

SUPERINFECTION WITH LEPROSY *

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PREVIOUS ATTEMPTS AT HUMAN INFECTION

Repeated attempts have been made to transmit leprosy from man to man by inoculation, but there is no certainty that leprosy was ever induced in this way. On the other hand there are numerous reports of persons who nursed lepers and themselves fell victims. It is believed that the leprosy bacillus is the cause of the disease, that contact is the way in which the bacilli are transmitted, and that the presence of lepers brings danger, however little, to the neighborhood.

These considerations have led many doctors to try to transmit the disease to themselves or to other healthy persons. Danielsen, who repudiated the infection theory, repeatedly inoculated himself and persuaded others to be experimented upon. Medical students, young doctors, nurses and others—a total of twenty persons—were inoculated without success. He used fluid from leprosy wounds and leprosy tissue, but the details of the experiments were not precisely recorded.

Various later experimenters have dared to make similar experiments, as Profeta, Holst, Witsch, and various Japanese researchers. Not one of these had success. Better success was had by Arning, of Honolulu, who inoculated leprosy material into the forearm of a Hawaiian prisoner condemned to execution. A year later there was a small ulcer at the site of the inoculation and a swelling of the ulnar nerve, and leprosy bacilli were found. In the course of the following year both lesions cleared up, but four years after the inoculation the patient developed general leprosy that went on to a severe form and continued till his death. But even this case is not entirely certain,

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for it was found later that there were two lepers among the patient's nearest relatives, so that he may possibly have been infected before the inoculation.

However, there are several recorded instances of typical leprous processes appearing after slight wounds with infected instruments. These cases make the skin a possible avenue of infection, though they give no certainty in the matter.

A CASE OF ACCIDENTAL INFECTION

We have personally observed a case of accidental infection that is not of less interest from the epidemiological viewpoint, though it also is not absolutely definitive.

A full blooded European, 48 years of age, in good material circumstances, living in one of our tropical cities, developed a severe attack of gallstones. A doctor gave him an injection of morphine but by mistake used, unsterilized, the syringe and needle that he had just used on a leper, who was suffering from an acute exacerbation of the disease—extremely sick, with high fever and pain.

Six months later a small anesthetic swelling appeared on the forearm, at the site of the injection. In the interval this place had sometimes itched, and now and then had assumed a dark red color. This swelling slowly extended peripherally and the ulnar nerve became thickened. Somewhat later small anesthetic areas of infiltration appeared on the upper arm, the hand and the right thigh, and some months after that similar infiltrations on the face. We saw the patient six months after the first small swelling was noticed and made a diagnosis of leprosy. Many bacilli were demonstrated in material from the first lesion.

For a year treatment was mild—small doses of chaulmoogra pills—and the process extended. The anesthetic patches on the forearm developed further, lepromata appeared on the back of the hand, and the lobe of the left ear became infiltrated. Intensive treatment was then begun—full doses of chaulmoogra pills, injections of E.C.C.O., and later the chaulmoogra esters, the injections being pushed to the limit of tolerance. The patient was a powerful man, and on one occasion received 10 cc. of chaulmoogra esters daily for fourteen days. He reacted strongly to this, but without unpleasant after-effects. The process promptly stopped extending, the existing lepromata gradually became smaller, and the bacilli in them gradually decreased and finally disappeared entirely. After several years of treatment the lesions had healed completely, with the exception of certain anesthetic patches. The patient has now been clinically cured for six years and bacilli cannot be found in sections.

The history of this patient was carefully considered to determine whether there was any possibility of a former infection. He had been thirty years in the tropics, with only the ordinary leave periods in Europe; he had never cohabited with a native woman; he had

always lived in the European residential sections of the cities in which he had been, and knew of no contact with a leper, but leprosy is endemic in the places where he had lived.

EXPERIMENTS ON SUPERINFECTION

Inspired by this case we decided to make experiments in regard to the infectibility of human beings. Not feeling justified in making experiments on healthy persons, we were restricted to tests with lepers. We chose patients with only slight skin and nerve changes, examined by biopsy the skin to be inoculated to make sure that it and the subcutaneous tissue were entirely normal, and gave the patients large doses of potassium iodide or a small dose of tuberculin to see whether they would undergo exacerbations of the disease with the formation of lepromata in the parts of the skin examined. Inoculations were made with various substances and under various conditions. Such tests do not have the same experimental value as if made on healthy persons, but they give further insight into certain points of the epidemiology of leprosy, and also have a distinct value in respect to therapy and prophylaxis.

Inoculations with leproma emulsion.—At first we used salt-solution suspensions of finely ground leproma tissue rich in bacilli, both from other patients and from the same patient. Different quantities were injected intracutaneously and subcutaneously in the normal skin areas. These injections caused limited red swellings that sometimes disappeared within 48 hours. In other instances they enlarged slightly for the first week, then came to a standstill and finally disappeared. In one instance an infiltration remained for one and a half months; in another it lasted some three months, but bacilli had disappeared as early as the third week.

We also made surface scarifications and rubbed in the tissue emulsion. There usually resulted no more than a redness of short duration, though in lepers of long standing a circumscribed infiltration sometimes persisted for a longer period. But here also there were no lepra bacilli to be found. In these experiments we did not succeed in making an inoculation take.

Inoculation with blister fluid.—Later we worked with inoculation material obtained by making blisters on lepromata with hot metal. The fluid, exceptionally rich in bacilli, was taken up in a syringe for injection. These experiments also gave negative results, even after repeated injections in the same place.

Inoculation with pus.—Pus and exudation products of leprous wounds, rich in bacilli, gave only local redness and swelling, once with a lymphangitis that did not, however, become a leprous process.

Result with reaction-case material.—A positive result was first obtained with an emulsion of a leproma from a patient who was quite sick, having had for some weeks a severe acute exacerbation, with fever and extensive swelling and reddening of the lepromata. This material was injected subcutaneously into another leper. On the following day there was slight redness that disappeared after several days but left a small persistent infiltration. This was so inconspicuous that it was not easily found. The patient noticed only a slight itching now and then. In the fourth week the patch became slightly larger; this developed so that at the end of the fourth month there was a sharply defined infiltration about 1 by 0.5 centimeter.

At first the sensibility was normal. In the sixth month there was definite diminution of the pain and temperature sensibility, though the sensibility to touch was entirely unaltered. In the fifth month smears showed numerous leprosy bacilli. Biopsy material removed in the eighth month showed masses of bacilli and lepra cells in a structure reminiscent of other lepromata.

During the first eight months the patient was not treated; then we felt that this could no longer be put off and it was started with moogrol. The leproma ceased to enlarge and became more superficial; in later excisions lepra bacilli were found only in the most scanty numbers, though sixteen months after inoculation they were still to be found and the structure was still lepromatous.

FURTHER EXPERIMENTS WITH REACTION-CASE MATERIAL

Patients with fever and acute exacerbation are infrequent with us, but on a few occasions we have been able to repeat this and other inoculation experiments. In choosing cases for experimentation we took those as young as possible, though without further justification such inoculation experiments could not be made on children. The age is important, susceptibility to infection being greatest in infancy.

Twelve inoculations have been made with such material. In eight cases the results were negative. In three they were positive after the first injection and in another after the second. In the eight negative cases the inoculation was repeated several times, but without effect until a positive result was obtained in one of them after the fourth

inoculation, the patient having been given a large quantity of the inoculation material subcutaneously, and two grams (30 grains) of potassium iodide per day for two weeks.

Control experiments were made with physiological saline, emulsions of healthy skin and of skin from a febrile malaria patient, a few drops of turpentine, and 1 cc. of blood, from both a leper and a healthy man. The results were entirely negative.

DISCUSSION

Our experiments show that at least leprous superinfection through the skin is possible, though we have not proved that infection of healthy persons is possible in this way. Such superinfection may play a role in the spreading of the leprous process in a patient, though spread by other avenues, as the blood or lymph channels are probable. This possibility at least points to the practical value of the care of the skin in leprosy, and of the external therapy that has been practised for centuries, above all by the use of medicated hot baths. Superinfection may be of importance in leper colonies where the patients are crowded and uncleanly, and failure of treatment in such places may be directly related to this.

In our experiments we followed the progress of an inoculation leproma under intensive treatment by the chaulmoogra acid esters, beginning in the fourth month, when there were many lepra bacilli. The development of the leproma continued for about three weeks, then it came to a standstill and gradually retrogressed. Further tests along these lines should be made to investigate the influence of modern methods of treatment on the leprous process.

All our experiments with various materials failed except for certain of those made with material from patients sick with fever and aggravation of their lepromata. Every worker knows these periods, which sometimes last only a few days, or may extend over weeks or months, with high fever and prostration. The lepromata swell, occasionally recover for a time a part of their normal sensitivity, and sometimes present actual hyperesthesia. New lepromata may develop and old ones retrogress or even disappear. Usually there form transitory red infiltrations that are gone within a day or two, as quickly as they were formed; often such lesions that at first are found negative for bacilli become positive in another week, and ultimately the foci become typically leprotic.

The fact that only material from these acutely sick lepers gave positive results raises the question whether there may not be here a partial explanation of the epidemiology of leprosy. It is certainly possible that most lepers when their disease is stationary or progressing quietly have only a limited influence on the spread of the disease, that the virulence of their bacilli is so reduced that they cannot transmit the leprosy process.

On the other hand it seems probable that lepra bacilli in the acutely sick cases have acquired such a character that when brought into the skin of a healthy person they can give rise to the leprosy process. From this follows the theory of a divided infectivity of lepers; that they are not infective during their rest period, and become so only at the times of acute exacerbations with fever.

Such a phenomenon could explain much in the epidemiology of leprosy. Definite settlement of this would provide a most important guide for efforts at the stamping out of leprosy. Obviously the patient in this phase must spread lepra bacilli about his surroundings. It seems that as with tuberculosis we must speak of "open" and "closed" leprosy, of fully and restrictedly virulent lepra bacilli. Perhaps the theory, based on incomplete data, loses itself in fancy, but in the light of these experiments the problem deserves consideration and further study.