THE EPIDEMIOLOGY OF LEPROSY
PRESENT STATUS AND PROBLEMS[1]

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In epidemiology, as in other branches of medicine, it is instructive not only to assess our present views but also to measure the progress that has been made since some readily identifiable point in history. In leprosy the obvious starting point is 1874, when the discovery of the leprosy bacillus was announced. It is proposed to commence a few years later, but still at the dawn of the bacteriological era, and take advantage of the comprehensive review of the subject by August Hirsch ([27]).

CONCEPTS OF 1880

August Hirsch, sometime professor of medicine in the University of Berlin, was one of the leading physicians of his day. His greatest work, entitled: Handbook of Geographical and Historical Pathology, published in an English translation by Charles Creighton by the New Sydenham Society in 1885, is a monumental work and the most comprehensive treatise ever written on the natural history of disease. The section on leprosy was completed about 1880. After reviewing all that was known concerning its etiology and epidemiology, and referring in particular to "a few cases which give evidence of a spontaneous origin of the disease even in regions where leprosy as an endemic had been extinct for centuries," Hirsch concluded with this discouraging remark: "We are here at the limits of our knowledge and there is not a single *well-founded* hypothesis to show us the way beyond."

The history of leprosy is as obscure today as it was at the time of Hirsch. He accepted early Egyptian accounts as showing that leprosy had been endemic in Egypt from the remotest times. Modern medical historians are a bit skeptical about these descriptions, and they are supported somewhat by failure to find the typical mutilations of leprosy among large numbers of mummies which have been examined. Biblical "leprosy" had been pretty well discounted; it may have included leprosy but was used in an inclusive sense for a group of skin diseases. The disease was probably present in ancient times in China and in India.

When and how leprosy reached Europe was and is unknown. It may have reached Greece from Egypt. Its subsequent spread through Europe, which has been greatly exaggerated, has been attributed to military movement, returning crusaders and increase in maritime commerce.

[1] Read at the Leonard Wood Memorial-Johns Hopkins University Symposium on Research in Leprosy, Baltimore, Md., May 8-10, 1961.

Virchow ([51]) pointed out that, in Germany, leprosy antedated the First Crusade, 1096-1099, but that its occurrence among the Knights of St. John and the Templars stimulated the establishment of hospitals. Some of the ancient German "leper houses" sheltered people afflicted with various chronic diseases. Sir James Simpson ([50]) listed more than one hundred "lazarets" that existed in England and Scotland during the Middle Ages. We now know from the studies of MacArthur ([35]) that some of these places never cared for any leprosy patients and others for very few. Nevertheless, leprosy was prevalent in Europe during the Middle Ages and declined after the 15th century. Norway shared in this decline but in the early decades of the 19th century an increase was observed which continued to about 1850 according to Vogelsang ([52]). In 1856 the number of known cases was 2858. Thereafter the disease declined steadily; in 1857, there were recorded 242 new cases, in 1907, 19 and in 1957 there were only 7 known cases in the country, none of which was in an active state. Why the disease increased so remarkably in Norway and not in Denmark or Sweden is one of leprosy's puzzling features. Its decline is equally puzzling.

The wide prevalence of leprosy in Asia had been attributed by various writers to migration of Chinese. Hutchinson ([28]), a strong advocate of the hypothesis that fish diet is an etiologic factor, explained this by the statement that the Chinese are skillful cooks and use decomposing and potted fish as delicacies. Hirsch did not admit that the disease ever spread from Chinese to other races. It was likewise widespread in Africa. In America, apart from localized foci in the northern hemisphere, it was chiefly a disease of the tropical zones to which it was supposed by many to have been introduced by infected slaves from Africa and by French, Portuguese and Spanish immigrants.

In assessing the position of leprosy Hirsch had one great advantage over earlier historians. In 1848 the Norwegian pioneers, Danielssen and Boeck ([7]) had published their classical work entitled: "Traité de la Spedalskhed ou Elephantiasis des Grecs." The names "nodular" and "anesthetic" were proposed to indicate the two principal forms. Gradually over the next decades the various clinical varieties of the disease were brought into unity; a great impetus was given to investigation of the disease, and reports of prevalence became much more reliable.

Examining the map of prevalence, Hirsch noted that leprosy was indigenous in all latitudes. Its appearance, spread and decline in Europe likewise told against any important influence of climatic conditions. The relative frequency of the disease in the tropics might be due to the debilitating effect of unfavorable climate. There was no special relation to the sea coast, and the theory that leprosy was caused or aggravated by eating fish either in immoderate amounts or after it was salted or spoiled had no scientific support. Poor environmental conditions such as inadequate shelter, deficient diet, filth and related factors, might

predispose to leprosy, and improvement in these conditions thus account for the reduction or extinction of the disease in certain places. On the other hand, cases were not infrequently observed among well-to-do individuals, removed from the harmful influences in question; also, the malady had disappeared from many localities which used to be much afflicted by it, although the most wretched hygienic conditions still existed. Furthermore, there were villages in endemic regions which were quite exempt whereas others apparently similar in all respects were subject to the disease.

As regards the basic question of contagiousness, Hirsch marshalled a great deal of negative evidence.

1. The extremely narrow limitation of the disease to certain centers, although free communication and sanitary conditions seemed to favor its conveyance.
2. Limitation to particular races or nationalities, notwithstanding unrestricted social intercourse throughout the community.
3. In innumerable instances the disease in one member of the family has not spread to others.
4. No case is known of a physician or nurse in a "leper house" having contracted the disease.
5. There is no instance of spread from a leper house to residents outside.
6. Although there are numerous cases in Europeans who have acquired the disease in leprous districts not one has ever been a source of transference to others.

Hirsch placed no weight on histories of contact obtained within endemic seats of leprosy, criticizing in particular the data published by Hansen ([22]) on such cases in Norway. Also indecisive to him were the opinions referring the origin of the disease in the Western Hemisphere to imported slaves; the fact might be explained in other ways. He dismissed as a fable the story of the introduction of leprosy into the Hawaiian Islands in the 19th century.

In common with the medical opinion of the day, Hirsch placed great importance on heredity. "There is only one kind of conveyance which cannot be questioned, I mean that which takes place by way of inheritance." The only doubt which he expressed was whether the disease as such was inherited or

> . . . whether it is only a predisposition thereto that we are concerned with, a morbid diathesis which inclines the individual to fall into the sickness, or makes him specifically susceptible to the morbid poison.

In another place he says that the facts go to prove that we must have a definite and specific noxious agent, a peculiar infective substance, which had once been more or less widely diffused throughout Europe but was now active only at certain points in this part of the world. Thus his concept was that of an "infectious" but not a contagious disease, that is, without the necessary implication of a living agent, to which an individual was predisposed by heredity and probably also by unfavorable elements in the environment.

In 1874 Hansen ([23]) had described small rod-like bodies in the cells of

leprosy nodules and this had been confirmed by several others, notable among whom was Neisser ([41]), who had no reservations in stating that in leprosy there is a specific kind of bacterium. Hirsch commented on these reports without accepting them. Nevertheless he had a concept of infectious agents that have the power of reproduction, as for example, the "virus" of syphilis. Forty years earlier Henle had laid down clearly the principles of the specific origin of infectious diseases. In 1862 Pasteur had published the results of crucial experiments which ended the doctrine of spontaneous generation. The bacillus of anthrax had been described in animal tissues in 1850 by Davaine and Rayer, and its essential role in the disease had been proved by Koch in 1876-77. With all this work Hirsch may be presumed to have been familiar.

It was therefore not lack of knowledge of the science of his day which made it difficult for Hirsch to accept leprosy as an infectious disease in the modern sense. It was rather certain peculiarities of the disease itself which obstructed his view. It should be borne in mind also that only the nucleus of the germ theory had yet been recognized; there were still major obstacles to be removed by the discovery of insect vectors and of the role of healthy carriers.

PRESENT CONCEPTS

During the eight decades that have intervened, leprosy has become generally accepted as a specific infectious disease. The overwhelming influence of analogy especially with tuberculosis, rather than direct proof, has been partly responsible for this change in viewpoint. Many facts have been learned concerning leprosy which fit this hypothesis better than any other which has been advanced.

The specific agent.—The bacillus observed by Hansen was undoubtedly that known today as *Mycobacterium leprae*. Experimental proof of this relationship is still lacking, although progress in this direction will be reported later today at this Symposium. There is no known method of cultivation of the bacillus on an artificial medium, and consequently there is no method of positive identification. Acid-fast bacilli which are similar to one another in morphology and staining properties are regularly and consistently found in the granulomas of the lepromatous type, less regularly in the tuberculoid. Noncultivable mycobacteria have rarely been found in other diseases and in healthy persons. Further study of this question has been discouraged by the impossibility of identifying these bacilli. Efforts should be made to confirm the report from Bombay by Desai ([9]) of finding almost one-half of contacts, free from cutaneous lesions, to be bacteriologically positive.

Skin testing with a heat-killed suspension of lepromatous tissue containing bacilli (lepromin) usually causes no reaction in patients suffering from the lepromatous type, but causes a characteristic reaction in a high proportion of those suffering from the tuberculoid type. No

other substance or bacillus conforms with lepromin in respect to both negativity in the lepromatous type and reactivity in the tuberculoid, and this is a point to be considered in identification of cultures purporting to be of *M. leprae.*

Ulcers of the skin and mucous membranes are common in lepromatous leprosy, and the discharges contain myriads of acid-fast bacilli. The skin lesions of tuberculoid leprosy also shed acid-fast bacilli in large numbers during acute exacerbations, but during quiescence few bacilli can be demonstrated in smears. Acid-fast bacilli may also be shed by unbroken skin; they have been reported in the epidermis by Muir and Chatterjee ([40]) and more recently by Weiner ([55]) and by de Andrade ([1]).

The assumption is made that transmission may occur by direct or indirect contact with an "open" case. This is the simplest hypothesis which is in agreement with the basic facts. It must be admitted that the proportion of cases even in children which can be traced to a known source is far short of what would be anticipated. Guinto *et al.* ([20]), for example, in a study of 19 cases, 5 lepromatous and 14 nonlepromatous, in children under 5 years of age found that all the lepromatous ones were in children living in household contact with prior cases of the lepromatous type. Of the nonlepromatous cases, 3 were in individuals exposed to the lepromatous type and one in a child exposed to a nonlepromatous case; the remaining 10 were in children whose contact could not be traced and was probably outside their immediate families. It should be added, however, that many of these cases were not discovered until considerable periods after onset.

With regard to the portal of entry, there is likewise uncertainty. The prevailing idea is that the bacilli usually enter the body through wounds in the skin. Rare cases give some support, such as that reported by Marchoux ([38]) in an assistant who was accidentally pricked with a needle during an operation for removal of a leprous nodule; those reported by Porritt and Olsen ([43]) in two United States marines following tattooing; and that reported by Hamilton ([21]) in a white attendant in a lazaret in Australia whose first sign was a reddish macule near a scar of a cut received 13 years before. Rogers and Muir ([46]) offer, as indirect support for this view, the observation that in India the earliest lesions are more frequently found on the feet in patients from hilly and stony districts than in those from districts where the soil is alluvial. If the portal of entry is through the skin it is obvious that injury, causing a break in the continuity of the skin, is a necessary predisposing factor. Insect bites are a common cause of such injuries, which may help to explain the higher prevalence of leprosy in moist, hot climates as suggested by Rogers ([45]).

From histologic studies of skin lesions in various stages of development, Khanolkar (30) contends that bacilli may enter through unbroken

skin, healthy or slightly altered, find their way anywhere under the epidermis through the superficial lymphatic network, and reach the fine nerve twigs of the dermis. It is, in his opinion, the nerves and not the lymphatics which are the pathway, and in these nerves the original foci of infection are found, forming epithelioid cells if resistance is good and Virchow cells if it is not. The possibility of *M. leprae* actually traveling up the axis cylinders is an interesting hypothesis.

Association between "heavy" infection and higher incidence rates.—Epidemiologic studies have been consistent in finding, in any given area, the highest incidence rates among these who are living in close contact with persons suffering from the lepromatous type of the disease. In the joint studies of the Leonard Wood Memorial and the Department of Health of the Philippines (Doull *et al.* ([10])) it was found that when the primary case was of the lepromatous type the average attack rate for household contacts over a period of years was equivalent to 6.2 cases per 1,000 persons per year. When the primary case was tuberculoid, on the other hand, the rate was 1.6 per 1,000. Furthermore, the concurrent attack rate for other persons living in the same communities but not known to have been subjected to household exposure was only 0.8 per 1,000. Thus the risk of contracting leprosy was almost four times as high for those in contact with the lepromatous type as for those in contact with the tuberculoid, and almost eight times as high as for persons for whom no history of exposure to either type could be obtained. In a more recent study of data for the same communities, Guinto *et al.* ([20]) found that the attack rate for those exposed to lepromatous leprosy was at a lower level (4.4 per 1,000), but again about four times that of those exposed to nonlepromatous forms. The rate for the latter group, however, was only one and one-third times that for unexposed persons.

Although the greater risk of association with lepromatous than with tuberculoid cases has been established with unusual exactness in the Philippine studies, the findings are, of course, not new. Similar results in household studies have been published by Lowe *et al.* ([34]), Lampe and Boenjamin ([32]), and others. Also the fact that contact can be traced to prior cases of the lepromatous type far more frequently than to those which probably were of the tuberculoid type was emphasized long ago by Dehio, Hansen, Rogers and Muir, and many others.

Contagiousness.—The principal difficulty in supporting the theory of contagiousness of leprosy is now recognized to be a long period of incubation or latency. Inquiries relate to events that may have occurred many years before. The experience of veterans of the armed forces of the United States is especially illuminating in respect to the long periods between exposure and clinical recognition. Thirty-two cases came to light over a period of almost forty years in men who served in the Spanish-American War, the Boxer Rebellion, or the

Philippine Insurrection. I have records of 21 cases in veterans who served in the Pacific Theater in World War II or in the Korean conflict, who were born in areas where leprosy is rare or absent and who had never lived in an endemic area except during military service. These cases are still turning up, and in almost all instances cutaneous lesions, or anesthesia were first noticed some years after return to the United States.

This long period of latency is only one of the complications which apparently break the chain. Although healthy carriers, if they exist, cannot be demonstrated there must be large numbers of instances in which mild cases go through life without detection. Some years ago Dr. Fred C. Kluth, then on the staff of the Memorial, demonstrated a potential instance of this kind to me at Corpus Christi, Texas. Leprosy had been diagnosed in a school boy, and his household associates were examined as a matter of routine. An elderly female relative was noticed to have what appeared to be a slight infiltration of the skin of the face. Smears showed many acid-fast bacilli and complete examination confirmed the diagnosis of lepromatous leprosy. Presumably she was the source of infection, but the point of pertinent interest is that if discovery of the case in the boy had been delayed until the elderly female's departure or death, his case would have been classified as one in which the source was unknown.

The slow development of secondary cases obscures the evidence of spread of the disease in new areas. Hirsch did not deny that such spread might occur but it was limited, in his view, to the families or class of people responsible for its introduction. The epidemic on the Island of Nauru (Pleasant Island) is the most notable example of spread to an indigenous population which was apparently not previously affected. According to reports, a leprous woman came to Nauru from the Gilbert Islands in 1912. The community was a small one comprising about 1,500 natives. There were also about 1,000 Chinese indentured laborers in the phosphate diggings who were not allowed to mingle with the natives. By 1920, three cases had occurred among contacts of the first one. In 1925 the whole population was examined, and it was found that more than a quarter of the Nauruan population was affected. Most of the cases were of the tuberculoid type, and the disease gradually diminished in frequency over the next 15 years (Wade and Ledowsky ([53])).

Although they are rare, contact cases are now known to have occurred in places in which the disease has never been endemic or in which endemic cases have not been present for centuries. These cases are of vital importance in refuting one of the principal arguments of Hirsch. In 1925 MacLeod ([37]) reported a series of four contact cases contracted in Great Britain. Three were in persons born in that country who had never been abroad. Hasseltine ([24]) tells us that, until 1943, no person

who has born in the New England states and who had lived all this life within these states was known to have contracted leprosy. In that year a man 24 years of age,

> . . . who was born in Massachusetts of foreign-born parents and who had never been outside of the state, was found to have leprosy. He was sent to the National Leprosarium at Carville, La. His father was known to have had leprosy . . .

Washburn ([54]) has published a valuable account of leprosy among the Scandinavian settlers in the upper Mississippi valley. The most interesting data are those for Minnesota, where the majority of the immigrants settled. To 1948, 98 cases of leprosy were reported in that state. Of these, 76 had apparently contracted the disease in Norway or Sweden, and 14 in other foreign countries. There were, however, 7 cases in the first generation of those born in the United States and one in the second generation. The first of these cases occurred in a male of 15 years in whose family there was no history of leprosy other than an uncle whom the boy had never seen and who had died of the disease in Norway. The other indigenous cases were in persons who had had household contact with leprous relatives. Subsequent to Washburn's report, Fasel ([14]) published an account of a case of lepromatous leprosy in a man of 42 years of age, born in Minnesota, where the disease was contracted about 15 years previously from an unknown source. His father was born in Finland and his mother in Illinois. The disease died out in Minnesota even more rapidly than in Norway, although the heredity factor—if its exists—overcrowding and insanitation were present.

Ebert and Sleypam ([13]) have described cases of leprosy in a mother and daughter neither of whom had ever lived in an endemic area. The daughter, who contracted the disease first, from an unknown source, was born in Kansas and had lived only there and in Illinois. The mother who was born in Virginia and had lived only there and in Kansas and Illinois, apparently received the infection from the daughter. She showed the first signs at the age of 54 years.

Probably all that Hirsch had in mind when he spoke of failure of leprosy to spread in the family is the transfer of the disease from one spouse to the other because all the reports cited, and discarded, refer to this matter. When both husband and wife contracted the disease he attributed the occurrence to some common source or to a general endemic influence and "not to conveyance of the morbid poison from one to the other."

There are many accounts of supposed marital transmission, but few of them can meet criteria that would satisfy Hirsch. One of the better older reports is that of Flandin and Ragu ([15]), who described six cases in white persons who had never left France and among them one in a white girl who married one of these persons. In three other instances there had been cohabitation with leprous females. A second instance of probable marital infection in Metropolitan France has been reported

recently by Chaussinand *et al.* ([6]).

The statement by Hirsch concerning the immunity of physicians working in leprosy hospitals is still true as far as I am aware. Except for the well known case of Sir George Turner ([42]), who saw patients every day in Pretoria and did many autopsies, a published report of a well authenticated case has not been found in a careful but not exhaustive search. With regard to nurses, the situation is perhaps different. The number of cases that have occurred in persons born in nonendemic areas who have worked in leprosaria, while not to be counted in the hundreds, is nevertheless large. Many of these were in close contact with patients and performed some nursing duties, but if the list includes fully qualified nurses they are not so designated. This statement also is subject to correction, as it is easy to overlook something of this sort. The occurrence among persons without medical training, although such persons are much more numerous than physicians and nurses, raises the possibility that precautionary measures taken after examining or treating patients have been a protection to the medically trained personnel.

Broad epidemiologic features.—Race: Leprosy occurs in the Caucasian, the brown, the yellow and the Negro, but there are no statistics of incidence relating to different groups living under conditions that are at all similar in relation to possible exposure. Consequently no conclusion can be made concerning comparative resistance.

Geographic and climatic differences: As noted by Hirsch, leprosy has spread in every climate from that of Iceland to the tropics. The higher prevalence rates of the latter were considered by him as possibly attributable to the debilitating influence of heat and humidity. Hirsch was quite baffled, however, as we are today, by the fact that some communities in endemic areas apparently similar to the others in all respects are nevertheless exempt from the disease.

Leprosy varies greatly in severity in different parts of the world, as was shown very clearly by F. Hayashi ([26]) in 1935. Lepromatous eye involvement with consequent blindness, for example, is far more frequent in Japan, Hawaii and the United States than in the Philippines, Malaya and India. The relative frequency of the two major types of the disease, lepromatous and tuberculoid, also varies greatly.

These variations in prevalence and severity are a challenge to the epidemiologist. It may well be that environmental differences could be demonstrated by careful inquiry between communities in endemic areas differing in prevalence which "apparently" are alike in all respects. Doull *et al.* ([11]) in their first report on leprosy in Cordova, Philippines, noted that families in which there was leprosy were much more crowded in their sleeping space than other families, although the other factors in sanitary status did not differ materially. There are many items which have not been adequately studied, including the association between

the incidence of leprosy and peculiarities of diet, occurrence of various kinds of insects, and presence of other skin diseases.

Sex: Prevalence rates for lepromatous leprosy are usually much higher for males than females. This is true alike for household contacts and for persons not known to have been exposed in the family. This has been shown in the Philippines by Doull *et al* ([10]) to be caused by higher rates of incidence and not by longer duration of the disease in the male. Some excess among males is seen in childhood, which suggests that males are inherently more susceptible. The tuberculoid type shows no sex selectivity. The male excess in the lepromatous type is not associated with lower frequency of reactivity to lepromin. Among large numbers of healthy persons tested in Cebu, Philippines, Guinto *et al.* ([19]), found that females over 10 years of age had somewhat higher Mitsuda positivity rates than males. For all ages the age-adjusted rates were 67 per cent for males and 70 per cent for females.

Age: Leprosy may manifest itself at any time from early childhood to old age. There have been several accounts of cases in infants under one year of age. A proven congenital case has not been reported, although suggestive lesions in the newborn have been described in two instances by Montestruc and Berdoneau ([39]) and more characteristic ones in an infant of 48 days by Ryrie ([47]). Dreisbach ([12]) has reported leprous macules with a few bacilli in a child of seven months, and Rodriguez ([44]) mentions a macule observed in a child of eight months which became bacteriologically positive ten months later.

In 1922 Gomez *et al.* ([17]) at Culion described lesions in children, positive or negative for acid-fast bacilli, which in a few instances disappeared without treatment. The period of subsequent observation was short, being only about nine months. Later, Lara and Nolasco ([33]) reported that about three-quarters of unquestionably leprosy lesions in children at Culion "actually healed spontaneously, a majority of them apparently permanently." More or less transient leprosy macules are perhaps not infrequent in children residing in endemic areas but it may be impossible to confirm their etiology. Macules showing sensory disturbance but negative for acid-fast bacilli have been encountered by Guinto ([18]) in field studies; in several instances these disappeared within a few months.

Turning to the other extreme of life, cases coming to light in older persons are not uncommon. Guinto *et al.* ([20]) give histories of 13 patients, 3 with lepromatous leprosy and 10 with tuberculoid, which were recognized for the first time after the individuals had passed 50 years of age. In 5 of these they had passed their 60th birthday at the stated time of onset. Eleven of these persons had been examined on one or more occasions prior to that time and found free of disease. There are also many cases, such as those of the veterans mentioned, in which adults born in places where leprosy is absent have contracted the

disease after entering endemic areas. It is clear, therefore, that advancing age does not necessarily confer immunity to leprosy.

In areas where leprosy is common, the average age when first signs are detected is very much earlier than in places where the disease is endemic but rare. In Texas, for example, Kluth ([31]) found that the average age at the stated time of onset was about 40 years.

The relationship of the age when first signs are noted to opportunity for exposure is well illustrated by the cases of leprosy in veterans of the United States military forces. Of the 32 veterans mentioned above who served in the Spanish-American War and are listed by Hasseltine ([25]), 27 were born in the continental United States but only 6 in Louisiana, Texas or California. The average age at which first signs were noted, from data published by Aycock and Gordon ([2]), was 46 years. On the other hand, of 51 World War I veterans who were admitted to Carville (Hasseltine ([25])), 18 were born outside the continental USA and 33 in the southern tier of states; that is, none was born in a northern state. The average age at the time of first signs, again according to the data of Aycock and Gordon, was 28 years. Presumably the leprosy of the Spanish-American War was principally due to exposure during service; that of World War I to exposure prior to service. The story of World War II and the Korean War is probably not yet completed.

In the communities studied in the Philippines to which reference has been made, the peak of the attack rate was found to be in the age group 10 to 14 years for both lepromatous and nonlepromatous leprosy. The median age, however, was considerably lower for the nonlepromatous. A rapid decline occurred after adolescence. These attack rates are shown in Fig. 1.

Among household associates, the peak of incidence was also found in the age group 10 to 14 years. The median age, however, was younger than for those developing the disease who were not known to have been exposed. Exposure to the disease under the circumstances prevailing in these households was probably not equal for all age groups, but must have been more nearly so than under any other conditions of ordinary civilian life. The explanation of the early peak and rapid decline under conditions of household exposure must be that resistant individuals become more and more frequent as age advances.

In so far as reactivity to lepromin may be depended on as a measure of resistance, the results of testing give support for the idea that increasing frequency of resistant persons may control the age distribution of leprosy. As a matter of interest the curve of *nonreactivity* to lepromin has been included in Fig. 1. There is, however, no intent to overemphasize any correspondence that there may be. A similar or perhaps closer resemblance might be shown between the leprosy attack rates and the results of tuberculin or Schick tests. Also Guinto ([18]) has under observation several persons who have contracted leproma-

tous leprosy although they were found by him some time before onset to be reactive to lepromin—but only weakly so.

It may be concluded, therefore, that the age at which leprosy is contracted depends primarily upon opportunities for exposure, but that in areas where the disease is common the controlling factor is the acquirement of resistance.

SPECIAL PROBLEMS

The phenomenon of decline of leprosy.—Many reasons have been offered for the decline of leprosy in areas where it was once prevalent.

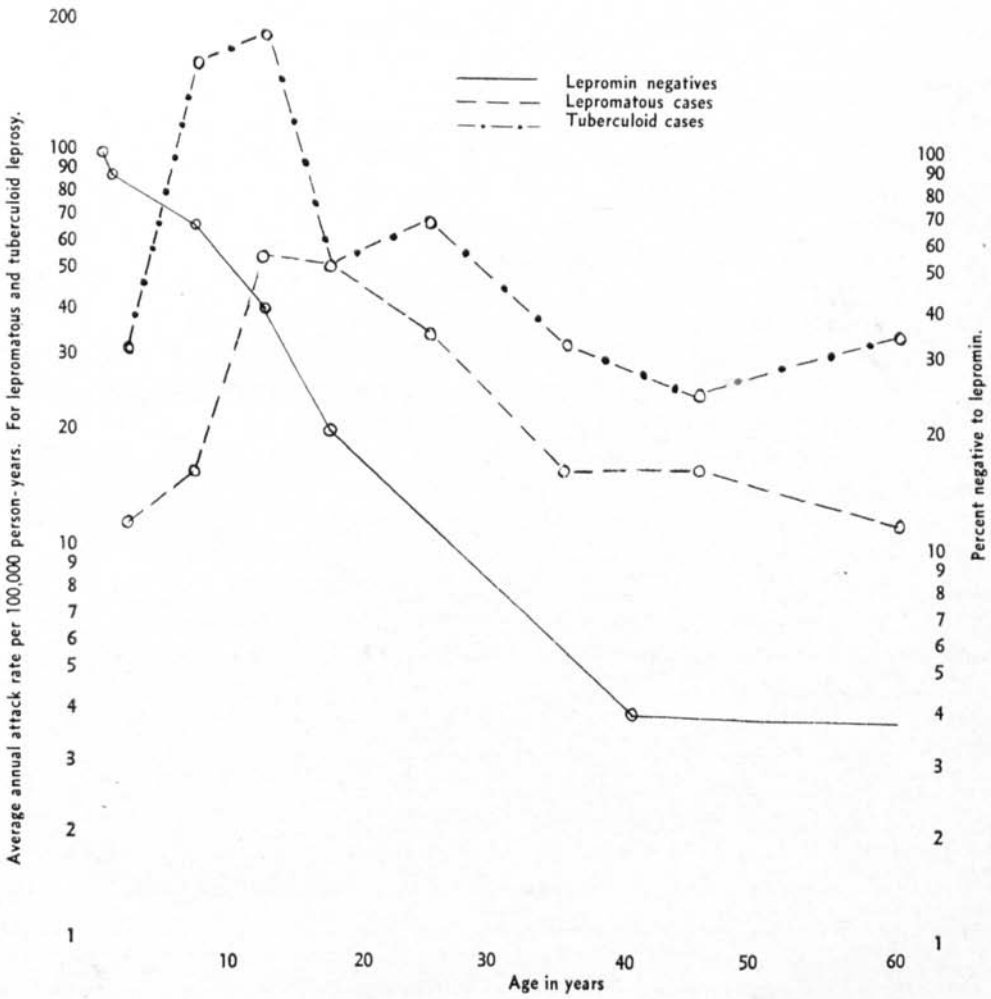

FIG. 1.—Attack rates for lepromatous and tuberculoid leprosy and percentages of nonreactors to lepromin by age, general population of Cordova and Talisay, Cebu.

In Norway, for example, segregation of infectious patients, improvement in general health by better diet, and many other explanations have their advocates. It is possible that several factors have operated, including a loss in pathogenicity of *M. leprae*. It is also possible that a relatively small reduction in exposure or a slight increase in resistance might have a major effect on the course of a disease that can do little better than maintain itself—as was suggested by Frost ([16]) regarding tuberculosis.

For some time, the lepromatous type of leprosy has been declining in the province of Cebu, Philippines. Evidence of this is to be seen in results of repeated prevalence surveys in two study areas of the Leonard Wood Memorial and the Department of Health, and is also apparent from the reduction in the number of patients admitted to the Eversley Childs Sanitarium, the sole leprosarium serving the province.

In the analysis of our data some time ago (Guinto *et al.* ([20])), an interesting point came out which is worthy of study in other areas where valid statistics can be obtained and of further study in the Philippines. To determine whether or not households in which lepromatous leprosy had been present had shared proportionately in the decline in that type of the disease, attack rates for persons exposed to lepromatous leprosy in the household and for persons in the community not known to have been subjected to household exposure, as estimated for the historical (presurvey) period were compared with rates prevailing during the interval between the initial and the more recent surveys. These rates in each case were calculated by a modified life-table method, and represent the averages for the life experience of those on the records for the period before the first survey (historical) and between the two surveys (observational).

It was found that for household associates the average annual attack rate was 59 per cent lower for the interval between the surveys than for the preceding period; for persons living outside these households the reduction was 72 per cent. If the reason for the decline of lepromatous leprosy in these communities were solely a diminishing opportunity for person-to-person contact, a wider difference would be expected between persons exposed in the household and other persons with respect to the amount of the reduction. Actually the factor or factors operated almost as well—possibly somewhat less—within the infected household as in the general population.

That something peculiar was going on which had affected the entire community is suggested also by the fact that, as the lepromatous type declined, a compensatory increase occurred in the nonlepromatous form ([20]).

Infectiousness of the tuberculoid type.—The part played by the tuberculoid type of leprosy in the spread and continuance of leprosy in a population is by no means clear, and intensive field studies are neces-

sary to determine it.

In parts of the world in which the great majority of recognized cases are of this type, the opinion is widely held that tuberculoid cases may play a significant part in spread of the disease. Davison ([8]), Macdonald ([36]) and Brown ([4]), for example, have objected strongly to classifying the tuberculoid type as noninfectious. This position appears to be a logical one as is shown by the following arguments:

1. If leprosy is being maintained or is increasing in any area, and the great preponderance of the cases are shown by careful surveys to be of the tuberculoid type, the simplest hypothesis is that open cases of this type are playing some part in the spread of the disease. There is no reason to doubt that lepromatous cases are, individually, far more dangerous than the tuberculoid, but they may be too few and too scattered to account for the observed prevalence.

2. If infective cases, of both lepromatous and tuberculoid types, are assumed to be distributed at random throughout the area, the populations coming into contact with each type would be proportionately to one another as the numbers of cases of each type are to one another. That is, if 50 per cent of the cases are lepromatous and 50 per cent tuberculoid, one-half of the population of the area may be assumed to be exposed to each type. If only 20 per cent are lepromatous, only 20 per cent of the population would be exposed to them and 80 per cent to the tuberculoid.

3. If the additional assumption be made that the relative risk of infection from the lepromatous and tuberculoid cases, respectively, is that which was observed among household contacts in the Philippines, that is, 4:1, the following results would be expected. In the case of a 50-50 distribution of lepromatous and tuberculoid cases, and of the respective populations exposed to each type, 80 per cent of subsequent cases would be derived from the lepromatous and only 20 per cent from the tuberculoid. But, if only 20 per cent of the original cases were lepromatous and 80 per cent tuberculoid, one-half of the subsequent cases would be derived from each type.

Granted that tuberculoid cases may contribute to leprosy prevalence and that their importance will vary in different communities according to the relative infectiousness and frequency of the two types, an interesting theoretical question arises. Can a high prevalence of leprosy, say 50 per 1,000 be maintained if the cases are predominantly of the tuberculoid type and the relative risk of contact with each type is that observed in the Philippines?

If the chance of effective contact in any area is a random one, it would require an average annual incidence of about 2.6 per 1,000 to yield a prevalence of 50 per 1,000 at the end of twenty years. If an average duration of 20 years be taken for the period in which the person is counted as having the disease (usually life), about the same annual

incidence (2.5 per 1,000) would be required to maintain a level of 50. If only 20 per cent of the infecting cases are of the lepromatous type and 80 per cent tuberculoid, such a cumulation would require that the attack rate for all the population of the area would have to be about as high as that observed in the Philippines for persons exposed to leprosy in the household. This can be checked, roughly, by noting that an annual attack rate of 6.2 per 1,000 for 20 per cent of the population, and one of 1.6 per 1,000 for 80 per cent of the population would yield a total annual rate of 2.5 per 1,000.

In theory, therefore, a high prevalence of the disease can be maintained indefinitely in an area where the great majority of the cases are of the tuberculoid type only by assuming that the effective contact rate for the general population is at least as high as that observed under conditions of household exposure in the Philippines, or by assuming that the tuberculoid type is relatively more infectious than it is in the Philippines. Neither of these assumptions is of course incredible. There is at present no way of determining whether the leprosy bacillus of the Philippines is identical with that of Africa or India, unless tests in the hamster or mouse prove to be of value. Climatic or other environmental conditions in certain areas may increase the frequency of reactions in cases of the tuberculoid type, rendering them infectious for a greater part of their clinical course than they are in the Philippines. Field and laboratory studies could throw light on some of these points, and until these have been made there is probably not much profit in speculating about the problem.

The question of a heredity factor.—It is quite certain that leprosy is not an hereditary disease. As to whether or not there are people who inherit a predisposition to it, there is no more evidence than was available to Hirsch. There are some studies that could be made, although the low incidence of the disease makes them difficult. The occurrence of the disease, its clinical type and course, in identical as compared to fraternal twins is a subject that might be studied further. There have been a few reports on this subject ([5]), ([29]), ([48]). Two pairs of apparently identical twins are under observation at the Leonard Wood Epidemiological Unit at Cebu. The disease in each pair is lepromatous and has been remarkably alike in its course.

Possibly some information might be gained by a study of the preponderance—if it occurs—of the tuberculoid or of the lepromatous type in certain families. It is known that both types occur among household associates of lepromatous cases, and also among such associates of tuberculoid cases. The question of a tendency toward the milder or the more severe form has never been studied as far as I am aware.

New techniques.—The production of granulomatous lesions in the ear lobe of the Syrian hamster by Binford ([3]) and in the footpad of the white mouse by Shepard ([49]), offers prospects for determining the

viability and pathogenicity of *M. leprae* in patients, in contacts, and in insects which may be suspected to be vectors. These new techniques may turn out to be valuable adjuncts in the newer epidemiology of leprosy. Also, Shepard has proposed a method for estimating the numbers of acid-fast bacilli in the nasal secretions which might be used as a basis for classifying cases according to their degree of infectiousness in epidemiologic studies.

SUMMARY

We may conclude that our knowledge of leprosy has been substantially extended since the day eighty years ago when Hirsch could see little that was hopeful. Additional and more convincing evidence of its contagiousness has been obtained. Although direct proof is still lacking that *M. leprae* is the etiological agent, the evidence is strongly in that direction and promising experimental studies are under way.

A great deal has been learned concerning the clinical varieties, and especially concerning the frequency and importance of the tuberculoid type. The lepromin test now provides helpful information as to the resistance of the individual.

Field studies have defined, much more precisely than before, the relative risk of household association with persons suffering from the lepromatous and nonlepromatous forms, respectively, and the influence of sex and of age. There is much more that could be learned, and some suggestions regarding future field studies have been made.

Perhaps the major difference between the present and the past is that we now have a good working hypothesis, admittedly with many weak points, but one that is coherent and in accordance with current biologic thought.

RESUMEN

Cabe concluir que nuestros conocimientos de la lepra se han extendido sustancialmente desde aquel día hace ya ochenta años en que Hirsch podía ver bien poco en que cifrar esperanzas. Se han obtenido nuevas y más convincentes pruebas de la contagiosidad del mal. Aunque falta todavía prueba directa de que el *M. leprae* sea el factor etiológico, los datos disponibles apuntan poderosamente en ese sentido y hay en camino estudios experimentales prometedores

Hemos aprendido mucho acerca de las variedades clínicas, y sobre todo acerca de la frecuencia e importancia de la forma tuberculoidea. La prueba de la lepromina facilita actualmente útil informacion en cuanto a la resistencia del individuo.

Estudios en campaña han definido, con precisión mucho mayor que antes, el relativo riesgo que entraña la convivencia casera con personas que padecen de las formas lepromatosa y no lepromatosa, respectivamente, y el influjo del sexo y de la edad. Resta aun mucho más que cabe aprender y ya se han hecho algunas indicaciones para futuros estudios en campaña.

La mayor diferencia entre el presente y el pasado quizás consista en que ya contamos con na buena hipótesis como punto de partida, reconocidamente con muchos puntos débiles, pero que es coherente y armoniza con las actuales ideas biológicas.

RESUMÉ

Nous devons admettre que notre connaissance de la lèpre a fort progressé depuis le jour, voici quatre vingts ans, où Hirsch n'entrevoyait que peu d'espoir. Des arguments supplémentaires ont renforcé la conviction du caractère contagieux de l'affection. Quoique la preuve immédiate n'ait pas été fournie de ce que le *M. leprae soit* l'agent causal, tout porte à se rallier à cette opinion et des études expérimentales pleines de promesses sont en cours.

Beaucoup a été appris en ce qui concerne les variétés cliniques, particulièrement en ce qui regarde la fréquence et l'importance du type tuberculoïde. Le test à la lépromine fournit à présent des informations précieuses sur la résistance des individus.

Des études sur le terrain ont dégagé, de façon beaucoup plus précise qu'auparavant, les risques relatifs de la cohabitation avec des personnes souffrant de lèpre lépromateuse ou non-lépromateuse, ainsi que l'influence du sexe et de l'âge. Il reste cependant encore beaucoup à apprendre, et certaines suggestions ont été avancées pour l'avenir en ce qui concerne les études sur le terrain.

Peut-être la différence fondamentale entre hier et aujourd'hui est-elle le fait que nous avons à présent une bonne hypothèse de travail, avec de nombreux points faibles sans doute, mais à tout le moins une hypothèse de travail cohérente et qui s'accorde avec les conceptions biologiques actuelles.

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