EPIDEMIOLOGICAL ASPECTS OF HANSEN'S DISEASE*

JOHN R. TRAUTMAN, M.D.
U.S. Public Health Service
National Hansen's Disease Center
Carville, Louisiana

Many definitions of epidemiology exist. Lechat[1] defines it as the study of diseases in populations. It measures frequencies to answer the questions: what, how many, who, when, where, and under what circumstances. It identifies the size and extent of the problem, the risk factors including agents, host, and environmental factors. It identifies vulnerable groups, designs control strategies, and evaluates control measures. A short definition, by Irgens,[2] is that epidemiology is the study of etiology. As is true with the history of Hansen's disease, there are countless references to various aspects of its epidemiology, and a large number of conflicting and confusing ones. The first item to consider is the problem. Briefly, we are dealing with a disease which probably affects between 12,000,000 and 20,000,000 people and is among the world's great public health problems.

GEOGRAPHIC DISTRIBUTION

Hansen's disease is found in almost every country in the world, but is most prevalent in India, southeast Asia, China, and central and east Africa. It is present but to a smaller extent in Japan, Korea, the Okinawas, Iran, Iraq, Turkey, Greece, Italy, Portugal, Spain, and north central Australia. It is also a problem of variable but not exceeding moderate magnitudes in Central and South America, except for mainland Chile.

In the United States, approximately 4,500 cases are known, with a rate of increase somewhat over 300 per year. The largest concentrations of patients reside in Hawaii, California, Texas, Louisiana, Florida, and New

*Presented as part of a *Symposium on Hansen's Disease* sponsored by the Committee on Public Health and the New York City Department of Health, held at the New York Academy of Medicine October 5 ,1983.

Address for reprint requests: National Hansen's Disease Center, Carville, LA 70821

York,[3] but no state or locality is exempt. In such cities as Chicago and other major metropolitan areas, foci of infection and need for control measures exist. The increased new cases during recent years are due primarily to the arrival of refugees and to a changing pattern of immigration from countries with low endemicity for Hansen's disease to countries which have a relatively high one. The disease is also endemic in the Trust Territories, in Puerto Rico, and in the Virgin Islands.[3]

When discussing the prevalence of Hansen's disease in the world, questions frequently arise why the disease is prevalent in one area but not in others. Answers to those questions are unclear, but it is known, for instance, that the disease has been present in India, China, southeast Asia, and central Africa for many centuries. In more recent years it spread to Europe and the Americas. It might be of some interest to single out Norway and to attempt to assess the reasons for the rise and fall of Hansen's disease in that country.

According to Irgens,[2] the disease was a problem in Norway, especially between 1850 and 1920, and reached a maximum caseload of almost 3,000 over a century ago. The southeastern part of the country, however, which accounted for about half that nation's population, had very few cases. The disease was most prevalent in coastal areas and in rural or farming areas rather than in cities. In those days travel was primarily by ship or boat, and the fishing industry of western and northern Norway may have been a factor, especially because the fishing industry brought people into close physical contact under less than ideal environmental conditions. However, the shipping industry fails to explain differences in prevalence between rural districts and cities, nor the virtual absence of the disease in the eastern parts of Norway which bordered the sea.

As concerns the Hansen's disease incidence on Norwegian farms, attack rates were similar in homes with large numbers of people and in those homes in which only small numbers of people resided. This suggests that overcrowding was not, in itself, decisive, and suggests further that direct physical contact may not be an important means of spread. It also suggests that upper respiratory spread may be more likely. A further analysis of the farms showed that members of the households of poor farmers had more disease than members of the more wealthy ones, and it was further concluded that malnutrition and sanitation may have been factors. During the endemic period, it was noted that the disease affected certain families more than others, which raises the possible effect of genetics, but it must

also be remembered that family members often live together.

What caused the Hansen's disease problem in Norway is not known. Most likely it was imported by the crews of vessels which had sailed to endemic areas of the world. That the disease did take hold and that it did become endemic is a fact. What, then, caused the disease to decline and finally to disappear? Certainly the cause of the decline was not treatment, because no effective therapy existed. One stated reason is that the nutritional status of the population improved during the latter half of the 19th century. Physical isolation of patients may have played a role, especially during the time when the incidence rates were highest. Dr. Irgens also reminds us that the chemotherapeutic regimens of today are, in effect, chemical isolation, and that drug therapy today is generally recognized as not only more effective but infinitely more humane than physical isolation.

Another factor which may have caused the Norwegian Hansen's disease problem to disappear was emigration to the United States. The highest emigration rate occurred from 1881 to 1890, and the highest emigration rate involved the Norwegian county with the highest rate of Hansen's disease. Moreover, the largest group represented among these emigrants were young men, regarded as that segment of the population at highest risk of contracting Hansen's disease. Genetics may have played a part, but there is no conclusive evidence one way or another.

The Norwegian experience has been examined closely by many people, and definite provable conclusions are few. The disease was brought to a variably susceptible population, flourished for a generation, then gradually died out. Why the disease disappeared remains unknown. The most widely accepted theory is that better standards of living were primarily responsible for its disappearance.

The Norwegian data and that accumulated from a number of other countries have thus far provided no indisputable answers to many epidemiologic questions about Hansen's disease. What they do tell us is that the disease can appear almost anywhere, that the experience in one country does not necessarily equate with experiences in other countries, and that patterns of prevalence, incidence, and morbidity can vary greatly within a country, indeed within the same regions of a given country. Additional data are needed, and possibly different ways to evaluate these data may be indicated before the puzzle can be solved. Then, too, we may never know all that we would like to know about the epidemiology of the

disease. The latter situation, however, does not preclude its control and eventual elimination as a world health problem.

Cause

The disease is caused almost certainly by the *Mycobacterium leprae* and, although Koch's postulates have not been fulfilled for the bacillus, they probably someday will be. However, were they never to be, it would not be reasonable to suggest that some other cause might be responsible for the disease. The footpad work of Shepard[4] and armadillo experiments, which began with the studies of Kirchheimer and Stoors,[5] also appeared to erase any doubts which might have existed. More recent studies involving primates add further confirmation.[6]

Incubation or Latent Period

It is often difficult to determine the time lapse between exposure and the onset of the disease, usually because exposure and the degree of exposure are often almost impossible to determine. From many studies, the consensus is that the duration of the latent period is from three to five years. One study performed in the Philippines by Rodriguez[7] showed that of 58 children with the disease, 24 (or 41%) were diagnosed by the time they were five years of age. Some cases, however, have been diagnosed in infants less than a year old, and in other instances the latent period appears to be 15 or 20 years or more, although both extremes are uncommon.

Race

Every race is affected by the disease, but no evidence supports the notion that one race or ethnic group is more susceptible to the disease than others, except that, to our knowledge, the disease has never been reported in a full-blooded American Indian. However, there is evidence that the type of Hansen's disease acquired, which in turn depends on the degree of resistance to the disease possessed by the contact, may indeed have racial relevance. Lowe[8] noted that the percentage of lepromatous to tuberculoid cases in Burma was as high as 70%. In India the lepromatous caseload seldom exceeds 30%.[8] Cochrane[9] stated that European and Asiatic races appear to be more likely to acquire the lepromatous type. Among Africans, the tuberculoid type is most prevalent.[10]

Heredity

Although not a hereditary disease, there may well be a genetically acquired resistance or susceptibility to the disease, which is probably true for a number of other diseases. Infants separated from their mothers reportedly seldom contract the disease, but when they do it is probably the result of another exposure. The history of Hansen's disease in Louisiana suggests a hereditary influence. Many cases have appeared in families of descendants of French Canadians who immigrated from Nova Scotia during the 18th century. This may be more apparent than real, however, according to Badger,[11] who, in analyzing existing data more than 25 years ago, pointed out that of the first 779 patients admitted to Carville from Florida, Louisiana, and Texas, only 98 (12.5%) gave a history of family contact. For Louisiana patients only, of 294 born in and admitted from that state, only 44 (14.9%) had known contact with an immediate family member who had the disease. And of the same 294, another 55 (18.2%) had a history of disease in related but not immediate household family members. Thus, of 294 patients, only 99, or 33.6%, had infected members in either the immediate or related families. Or, from the other viewpoint, 195, or 66.3%, apparently were infected by open cases of disease in the community.

Data concerning the United States compiled in the future may show somewhat different results because during recent years approximately 90% of patients newly diagnosed in the United States are foreign born and come from highly endemic areas where genetic influences may be even more of a reality.

Hundreds of references tend to support the influence of genetics on Hansen's disease. One example presented by Spickett[12] indicates that "genetic control over the form of leprosy contracted should result in there being a higher degree of concordance between the types of leprosy suffered by identical twins than between fraternal twins." Twin data available at the time so indicated, but numbers were too few for true statistical significance. Of 14 sets of fraternal twins of the same sex, 10 developed identical disease. Of 14 sets of identical twins, all 14 developed the same type of disease. The literature otherwise contains many references to twins developing Hansen's disease at about the same time, which strongly suggests that identical twins are much more likely to develop the disease in this way than are fraternal twins. These reports involve only a single set or, at most, small numbers of subjects. In 1966,

however, Ali and Ramanujam[13] reported on 35 sets of twins. One or more of each set had Hansen's disease. Of this group, both members of 19 sets of identical twins had Hansen's disease, and 17 of these 19 had the same type of disease. In only four sets in the group was the disease present in just one twin. Of the 12 fraternal sets, 10 sets showed only one member with the disease and two sets with both members infected, but in these two instances each twin had a different type of Hansen's disease. Although these numbers are not large, they still reveal a concordance with respect to Hansen's disease of 89.5% in identical twins and 0% in fraternal twins, which the authors state supports the view that the type of Hansen's disease contracted may be genetically influenced.

Sex. Most studies throughout the world indicate that men are approximately twice as likely to contract lepromatous Hansen's disease as are women, but with tuberculoid Hansen's disease the ratio is very nearly 1:1. The reasons are unknown. Perhaps men have a greater degree of exposure, but this would not account for the evenness of the tuberculoid form.

Age. Some authors believe that children are more susceptible than adults. The young have a greater opportunity for exposure by an infected parent, and in some societies children sleep with a parent and the spouse sleeps elsewhere. Overall, spouses tend to be less susceptible to contracting the disease than are the children of infected parents. It is, of course, possible that children may be somewhat more susceptible and that as these individuals grow older they somehow acquire a greater immunity to the disease.[14] Genetic factors may also be involved.

Climate. Hansen's disease may appear to be a tropical disease, but it was widely prevalent in Europe centuries ago, and still is to some extent; and it was and still is fairly common in Japan and in widely scattered areas of China where temperatures are moderate to cold. In the east Bengal area of India, where it is hot and humid, the incidence is much lower than in the cooler, drier West Bengal area. A similar situation exists in Burma.[15] Complications of the disease, especially involving the eyes, are said to be more severe in northern Japan than in the south and in the highlands of Peru as compared to the lowlands.

Environment. Currently, Hansen's disease is more prevalent in the warmer regions of the world, but, as stated earlier, this by itself may not be as important as it may seem to be. The areas of greatest prevalence are also areas where the standard of living is less than ideal. Crowding, poor sanitation, and other environmental factors are probably of

considerable importance. Malnutrition may well increase susceptibility. Some workers have suggested that *M. leprae* exists in the ground, and thus going barefoot or living in houses with dirt floors may increase exposure. Again, there is no convincing evidence for this, but the finding of naturally infected armadillos in Texas and Louisiana[16] at least raises a question in that this observation is thus far unexplained.

Transmission and communicability. The mode of transmission of Hansen's disease is unknown. Skin to skin contact has long been suspected, but in most instances bacilli are not present on the surface of the diseased skin in large numbers. Insects have been suspected, but a careful study of this possibility in India tends to exclude such transmission as a major factor.[17] Soil has been mentioned as a possible source, as has various food stuffs, but present thinking is that the most probable transmission involves the upper respiratory tract. One study by Rees and McDougall,[18] using immunosuppressed mice, tends to support this possibility. Ultimately, it may be found that the disease is transmitted by more than one method.

There are no proved successful attempts deliberately to transmit the disease to humans, although several claims of success are reported. The one most frequently cited involved the "inoculation" of a convicted murderer in Hawaii, who in 1884 volunteered for the experiment. A large, fresh leproma was imbedded in his forearm and sutured in position. Twenty-five months later he developed widespread cutaneous nodules. A definite diagnosis of lepromatous leprosy was made in the fall of 1887. The disease progressed rapidly and he died, presumably of complications of the disease, in 1892.[19] It is, of course, quite possible that the disease was surgically transmitted to the subject. However, the method used involved the transplantion of a large amount of infected tissue. This degree of exposure could not occur in a real life situation. Otherwise, the subject had close relatives with Hansen's disease, and he had lived in the same household with them for a considerable time prior to the experiment.

Accidental transmission has occurred during surgical procedures, but is uncommon. Lowe and Chatterjee[20] refer to Hansen's disease lesions following tattooing, and Porrett and Olsen reported two marines who were tattooed.[21] Both men had been residents of the same town in eastern Michigan where there was no known Hansen's disease. Both were tattooed in the same shop in Melbourne, Australia, and three years later each developed a tuberculoid lesion in and surrounding the tattooed area.

The spread of Hansen's disease appears to be influenced by hygiene and socioeconomic conditions. Studies from Indonesia support this thinking.[1] They showed that children of Hansen's disease patients who slept on the same mat with their infected parents developed Hansen's disease about seven times more frequently than children sleeping on separate mats. One could, of course, suggest that the same sleeping habits in a mansion might produce similar results. However, standard of living does appear to be the one constant factor in studies of the prevalence of the disease and its rise and fall.

It is stated that more than 90% of people are probably immune to Hansen's disease. Lepromin testing can apparently provide strong clues as to the degree of susceptibility in a given person. A negative lepromin test suggests that the individual, were he to develop Hansen's disease, would have the lepromatous type, and a positive lepromin test indicates resistance to the point that, should the person develop the disease, it most likely will be of the tuberculoid variety.[22] The lepromin now produced is almost exclusively derived from armadillos. Further testing will be necessary before it can be made readily available in the United States.

The high degree of immunity mentioned might well hold true for countries where the disease is of low endemicity, such as the United States, but in other areas of the world numbers of susceptible persons may be greater. The statement that Hansen's disease is the least communicable of communicable diseases has also been challenged on a number of occasions. Experience at Carville and that of others apparently shows that clinically active disease seldom develops in workers assigned to Hansen's disease hospitals or as a result of casual contact in a normal society. But in different situations attack rates may be much higher. For instance, from the experience in Hawaii it was concluded by Badger[11] that Hansen's disease cannot always be said to be "feebly contagious." It was first recognized among native Hawaiians in 1835. From then until 1865 686 cases were diagnosed; from 1866 to 1915 more than 10,000 patients were admitted to hospital.

On the island of Nauru, in 1920, four cases of Hansen's disease had been recognized. Within four years almost 35% of the total population of some 1,200 persons had contracted the disease. A similar situation developed in the island of Malulu, off the coast of New Guinea. The disease was first noted among native residents during World War II, but within a decade some 15% of the population was affected.[12]

Badger's[11] study of 2,522 family contacts in 1,167 families in the United States revealed that 131 were infected—a contact rate of 5.1%. Stanley Browne[23] stated that "lepromatous cases are grossly infectious, but they are not the only, nor always the most, important sources of infection. Most patients, at some time or other, may be infectious to susceptible individuals." The consensus, however, is that lepromatous and borderline lepromatous cases are communicable if not under effective treatment, whereas the more tuberculoid forms of the disease are, for practical purposes, noncontagious. Doull and Gunito,[14] in Cebu, the Philippines, showed that the risk of developing Hansen's disease by household contacts was four times greater in contacts of lepromatous patients than in contacts of nonlepromatous types.

Missionaries, especially when working closely with native residents in areas of the world where Hansen's disease is highly endemic, appear to be more likely to contract the disease.[24] Father Damien's experience on Molokai is a notable example.

By comparing attack rates in children born of treated or untreated mothers, Worth,[25] in Hong Kong, showed that patients with lepromatous Hansen's disease who are adequately treated no longer transmit the disease. Many studies since confirm these results, and this is the main reason that isolation should no longer be considered a viable method of treatment. In addition, forced isolation leads many patients to avoid medical care until it is often too late to reverse the damage already done.

Undeserved stigmata and unwarranted fear of the disease remain problems which can be further diminished in the future. But, in this respect, a total absence of fear which occurs in some areas of the world, while a good thing for the patient, can be a factor in the spread of the disease. Fear, on the other hand, tends to drive the disease underground and can also increase the chances of spread. Thus, a healthy respect for Hansen's disease without unwarranted fear appears to be justified and in the best interests of all concerned.

Knowledge about almost every facet of the epidemiology of Hansen's disease is incomplete, yet more is probably known than is realized. To prove what is probably already known and to fill the remaining factual gaps continue to be interesting and difficult challenges.

REFERENCES

1. Lechat, M. D.: Epidemiology of leprosy. *Health Coop. Papers* (Quaderni de cooperazione sanitaria) *1:*29-32, 1982.
2. Irgens, L. M.: Epidemiological aspects and implications of the disappearance of leprosy from Norway; some factors contributing to the decline. *Lepr. Rev.* (Suppl. 1) *52:*147, 1981.
3. Enna, C. D., Jacobson, R. R., Trautman, J. R., and Sturdivant, M.: Leprosy in the United States. *Pub. Health Rep. 93:*469-73, 1978.
4. Shepard, C. C.: The experimental disease that follows the injection of human leprosy bacilli into footpads of mice. *J. Exp. Med. 112:*445-54, 1960.
5. Kirchheimer, W. F. and Storrs, E. E.: Attempts to establish the armadillo (*Dasypus novemcinctus* Linn.) as a model for the study of leprosy. I. Report of lepromatoid leprosy in an experimentally infected armadillo. *Int. J. Lepr. 39:*692-701, 1971.
6. Meyers, W. M., Walsh, G. P., Brown, H. L., et al.: Naturally-acquired leprosy in a mangabey monkey *(Cercocebus sp.). Int. J. Lepr. 48:*495-96, 1980.
7. Rodriguez, J. N.: The importance of epidemiological studies in leprosy. *Monthly Bull. Bur. Health Philipp. 19:*323, 1938.
8. Lowe, J.: The leprosy problem in Burma. *Lepr. India 10:*120, 1938.
9. Cochran, R. G.: *A Practical Textbook of Leprosy.* London, Oxford University Press, 1947, p. 13.
10. Cap, J. A.: The epidemiological situation in Africa. *Lepr. Rev.* (Suppl. 1) *52:*53-60m, 1981.
11. Badger, L. F.: Epidemiology. In: *Leprosy in Theory and Practice.* 2nd ed. Baltimore, Williams and Wilkins, 1964, pp. 69-97.
12. Spickett, S. G.: Genetic Mechanisms in Leprosy. In: *Leprosy in Theory and Practice,* 2nd ed. Baltimore, Williams and Wilkins, 1964, pp. 98-124.
13. Ali, P. M. and Ramanujam, K.: Genetics and leprosy. A study of leprosy in twins. *Lepr. India 36:*77-84, 1964.
14. Doull, J. A., Rodriguez, J. N., and Bancroft, H.: Risk of attack in leprosy in relation to age of exposure. *Am. J. Trop. Med. 25:*435, 1945.
15. Dharmendra: Notes on leprosy. *Int. J. Lepr. 15:*424-30, 1947.
16. Walsh, G. P., Storrs, E. E., Meyers, W. M., and Binford, C. H.: Naturally-acquired leprosy-like disease in the nine-banded armadillo (*Dasypus novemcinctus*): Recent epizootiologic findings. *J. Reticuloendothel. Soc. 22:*363-67, 1977.
17. Kirchheimer, W. F.: The role of arthropods in the transmission of leprosy. *Lepr. India 45:*29-33, 1973.
18. Rees, R. J. W. and McDougall, A. C.: Airborne infection with *Mycobacterium leprae* in mice. *J. Med. Micro. 10:*63-68, 1977.
19. Mouritz, A. A.: Human inoculation experiments in Hawaii including notes on those of Arning and Fitch. (Condensed, arranged and annotated by Wade, H. W.) *Int. J. Lepr. 2:*203-215, 1951.
20. Lowe, J. and Chatterjee, S. N.: Scarification, tattooing, etc. in relation to leprous lesions of the skin. *Lepr. India 11:*14, 1939.
21. Porritt, R. J. and Olsen, R. E.: Two simultaneous cases of leprosy developing in tattoos. *Am. J. Path. 23:*805, 1947.
22. Leprosy Unit, WHO, and Seal, K. S.: Present Knowledge of the Epidemiology of Leprosy. In: *A Guide to Leprosy Control.* Geneva, World Health Organization, 1980, p. 14.
23. Browne, S. E.: Factors influencing the transmission of leprosy. *Trans. R. Soc. Trop. Med. Hyg. 53:*197, 1959.
24. Gray, H. H. and Dreisbach, J. A.: Leprosy among foreign missionaries in northern Nigeria. *Int. J. Lepr. 29:*279-90, 1971.
25. Worth, R. M.: Is it safe to treat the lepromatous patient at home? A study of home exposure to leprosy in Hong Kong. *Int. J. Lepr. 36:*296-302, 1968.