

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.

III. SYPHILIS.

Syphilis has hitherto been held to be the infectious disease most nearly related to leprosy. But now it is certainly determined that there is no connection in any direction between leprosy and syphilis, since a leper may also acquire syphilis. On the other hand, we know now that tuberculosis and leprosy represent a group of diseases belonging together through their striking resemblance, while syphilis is farther removed from them. Nevertheless the near kinship of these three affections to one another is not to be disputed, so that we feel justified in looking upon the contagion of syphilis as an organized, bacterial one. This reasoning from analogy becomes all the more important because the positive demonstration of the "bacteria of syphilis" seems to be still lacking. But recently Birch-Hirschfeld has published investigations to which I refer more in detail on account of their remarkable character:

On examining gummous tumors, he constantly found micro-organisms. The majority of the gummous patches were of relatively recent date. The bacteria were most numerous at the border of the granulation tissue as compared with the more centrally located cheesy infiltrations. They could be best demonstrated where the spindle-shaped and round cells of the granulation tissue were less dense. As a rule, they were altogether absent in the firmly fibrous parts of syphilomata, as well as in fully cicatrized gummous patches.

Wherever the bacteria are free in the tissue, they are always aggregated into small colonies. Then reference must be made to the presence of intercellular bacteria which could likewise be demonstrated in gummous tumors. The cells inclosing bacteria were roundish, oval, and also spindle-shaped elements of the granulation tissue; they were often spread over larger regions of the section, but the number of similar cells without bacteria in the neoplasm was by far the larger. The short, thick formations within the cells, exactly resembling those of the smaller colonies, partly filled them completely, partly they were distributed circularly in the periphery of the cell.

The micro-organisms thus described, however, are not to be interpreted as rods or bacilli, but they are cocci united into chains, thus simulating rod-like formations. The segmentation, it is true, is much more indistinct than in the majority of micrococci joined into chains; besides, the cocci, as a rule, are not round, but longitudinally oval. Usually we see micrococci and diplococci, more rarely three to five individuals united into one.

The demonstration of the above-described free colonies of bacteria is very simple. The sections (hardened in absolute alcohol and cut with the Rivet-Leister microtome) are placed for a short time in glacial acetic acid, then examined in glycerin. The colonies of bacteria can now be readily seen; they differ from the faded and swollen elements of the tissues by a certain lustre. The best staining agent is fuchsin in moderately concentrated aqueous solution. With this, the bacteria of the colonies, but especially the intercellular rods, exhibited a very beautiful red color which is again destroyed by concentrated acetic acid. Still better is a simple clarifying of the sections in caustic potassa, after which the cocci become visible in the tissue as strongly refractive corpuscles.

In the above-described manner examinations were made of gummous tumors, hardened in absolute alcohol (of the brain, of the lung of an adult and a new-born child, of the liver, of the supra-renal bodies, of the wall of the stomach, and of the intestine). In all cases the result was positive, although the quantity of the bacteria varied considerably, and in several objects only the smallest rows of cocci were found.

For the sake of comparison, portions derived from the living were examined in the fresh state; they were excised portions of broad condylomata, of an indurated chancre, of an excised papule of a papular syphilide. Here likewise were found the above-described colonies of small, relatively strongly refractive diplococci; most numerous in a broad condyloma, where they lay chiefly in the cells of the rete Malpighii and in the connective tissue of the papillary body. It is also feasible to demonstrate the micro-organisms by incising a fresh, non-ulcerated broad condyloma from its basal surface, scraping the juice from the cut surface, drying it on the covering glass, and staining it, best with fuchsin and gentian violet.

The blood of a patient suffering for a few days from roseola syphilitica showed no bacteria.

The demonstration of the same bacteria within gummous patches of different organs renders it very probable that these micro-organisms are indeed the carriers of the syphilitic contagion.

Whether these results will be confirmed or not, we believe it to be perfectly justifiable to interpret *syphilis as a bacterial disease* and shall attempt to explain the relations of the morbid process, of the infection, of the heredity, etc., from this standpoint. Of course, in entering on the details of the pathological process, we miss at every step the possibility of demonstrating the bacteria; in discussing such questions minutely, we are almost entirely confined to reasoning from analogy.

In still another, very important question, the demonstration of specific micro-organisms would bring the definite, longed-for decision: I mean the question of unity and duality of the venereal chancre poison.

I shall merely give expression to my conviction that the dual theory appears to me by far more firmly established; that therefore the syphilitic virus is altogether different from all those noxæ which produce the forms generally termed "soft chancres." Even if solitary cases appear ever so obscure in regard to the relation between the source and the product of infection, even if they seem to prove the unity of syphilis and soft chancre, it will have to be admitted that, with such involved factors and strange complications as are brought about by prostitution and extra-marital intercourse of the sexes, no basis can be gained for a positive theory from such incalculable observations.

To me the fact appears decisive that all cases of syphilis coming under observation are derived from syphilitic individuals, and not in a single case from a soft chancre without syphilis.

The acceptance of the mixed chancre which has been so freely assailed, moreover, corresponds altogether with the universally recognized observation that vaccine plus syphilis virus can be transmitted simultaneously and produce their respective effects one after the other, first small-pox pustules, then syphilis. It would even be remarkable if fewer cases of mixed infection were to occur than is actually the case. For the sources of infection are "mixed," that is to say, the preponderating majority are prostitutes who, besides the syphilis of long standing, harbor other ulcerations, vulgo "soft chancres." These latter are transmitted either alone or combined with syphilis, as the one or both of the poisons penetrate through the point of infection. Syphilitic virus, *i. e.*, parts of syphilitic neoplasms or blood (?), must be mixed with the infecting secretion if syphilis is to be transmitted. Inversely, if a man has exposed himself to the danger of infection and has not acquired syphilis, we can only conclude that no syphilitic particle has gained entrance into his system.

We must not identify syphilitic secretion with purulent secretion on a syphilitic person. Accordingly, no value can be ascribed to experimental inoculations with secretions derived from syphilitic persons, but the nature of which is not determined, whether it contains syphilis or not.

As regards the experiments on animals, it has been ascertained that monkeys, cats, and others were specially susceptible to soft chancres, while the attempts to inoculate animals with syphilis have given no positive results.

The transmissions to monkeys have, in another quarter, been referred to tuberculosis in their results, and can therefore as yet claim no full validity, for there is no proof that the neoplasms artificially produced were really of a syphilitic nature.

Moreover, there is on record a preliminary communication on inoculation syphilis of the iris and cornea of the rabbit, by Dr. Paul Haensell. Syphilitic particles were introduced into the anterior chamber; the thin-fluid purulent contents of an intact gum-

mous node, portions of mucous patches, pieces of a sclerosis before it had ulcerated. After a period of incubation of about one month, there were developed an iritis having a subacute character; then, several days later, those strongly vascularized nodules which in man are generally termed gummous tumors of the iris. In an animal which died in the sixth month after inoculation, with considerable emaciation, it was found that the lungs and liver were interspersed with small, rather hard nodules, which proved to be composed of round cells and larger, multinuclear epithelioid, at times also giant-cells.

A rabbit which had been inoculated with the products of this inoculation syphilis into the anterior chamber, presented the like appearances.

Compared with inoculated tuberculosis, the time of incubation here is much longer, and the whole course bears a much more chronic character. Of the greatest importance, however, are especially two differences. First, the nodules of inoculated syphilis are throughout their whole extent traversed by minute vessels which are altogether absent in inoculated tubercles; second, they never fall a prey to cheesy metamorphosis, which is always the case with the latter.

An attempted transmission to the monkey, which Martineau claims to have been successful, is still under observation. J. Neumann recently declared himself in favor of the doctrine of non-transmissibility to animals. He did not succeed in establishing the syphilitic poison in horses, rabbits, martens, rats, cats, or pigs; at most, there appeared local symptoms of reaction in consequence of the inoculation.

It may here quite briefly be stated that for the decision of the question above discussed, as to the unity and duality of the virus, the form of the primary ulcer ("soft" or "hard" chancre) is comparatively immaterial. We shall again revert to this point.

Nevertheless, fully conscious of the difficulties arising from this lack of sufficient and especially objective demonstrative material, I have thought it incumbent on myself to approach these questions. It appeared to me more valuable that a consistent interpretation of the pathology of syphilis be carried out from a single standpoint, even if at present still hypothetical.

In the first place, in regard to the relations of the modus of infection, we must bear in mind that the bacteria have to penetrate directly into the plasmatic channels of the organism. In the case of the external skin and the superficial mucous membranes (of the oral cavity, on the genitals), there are required, generally, mechanical injuries which arise at the moment of infection or existed previously. According to experience to date, an infection through the intact epidermis is not possible. It seems also that the mouths of the hair follicles and glands in their normal condition do not serve as points of entry to the virus. But whenever the virus meets open permeable fissures in the tissue, even if it be the most minute erosion, it adheres, and penetrates into the organism. Hence it does not require—as the bacilli of tuberculosis do—a specially protected locality; but on the contrary, in spite of the most rapid and careful efforts, it can no longer be removed from the supposed points of infection. This mode of infection by direct contact holds good for all syphilitic diseases acquired in extra-uterine life.

Non-effectuation of the infection (through a firm epidermis, etc.) must, of course, not be identified with immunity against the virus. As far as we know, this immunity does not exist in any man. (Whether the assertion that syphilis does not occur in Iceland, in spite of the plentiful nautical intercourse, corresponds to the actual conditions, and whereon they are based in that case, is to be ascertained by further investigations. Otherwise the spread of syphilis has kept equal pace with the advance of infected nations.)

Another mode of infection consists in direct introduction of the virus into the blood, such as takes place in intra-uterine syphilitic infections by means of the placental circulation.

Finally, the most direct and highest imaginable degree of infection is represented by the genuine hereditary transmission by the semen or the maternal ovum, for here all the formative material of which the new body is composed, harbors the infectious matter and develops under its injurious influence. But syphilitic semen or ovum is not to be identified with the semen or ovum of a syphilitic person. In the former case the virus is transmitted with it and will produce its specific effects, in the other case there is merely a certain cachexia of the parents, which (not being of a specific nature) will manifest itself perhaps in some constitutional anomaly (of a non-specific nature), for instance, rickets, etc.

In the two last-described modes of intra-uterine infection (*i. e.*, the "hereditary" and the syphilis acquired in utero), of course, there are no local primary places of infection.

As opposed to these forms, syphilis acquired in extra-uterine life begins always locally, *i. e.*, from a local point of infection. But this point of infection, in its appearance and the form in which it becomes manifest, is subject to the greatest variations which depend chiefly upon the anatomical configuration of the point of entry. On the skin there arise usually those neoplasms (syphilomata) which are termed "hard chancres," primary "indurations." On the mucous membranes, however, "hard chancres" are almost never seen to develop; there is a formation of superficial, corroding, non-indurated ulcerations or erosions, without any specific new-formation at their seat. (However, I wish to explain particularly that in my estimation these soft primary affections stand in no relation to the soft contagious chancre which owes its origin to a specific virus totally different, I am sure, from that of syphilis.) Only at the vaginal portion of the uterus indurated primary affections—dependent on the anatomical structure of the submucous tissue—develop frequently. Of course, with such insignificant primary affections, it may happen that they run their course unnoticed. In reference to these cases, which chiefly affect women, more rarely men, and in whom the infection naturally occurs on mucous membranes (because it is on the genitals) a syphilis *d'emblée* has been spoken of. If this is to mean: syphilis without a primary affection on the skin and mucous membrane discoverable by our eyes and fingers, this doctrine may be accepted. But if it is to signify that in these cases there is absolutely no local focus of infection present, we must object; for indeed it exists; although not visible to us on the skin or mucous membrane, it is in the lymphatic glands belonging to the point of infection (cutaneous or mucous).

The first discoverable sign of the disease (the primary effect, if you choose), then, lies in these very lymphatic glands in which the multiplication of the penetrated bacteria or their germs is effected.

Only subsequently, after a variable period of incubation, the general infection is brought about from these depositories, still representing local foci, as it were from within outward. Either the lymph channels serve this end—the ordinary course of the spreading syphilitic virus (also in leprosy, in certain cases of acute miliary tuberculosis)—or the infection of the blood produces the general disease (as in most of the acute miliary tubercloses) (Weigert).

In syphilis, therefore, we have to deal (in the form acquired in extra-uterine life) with a local infection, mostly with a so-called primary affection at the point of infection.

But what significance has this local disease in reference to the general infection? Is it the focus in which the bacteria multiply during the period of incubation, and from

which the general saturation of the whole body takes place? Or have we to deal with an instantaneous general intoxication; a "primary" alteration at the point of infection developing only partly on account of the larger quantity of the infectious material acting at this point, partly on account of the local processes preceding or accompanying the penetration of the virus?

Unfortunately, it has been impossible hitherto to gain perfect clearness in this question. In the last few years it has been attempted to satisfy even this scientific want, with the therapeutic indications, by the excision of the syphilitic primary affections. However, the results are so variable that no definite conclusion can be reached. Where, after operative removal of an ulcer or node appearing after suspected coition, no general disease followed, it must be proved that the structure removed was actually of a syphilitic nature. I am of opinion that this proof cannot be brought with certainty for the early stages of a syphilitic primary affection, because the microscopic appearances which are looked upon as characteristic by Auspitz, Unna, and Cornil do not seem to me to possess the value claimed for them. Where the excision was still followed by general syphilis, it could be objected that the operation was done too late.

According to our view, this question cannot be decided positively. As in other infectious diseases, the space of time within which the general infection is brought about will vary with the manner in which the virus penetrates into the body.

If it enters at once into the circulation, an instantaneous general intoxication will result sooner than when the bacteria, multiplying in the lymph spaces of the infected district, reach the blood at a later date. If intense inflammatory processes accompany the development of the initial affection, the penetration of the syphilitic germs into the deeper tissues and thus into the general organism, is influenced by the inflammation (it seems to me injuriously). Clinical observation (in experimental inoculations and in accurately known infections) has actually taught that the lapse of time between local infection and general disease varies between wide limits. At all events, there is a lack of any constant relation between the intensity, course, etc., of the primary affection on the one hand, and the progress of the virus in the organism on the other hand. The chief importance attaches in every case to the quantity of the virus introduced.

We know quite analogous facts in other infectious diseases. I call to mind the experiments of Renault (d'Alfort) upon the absorption of the glanders poison, and those of Colin upon anthrax. In these experiments the absorption of the virulent substances was effected within a few minutes. Opposed to this fact we have the results of Davaine, who brought anthrax matters to the surface of wounds which had been caused in rabbits by means of vesicants, energetic friction, or excisions of portions of the skin. Some of the animals were saved from general infection when cauterization was performed with caustic potassa one, two, or even three hours after. Davaine gives the following explanation of the fact. "In a subepidermal inoculation, a small number of vessels is opened, which are in immediate collateral communication with others in which the circulation continues undisturbed. Therefore, the poison is at once introduced into the general circulation. In an extensive wound, however, most of the vascular trunks are severed and without any communication with the general circulation."

It appears to us that in syphilis the greatest stress is to be laid on the fact that the general infection proceeds gradually, and that we cannot say at a given moment that it is now present, while only a little while before nothing but a local trouble existed. I believe, therefore, that hand in hand with the development of the local primary affection and the great multiplication of bacteria taking place in it, the general disease is effected from that point. The formation of an induration ("hard chancre") has nothing to do with the process of infection. The induration is nothing but a peculiar reac-

tion of the healthy skin on the effect of the syphilitic virus. With or without induration, the primary affection is a focus of infection for the general organism. The sooner it is removed, the smaller will be the quantity of the virus penetrating into the body, and the greater will be the probability that no general infection will take place, for the latter presupposes a certain large quantity of infectious material. It can hardly be doubted that this multiplication may also occur subsequently in the organism, but it requires certain preliminary conditions—resting quietly in depositories—which do not exist from the start and do not form until after the more abundant presence of the bacteria in the tissues (local foci of inflammation).

Moreover, in this question a fundamental error is committed in considering only the hard chancre as the primary affection. The lymphatic glands appertaining to the initial affection have the same importance. Two facts are in favor of this view:

1. The concurrence in time, or separation by but a few days, of the disease of the glands with the induration at the point of infection.

2. The anatomical structure of these lymphatic glands. Several times I have had the opportunity of extirpating and examining them in very early stages of the disease. The appearance is essentially the same as in the indurated ulcer, *i. e.*, inflammatory hypertrophy and new-formation in the connective-tissue portion of the glands. But if the glands in the same stage are equally diseased as the initial affection of the skin, they must also have become diseased at the same moment; that is to say, we are forced to the assumption that at the moment of infection some germs penetrated also into the open fissures of the tissues, and migrating onward, reached the glands. This consumes several days—an interval which repeats itself with the disease of the glands. (It would even be by no means surprising if the bacteria of syphilis were to get into the circulation at once; the general infection, therefore, immediately following the local infection.)

The positive demonstration of the correctness of the above-defended view has been recently brought by Bumm (*l. c.*, 11, p. 285), by an experimental inoculation.

He extirpated from a patient, in whom the syphilitic nature of a sclerosis had been assured by a macular eruption, two lymphatic glands which had swelled in direct connection with the primary affection (in the fourth week after the infection); they were scrupulously cleansed of all foreign tissue, split longitudinally with a scalpel, and with the milky-looking lymphatic serum which presented, the following inoculation was made on a non-syphilitic person: two punctures, on each arm, at a distance of twenty centimetres from each other.

On the seventh day after the inoculation, all the points of puncture, excepting one on the right upper arm of which nothing was to be seen and which subsequently also remained sterile, were marked by red dots the size of a pin point and barely recognizable. These points developed within five more days into slightly raised spots the size of a pin's head, and increasing rapidly, reached by the eighteenth day after the inoculation about the size of a cent. The surface was formed by a brownish crust, after the removal of which a small shallow ulcer remained behind. No further enlargement of the ulcers took place, but after ten more days an infiltration of the base occurred and a slight elevation of the margin which was surrounded by a red areola. At the same time it was possible to demonstrate some swollen and sensitive glandular bodies in both axillæ.

One peripheral point of inoculation of the left arm showed a very retarded course, and did not reach the phase of the other ulcers until a week later.

By the forty-third day after the inoculation, the sclerosis of both the base and the margins had developed more distinctly and the red areola around them had considerably increased. Its peripheral limitation was serrated in many ways and surrounded by a series of small papules. By the fifty-second day the outbreak of a maculo-papulous syphilide followed, with slight symptoms of fever. The macules appeared specially crowded together around the point of inoculation, where they partly changed into desquamating papules. A few days later, a multiple swelling was per-