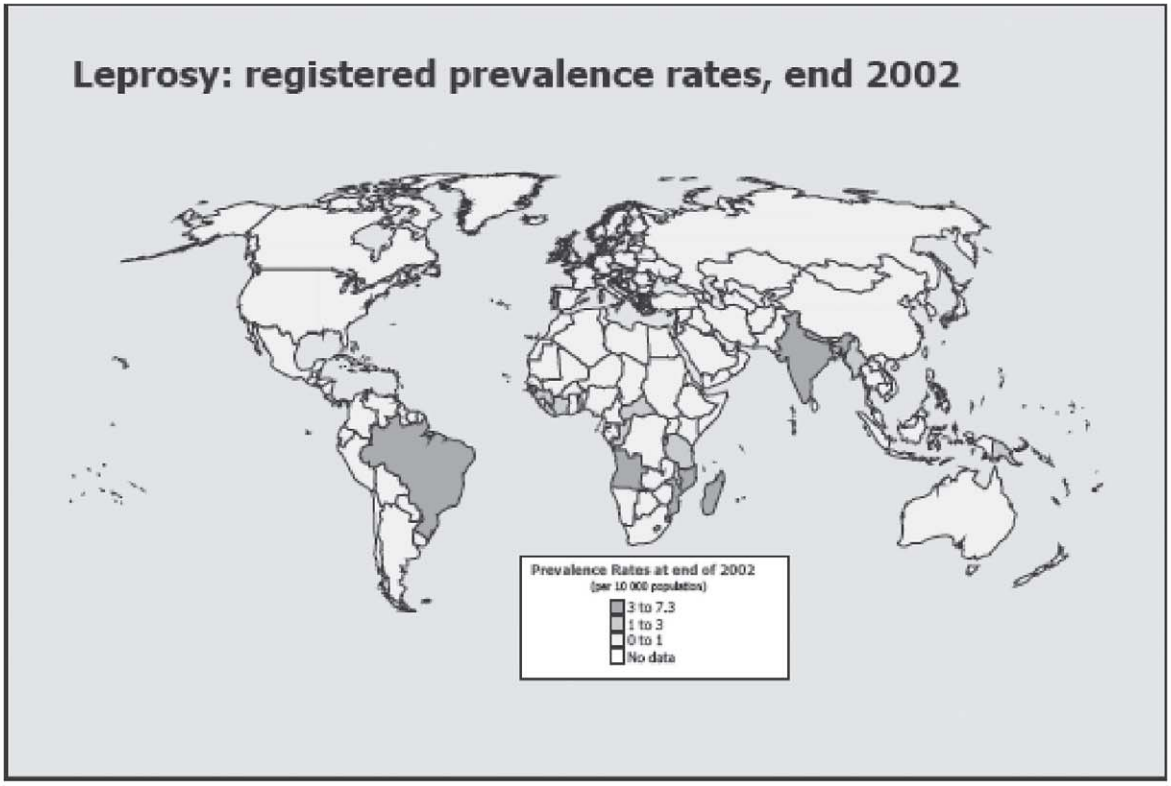
Working with local governments, health-care professionals, and NGOs (such as the Nippon Foundation, the International Federation of Anti-Leprosy Associations, the World Bank, and Novartis), WHO-supported programs using the revised MDT regimens were very successful in treating HD patients. The control activities were multipronged, with efforts in enhanced diagnosis, provision of MDT, and follow-up care, including patient counseling and community education to decrease stigma and increase self-reporting.[1] In 1985, 122 countries were reporting endemic disease (prevalence rate >1 per 10,000 population) with an estimated global prevalence of 10 million to 12 million cases (Figure 1).[8] By 1994, the estimated number of cases had dropped to 2.7 million, of which WHO estimated 1.9 million cases were being followed on disease registries.[16] Starting in 1995, WHO further strengthened its programs by providing MDT medications free to endemic countries. By 2002, the number of countries reporting endemic HD had dropped from 122 to 12 (Figure 2).[18] This number subsequently dropped further to nine countries by 2003.[1] At the end of 2003, these nine countries—India, Brazil, Nepal, Mozambique, Madagascar, Angola, Central African Republic, Democratic Republic of the Congo, and United Republic of Tanzania—accounted for 84% of the global prevalence and 88% of the

Figure 1. Distribution of leprosy in the world



SOURCE: Noordeen SK. The epidemiology of leprosy. In: Hastings RC, editor. Leprosy. 1st ed. Edinburgh (Scotland) and New York: Churchill Livingstone; 1985. p. 16.

Figure 2. Registered prevalence rates of leprosy, 2002



SOURCE: World Health Organization. Leprosy elimination project: status report 2003. Geneva: WHO; 2004.

515,000 new cases detected. From the 1980s through 2004, more than 14 million cases of HD had been treated with MDT.[1]

Perhaps of equal or greater importance is the progress that HD treatment programs have made in decreasing social stigma and increasing community and health professional awareness that HD is a treatable condition, though it must be acknowledged that overcoming centuries of ingrained cultural beliefs is not easy. Progress in overcoming social stigma and the provision of effective chemotherapy to millions of patients in treating active infection is indeed an enormous accomplishment that should not be minimized. However, it is the coordination of efforts in increasing the awareness of governments, health professionals, and the public to the benefits of early detection and treatment of the disease, followed by the management of disease reactions, that allows for the avoidance or minimization of permanent nerve damage and potentially devastating sequelae. The hallmark of the program's ultimate success is the minimization or avoidance of permanent disability, enabling individuals with HD to lead productive lives as an integral part of their community.

Sustaining progress and future efforts

In the span of two decades, the reported global prevalence of active HD infection had dropped by almost 90%.[18] Of potential concern is the lack of a parallel drop in the detected disease incidence. From 1994 through 2003, the annual new case detection rate has persistently been >500,000 new cases annually.[18] Acknowledging the limitations inherent in the use of operational data in the absence of true incidence data, the question arises whether the current chemotherapy program efforts are breaking the chain of disease transmission.[2] Once again, the gaps in fundamental knowledge about the disease reservoir(s), mechanism of disease transmission, and inability to screen for latent or subclinical disease leave the question of the role, if any, of antibiotic treatment in eradication of the disease unanswerable at present. It is illustrative to note that the marked decline in incidence and prevalence of HD in many developed countries preceded the onset

of antibiotic treatment. The factors associated with this decline remain unknown, although associations with improved living conditions have been postulated.

Also of concern is the potential impact of success. Public health programs depend on public funding, and these limited resources are focused on areas with the greatest perceived need or potential benefit. As progress in treating HD is celebrated, and rightfully so, there is a potential risk that this progress will lessen the perception of the benefit in continuing to spend resources on HD, as other competing priorities (e.g., human immunodeficiency virus/acquired immunodeficiency syndrome, malaria, and tuberculosis) may appear to be of relatively greater importance. The experience of the resurgence of drug-resistant tuberculosis in the U.S. after public health resources were diverted to other priorities might be instructive of the need to continue to devote appropriate resources to a communicable disease that has at present left one million to two million individuals around the globe with permanent disabilities.[19] It should be remembered that the management of this disease requires both treating the bacterial infection as well as minimizing the potential for permanent nerve damage and subsequent impairment.

Additionally, the question of whether success can lead to a paradoxical delay in treatment and an increase in the severity of impairment should be considered. As a disease or condition becomes more rare, it takes a higher index of suspicion for a treating physician to appropriately diagnose or refer a patient for care. The average time from case presentation to diagnosis in the U.S., where the disease is rare, is about two years.[20] During this time of misdiagnosis (or, perhaps more appropriately, missed diagnosis), there is a risk of avoidable permanent tissue and nerve damage. Some have suggested that a lowered index of suspicion and delay in diagnosis may explain the increase in proportion of multibacillary and disability cases seen in some countries where marked success in treating HD has occurred.[21]

CONCLUSION

HD continues to exhibit a number of paradoxes. It is one of the oldest diseases known to man and was the first human bacterial pathogen discovered; however, substantial gaps in our fundamental knowledge of this disease persist relative to other infectious diseases. More than 95% of the population has natural resistance to the disease, modern antibiotic treatment is available to eradicate a patient's infection, and early treatment can prevent or substantially limit the consequences of the disease. Yet, there remain substantial cultural myths, superstitions, and stigma associated with HD that inhibit early recognition of the disease and treatment-seeking behavior.

Despite many obstacles and barriers, substantial progress has been made in providing treatment to millions of individuals and in overcoming social stigma and myths.[22,23] Hopefully, the progress made to date will be maintained and further advanced through the application of the sustained political will of governments, ongoing research into basic understanding of the disease and improved treatments or vaccines, and maintaining a high index of suspicion in both the public and medical communities that HD might be a treatable cause of a patient's condition. If so, there may be hope that HD will some day no longer be one of the leading causes of physical disability in the world.

REFERENCES

1. World Health Organization. Global strategy for further reducing the leprosy burden and sustaining leprosy control activities (plan period: 2006–2010). Geneva: WHO; 2005.
2. Scollard DM, Adams LB, Gillis TP, Krahenbuhl JL, Truman RW, Williams DL. The continuing challenges of leprosy. Clin Microbiol Rev 2006;19:338-81.
3. Feeny P. The fight against leprosy. New York: American Leprosy Missions; 1964.
4. Browne SG. The history of leprosy. In: Hastings RC, editor. Leprosy. 1st ed. Edinburgh (Scotland) and New York: Churchill Livingstone; 1985. p. 1-14.
5. Trautman JR. A brief history of Hansen's disease. The Star 1990;50: 3-16.
6. Manchester K. Tuberculosis and leprosy in antiquity: an interpretation. Med Hist 1984;28:162-73.
7. Monot M, Honoré N, Garnier T, Araoz R, Coppée JY, Lacroix C, et al. On the origin of leprosy. Science 2005;308:1040-2.
8. Noordeen SK. The epidemiology of leprosy. In: Hastings RC, editor. Leprosy. 1st ed. Edinburgh (Scotland) and New York: Churchill Livingstone; 1985. p. 15-30.
9. World Health Organization. Leprosy: learning from success. Geneva: WHO; 2001.
10. Brown W. Can social marketing approaches change community attitudes towards leprosy? Lepr Rev 2006;77:89-98.
11. Manchester K, Roberts C. The palaeopathology of leprosy in Britain: a review. World Archaeol 1989;21:265-72.
12. Jacobson RR, Krahenbuhl JL. Leprosy. Lancet 1999;353:655-60.
13. National Institute of Allergy and Infectious Diseases, National Institutes of Health, Division of Microbiology and Infectious Diseases. Leprosy—Hansen's disease. Bethesda (MD): National Institute of Allergy and Infectious Diseases; 2005.
14. Bullock W. Leprosy (Hansen's disease). In: Wyngaarden JB, Smith LH, editors. Cecil textbook of medicine. 18th ed. Philadelphia: W.B. Saunders; 1988. p. 1696-1701.
15. Curtiss R, Blower S, Cooper K, Russell D, Silverstein S, Young L. Leprosy research in the post-genome era. Lepr Rev 2001;72:8-22.
16. World Health Organization. Chemotherapy of leprosy: report of a WHO study group. WHO technical report series, 847. Geneva: WHO; 1994.
17. Morel CM. Reaching maturity—25 years of the TDR. Parasitol Today 2000;16:522-8.
18. World Health Organization. Leprosy elimination project: status report 2003. Geneva: WHO; 2004.
19. World Health Organization. Special programs for research and training in tropical diseases. Strategic direction for research, February 2002 [cited 2006 Feb 18]. Available from: URL: http://www.who.int/tdr/diseases/leprosy/direction.htm

20. Hartzell JD, Zapor M, Peng S, Straight T. Leprosy: a case series and review. South Med J 2004;97:1252-6.
21. Stearns AT. Leprosy: a problem solved by 2000? Lepr Rev 2002; 73:215-24.
22. World Health Organization. Report of the seventh meeting of the WHO technical advisory group on the elimination of leprosy; 2005 Apr 4–5. Geneva: WHO; 2006.
23. World Health Organization. Guide to eliminate leprosy as a public health problem. 1st ed. Geneva: WHO; 2000.