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HEREDITY IN LEPROSY¹

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There can be no doubt that leprosy is a family disease in the sense that it often occurs in many members of one family. There can also be no doubt that prenatal transmission of leprosy from parent to child is of such rare occurrence that it can be regarded as unimportant, if not negligible, as a cause for the prevalence of leprosy in families. The mooted question is whether or not a predisposition to the disease is an hereditary family characteristic.

Statistical facts can be presented in support of the view that there is an absence of immunity in certain families, but the same facts can be advanced as arguments for the theory that the contagiousness of leprosy is the sole cause of familial infection.

In regard to the inferences made in this paper concerning an inheritable predisposition it should be understood that it is recognized that leprosy is an infectious disease and that infection is always the direct cause of its transmission. The inferences suggested are tentatively submitted in further explanation of some facts observed in Louisiana that do not seem to be adequately accounted for by infectiousness alone.

RACE

As is well known, leprosy was prevalent in Europe in the thirteenth century. Leloir (1885) estimated that at that time

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there were nineteen thousand leprosaria in Europe, and two thousand in France alone. Leprosy is now a rare disease in Europe. Its gradual disappearance during the seven centuries since it was at the peak of its incidence may be explained by the assumption that during this long period of years succeeding generations in those countries have developed an increasingly great degree of immunity and that this immunizing process has resulted in a people in whom the number of susceptible individuals has become very small. It is true that such an immunization can not be shown to be the sole cause of disappearance of the disease. The isolation of lepers in the Middle Ages, improved methods of living or the disappearance of unknown factors necessary for the transmission of the disease from person to person, may explain this almost complete disappearance in the white races. However, in the absence of knowledge of the method of transmission from individual to individual the assumption that individual susceptibility plays no part in acquiring leprosy is unwarranted, and the belief that lesser susceptibility is an inherited characteristic is not unreasonable.

Leprosy resembles tuberculosis more closely than it does other diseases, and what has been said of hereditary immunity in tuberculosis is equally applicable to leprosy, if not more so (Rich, 1936). "Hereditary differences in individual resistance are, in all probability, of great importance in slowly elevating the average level of resistance of a race through the principle of survival of the fittest." The rarity of leprosy among Europeans at the present time, if due to the operation of this principle, indicates a far more efficient action in leprosy than in tuberculosis.

Conversely to the disappearance of leprosy in Europe, its rapid spread in the Hawaiian Islands, where it did not exist until comparatively recent times, is an instance in which a race without hereditary immunity becomes widely infected when leprosy is introduced.

From Texas there have been admitted to the National Leprosarium 130 lepers. In connection with the question of possible differences in the degree of susceptibility in different races it is interesting to note that 63 of the lepers admitted from Texas were of Mexican descent, 2 were of half Mexican descent, and the remaining 65 were Americans of more or less remote European ancestry, or approximately one half of the number of lepers from Texas were of Mexican stock and one half American. Numerically, the ratio of the white to the Mexican

race as given by the United States Census of 1930 is more than six to one in Texas. If the number of admissions be taken as an index of the prevalence of leprosy in the two races in Texas it must be recognized that the incidence among Mexicans is greater than among Americans. Furthermore, it may be said that very few Negroes have been sent to the Leprosarium from Texas, which seems to indicate that the fact of being of a dark-skinned race does not of itself explain the comparatively large number of Mexicans received at the institution. It can not be determined accurately whether the Mexican lepers contracted the disease in Mexico or in Texas, but it may be said that no patients are retained at the Leprosarium who are not citizens of the United States. If the greater incidence of leprosy among Mexicans be granted, nevertheless, it might be said, it does not follow that the race is less immune, but, on the contrary, that conditions of living of the Mexicans are inferior to those of Americans and that it is on this account that infection spreads among them to a greater extent. An answer to this argument is found in the comparable fact that in the adjoining state of Louisiana leprosy is much rarer among Negroes than among white people.

From Louisiana there have been admitted to the National Leprosarium 261 lepers. Of these, 61 were Negroes and 200 were of Caucasian or other than Negro descent. According to the United States Census of 1930 the Negro population is more than half that of the white. The percentage therefore of Negroes admitted to the Leprosarium in proportion to their population in the state is smaller than that of the white race in proportion to their population, and it may be inferred from these figures that the incidence of leprosy in the black race is less than that in the white, because it is not probable that, in Louisiana, Negroes, if afflicted, could more easily avoid isolation than their more influential and resourceful white neighbors.

A comparison of the incidence of leprosy in the Mexicans of Texas and the Negroes of Louisiana discloses a difference which can not be explained on the basis of the communicability of the disease alone. The average Mexican in Texas and the average Negro in Louisiana may live under conditions more adapted to the transmission of communicable diseases than does the white population of these states, but in Texas leprosy apparently is more common among the Mexicans than among

the Texans of Caucasian ancestry, while among the Negroes of Louisiana the reverse obtains. The theory that poor living conditions favor the communicability of leprosy may apply to the Mexicans, but it certainly does not apply to the Negroes. It is quite possible, however, that the Mexican is racially less immune and the Negro more immune than individuals of the white race.

It is believed that one source from which leprosy came to Louisiana was the importation of Negro slaves from Africa. Why the foci then established have not caused a wide-spread prevalence of the disease in the race in which it has existed for such a long period is difficult or impossible to explain, except by the assumption of partial immunity in the Negro race. Living conditions of the Negro, though admittedly bad in the United States, yet are presumably much better than were those in his native African environment. It is tentatively submitted that in his native home his resistance was comparatively high or that his racial immunity became augmented when he was abruptly transplanted to America into better hygienic surroundings. Confessedly, this argument would be stronger if it could be applied to tuberculosis as well as to leprosy.

Leprosy is not the only disease to which greater immunity is found in the Negro than in the white race. Epithelioma of the skin is so rare in the black race that cases can be regarded as medical curiosities, and psoriasis is much less common in the Negro than in the white man. It is true that in both of these diseases cutaneous pigmentation may be considered as an explanation of the immunity.

It can not be said, however, that pigment in the skin is the cause of the Negro's high resistance to leprosy, because the skin type of leprosy occurs as frequently in proportion to the nerve type in the Negro as it does in the white race, which obviously would not be the case if the skin were protected by its pigment. Furthermore, the occurrence of nerve lesions as found in the nerve type indicates that the color of the skin *per se* is not the cause of either high or low resistance to neural leprosy because protection in the skin could hardly extend its influence as deeply as the nerves affected in this type. Expressed in the vernacular, the immunizing factor is more than "skin deep."

In certain parishes in Louisiana leprosy is quite common among the French-speaking population, many of whose ances-

tors emigrated from Canada. The story of this emigration has been told by Longfellow in his poem "Evangeline." These immigrants very probably brought leprosy with them from Canada to Louisiana, and the persistence and spread of the disease among them and their descendants must be regarded as an indication either of the communicability of leprosy or of the hereditary predisposition of a racial strain, and it does not seem improbable that the latter factor is at least partly responsible when the greater incidence of leprosy in these French-speaking parishes is compared to the rarity of the disease in the adjoining English-speaking parishes.

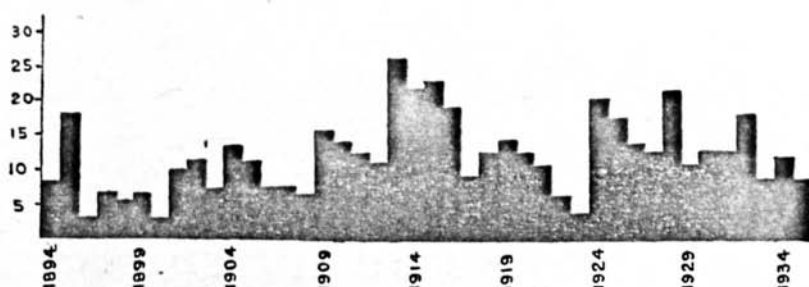


CHART 1. Admissions of lepers from Louisiana by years from 1894-1935.

FAMILY

In a previous publication Denney and the author (1929) noted that, of the inmates of the Louisiana Leper Home, which received patients from the entire state, 33 per cent. were as closely related as parent and child, brother and sister, uncle or aunt, nephew or niece.

In one group of 36 families there were 119 lepers. In this group there were five instances in which the disease occurred in a father and one or more of his children, fourteen instances in which the disease occurred in a mother and one or more of her children, fifteen instances in which the disease occurred in sons of lepers, twenty-one instances in which the disease occurred in daughters of lepers, thirty-eight instances in which the disease occurred among brothers, and thirty-one instances in which the disease occurred among sisters. In less close relations leprosy occurred in: eight uncles, eight aunts, eighteen nephews, nine nieces, five grandfathers, three grandmothers, six grandsons and five granddaughters. There were only three instances of hus-

band and wife, and there was some doubt as to whether or not these three were all cases of conjugal infection.

Charts were also exhibited showing family trees in which numerous members of several families were lepers. One of these charts (No. 2) is reproduced to show additional members of the family affected since the publication of the first chart. The second family tree shows the occurrence of leprosy in a very large percentage of the third generation. A count of the black circles, which indicate leprous members of the family compared to the white circles, which indicate unaffected members, leaves little doubt that some factors existing in the family or in the familial relations have been the cause of the occurrence of leprosy in such a large number of closely related individuals. If leprosy were a common disease and as infectious as influenza, it would not be surprising that so many cases should occur in

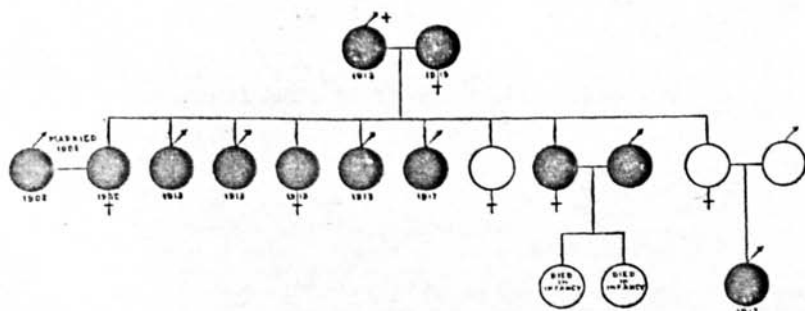


CHART 2. Ten known cases of leprosy in three generations of one family; also husbands of two women of second generation.

one family, but, even in Louisiana, where it is endemic, leprosy is a comparatively rare disease. If the cases shown in the charts represented a few isolated instances of great family incidence, they might be considered as accidental happenings, but during the last forty years or more a constant and continuous occurrence of leprosy in closely related members of families has been observed both in the former Leper Home of Louisiana and in the National Leprosarium. Its occurrence in three or four generations has almost exterminated not a few large families.

That leprosy is a communicable disease, that prolonged and intimate contact affords the most favorable conditions for infection, and that children are more prone to infection with Hansen's bacillus than are adults, must be granted; but it remains difficult to understand how these factors alone can be a sufficient

explanation when it is considered that the leper often has many and more than casual contacts over long periods of years, in addition to those with his family, and that the vast majority of those exposed, but unrelated by blood, do not contract the disease. A notable instance in which such prolonged and intimate contact has only infrequently resulted in infection is in the conjugal relationship. Comparatively few husbands have infected their wives or wives their husbands. A partial explanation of this surprising fact is that children are more prone to infection than adults, but this reason alone is not satisfactory, because leprosy can by no means be said to be a disease entirely of childhood. However, the explanation becomes more satisfactory if it is further assumed that husband and wife, being unrelated by blood, do not share the same heredity and

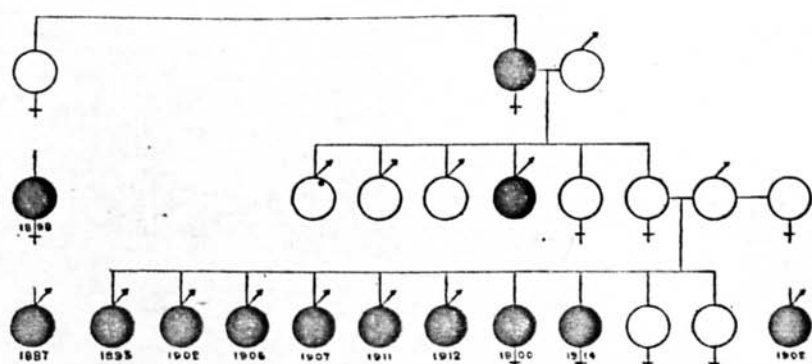


CHART 3. Thirteen known cases of leprosy in three generations of one family; one mother infected years after her son.

in consequence one may be hereditarily susceptible while the other has inherited such a high degree of immunity that the disease is not contracted from a leprosy spouse even though contact be as prolonged and intimate as it is in the marital state.

Other instances of adult infection have apparently occurred when leprosy has developed in children years before its appearance in their parents. This reversal of the chronological sequence usual in hereditary diseases does not disprove the theory of a familial inherited susceptibility, but merely indicates a lack of resistance in both parent and child. When susceptible individuals of different generations are exposed to contagion it is not to be expected that the parent should always be the first to acquire the disease. The sequence of events depends solely on which individual is the first to be exposed to contagion.

SEX

Since the establishment of the National Leprosarium 809 lepers have been admitted. The number of males has been more than twice that of the females. This disproportion of males to females is approximately the same as that previously observed in the Leper Home of Louisiana and in all other countries in which surveys have been made. Sex characteristics can not be regarded as hereditary in the same sense in which a predisposition to disease might be, but the apparent greater immunity of females is evidence of the fact that there is some factor controlling the transmission of leprosy in addition to that of exposure to infection. The sex difference in incidence occurs in such widely separated countries and among peoples of such various habits and customs that the conclusion is almost inescapable that females are inherently less susceptible than males and that they do not owe their greater immunity to accidents of environment or to lesser exposure to contagion.

FOCI

Chart Number 1 shows the number of admissions from Louisiana from the time of the establishment of the Louisiana Leper Home in 1894 to the end of the year 1936. The decreased number of admissions in the years 1922-23 is explained by the fact that in those years admissions of patients from Louisiana were restricted because of lack of housing facilities in the institution, caused by numerous admissions from other states when the Federal Government bought the State Home. The laws of Louisiana require the isolation of lepers in the institution, but it is believed that many evasions of the law occur. The number of admissions may, however, if taken as an index of the prevalence of leprosy in the state, show a slight decrease in recent years.

The belief that the incidence of leprosy in Louisiana is growing less becomes more credible when this slight decrease is considered in connection with the probability that a greater proportion of the lepers in the state are now being segregated than in former years. The evidence of decline is not conclusive, but at least there is no evidence of increase, and speculation is interesting, because of the possibility of several factors that might be the cause. Isolation of lepers has been more or less enforced at different times since Louisiana was a French colony; immunity may be gradually becoming established; or

the foci may be gradually disappearing for reasons unknown, as they are in Minnesota and in certain parts of Canada.

That foci disappear may be attributed to environmental changes which make the transmission of Hansen's bacillus impossible, but this view does not preclude the possibility of heredity as a predisposing factor in those communities in which leprosy is indigenous. Neither does the fact that only sporadic or imported cases are found in some communities prove that leprosy is not infectious where conditions are favorable for its transmission, nor that predisposition is not a characteristic important in the propagation of the disease.

Although leprosy is more common in Louisiana than in other states its incidence is very small compared to that of most other diseases. It certainly is much more rare than is tuberculosis, and its relative rarity may well be due to an inherited immunity in a very large percentage of the population.

INDIVIDUAL IMMUNITY

The personnel of the Leprosarium now numbers 199 and there has been no instance of leprosy developing among them, nor was there any instance in the personnel of the former Leper Home of Louisiana. Included in the personnel are Sisters of Charity now numbering 19. Sisters have been in attendance upon the lepers as nurses during the last 41 years. The belief now generally accepted that leprosy is but feebly contagious would be a satisfactory explanation for the fact that no cases have developed in the attendants, were it not for the fact that in the familial relation leprosy shows itself to be by no means feebly contagious but quite the contrary. It is true that precautions are taken to safeguard the personnel, and it may be true that these precautions alone have been sufficient for the protection of the attendants. However, the thought naturally occurs that leprosy is not easily acquired by the average adult individual because of characteristics that are inherent in himself.

In explanation of the relatively great resistance of adults it has been said of tuberculosis: "that adults possess acquired resistance as a result of previous, well-resisted, immunizing infections, whereas many of the children of tuberculous parents will be exposed to the massive infection before they have acquired those slight, immunizing, primary infections" (Rich 1936). This view may apply to tuberculosis, but it does not apply to leprosy,

because the rarity of leprosy in these days precludes the possibility of sources of infection in sufficiently great number, and sufficiently dispersed throughout entire countries, to furnish the necessary material for those slight immunizing infections. If this principle is the cause of the greatly reduced incidence of leprosy in the white race, it is because of its operation in past times when leprosy was prevalent, not in the present time, when in most communities the source of these immunizing infections is non-existent. In other words, the resistance which has developed through this process is now an inherited rather than an acquired characteristic.

CONCLUSIONS

It is possible, even probable, that Europeans and descendants of Europeans have acquired a high average level of resistance to leprosy.

The high incidence of leprosy in the Hawaiian Islands is an instance of the rapid propagation of leprosy in a people lacking hereditary resistance.

The Mexican in Texas has less resistance to leprosy than the Texan of American ancestry.

The Negro in Louisiana has a higher degree of resistance to leprosy than has the Louisianian of Caucasian ancestry.

The lesser incidence of leprosy in females than in males is attributed to inherent feminine characteristics and not to habits, occupation or environment.

The extent to which leprosy occurs in family groups suggests an hereditary familial lack of resistance. The small number of cases occurring in husband and wife indicates an inherited high degree of resistance in the unaffected spouse.

The fact that no cases of leprosy have developed in the attendants at Carville during a long period of years is attributed in part at least to inherited immunity.

Recognition of the possibility of an hereditary predisposition to leprosy emphasizes the importance of the segregation of lepers in whom the disease is active. Prolonged and intimate contact of lepers living with their families exposes to infection certain individuals in whom there is a probability of less than average resistance to the disease.