

volume which bears no relation to the thickness of the wall. The cells are deposited in an uncolored filamentous basis substance looking like coagulated fibrin, and generally are the size of a white blood-corpusele, with a large dark-colored nucleus which nearly fills the cell. Now and then there are also several small nuclei instead. At the same time there are numerous epithelioid cells, especially in the neighborhood of the blood-vessels, of very variable form, and some young spindle-shaped connective-tissue cells.

In striking contrast to these small cells are others five or six times larger, with very voluminous, bright, vesicular nucleus, which contain masses of beautiful smooth bacilli (with and without spherical spores).

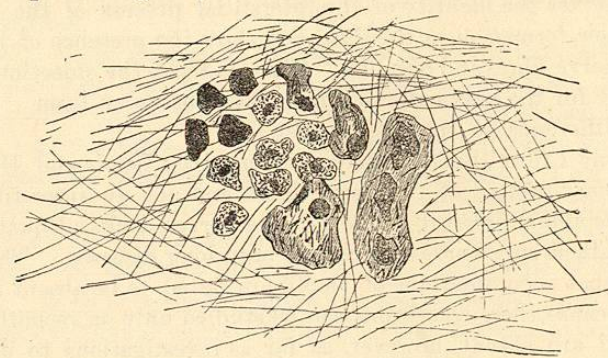


FIG. 25.—Section from wound granulations.

At times it seems as if these cells lie singly or together in lacunæ of the basis substance. Also giant-cells with three or four nuclei, with or without bacilli, are not rare. Besides the exceedingly well-preserved rods, we find smaller corpuscles tapering conically which are not bacilli viewed obliquely or vertically. I might add that these granulations proliferate with uncommon rapidity on leprosy excision wounds. The formation of epidermis is long delayed through the crusting of the drying granulations.

B. Still more conclusive appear to me the experiments on animals. A freshly extirpated tubercle is under antiseptic precautions inserted into the peritoneal cavity of a rabbit (G. operated on November 6th, killed on November 11th). The autopsy shows the tubercle inclosed in a connective-tissue capsule adherent to the great omentum. Microscopic examination: The mass of the original tubercle has perished by necrosis; not a single nucleus is stained. Only the arrangement of the clearly stained hives of bacilli still represents a picture of the tubercle cells formerly constituting the basis. Externally to this is first a zone so densely packed with granular detritus that bacilli are no longer recognizable. But the adjoining layer of connective tissue—in which we trace from the centre toward the periphery layers of all stages of inflammation and inflammatory connective-tissue formation to the development of ordinary narrow bright caudate connective-tissue cells—contains a considerable number of strikingly large, round, longitudinally oval and elongated bacilliferous cells with large bright nucleus, in form intermediate between epithelioid and completed connective-tissue cells.

Also in the newly formed fine-fibrillary connective tissue of the surrounding capsule we find bacilliferous cells in which the rods lie either in small agglomerations or scattered singly by the side of the nuclei. Everywhere the bacilliferous cells distinguish themselves by their size and by a retardation in development as compared with their neighbor cells of the like age in the same layer. The fact is noteworthy that the bacilli represented specially smooth and intact rods.

That white (inflammatory) blood-corpuseles generally can harbor bacilli may be demonstrated on every dry preparation of leprosy nodular pus (after ulceration of such nodes). Cells in no way differing from ordinary pus-corpuseles are full of beautifully stained bacilli.

V. It may be demonstrated that corresponding to every developmental phase of the lepra cell there is a corresponding state of the bacilli.

The older and larger the cell, the greater become the number and density of the bacilli and their derivatives deposited in the protoplasm. Finally there arise large round, sharply limited agglomerations which untinted present a strong waxy lustre, but in anilin colors take an almost homogeneous deep stain. These agglomerations (globi) represent the acme of the bacillar infiltration in the protoplasm. At the same time, however, it is possible to demonstrate a change of protoplasm by chemical staining (by a distinct red coloration in gentiana violet instead of the normally obtainable decoloration of the body of the cell). Finally there is a direct connection between the vacuole formation and the condition of the bacilli, namely, the dropping out of the bacilli deposited in clusters in the protoplasm.

If we draw the conclusions from the facts thus far enumerated, we are justified, as far as I can see, in assuming:

The specific form and nature of the lepra cell is incited etiologically by the immigrated specific bacillus. This leads in natural sequence to the further conclusion: The entire affection is a bacterial disease.

And indeed, in our opinion, no doubt can exist about this point, even if the strictly scientific proof is still lacking for leprosy, as has been furnished for tuberculosis by Koch's cultivations.

That these cultivations are possible I have convinced myself by a number of successful trial cultures on boiled egg albumen and on blood-serum gelatin. It will be more difficult to find a species of animal appropriate for inoculation, nor is there on record a single positive observation of a (non-experimental) spontaneous leprosy affection in animals. In two instances I succeeded in producing in dogs, by the introduction of small leprosy particles into the subcutaneous connective tissue, local neoplasms identical with human lepra tubercles both histologically and by the presence of bacilli in the tumor cells. General disease did not follow these local processes.

VI. Leprosy is a contagious infectious disease. This is demonstrated, aside from the arguments thus far advanced, by the manner in which this plague formerly spread over the earth.

In the first place it is certain that lepra has been introduced into islands and countries formerly free from this disease.

We shall not dilate upon the more remote importations, and confine ourselves to two islands of which accurate data are on record.

On the island of Trinidad there were in:

1805, among 29,940 inhabitants,	3 patients;
1813, " 32,000 " "	73 " "
1878, " 120,000 " "	860 " "

The most instructive example, however, is presented by the Sandwich Islands. On these islands, distinguished by the healthfulness of their climate, the excellent fertility of the soil, the fine and vigorous physical development of the natives, the disease had occurred until 1859 only in isolated cases carried thither by landing sailors; among the natives it was altogether unknown. In 1859, a German physician, Dr. Hillebrand, observed the first two cases of leprosy on the islands themselves, on two immigrated Chinese who came under treatment at the Hospital in Honolulu. Since then the disease has increased rapidly to such an extent that as early as 1866 the government was forced to resort to measures of isolation, and forwarded four hundred patients to a smaller adjoining island (Molokai). In 1881, the number of patients in Molokai is eight hundred; the last statistics of the Board of Health estimate that about 4,500 natives, that is, one-tenth of all the aborigines, are affected with leprosy.

The native population amounts to about 45,000. From the publications of this Board of Health we learn also that in the last fifteen years about 2,000 lepers have died at Molokai. All those familiar with these islands are agreed that the morals and character of the natives specially favor the spread of an infectious disease; while their physical development, and the excellence of the climate must appear absolutely inadequate to explain the etiology. Stress is laid on the dwelling of large families in small huts, the common use of the same vessels and utensils, eating from a single dish, the fingers being employed for taking out the eatables, drinking from one and the same vessel, smoking the same pipe, the very loose morals, the absence of any dread of the disease, whence patients are not only not isolated, but, on the contrary, secreted as much as possible by the authorities; hence also cohabitation and marriage between the well and the sick, etc. The natives, however, even hold the disease to be contagious.

Still not only natives suffer the disease, but often enough immigrated Europeans, in whom the disease can almost generally be traced to longer, more intimate intercourse with other lepers. That such an infection does not take place in every instance can be enumerated as a counter-argument in leprosy as little as in similar cases of syphilis.

Genuine cases of leprosy, in countries free from the disease, however, do not exist. Such, at best sparse, reports date altogether from a time when the only pathognomonic sign—the demonstration of the bacillus—was not known. All cases of true leprosy occurring in Germany, England, France, etc., can without exception be traced either to infection from lepers or, more commonly, to residence in tropical leprosy countries.

Like the appearance of leprosy, so its spread and disappearance can be traced only to contagiousness, not to miasmatic conditions. For we may formulate the law: The spread of leprosy stands in inverse relation to the measures of isolation to which the patients are subjected in the several localities. By the rigorous seclusion of lepers this plague was exterminated several centuries ago in Germany and France; and the same fact is repeated on isolated islands by appropriate measures taken by the government.

In Norway, too, the number of patients is steadily diminishing, since the majority of lepers have been more or less isolated in the hospitals erected.

However, it should be stated here that the relations of the disease prevailing at the present time in Norway, Spain, Livonia, etc.—for instance, the rarely demonstrable occurrence of direct infection (of the hospital attendants, from husband to wife, etc.)—cannot be utilized in the settlement of the present question without qualification.

In these countries we are undoubtedly dealing with a weaker quality of virus—a fact demonstrated by the average duration of the disease in Europe, 15 to 25 years, as compared with that on the Sandwich Islands, 3 to 5 years.

Thereby the factors above indicated, which are necessary for the actual effectuation of the infection, gain still greater importance. The more scrupulous the cleanliness, the more airy the living-rooms, the more the patients are isolated in the family, and the greater the fear of the disease, etc., the less the affection will be able to spread—relations which are present in an absolutely equal manner in syphilis and are universally recognized.

It remains for us to state that the inhabitants of the Sandwich Islands were seized in an equally terrible and rapid manner with syphilis, and for the same reasons, above given, which allowed so swift an extension of leprosy.

The transfer takes place from man to man, and may be direct, or indirect when only the bacilli or their spores are transmitted. Pus containing bacilli (spores), therefore, will be liable to infect, but not any kind of pus coming from a leprosy patient. Whether, in analogy with anthrax, the spores possess so great a power of resistance that they retain

their vitality outside of the animal body in the corpses of lepers, and thus are able to provoke the disease when they subsequently reach the human organism, has not been ascertained. This infection—by the spores of former human leprosy bacteria—is by no means a purely miasmatic one; nor do I believe that, in order to produce the disease, formerly non-pathogenetic bacteria change into pathogenetic ones within the human body.

The way in which the infection is brought about is likewise still a matter of supposition, though well founded. At any rate, here as in tuberculosis, there is required a lesion of the external layers of epidermis which allows the penetration into the subcutaneous or submucous connective tissue. Inasmuch as the growth of the bacilli is very slow, a superficial excoriation, from which the bacilli can be easily removed, will not suffice, but there must be the establishment of a more deep-seated protected focus of infection. The bacilli enter the organism either as such or, more probably, as spores; remain in incubation, varying with circumstances, in depositories, perhaps the lymphatic glands, and thence migrate into the rest of the body. Judging from the participation of the lymphatic glands, in the majority of cases the first infection takes place on the skin of the face, the hands, the genitals, and on the mucous membrane of the first respiratory passages. At least great swelling of the glands in the inguinal or submaxillary region is a regularly recurring condition. (Recently, indeed, Koch has demonstrated in anthrax that the participation of the lymphatic glands furnishes no certain landmark respecting the point of infection in any infectious disease.)

The duration of the incubation in leprosy is extremely variable. Its determination is all the more difficult because a true primary affection is altogether absent, and leprosy really always presents itself to us as a complete constitutional disease. Men have contented themselves with reckoning from the approximate date of the infection—sojourn in a leprosy country—and accordingly have assumed incubations extending over years, even decades.

The spread of the bacilli or their spores in the organism takes place chiefly, if not solely, by way of the lymph channels.

According to my investigations, the blood-vessels under ordinary conditions do not seem to transport either bacilli or spores. I did not succeed in a single instance in demonstrating bacilli in the lumen of blood-vessels, and I have always had negative results with dry preparations of blood. Also cultivations of blood taken from healthy portions of skin remained without positive results. On the other hand, if the blood be drawn from leprosy new-formations, spores and bacilli, demonstrable microscopically or by cultivations, get into the escaping blood, through the mechanical lesion, from the neoplasm out of the lymph channels. The opposite view is entertained by Majocchi and Pellizari. Köbner, too, noted the isolated presence of bacilli in the blood, but agrees with me in this, that the lymphatic vascular system is the main channel for the spread of the bacilli. The latter are transported either in the free state or by white lymph-corpuseles.

In favor of this view are further:

1. The arrangement of the infiltrations around the adventitiæ of the blood-vessels which have been demonstrated to contain lymph spaces, while within the blood-vessels bacilli could not be shown with certainty.

2. The clinical observation that both the first outbreak and the relapses of tubercular eruptions on the skin appear with erysipelatous cutaneous inflammations known to us as diseases of the lymphatic vascular system. Suppuration never occurs with them,

from which we may deduce the peculiar character of this disease which is akin to erysipelas. These same forms of dermatitis, on the other hand, always lead to local recoveries on the affected regions—disappearance of the tubercles, leaving brown spots containing an abundance of amorphous blood pigment—but invariably give rise to an exacerbation of the entire course, with renewed leprosy eruptions in other cutaneous regions, that is to say: plentiful transportation of fungi from one region into another.

It is likely that the blood vascular system participates in this transportation of spores in "erysipelas," but thus far this supposition remains unproved. Majocchi and Pellizari state that the presence of schizomycetes in the blood will manifest itself best in the eruptive period of leprosy, or, to speak more correctly, with every repetition of an eruption.

3. The above-mentioned experiments on animals (introduction of freshly extirpated tubercles into the body of rabbits and dogs) prove the fact that there are local transportations of bacilli and spores without the participation of blood-vessels.

Presumably only spores are carried from one region to another, while the local progress of the leprosy infiltration probably takes place by the peripheral migration of bacilli (*e. g.*, in the cornea).

Finally, in favor of the view that the lymphatic vascular system transports the spores or bacilli, is the extraordinary swelling of the largely bacilliferous lymphatic glands and their great painfulness during all the erysipelatous affections accompanying the eruptions.

But is the contagion of leprosy transferable by way of intrauterine infection; IS LEPROSY HEREDITARY OR NOT?

Most authors incline to the view of hereditary, by the side of direct infection in extra-uterine life. Others speak of inherited disposition. In our opinion, there is no satisfactory PROOF for either of these views; but more for the former than for that which would only grant inherited disposition. On the other hand, we must admit the POSSIBILITY of heredity, and especially of an hereditary disposition.

The doctrine of heredity is based exclusively on statistical data. Against this it must be objected:

1. These tables do not give such high figures in favor of the asserted heredity as to appear demonstrative by reason of striking numbers.

2. But these tables and their results admit of another interpretation—infectiousness without heredity. In most of the countries in which leprosy still prevails, the patients live more or less isolated from the healthy population. The patients intermarry, the children grow up surrounded by their diseased parents, relatives, and neighbors.

3. The fact that the disease occurs very rarely previous to the third to fifth year of life, in most cases not before the second decennium, has more force against than for heredity. In all these cases we should have to assume an incubation lasting for years, even in regions in which the course of the disease itself is more rapid than this asserted latent stage. A case of congenital leprosy has never been recorded, as far as I know.

4. I hold it to be altogether erroneous to try to explain the spread of the disease by heredity only, without infection. We need but point to the rapid spread of the disease in the Sandwich Islands—from 2 to 4,500 in twenty-two years; this would be absolutely inconceivable by heredity alone.

But, while the proof of a direct inheritance is still completely lacking, the assumption of an inherited disposition can be more easily defended.

For the two forms of leprosy, viz., lepra tuberculosa and lepra nervorum, are fre-

quently sharply demarcated geographically, so that in certain sections the one or the other form occurs almost exclusively. Besides, the cases in which hereditary transmission can be assumed are considerably more numerous in lepra nervorum than in tubercular leprosy. In explanation of this fact, I think, we might assume a congenital disposition, either of the cutaneous tissues or especially of the nervous connective tissue, which brings about the affection of these organs particularly.

As to the sex of the patients, we find a preponderance of males in all districts and in every form of leprosy.

Cases between the first and the tenth year are very rare, more frequent are attacks in the second, and most numerous in the third decennium, after which they decrease.

DIAGNOSIS.—The diagnosis presents no difficulty in the tubercular form. But it is the demonstration of bacilli which facilitates the diagnosis of tubercular leprosy in the same way as it places each individual case beyond doubt.

More difficult is the diagnosis of pure lepra anæsthetica, especially in the initial stages. An accurate knowledge of the symptomatology is all the more requisite for these cases because the criterion valid for the tubercular form, the presence of bacilli, cannot be utilized during life, of course, owing to the localization of the leprosy process in the peripheral nerves.

Once for all it must be borne in mind that there is no genuine leprosy in countries otherwise free from the disease, that the possibility of infection, by residence in leprosy regions or by intercourse with lepers, must always be present.

TREATMENT.—Leprosy is an absolutely incurable disease. Although from year to year new therapeutic propositions are made which have proved effective in isolated cases, none of them have proved available for the extirpation of the malady.

All the more weight will have to be laid on prophylactic measures:

1. Isolation of the patients in hospitals; quarantine regulations against the introduction of the disease.

2. Prevention of the possibility of infection given by every single patient for his surroundings.

I refer in the first place to the careful, disinfecting local treatment of open ulcerations, the secretion of which contains bacilli and spores in specially large quantities. In the second place, the attempt will have to be made to remove the tubercular eruptions previous to their softening, which can be done, for instance, by chrysarobin. At any rate it seems to me as if the local treatment in general had not hitherto received the attention it deserves.

I shall merely mention the reported successful (?) attempt at securing improvement in lepra anæsthetica by nerve stretching, and even by suturing the nerve.

Change of residence to a non-leprosy country or otherwise healthy climate has proved effectual. The course of the disease thereby usually becomes milder and slower.

This experience refers mostly to Europeans who return to their native country after they have acquired the disease in tropical zones. In these cases, the improvement should be ascribed to the fact that the patient is again surrounded by the accustomed and more appropriate climatic and other conditions. The little patient whom I have had under observation for two years (born in Surinam; sick from his fifth year; in Germany two years) shows no improvement in his condition, in spite of favorable surroundings and extensive therapeutic experiments.