

ceptible in all palpable groups of glands on the upper half of the body, which could by no means be felt on the lower half of the body, especially not in the inguinal region.

This last observation teaches in an incontrovertible manner that the primary lymphatic glands are a focus of the virus equivalent to the hard chancre, and renders clear why the extirpation of the latter alone so rarely secured a radical result. As early as 1871, P. Vogt had therefore made the proposition, and Hardaway in 1877 had repeated it, to remove the glands together with the sclerosis. Although the results were not very brilliant, still the proposed method is to be adhered to. His cases came under treatment in a rather advanced stage of the disease in which the virus probably had already extended beyond the limits of the glands.

The removal of the glands was performed before that of the chancre and in every case was a very simple affair; the indurated glands can be enucleated together with their capsule with great facility from the surrounding loose connective tissue without any considerable hemorrhage occurring. A thin drainage tube was inserted into the remaining cavity, often pretty large, and the wound closed over it with deep sutures. Under an antiseptic pressure bandage the cavities closed by first intention in the majority of cases.

Finally it must be taken into consideration that we can hardly determine clinically when general infection has been effected in syphilis. Usually the view prevails that the time of general infection is to be identified with the appearance of visible symptoms (exanthem, polyadenitis). That this doctrine, in its general application at least, is erroneous is proved by a communication published by Finger, in which, in a patient recently infected, syphilitic efflorescences appeared on a previously irritated part of the skin two weeks before the macular general eruption developing subsequently in a typical manner, hence in that early period of syphilis which is usually designated as the second period of incubation.

If we adhere to the above developed view of the gradual poisoning of the organism from the focus of infection, we shall not be surprised on the one hand by the contradictory results of excision, on the other hand excision will still appear to us a very useful operation weakening the general infection. Wherever it is at all possible, the excision of the chancre will have to be combined with the extirpation of the glands.

As regards the general infection, this is effected, as above mentioned, most probably by way of the lymph channels; this explains those diseases of the lymphatic glands of the body which may be controlled step by step and followed anatomically, while the morbid foci occurring simultaneously in the skin will have to be traced to the participation of the blood channels.

But no matter in what way and at what time the spread of the infectious substances takes place, finally local pathological processes are produced at those points, and there only where the bacteria settle and find rest so as to unfold their activity.

In fact we see that from this period on (after the so-called second incubation) there are developed in all organs of the body in more or less regular order, pathological processes which provoke the most manifold symptoms. But another question presses into the foreground: To what factors can we trace the fact that these products developing in the course of syphilis, the etiological unity of which is certain, and which in their initial stages represent almost identical formations (heaps of granulation cells) give rise to such differences in their further course that finally that well-known polymorphism is effected which is characteristic of syphilis and which is capable of simulating all possible forms of efflorescences?

This question has been often raised and has found its expression in the many attempts at dividing the course of syphilis into several periods according to the varying morbid processes. Especially two great groups have been always placed opposite to one another.

From the anatomical standpoint the papular were separated from the gummous products (Zeissl, the condylomatous from the gummous stage). Virchow divided irritative inflammatory or hyperplastic processes from the gummous. According to the time of their appearance, they are separated into symptoms of the early and those of the late period, or according to the ordinary mode of expression originated by Ricord, secondary and tertiary symptoms. This difference in time corresponds with a clinical one: The early symptoms as a rule have a tendency to spontaneous absorption, are "benign," while in the late period the tendency to disintegration prevails.

But here a remarkable phenomenon must be taken into account, namely the different systems of tissue have a certain independence in reference to the time, and accordingly to the manner of their affection, so that every group of tissues must be considered specially by itself. For instance, for the syphilides of the skin and mucous membranes we reckon the division as to time from the day of infection; however, another measure must be applied to the syphilitic diseases of the peritoneum and vessels, to the syphilis of intestinal organs. Thus the endarteritis syphilitica described by Heubner, which belongs almost invariably to the late period of syphilis, is to be counted, both anatomically and clinically *per se* (aside from the secondary alterations in the brain), altogether among the benign new-formations corresponding to the early symptoms of the skin. On the other hand, we know in every tissue, in every organ, those two forms of disease which we have above opposed to one another as "benign" and "malignant" (by the side of the ordinary endarteritis also the gummous form), corresponding to an earlier and a later implication of the system. But in that case "early" and "late" mean something altogether different from what they do in cutaneous syphilis, with which we are most familiar. Hence, to speak of a secondary and tertiary "period" is correct only with these limitations. Furthermore, it must be taken into consideration, especially for the diseases of the bones, that osseous new-formations of a permanent nature frequently occur in them; hence that the date, often late, at which such tophi, periostoses, are still demonstrable, is not to be confounded with the far earlier time of their origin.

The mere number of the attempted divisions must lead to the supposition that a strict (schematic) subdivision is really impracticable. Indeed, mixed exanthemata of anatomically the most divergent forms are not at all rare, and especially observations of simultaneously developing "secondary" and "tertiary" efflorescences are so frequent that the question appears justifiable: Is there actually any such strict separation between the several forms of syphilis as authors have made? Is there really an essential difference between the papulous and the gummous neoplasms, and can an explanation be found for the variation of the two forms?

Bäumler (p. 37) assumes for this purpose a changed quality of the tissues in the gummous stage. "At first the syphilitic virus itself is the cause of the neoplasms in the normally reacting tissues; however, in the development of gummata, we have to deal, probably, no longer with the effect of the specific virus on a normal tissue, but with the specifically altered reaction to any irritation of tissues modified by the preceding blood-poisoning." This view indeed has something very taking in it. There is nothing to prevent our assuming a modification of the tissues, even if we do not as yet know positively wherein it consists; we find like conditions (acquired immunity) existing unquestionably in other infectious diseases (in vaccinia, etc.); even in syphilis we are acquainted with such a modification in the fact that the induration of the primary affection can develop only in persons free from syphilis, but cannot be produced in an individual

affected with syphilis. Inexplicable though this "modification" of the tissues be in this observation, it is confirmed by a thousandfold experience.

To explain how this "modification of tissue" is effected and what is its nature, we might perhaps suppose a chemical incidental effect of the bacteria, of the kind with which we are well acquainted in fermentation, decomposition, the growth of *aspergillus*, etc.

Bumm makes the following remarks in reference hereto: If we have the opportunity of making an early auto-inoculation from an indurated chancre to its bearer, and especially if we choose for this purpose a spot as far as possible removed from the primary focus of infection, we can often make very instructive observations about the relations above mentioned. The following extract from the history of a case may serve in illustration.

K. C., *set.* 25. Infection took place on August 5th, 1881. A couple of weeks later, moist spots were perceived on the prepuce which gradually changed into ulcers.

On August 23d, one larger and two smaller indurated ulcers were noticed, and with the secretion present, of which there was a sufficient quantity, an inoculation was made on the right upper arm. After three days the small crust of blood had become detached and the skin at the point of inoculation appeared perfectly intact.

On the tenth day after the inoculation, a red spot the size of a pin's head was first noticed at that point which slowly increased during the following days. At the same time swelling of the inguinal glands occurred.

On the twentieth day, a papule somewhat larger than a lentil, with slightly scaly surface, was found; it had a distinctly infiltrated feel. The next few days the papule underwent a grayish-yellow discoloration, and thenceforward retrogressed so that by the thirtieth day after the inoculation (the forty-seventh after infection) the entire formation had disappeared. Simultaneously with the retrogression of the inoculation papule, swelling of the cervical glands and an angina occurred. As the ulcers on the penis had healed in the mean time, the patient left the clinic, but soon returned with secondary symptoms.

In this case the inoculation at first progressed as in a healthy person; a quite characteristic papule developed which was about forming an ulcer by its disintegration, when suddenly the whole process, at the very time when the general infection commenced, came to a standstill. Such processes we can explain only by supposing that the organism at the time of the inoculation and for three weeks thereafter was not yet infected, and that therefore an inoculation papule could develop which of course made no further progress with the constitutional disease then ensuing, owing to the immunity conferred by it.

I might here briefly remark that perhaps it is incorrect to say: a syphilitic person possesses an immunity against fresh infection during the time the disease exists. For the time being, it is true only that during this time no typical primary affection is formed; but whether there is not a new invasion of virus with additional infection is an open question which can by no means be negated without further investigations. Practically this relation is important only in so far as physicians and patients believe in immunity after infection without any qualification, and as the latter imprudently expose themselves to fresh invasions of virus.

Of Bäumler's view, therefore, we accept as proven only one part: the modification effected in the tissues of the body by the poisoning of the organism with syphilitic virus. It is more questionable, however, whether we shall, with Bäumler, charge "any kind of irritation" with the production of gummous processes, or rather, in their stead, again the specific syphilitic virus.

Those who reject the view that the gummous process is produced by the syphilitic

virus in propria, base their opinion on the slighter infectiousness in the gummous stage. Indeed, in this period, syphilis is more rarely transferred to other persons than in the early papular period. But this rests only on external accidental circumstances. The gummous processes are almost always present in but few numbers at one time, and are situated on parts of the body unfavorable to the propagation; while the numerous early efflorescences which preferably affect the mouth and the genitals, and which are distinguished by a decided tendency to relapse, are naturally the chief propagators of syphilis; as is well known, even more frequently than the primary affections, and for the same reason.

The possibility at least that gummous masses are infectious, as well as the secretions of the early period, has been recently demonstrated by Haensell by inoculations on animals. Moreover, I call to mind that Birch-Hirschfeld has made the discovery of the micro-organisms described by him, in gummata. Accordingly we hold that a direct cooperation of the bacteria of syphilis in the production of gummous products is at least of frequent occurrence, although no positive opinion can as yet be given as to the constancy of this fact.

If now we ourselves attempt an explanation of the variability of the several forms of syphilis, we must bear in mind:

In all syphilitic neoplasms without exception we have to deal, in the first stages of development, with a heap of granulation cells, no matter whether this process occurs earlier or later, or in whatever organ it may take place. It is the further developmental stages of this mass of cells which take different courses and lead to the formation of all the manifold forms which we "meet with in almost all organs as hard chancre, tubercles and abscesses, tubercular and gummous processes, interstitial formation of membranes, etc." Gummous, therefore, does not by any means designate a peculiar form of new-formation, but only that of decay.

What are the factors causing this difference in the development of the syphilomata?

There is, in the first place, the active effect of the virus, which is:

First, an inflammatory one;

Second, one specifically modifying the course of these inflammatory products;

Third, an alteration manifesting itself in the entire organism—vessels, permanent tissue cells, etc.

This alteration of the tissues becomes an independent factor soon after the infection, whenever the disease has become constitutional; a factor which has to be taken into account with every inquiry into the effect of the virus *per se*. Here we have not to deal with those so-called constitutional anomalies (scrofulosis, scurvy, etc.), but with a specific modification suffered by the tissues when they are poisoned with the SYPHILITIC VIRUS ITSELF.

This modification manifests itself at once in two directions:

1. In that only the healthy tissue (*i. e.*, before the infection and after perfect cure) possesses the capacity to form an "induration"—an essential difference from the later periods in which the products of all stages of syphilis are less variable histologically so that numerous transitional forms render nugatory any attempt at schematic classification.

Very remarkable indeed are the rare observations of reinfections (Merkel, Gascoyen) during still present gummous eruptions. However, they do not militate directly against the correctness of the view just defended; they merely strengthen the view maintained by the above authors as well as by Finger, that in tertiary syphilis the diathesis, the general disease has disappeared, that

syphilis may have lost its character of a general nutritive disturbance, the symptoms present having the significance rather of a local sequela.

But how does the primary syphilitic affection look, and wherein lies the essential difference of the primary syphilitic tumor from all others?

The primary induration, the hard chancre, the initial sclerosis *per se* is an ordinary, granulation-cell tumor. The cells are derived from the vessels and are inflammatory, emigrated white blood-corpuscles which take on a specific course under the influence of the syphilitic virus; that is to say, they all develop rather quickly into an elongated, squat spindle cell with a small nucleus and relatively abundant mass of protoplasm. The vascular development is proportional to that of the cell-mass so that the tissue represents a very high degree of the inflammatory new-formation of tissue. The wavy connective tissue has nothing to do with the formation of the hard infiltration, but constitutes a fine, barely recognizable fibrillary network between the mass of the tumor consisting of closely packed cells; only here and there we see broader bundles interwoven between the cells—remnants of the tissue originally present. In the great majority of cases this cell-mass perishes before it has reached the terminal stage—common in normal inflammation not specifically influenced—of a fibrous connective tissue; according to our assumption, by the influence of the virus on the individual cells. The latter die, and at the same time the vessels become thrombosed and disappear. Blood pigment then remains for a time. (Exceptions occur in two directions: 1. Persistence of a cellular tumor for years, *i. e.*, transition to gumma; 2. Actual connective tissue new-formation, but also of a temporary nature.)

The great majority of the cells composing the granulation tumor are emigrated white blood-corpuscles. In recent stages this may be clearly recognized in the cellular tubes which traverse the tissue along all the vessels. The virus probably extends in the lymph sheaths surrounding the blood-vessels and thus causes the inflammation of the vessel-walls. Whether the thickening of the vessel-walls finally present is effected by the fixed cellular elements of these vessels themselves or by immigration is an open question. It seems the veins participate more largely than the small arteries.

Besides the migratory cells, however, there exists in the syphilitic primary ulcer also a hyperplastic process of the fixed connective-tissue cells. In the mass of the granulation tumor they cannot be recognized; but they are uncommonly numerous in the tissue beneath the induration, so that even in this connective tissue are found at times only these large, big, granulated, comparatively short cellular elements with large nuclei otherwise no spindle-shaped elements whatever, or at most migratory cells with their small granular nuclei. But it follows from this fact that in the case of these cells we are not dealing with immigrated and further developed elements. Were this the case, then the ordinary narrow spindle-cells of the connective tissue would be found by the side of the large cells and the lymphoid round cells.

These hyperplastic cells I take to be altogether specific for the hard chancre; not in a single instance have I failed to find them (they are especially well visible after staining with Bismarck brown, while they remain uncolored in strongly acid dahlia solutions, *i. e.*, they are no mast cells).

Whether they take part in the formation of the specific hardness I am unable to say. The latter seems to me to find sufficient explanation certainly in the spindle shape of the closely packed granulation cells.

How these enlarged cells are produced and what they really mean can of course not be positively decided. They might, on the one hand, owe their origin to a direct irritant effect of the

poison. On the other hand, according to the theory defended by Weigert, which denies primary "irritations" *in toto* and assumes only primary "noxæ," we would have to deal with a kind of necrosis with an imbibition of tissue lymph rendered possible thereby. The decision of this point is still open. As has been stated, they are not the mast cells of Ehrlich, for they lack the specific granulation of the protoplasm and their characteristic color in strongly acid anilin solutions (especially dahlia). Possibly they are cells filled to repletion with the syphilitic micro-organisms.

Auspitz and Unna speak of a fibrillary hypertrophy of the connective tissue, with deposition of a collagenous substance, of a solid, little alterable product of young connective substance, and hold this hypertrophy of the fibrillary tissue to be the characteristic condition of the syphilitic initial sclerosis. The description given by the above-named authors is correct in itself for some specially advanced indurations in which there was not only a formation of spindle-cells, but also of fibrous connective tissue. But this "connective-tissue hypertrophy" exists only in isolated cases, while the cellular swelling is present in *every* one. I have examined scleroses not inferior in size to those described by Unna; but there was no trace of fibrillary connective tissue, nothing but spindle-cells. This condition could be demonstrated at first sight on preparations of (recently) boiled scleroses stained with picro-carmin. All fibrillary connective tissue obtains an intense red color by this method. Such red cords, however, occurred only as isolated narrow strips in the cellular tumor, the elements of which were closely packed and formed a compact mass only in the environment of the induration.

As to the microscopic difference between a hard and a soft chancre, this lies, in more advanced cases, in the spindle shape of all the cells forming the *hard* tumor, as opposed to the (less dense) infiltration with round and small (also more markedly stained) cells in chancroid; that is to say, in hard chancre we have inflammatory cells in progressive development; in soft chancre, the same cells necrosed by the virus of pus. In the early stages of both, in a series of clinically doubtful cases in which excisions were performed, I have never erred heretofore when forming the diagnosis from the presence of the hyperplastic connective-tissue cells. Wherever these were present, general syphilis broke out regularly, even in cases where the excision was performed at a time when no "induration" was as yet noticeable. When the large connective-tissue cells were absent, no matter how intense the infiltration, the process remained local. But these examinations are not definite enough to enable us to draw a positive conclusion. However, I believe I may be justified in concluding from these investigations why—aside from the primary affection of the lymphatic glands which had not been sufficiently attended to—the excisions did not furnish the desired positively curative result, why a secondary infiltration so frequently develops in the cicatrix of the wound which had closed by first intention. As far as the eye and palpation could determine, everything morbid seemed to have been removed. But the microscope showed that the connective-tissue cell-hyperplasia in the portion removed existed even in the lowest layers immediately adjoining the cut surface, so that we are forced to the conclusion that also the contiguous layers of connective tissue which had been left behind contained similar cell forms, *i. e.*, were likewise diseased.

Accordingly it will be necessary to excise more of the apparently healthy tissue, perhaps with microscopic control of the remaining connective tissue portions, or perhaps take into consideration an energetic cauterization of the excision wound surface.

In hard chancre, therefore, the action of the virus consists, on the one hand, in the formation of an inflammatory cell-mass which develops progressively only under the influence of the virus (spindle shape, at times connective tissue), but later perish by the action of the same virus; furthermore, in the hyperplasia of the cellular connective-tissue elements.

The alterations of the epithelium into active proliferative processes I hold to be "specific" neither here nor anywhere else.

The greatest analogy with the induration of the skin is presented by the endarteritis of the small arteries, the relation of which to the early processes we have pointed out above.

In all later new-formations there is an absence mainly of the hyperplasia of the connective-tissue cells which we have declared above to be the anatomical expression of the

completed syphilization of the tissues. But there is superadded to it the second factor which increases in importance with the longer duration of the disease—the chemical modification of the tissues, a greater liability to decay of the cell masses produced, anatomically indicated by the lesser degree of progressive development exhibited by the migratory cells. The cells, it is true, may become larger, epithelioid forms are found, but the “fibre-cell” is no longer developed.

The nature of this “modification” by syphilization may consist in, first, the fact that the cellular elements furnished by the body which constitute the syphiloma are from the start less viable and succumb more quickly to the necrosis induced subsequently by the virus than cells furnished by a healthy body.

Secondly, however, the modification may have influenced the growth of the vessels; they do not participate sufficiently by new-formation, as in a normal organism, in the nutrition of the granulation tumor; perhaps also the young vascular shoots are destroyed soon after their formation.

But if this new basis, the modification of the tissues, is once established, then again the variable intensity of the virus comes into action as the determining factor in shaping the several syphilitic processes, and it is mainly the changeable quantity of the virus circulating in the organism and coming into play locally at once.

We have already become familiar with similar relations in tuberculosis; they are also found in vaccination. A. Nourney made experiments with diluted lymph, with punctiform inoculation in very small incisions, whereby the quantity of the virus introduced into the wound was diminished. It was found that: 1. the duration of the course of the inoculation undoubtedly depends on the quantity of the virus introduced, the onset of the vaccinal fever, the appearance of the areola being delayed two or three days by diminution of the virus; 2. diminution of the virus causes in most cases a lesser maximum of fever and certainly a more circumscribed expansion of the areola; 3. general infection is brought about immediately with the inoculation; 4. the rapidity of the reproduction of the virus in the organism seems to stand in causal connection with the local phenomena.

The quantity circulating at any one time is greater in the periods closer to the infection than it is subsequently; but locally smaller numbers of bacteria usually come into action. Hence the early exanthems are more numerous, more disseminated over the body, and acute in their onset. Within a few days a small granulation tumor arises with copious vascular development so that the persistence of the neoplasm is assured for a certain time. Not until weeks afterwards do the cells and vessels gradually perish so that finally a complete *restitutio ad integrum* ensues. The analogy of these formations with the primary affection is obvious; in both there are comparatively high further development of the several cellular elements, sufficient vessel formation, healing by absorption of the neoplasm without loss of substance.

The course of the gummous form is altogether different! At very few places a slow tardy accumulation of exudation corpuscles with sparse development of vessels. This mass may remain unchanged for months until finally the cells, the development of which was very moderate from the start, perish. But the tissue in which the tumor was embedded is implicated in this disintegration, and thus results a defect healing only with cicatrix, etc.

It cannot be positively decided whether these defects of tissue are merely processes of deliquescence due to the necrosing mass of the tumor, or whether we have to deal with a simultaneous primary necrosis of the constituents of tissue by the virus itself. In the case of gummata it seems to me untenable to assume the direct necrosis of tissue. The possibility of causing even large “gummous” new-formations to regress by appro-

priate early treatment, without any damage to the mother tissue, indicates that this gumma consisted only of newly superadded cells, after the removal of which the previous state was re-established. Only when the (newly superadded) cell mass perishes, does the destruction in the fundamental tissue commence.

The disintegration of the tumor begins in the centre with a necrosis of the cells corresponding to the necrosis of coagulation (Weigert): destruction of the nuclei, coagulation of the cellular protoplasm. Accordingly the whole cellular new-formation becomes necrosed, but in a variable manner depending on external circumstances: in the superficial gummata, with very early and great fatty degeneration of the infiltration cells; in the subcutaneous connective tissue with melting down of the contents by the formation of a tough, mucoid (“gummous”) substance, occasionally with subsequent ulceration; in the internal organs, in which “strong rugous thickenings of the tissue have taken place round about,” with the formation of a dry, cheesy, pultaceous, more persistent patch.

I hold this persistent, permanent connective-tissue new-formation surrounding the gumma to stand in no relation whatever to the virus itself. It arises around the necrotic syphilitic patch as it does around every dead patch in process of absorption, nomatter how it originated. The same interpretation I apply to the giant cells of the gummata. They are a sign of the attempt at reproduction of the surrounding connective tissue having no character specific of the syphilitic virus.

Years ago I made investigations into the regenerative capacity of liver substance, a necrotic focus having been produced in the liver tissue by the injection of a drop of concentrated carbolic acid. Subsequent examination showed conditions absolutely parallel to those of a gummous affection of the liver.

Owing to their tendency to decay, gummata are to be interpreted patho-anatomically as malignant products of syphilis. But looked at clinically they lose this malignant character, because, if recognized in time, they offer less difficulties to treatment than the early forms which are benign *per se*. Of course, it must not be overlooked that it is just this “early recognition” which is often rendered very difficult by the exceedingly chronic and insidious course. A recognized and correctly treated gumma does no damage to the tissue affected; left to itself, the tumor and the corresponding mother tissue disintegrate. Altogether the syphilitic virus, in the majority of cases, is relatively benign, because it generally limits its effect locally, and therefore permits the reparative efforts of the organs, consisting in inflammatory connective-tissue formation, to take place unhindered. Exceptions occur here likewise, for instance in the serpiginous syphilide of the skin, in certain interstitial affections of the liver, etc. But even such cases may heal spontaneously, although they leave permanent defects and cicatrices.

We must here in a few words touch upon the chemical difference between the papular and gummous formations; namely, the well-known absorption which gummous infiltrations undergo by the use of potassium iodide, as opposed to the slight and rarely observable influence of the same agent on the products of the early period. These latter again heal more quickly under the use of mercurial preparations which, though they aid in the treatment of gummous syphilis, do not approach the effectiveness of iodine. The effect of potassium iodide on gummata is almost equivalent in its positiveness to a chemical reaction. Well-known and constant as this fact is, its explanation is still to be furnished; but the fact is so certain that we, inversely, employ the absorbability of gummous tumors by iodine as a proof of the slight viability of their cells.