

## RISK OF ATTACK IN LEPROSY IN RELATION TO AGE AT EXPOSURE\*

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### INTRODUCTION

It is a common opinion among leprologists that the risk of developing leprosy is affected predominantly by the age at which exposure takes place. Recently, this opinion has been expressed clearly by one of the leading students of the disease, Dr. R. G. Cochrane, as follows: "The greatest individual cause of infection is close contact, . . . this and the age of the individual play a far greater part in the epidemiology of leprosy than all the other factors frequently suggested" (1). It is on this conception that the practice of prompt segregation of patients with lepromatous leprosy and the policy of early removal of infants from contact with leprous parents are based.

There is now sufficient evidence that the risk of contracting leprosy is far greater for individuals exposed to lepromatous patients in the household than for other persons living in the same community. In the Philippines the relative risks are five or six to one (2). Also, for the same area (2) statistical evidence shows that the average age at onset is somewhat younger for patients known to have been subjected to household exposure than for others, although in both exposed and non-exposed the highest incidence occurs in the age group of 10 to 15 years.

More precise measurement of the influence of age at exposure is obviously desirable but very detailed epidemiological studies are necessary for this purpose. The total number exposed must be determined, a fact obtainable only for households in which a case has occurred. It is necessary to learn also the type of leprosy, both for primary and secondary cases, and, as closely as possible, the date

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of onset. In addition, dates of birth, and subsequent histories through a sufficient period of years, must be ascertained for all members of these households.

For milder forms of leprosy, incidence can be measured accurately only by keeping such individuals under close supervision for a long time. For lepromatous cases, it is, however, quite possible to estimate rates of incidence from the study of the past experience of existent households.

#### SOURCE OF DATA

Data for the present analysis were collected in 1933 and in 1936-7 in two municipalities in the Philippine Islands, Cordova and Talisay, in the province of Cebu. Surveys were under the joint sponsorship of the Bureau of Health of the Philippines and the Leonard Wood Memorial Fund.

Cordova, the first area studied, is situated on the small island of Maectan about one mile east of the city of Cebu. The island is low-lying and of coral formation. At the time of the survey few crops were grown and the population was economically dependent on fish, copra, and hemp which is derived from the maguey plant. The general economic condition of the municipality was very poor.

Talisay, on the main island of Cebu, is situated about 7 miles south of the city of Cebu. The area surveyed included not only the low-lying plains but also a river valley and hills. Unlike Cordova, the soil is relatively fertile, the principal crop being sugar cane. At the time of the survey some fishing was done and in most areas fruit and vegetables were grown. The general economic level of the population was appreciably above that of Cordova.

The procedures which were followed in both communities included (1) a house-to-house census of the inhabitants, (2) physical examination of the inhabitants for leprosy and other skin diseases, and (3) epidemiological investigation of all cases of leprosy. Cooperation of the population was excellent; 99.3 per cent of 10,672 inhabitants in the Talisay area and 98.3 per cent of 6,063 in Cordova, submitted to examination.

The two municipalities were alike in that each had a relatively high prevalence<sup>2</sup> of leprosy (3, 4). In Cordova in 1933, the prevalence rate was 17.2 per 1,000, but exclusion of neural cases considered to be quiescent or arrested, lowered the rate to 13.4. In Tali-

<sup>2</sup> By prevalence is meant the number of cases existent in a community on a specified date. In contrast, incidence refers to the number of new cases occurring in a specified period of time.

say in 1936-7, the total rate was 19.5, reduced to 15.2 by exclusion of inactive neural cases. In Cordova 44.2 per cent of the patients were known to be bacteriologically positive and in Talisay 50 per cent. The prevalence in both areas was higher in males than in females.

The epidemiological investigation included for each household the complete family roster, with birthdate, sex, and leprosy status for all past and present members. For exposed persons not present in the household the date of death was ascertained, or the date of departure, if moved to another residence. The date of onset and type of leprosy were determined for each patient with leprosy. Information obtained from the family was checked against the records of the Culion Leprosarium and of the Eversley Child's Treatment Station at Cebu.

The data relating to influence of age at exposure were considered to be sufficiently complete only for the study of lepromatous leprosy; that is the analysis is restricted to records of individuals exposed to lepromatous cases in the household and the secondary cases included in the study are only those of the lepromatous type.

The families included are those for which it was possible to complete the life experience of every known member from entrance into the family, either to death, to development of leprosy, to departure to another household or community, or to the end of the period of observation, taken as June 30, 1933, for Cordova and as October 30, 1936, for Talisay.

#### METHOD OF ANALYSIS

To determine the risk of developing leprosy a modified life-table method was adopted. This method involves determination of person-years of risk, that is, each year of life of an individual is regarded as a unit. For any given group the incidence rate is expressed as the average number of cases per 1,000 person-years, which is regarded as equivalent to observation of 1,000 persons for one year. The schedules include individuals who were born eighty years or more before the date of investigation and infants born only a month or two before. It should be borne in mind, therefore, that the incidence rates are not applicable to the present but are a statement of what has occurred during the life experience of households of Cordova and Talisay, in which one or more members were living and present at the time of the inquiry.

An individual was considered to have been exposed if he had lived under the same roof as a leprous person for a period of at least one month. Subsequently he was considered to be at risk as

long as he remained in the community, regardless of the removal of the patient from the household or of the removal of the individual to another residence in the community.

Individuals born in any household in which there was an existent case of leprosy were considered to be at risk from birth. Those present at the time of onset of the primary case were allotted one-half year of risk at their age at time of onset. Individuals entering the household while a leprous person was present were likewise given one-half year's experience at their age at entrance. Departures, either because of death or removal, were given one-half year's experience at their age at time of departure.

Since previous analysis had shown that the two areas were similar as regards both prevalence rates and incidence rates, data from Cordova and Talisay were combined. On the family schedules there were included the records of 755 males and 765 females, who gave a history of exposure in accordance with the definition adopted. For each of these individuals the years of risk were calculated, yielding a total of 19,553 person-years. In this experience there occurred 89 secondary cases of lepromatous leprosy, or an average annual incidence of 4.6 per 1,000 person-years. It may be noted that this is approximately 5.5 times the incidence rate for persons in the general population not known to have been subjected to household exposure.

#### INFLUENCE OF AGE AT EXPOSURE

The life experience of these households, classified according to the ages at which the individuals were first exposed, the cases of lepromatous leprosy developing, and the incidence rates, are given in table 1, by sex and age.

This table indicates clearly a definite relationship between age at exposure and age at which signs of leprosy were first observed. Among children who were exposed at ages under 5 years, the majority at birth, no cases occurred before they reached 5 years of age. Lepromatous cases have been reported in young children but are rare (5); most have been of the neural (macular) type. Between 5 and 10 years of age the annual incidence rate averaged 7.9 per 1,000. The rate increased to a maximum of 17.8 at 10 to 15 years and fell to 12.4 at 15 to 20 years. The rate for persons 20 years and over who were exposed before 5 years of age was only 3.5 per 1,000. Thus the experience, at successive ages, of those exposed in infancy and early childhood in these households, shows that the highest incidence of lepromatous leprosy is reached about 10 years after exposure.

TABLE 1

*Secondary attack rates for lepromatous leprosy following household exposure to lepromatous leprosy, according to age at exposure and age at attack.  
Cordova and Talisay, Cebu, Philippine Islands*

Age at Exposure	Sex	AGE AT ATTACK												All Ages	Ratio of Rate to Rate at All Ages					
		Under 5 Years		5-9 Years		10-14 Years		15-19 Years		20 Years and Over										
		Person-yrs.	No. of Cases	Person-yrs.	No. of Cases	Person-yrs.	No. of Cases	Person-yrs.	No. of Cases	Person-yrs.	No. of Cases	Person-yrs.	No. of Cases	Person-yrs.						
Years																				
Under 5	Male	955	0	0.0	983	12	12.2	699	17	24.3	453	7	15.5	497	2	4.0	3587	38	10.6	1.6
	Female	812	0	0.0	781	2	2.6	540	5	9.3	354	3	8.5	349	1	2.9	2836	11	3.9	1.6
Total		1767	0	0.0	1764	14	7.9	1239	22	17.8	807	10	12.4	846	3	3.5	6423	49	7.6	1.7
5-9	Male			245	0	0.0	383	7	18.3	233	3	12.9	284	1	3.5	1145	11	9.6	1.4	
	Female			214	0	0.0	372	0	0.0	254	3	11.8	317	1	3.2	1157	4	3.5	1.4	
Total				459	0	0.0	755	7	9.3	487	6	12.3	601	2	3.3	2302	15	6.5	1.4	
10-41	Male					205	1	4.9	338	1	3.0	477	5	10.5	1020	7	6.9	1.0		
	Female					224	2	8.9	333	1	3.0	504	0	0.6	1061	3	2.8	1.1		
Total						429	3	7.0	671	2	3.0	981	5	5.1	2081	10	4.8	1.0		
15-19	Male								161	2	12.4	738	2	2.7	899	4	4.4	0.7		
	Female								178	0	0.0	945	2	2.1	1123	2	1.8	0.7		
Total									339	2	5.9	1683	4	2.4	2022	6	3.0	0.7		
20 and Over	Male											2916	4	1.4	2916	4	1.4	0.2		
	Female											3809	5	1.3	3809	5	1.3	0.5		
Total												6725	9	1.3	6725	9	1.3	0.3		
All Ages	Male	955	0	0.0	1228	12	9.8	1287	25	19.4	1185	13	11.0	4912	14	2.9	9567	64	6.7	
	Female	812	0	0.0	995	2	2.0	1136	7	6.2	1119	7	6.3	5924	9	1.5	9986	25	2.5	
Total		1767	0	0.0	2223	14	6.3	2423	32	13.2	2304	20	8.7	10836	23	2.1	19553	89	4.6	

Turning to those exposed at 5 to 10 years of age, no cases occurred before the age of 10 years. Between 10 and 15 years the incidence rate was 9.3 per 1,000, increasing to a maximum of 12.3 at 15 to 20 years, and falling off sharply to 3.3 at 20 years of age and over. Again, the age of maximum incidence occurred 10 years after exposure.

For those exposed at 10 to 15 years, the maximum incidence rate, 7.0 per 1,000, occurred in this same age group. The rate fell to 3.0 at 15 to 20 years and increased to 5.1 at 20 years and over.

Similarly for those exposed at 15 to 20 years the maximum incidence rate, 5.9 per 1,000 again occurred in the same age group. The rate fell to 2.4 for those of 20 years and over.

These data indicate a variable period between exposure and development of noticeable lesions of lepromatous leprosy. Taking the statistics at their face value, this period must be much longer when exposure occurs in infancy and early childhood than when

it occurs in later childhood and adolescence. The average interval between exposure and recognition of the disease in 64 persons exposed before the age of 10 years was 10.5 years; and for 25 individuals exposed after the age of 10 years, it was only 6.0 years. It may be that some secondary factor more common to adolescents than to young children is necessary to bring a latent infection to light.

These data also reveal a definite relationship between the age at which exposure takes place and the probability of developing leprosy. The average annual incidence rate for those exposed before 5 years of age was 7.6 per 1,000; for those exposed between 5 and 10 years, 6.5; for those exposed between 10 and 15 years, 4.8; for those exposed between 15 and 20 years, 3.0; and for those exposed at ages over 20 years, it was only 1.3 per 1,000. The ratio of the attack rate for each group to the rate for all ages thus decreases regularly, for each age band at exposure, from 1.7 to 1 for those exposed before 5 years of age to 0.3 to 1 for those exposed after the age of 20 years. This suggests greater susceptibility of young children to the disease; the earlier the exposure the greater the risk. In available records there are insufficient data to exclude the possibility that some or all of the excess incidence observed in those exposed at the younger ages may be attributable to greater intimacy of exposure. An infant crawls about, handles contaminated objects, and may be fondled by a leprous member of the family. The comment may be made, however, that in these households, the primary case occurred infrequently in the mother.

Nothing has been said regarding the possible effect of duration of exposure. In the Philippines, for many years, lepromatous cases have been segregated promptly following discovery. It is not likely that the period between onset and discovery would be affected by the ages of those exposed in the household.

Examining the data for males and females separately it will be seen that the major fact previously noted is true for both sexes, namely, there is positive correlation between age at exposure and risk of contracting leprosy. This risk is very much higher for males than for females regardless of age at exposure. From other studies it would appear that this finding may be peculiar to lepromatous leprosy. Incidence rates for neural leprosy do not indicate a pronounced selectivity for either sex (2). The marked difference between incidence rates for the sexes in early childhood, and especially for those exposed at birth or shortly after, leads to a first assumption that the responsible factor is not greater exposure of males than of females but rather greater susceptibility of males.

Judging from the experience of those exposed under 5 years,

admittedly too limited an experience to justify a final conclusion, it would appear that if a difference in susceptibility between the sexes exists, it tends to decrease as adult life is approached. For children in successive quinquennial age groups from 5 to 9 years upwards, the ratio of male to female incidence was 4.7, 2.6 and 1.8 to 1. For those 20 years and over, it was 1.4 to 1. This decreasing ratio is difficult to explain, assuming about the same number of males as of females to be infected, some secondary factor must reduce the resistance of the former. This factor, whether it be an inherent susceptibility as we have previously suggested (2), or some external factor, becomes progressively less important as the children grow older.

In reaching the conclusion that greater susceptibility of the male is the chief factor, it has been assumed that environmental conditions are identical for male and female children. It should be mentioned, however, that in the localities under consideration, there was a conspicuous tendency to provide small female children with clothing to a greater extent than male. This would be protective if *Mycobacterium leprae* enters through the skin.

In favor of the view that males are more susceptible than females is the fact that the overall picture, when exposure to the disease takes place in later childhood, also indicates a substantially greater risk for males. Unfortunately the data are too limited to justify further speculation on this matter.

#### SUMMARY

A study of the life experience of 1520 individuals living in the province of Cebu, P. I., and exposed in the household to lepromatous leprosy reveals the following facts:

1. There is a clear relationship between age at time of exposure and the risk of developing lepromatous leprosy. It is highest for those exposed before the age of 5 years, decreasing progressively as the age at time of exposure increases. This is true for both males and females.
2. The ratio of the incidence rates for males to those for females, for those exposed before 5 years of age, varies from 4.7:1 for rates in the age band of 5 to 10 years to 1.4:1 for those of 20 years and over.
3. The average interval between exposure and development of lepromatous leprosy was 10.5 years for those exposed under 10 years of age but only 6.0 years for those exposed after the age of 10 years.

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