Otis (F. N.) With the Author's regards

ON THE

PHYSIOLOGY

OF

SYPHILITIC INFECTION,

AS APPLIED TO THE

SUCCESSIVE MANIFESTATIONS OF THE DISEASE.

BY

FESSENDEN N. OTIS, M. D.,

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PART SECOND.

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ON THE PHYSIOLOGY OF SYPHILITIC INFECTION, AS APPLIED TO THE SUCCESSIVE MANIFESTATIONS OF THE DISEASE.[1]

On a previous occasion I had the honor of reading a paper before this Society entitled "The Physiology of Syphilitic Infection." In this paper it was claimed that the infection took place through the agency of the lymphatic system *alone;* that it was the germinal matter of the tissue-fluids and of the blood—the unformed material—the white corpuscular element alone, that was capable of entering into combination with the abnormal germinal cells in which the syphilitic influence was supposed to reside. These abnormal cells or disease-germs were assumed to be analogous to the disease-germs discovered by Beale and Chauveau in the blood of animals diseased by the cattle-plague, and in the fluid of the vaccine virus—germinal corpuscles, probably originating in the human organism, but possessing, besides the properties and powers of the white blood-corpuscle, a peculiar tenacity of existence, a capacity to grow and multiply when removed from the seat of their development and transferred to another situation, provided only that they were supplied with sufficient nutrient pabulum. It was further claimed that, through the current of the tissue-fluids which moves constantly toward the lymphatic vessels, such disease-germs, deposited upon an abraded cutaneous surface, would necessarily be drawn toward, and might finally effect an entrance into, the underlying

[1] Read before the County Medical Society, May 27, 1872.

lymphatic vessels of the part. It was also shown that, as the influence of such disease-germs would be to induce a coagulation of the tissue-fluids, such coagulation would of necessity delay the transit of the disease-germ from the surface of inoculation to and into the lymphatic vessels, and that this delay favored the proliferation of the disease-germs; that the fibrinization of the tissue-lymph and the increased development of the connective-tissue cells at the point of inoculation would thus be effected to an extent sufficient to produce the induration which is looked upon as a characteristic of the initial lesion of syphilis. It was then claimed that the so-called *period of incubation* of syphilis corresponded to the time required for the disease-germ or its descendants to accomplish the transit from the inoculation-surface to and into the interior of the underlying lymphatic capillary; and that, after having effected an entrance into the lymphatic vessel, it passed directly along this canal until it was arrested by the lymphatic gland with which it was in connection.

Half a year subsequent to the publication of the foregoing views in the *New York Medical Gazette*, and in the *American Journal of Syphilography and Dermatology* (July, 1871), it was announced at a meeting of the Medical Society of Vienna, January, 1872, that Dr. Lostorfer, of that city, after researches and experiments in the laboratory of Prof. Stricker, and in the syphilitic wards of Prof. Zeissl, covering a period of several months, had finally discovered and demonstrated the existence of the living syphilitic corpuscle or disease-germ, and its presence in the blood of persons affected with syphilis. This corpuscle was described as living bioplast, growing and multiplying after having been removed from the seat of its development; in short, corresponding most completely with the disease-germ which I had assumed as the infecting agent in syphilis. Out of about fifty specimens of healthy and diseased blood, marked and numbered, and presented to Dr. Lostorfer by Profs. Hebra and Stricker, *twenty* were selected as containing the syphilitic corpuscle, and, by reference to marks and numbers, in every instance it was found that the specimens had been taken from persons affected with

syphilitic disease. The conditions under which this corpuscle was found, and the manner of its development, were so in harmony with the probabilities of such a discovery, that, with the corroboration thus afforded by Dr. Lostorfer, the syphilitic corpuscle was publicly accepted and confirmed by Profs. Skoda, Stricker, and Hebra. It was, however, soon after disputed by Profs. Wedl, Gruber, and Neumann, although no especial investigation of the subject appears to have been made by these gentlemen. Prof. Stricker, however, at once commenced a series of independent observations, for the purpose of ascertaining the validity and real significance of Dr. Lostorfer's discovery. Advices received from Prof. Bumstead, by the last steamer, are to the effect that the corpuscle described by Dr. Lostorfer was actually found by him in syphilitic blood, but it was also found to have been present in the blood of persons not syphilitic, but who were the subject of cachexia from other causes. He then concludes that the corpuscle of Lostorfer is a product of the cachectic condition from any cause. The significance of this cachexia-corpuscle, when present, has not yet been ascertained.

Had the discovery of Dr. Lostorfer's corpuscle and its exclusive association with syphilis been confirmed, it must have been accepted as a corroboration of the views I have advanced. It has, however, proved otherwise, and yet I claim, as confidently as before, that the necessity for such a corpuscle still exists, and that a present failure to demonstrate its actual presence in the blood of syphilitics does not militate against its acceptance as a reasonable and probable initiative point in the attempted elucidation of the acknowledged mysteries of syphilitic disease.

I propose to-night to resume the subject of syphilitic infection at the point which is recognized as the termination of the first incubation of syphilis, and to consider the disease-germ, in its passage through the lymphatic glands adjacent to the surface of inoculation, in its relation to a second period of rest which is known to elapse between the induration of the initial lesion and the earliest period at which the constitutional manifestation of the disease ever takes place, a

period termed, by some authors, the *second incubation* of syphilis.

It is a universally-accepted clinical fact in the natural history of syphilis that a distinct period of rest succeeds the appearance of the initial lesion or chancre; that, for a time, the chancre is the only recognizable evidence of syphilis in the individual bearing it. That by no external sign or internal sensation is it possible to discover any variation in the normal physiological processes of such subject that can be attributed to the influence of syphilitic disease. It is, however, claimed, and by a very great weight of authority, notwithstanding the complete absence of proof, that the development of the disease is steadily and surely progressing in the blood, and that it will finally acquire and exercise the power of producing general manifestations of the disease; and hence it is claimed that this period of apparent rest is an incubation as actual and complete as that which is known to elapse between the date of vicious contact and the appearance of the initial lesion or chancre.

According to authorities, the earliest and most common general manifestation of syphilis is a *roseolous eruption.*

Accepting the occurrence of this exanthema as the termination of the second period of incubation, Ricord places its accession at three weeks from the appearance of the chancre as the earliest, and at six months as the latest date at which he has ever known it to occur. Cullerier makes a similar statement. Lancereaux places it at from six weeks to two months, Sigmund from four to six weeks, Henry Lee from four to eight. Zeissl has never seen this eruption before the eighth week after contagion. Berkeley Hill confirms this experience, and further states that the longest interval he had observed was fifteen weeks. Diday cites fifty-two cases carefully observed, where the appearance of the chancre was ascertained, and where no treatment was resorted to, where the interval varied from twenty-five to a hundred and five days. Fournier, from an examination of three hundred and seven cases, concludes that this eruption, "the earliest general manifestation of the disease," appears from the for-

tieth to the fiftieth day after the development of the chancre. Puche and Cullerier the younger state that roseola is never wholly absent in syphilis, and concur in the previous statement as to the date of its appearance. Bumstead regards the occurrence of the syphilitic roseola between the fortieth and fiftieth day after the development of the chancre as almost certain, and states that he has never seen a case, carefully observed, where it had failed to show itself within three months.

Thus it appears that, with great unanimity, authorities agree upon a period of rest, following the appearance of the initial lesion or chancre, of at least three or four weeks. Absent in none, it is shown to have been prolonged in exceptional cases to three or four months. Virchow, in his "Cellular Pathology," p. 221, has furnished a parallel to this apparent cessation of progress in the early stages of syphilis, by showing what is known to occur in cases of mammary cancer, where, during a long period, only the axillary gland becomes implicated, the groups of glands next in succession, as well as all other organs, remaining free from disease. "We can account for this," he remarks, "upon no other supposition than that the gland collects the hurtful ingredients absorbed from the breast, and thereby, for a time, affords protection to the body; but at length proves insufficient, nay, perhaps, at a later period, itself becomes a new source of independent infection to the body, inasmuch as a further propagation of the poisonous matter may take place from the diseased parts of the gland." I have, however, yet to find this view of Virchow's accepted, by any of the numerous writers on syphilis, as applicable to the interval of rest following the appearance of the initial lesion. The explanation of this remarkable phenomenon, given and generally accepted, is, that the disease has an inherent cyclical tendency—proceeding throughout its course by successive stages or bursts; that, notwithstanding the apparent rest, the vitiation of the circulatory fluids is going steadily, relentlessly on; and that, when the system becomes fully charged, an outbreak takes place, and is recognized in the syphilitic roseola. Thus a mystery, wholly in-

compatible with known physiological and pathological facts, is quietly accepted, almost without comment, and designated *the second period of incubation.*

A certain and positive value must attach to a theory which shall even plausibly account for and explain a mystery. A *point d'appui* is thus fixed, about which the results of observation and investigation may crystallize—it is a step out of the *unknown* toward exact science.

In the case of the first incubation of syphilis, clinical cases were adduced, supporting the theory of a gradual local development of the influence of the disease-germ, up to the point of its final entrance into a lymphatic vessel. It was then shown that, through natural physiological processes, the disease-germ or its descendants would be carried along the lumen of the lymphatic canal until it reached the lymphatic gland in connection with that vessel, and that the arrest of the vitiated corpuscle in the substance of the gland was in accordance with the previously ascertained influence of the so-called syphilitic virus, viz., to induce a coagulation of the tissue-fluids with which it was brought in contact.

The anatomical arrangement of the lymphatic glands has long been a point of inquiry. By early observers considered as consisting simply of coils of lymphatic vessels, they were demonstrated by Kölliker to possess a parenchyma in which the afferent vessels were wholly lost, and out of which the efferent vessels constituted themselves at the opposite side of the gland. This view, confirmed by Virchow, was generally accepted by histologists until within the last two years, since when, through the investigations of His, Frey, and Teichmann, and substantiated by Recklinghausen, it has been shown, that the circulation through the glands is continuous by the presence of lymph-paths lined with epithelium throughout the supposed parenchyma, and that consequently a continuous lymph-current through the substance of the glands could be demonstrated.

Accepting this view, we have, then, as in the application of the disease-germ to the original abraded surface of a syphilitic inoculation, the same two distinct forces by which the

progress of the vitiated corpuscle through the tissues of the lymphatic gland would be facilitated, viz., the independent power of amœboid movement of the corpuscle, and the force of the lymph-current through the substance of the gland. Delayed in its progress by the same cause which produced the interval of apparent rest occurring between the application of the virus to the surface of inoculation, and its arrival at the portals of the lymphatic gland of connection, corresponding to the period of first incubation, the coagulation of the lymph, effected by the presence of the disease-germ, may be accepted as producing a similar retardation in its passage through the substance of the lymphatic gland in connection, and thus reasonably explain the period of rest known as the second incubation of syphilis.

As a result of the coagulating influence of the disease-germs or their descendants, in the lymph-paths traversing the lymphatic glands, we have, then, an arrest more or less complete of the lymph-current. The natural result of this would be an increased proliferation of the lymph-corpuscles both normal and vitiated, and their rapid accumulation within the gland, and we should expect to find following such occurrences an immediate enlargement of the substance of the glands. This is exactly what we *do* find in every case: a development, a condensation of the normal constituents of the gland, a simple hyperplasia, which is always sluggish and non-inflammatory, and is recognized as characteristic of syphilis. We must also have, to a greater or less extent, and from the same causes, the same retardation of the vitiated corpuscles on their passage through the lymph-vessels and glands, which still interpose between the glands of original implication and the thoracic duct, through which they finally effect their entrance into the general circulation. As an evidence that this is the course and influence of the disease-germs, after their passing through the first order of glands, we have a sudden increase in size of the glands of the second order—glands remote from the point of inoculation, the cervical, the submaxillary, the epitrochlear, etc., the slight but well-marked increase of temperature, a marked increase of the white corpus-

cular element of the blood, and various other evidences that the constitution at large is in embarrassment and distress in the performance of its normal nutritive and nervous functions. Prominent among these stands the roseolous eruption of this period, which is claimed to mark the termination of the second period of rest or incubation, and to usher in the active secondary or constitutional stage of syphilis.

The period of so-called second incubation, then, whether caused by a necessity in the nature of the syphilitic virus, requiring a certain accumulation in the blood before general constitutional disturbances can take place, or caused by the gradual passage of the vitiated germinal matter through the glands and vessels of the lymphatic system, intervening between the point of inoculation and the general circulation, is nevertheless an admitted fact, and the roseola is accepted as marking its termination.

Let us inquire into the significance of this roseola. Is it really the result of pathological changes, necessarily dependent upon the syphilitic influence? Or may we not be able to class it among the physiological phenomena, and thus show that it is not due to an elimination or an attempted elimination of syphilitic material from the infected organism.

Mr. Wilson, the distinguished English dermatologist and syphilographer, gives the following description of this exanthem: "Roseola syphilitica commonly presents itself in the form of undefined patches, giving to the skin an appearance identical with that of common idiopathic roseola or measles, and is due, like the two latter, to the manner of distribution of the blood-vessels of the skin. Perhaps," he says, "the congested patch represents the ramifications of a single arterial trunk; perhaps it embraces that small capillary system which is normally emptied by a separate venous trunk; perhaps, again, it includes the small district of skin, the circulation of which may be governed by the ultimate divisions of one small nervous twig."[1]

With this evident uncertainty as to the manner in which

[1] "Diseases of the Skin, a System of Cutaneous Medicine," by Erasmus Wilson, F. R. S. Sixth edition, p. 472. London, 1866.

simple roseolas are produced, he does not hesitate to express a decided opinion that the syphilitic roseola is caused by an effort of Nature to expel the syphilitic poison from the system, and compares the syphilitic disease to the simple exanthemata. "It is preceded, he says, "by a peculiar fever called the syphilitic, and bears a resemblance in its pathognomonic symptoms to measles, scarlet fever, and small-pox, as follows: 1. The nervous depression, showing the stagnating influence of the accumulated poison. 2. In the congestion of the mucous membranes, particularly that of the fauces, showing the effort made by the blood-vessels to eject the poison through that tissue; and 3. In the cutaneous exanthema which *completes the triumph of the pressure from within, and is the sign that the poison is driven to the surface, and is in process of expulsion.*" There is, then, no uncertainty about the fact that Mr. Wilson considers syphilitic roseola the result of the process of the elimination of the syphilitic material through the skin. This view, elaborated more fully by Mr. Wilson than by any other writer on cutaneous or syphilitic disease, I do not find contradicted by any except M. Diday, of Lyons, but is accepted directly or through implication by all the other authorities I have been able to consult. Very naturally, Mr. Wilson does not stop at this point, but goes on to trace a connection between syphilitic roseola and the subsequent manifestations of the disease. Thus, in his last "Lectures on Dermatology" (published London, 1871), he says: "Chancre, the focus of inlet of the poison, has run its course and healed up. Six weeks afterward, an exanthema, which is identical in appearance with roseola, is developed in the skin. . . . Another six weeks passes by, and a second exanthema appears, no longer a roseola like the first, but an eruption of *papulæ*, corresponding to the common *lichen*. Then another interval of six weeks transpires, and the eruption may appear for the third time, but with dimensions still further augmented, viz., as a large papula or tubercle." In an earlier work on syphilis, he says: "The transition of *syphilitic roseola* into *lichen* is so obvious that it may be observed through every stage of its progress. A roseolous patch may be seen to develop papules . . . and I have furthermore seen the small papules of lichen converted

into the larger elevation called tubercle, by a sudden aggravation of the syphilitic fever, or from exposure to cold." Of the *simple roseola*, however, he says in his last published lectures (1871), "it is now well understood that the influence of the *vaso-motor nerves* is involved in the production of roseolas." But for the syphilitic roseola, Mr. Wilson has assumed a pathological importance which could not attach to it, were it shown to be possibly due to the impression made upon the sympathetic nervous system by the syphilitic influence.

Characteristic prodromata are recognized by modern syphilographers as constantly associated with the advent of constitutional syphilis in representative cases. They are numerous and varied, as follows, viz., slight persistent increase of temperature, 99° to 101°, general *malaise*, headache, rheumatoid pains, irregular, chiefly nocturnal, loss of appetite, indigestion, nausea, diarrhœa, giddiness, mental irritability, sleeplessness, great prostration, unnatural acceleration of breathing on slight exercise, the circulation generally disturbed, in some cases exacerbations of fever of an intermittent character, temperature running up to 103° or 104°, followed by profuse sweats, etc. These are among the most prominent of the prodromata cited by authors, and are grouped together under the title of *the syphilitic fever*. This title is then applied not simply to an acceleration of the pulse, heat of skin, etc., which is usually understood by the term fever, but any one of the foregoing conditions or symptoms, or any modification or combination of them, is claimed to merit this title. Diday uses the more exact and appropriate term *syphilitic prodromes*. It will then be readily seen that, when authors speak of *syphilitic fever* as ushering in, or being associated with, syphilitic roseola, a very considerable degree of uncertainty may be claimed as to the dependence of such varied and common aberrations from the healthy state upon the development of syphilitic roseola.

The connection assumed by Mr. Wilson between syphilitic fever and syphilitic roseola is, however, not universally accepted. His statement that the syphilitic roseola is preceded (ushered in) by fever, especially with the broad interpretation previously given to the term, would lead us naturally to infer

that this was *the rule*. Ricord, on the contrary, says that it is *never* associated with fever, except as an accidental coincidence; and that, when fever is present, it is invariably due to some cause *quite independent of the roseola*. Bassereau affirms that it was entirely absent in fifty-six out of the one hundred and ninety-nine cases critically observed by him, but it occurred in thirty-four out of fifty cases of the later papular eruption. Coulson states that one-third of the cases of syphilitic roseola are not preceded by any premonitory symptoms. McCarthy (quoted by Lancereaux), that of sixty cases only forty were preceded by any well-marked prodromes. Of these forty, twenty-one had nocturnal cephalalgia alone, eleven cephalalgia and rheumatoid pains, and eight the *latter* alone; leaving twenty cases, or *one-third*, occurring absolutely without any premonition of any sort. Bumstead says that syphilitic roseola is so free from febrile excitement, heat, and pruritus, that the patient may not discover its presence except by accident.

Besides the records of observations covering a period of nearly two years in the Blackwell's Island Venereal Hospital of this city, in 1851 and 1852, and, during the subsequent years, meeting frequent cases in private practice, I have called especial attention to this matter in every case presenting at my clinique in the College of Physicians and Surgeons of this city for the past two years, and for the last year, in the venereal wards of the Strangers' Hospital under my charge, and I do not hesitate now to express my entire accordance with the views of M. Ricord, viz., that the syphilitic roseola is *never* preceded by *nor associated with* any fever or other prodromata that cannot readily and reasonably be accounted for through causes entirely independent of the approach or the presence of the roseola. For the past twenty years, Mr. Wilson has taught, without qualification and almost without contradiction, that syphilis, with roseola as its early exponent, was a distinct element; that the organism in process of infection was gradually invaded by it, until Nature, no longer able to endure its presence, concentrated all its forces, at a given stage, to expel it, with the directness and urgency of a woman in labor. As he puts it in his climacteric in describing the

roseola, "*completes the triumph of the pressure from within, and is the sign that the poison is driven to the surface, and is in process of expulsion.*"

In the effort to understand the mysterious workings of syphilis in the human organism, analogical reasoning has naturally been resorted to; and from the fact that there occurs a well-ascertained period of rest in its early development; that it is associated with varied disturbances of the nervous and vascular systems; and that preceding, during, or succeeding these disturbances, an exanthematous eruption occurs, it has been the fashion, for the want of a better place, to class it among the exanthemata, and further, inasmuch as it has been the accepted conclusion that these diseases are the result of an effort of Nature to rid itself of the peccant material causing them, a like interpretation has been seized upon to explain the significance and value of the syphilitic roseola. The very important fact that, at the point of commencing constitutional disturbance in syphilis, *the entire lymphatic vascular and glandular system is the subject of recognized and grave interference*, seems to have been entirely lost sight of. There is nothing better understood than that, among the first constitutional evidences of the syphilitic influence, an engorgement and enlargement of numerous lymphatic glands remote from the point of inoculation take place, and that there is a marked proportional increase of the white corpuscular element of the blood coincident with this glandular enlargement. Has this undoubted disturbance in a system of important functional use, one now recognized as occupying a place of acknowledged value among the hæmatopoëtic organs, no influence in producing the *prodromes* of constitutional syphilis? Or must this be ignored, and all aberrations from the healthy condition be attributed to the influence of a simple roseola which has been shown to be present and associated with recognized deviations from the healthy state in but a very limited proportion of cases?

Diday states it as his opinion that, in the prodromes of syphilis, mercurials are contraindicated, and that iron and iodine will be found the best means of combating them. In this view, Lancereaux explicitly concurs, although he depre-

cates the natural inference to be drawn from such concurrence. "But are we," he[1] says, "like Diday, to conclude, from the fact that iron and iodine are the means to be employed for combating syphilitic fever, that this morbid condition has not the same relation to syphilis as the constitutional lesions? that it is *occasioned*, and not *directly* caused, by that disease? Not absolutely," he answers, "for, if it be permitted to attribute to the debilitation, impressed upon the organism by the syphilitic poison, *some* of the disturbances in question, a great number remain which do not explain either the chlorosis or the anæmia." Forced *practically* to acknowledge the functional disturbances as in no immediate relation to the syphilitic virus, he is still unwilling to admit that the direct action of that virus is not in some mysterious way the local cause of certain of the prodromes, viz., those which cannot be made to connect with the immediate and perceptible blood-changes. That these changes, well-recognized departures from the healthy state of the blood, do occur, is no longer a question, but there is a considerable variance of opinion as to the *cause* of the disproportion of the normal constituents of the blood which obtains in the early stage of syphilis. Virchow claims that it is a leucocythemia. "In any considerable irritation of a lymphatic gland," he[2] remarks, "there is an increased formation of cells in it, and this is followed by an increase in the proportion of lymph-corpuscles in the blood. Billroth,[3] on the contrary, thinks it unlikely that the hyperplasic lymphatic glands should be the source of an increased supply.

"1. Because extensive adenopathies occur independent of such increase.

"2. That it is very improbable that, when the normal channels of the glands are obstructed, they should continue to perform their physiological functions." In the attempts made by Frey, O. Weber, and Billroth, to inject the vessels of hyperplasic lymphatic glands, there was failure in every instance, thus affording negative proof that the enlarged glands were physiologically insufficient. Rindfleisch,[4] however, distinctly

[1] Lancereaux, vol. i., p. 131. [2] Virchow, p. 222.

[3] Billroth, "Surgical Pathology," p. 209.

[4] Rindfleisch, "Text-book of Pathological Histology," p. 186, 1870.

states that lymphatic glands, the subject of aggravated hyperplasia, are still readily injected. "One is able," he says, "to fill the lymph-sinus of such glands, as well by the afferent vessels, as by piercing them."

In reports of the experiments made by Grassi, under the direction of M. Ricord, the disproportion found existing between the white and the red corpuscles was claimed to have been caused by a *diminution* of the *red* corpuscles.[1] It is now known that the red blood-corpuscles are regenerated at the expense of the white; and, with this in view, Mr. T. Henry Green, of London, suggests that "conditions obtained when the white corpuscle already in the blood is arrested in its development into the red, and that possibly the white corpuscles increase by multiplication in the blood."[2] With this present disagreement of authorities as to the cause and absolute value of the leucocythemia, or chloro-anæmia, always associated with the real prodromes of syphilis, it may still be accepted as exercising a profound influence upon the nutritive and nervous functions during the period of its presence, which, curiously enough, coincides and passes away with the period of the prodromes of syphilis.

In his elaborate and exhaustive work on diseases of the skin, Mr. Wilson treats of eighteen different varieties of roseola. Of these, six, viz., roseola rheumatica, roseola vaccinia, roseola cholerica, roseola arthritica, and roseola febris continuæ, occurring exceptionally in the course of the corresponding diseases, he calls the *symptomatic group* of roseolas. "The cause," he says, "may be *nutritive*, *nervous*, or *assimilative*." He has already told us that the *vaso-motor nerves* are concerned in the production of roseolas, that is to say, *all* roseolas *except* the roseola which occurs during the early evolution of syphilitic disease. *This* is claimed to be the result of a *pathological* condition, and to be but the first stage of the later eruptions, papular, tubercular, etc. That the papular eruption may be developed at a later period, and upon the exact spots previously occupied by the roseola, and that these

[1] Stricker, "Human and Comparative Histology," Sydenham Society's edition, vol. i., p. 421.

[2] "Pathology and Morbid Anatomy," Green, London, 1871, p. 132.

in turn, passing away, may be replaced by a still later *tubercular* eruption, is not only possible but almost inevitable, where they occur at all; but how are we to understand this gradual development when we find both the papular and roseolous eruptions associated together at the same time, each distinct and characteristic, and absolutely independent of the other? This fact, which I have often seen, and have demonstrated in my clinique on numerous occasions, will, I doubt not, be confirmed by every critical observer of the early eruptions of syphilis.

Virchow[1] states that, on a section of the sympathetic nerve in the neck of an animal, "a state of hyperæmia ensues in the whole of that half of the head. The ears become dark red, the vessels greatly dilated, the conjunctiva and nasal mucous membrane turgidly injected; and this," he says, "may continue for days, or weeks or months without the least appreciable nutritive disturbance necessarily arising thereupon." From deductions based upon the electric experiments of Claude Bernard upon a bisected sympathetic, he states that, "whether the relaxation of the muscular fibres of a vessel be produced directly by a paralysis of the nerve, or by an interruption of the nervous influence, or whether it be the indirect result of a previous stimulation, giving rise to exhaustion, in *every case*, we have to deal with a *kind of paralysis* of the walls of the vessel, and that the process is incorrectly designated *active hyperæmia*, inasmuch as the condition of the vessels in it is always a *completely passive* one."

Belladonna is well known as a relaxing agent in its effect upon the iris, and also in producing an eruption similar to the roseola of syphilis.

Mental emotions are recognized as the cause of eruptions in not dissimilar cases. I have at present under observation, a lady upon whom an eruption, in no way to be distinguished from a classical, recent, syphilitic roseola, is brought out over the breast, back, and arms, whenever she is subjected to any unusual mental excitement, and which remains distinct for several hours, and we know that similar roseolas are initiated by

[1] "Cellular Pathology," Virchow, p. 156.

causes that can only be referred to impressions made upon the sympathetic nervous system.

But, it may be remarked, while certain of the syphilitic roseolas pass away in a few days, or even hours, yet, in a very considerable proportion, the eruption is much more persistent than in the simple roseolas, and besides, in finally passing off, they leave a coppery stain which is considered characteristic of syphilis.

To this it may be answered that the causes of simple roseolas are transitory, and yet *a thought*, in the lady above referred to, caused a rash which remained for several hours. Is it, then remarkable, that a cause dependent upon actual changes in the blood proportions and quality should be more persistent? It is certainly *the fact*, and to this very persistence, and to it alone, are due the pigmentary sequelæ which are thought to be so significant. From the complete and prolonged stasis of the blood in the relaxed capillaries, the *hæmaglobin* (the coloring-matter of the blood) escapes through the vascular walls to some slight extent, and into the superimposed tissue; after a time crystallization of the *hæmaglobin* takes place, forming *hæmatoïdin*, the reddish-yellow crystals of which occasion the coppery stains of the skin—a result which may occur not alone in syphilitic roseola, but in any prolonged blood capillary engorgements from any cause. May we not, then, reasonably infer, from the foregoing, and in the absolute absence of proof to the contrary, that the syphilitic roseola is, like the simple roseolas, the result of an impression upon the sympathetic nervous system—a paresis of the vaso-motor nerves of the cutaneous envelope, caused by a limited but special paralyzing influence exerted upon the great sympathetic nerve through occult but positively recognized blood-changes?

We have now followed the progress of the syphilitic disease-germ, from its original point of contact with the surface of inoculation, to its lodgment in the second order of lymphatic glands. If the foregoing view of the nature of the roseola of syphilis be accepted, we have *no positive evidence that the disease has yet reached the blood.* Delayed for a limited period at the point of inoculation by unavoidable physical and

physiological obstructions, it finally reaches the first order of glands (the glands of connection); delayed here again for another period by the same causes that obtained in the first instance, it finally passes on through the afferent lymphatic canals to and into the second order of glands, which become involved in precisely the same manner as the first. Thus, if we are willing to accept the view of Diday, that the prodromes of syphilis are due to the chloro-anæmia, the sole evidence of the presence of the so-called *syphilitic* virus is still to be found in the lymphatic system. We have, it is true, at about this time, in a considerable proportion of cases, an inflammatory engorgement, more or less intense, occupying the mucous membranes of the pharynx and tonsils; but the tonsils have been recently accepted as belonging to the lymphatic system, representing a simple form of lymphatic gland, although no direct communication has yet been demonstrated between the follicles composing the tonsil and the adjacent lymphatic vessels; these cover them in almost completely, and they are besides so dilated that they are rather lymph-sacs or lacunæ surrounding the follicle.

The entire pharynx is much richer in lymphatics than the surrounding mucous membrane. At this point, then, we should expect, with the general engorgement of the lymphatic system, early evidence of disturbance. Brought here into more intimate relations with the blood vascular system than occurs in lymph-glands of a higher order, the implication of these lymphatic accessories is often followed by a true inflammatory engorgement, which not unfrequently results in a rapid gangrenous or ulcerative destruction of tissue.

In the necessarily frequent allusion to different authorities, as the subject of syphilis is considered, the term *virus* constantly occurs; it is, therefore, perhaps not out of place here to repeat that, according to the views advanced in this and in the preceding paper, it is not a *virus* which is accepted as producing syphilis, but an abnormally active natural germinal cell or corpuscle, that, being introduced into a healthy organism, impresses the normal germinal molecules with an action similar to its own; that the nutritive changes and deviations from health in syphilis are simply the result of a too

rapid development of such germinal material as the hyperactive corpuscle may have been able to impress with its influence; that in no case is the disease-germ or its descendants able to arrive at any maturity; that they never become elevated into red blood-corpuscles, nor ever form a permanent ingredient in any useful tissue; that, as certain conditions of vascular excitement, which we call inflammatory, hasten the development of the white blood-corpuscle, up to the point of emasculation, resulting in the pus-corpuscle, so a more subtle influence imparts to certain of the white blood-cells a greater tenacity of life and a capacity of somewhat higher development; capable of a certain low power of organization, but still falling short of the ability to combine with the normal tissues, in any way, except as foreign material, to embarrass and disturb their normal development and functional integrity.

The vitiated corpuscles, then, holding on their course through the lymphatic system in which we have observed them repeatedly, and for a time effectively, arrested by glandular barriers, finally gain an entrance into the general circulation.

It is by no means improbable that the lymphatic glands act as depots, as claimed by Virchow, and that, in occasional cases, the vitiated corpuscles are retained in these organs, until a normal or artificially excited fatty degeneration has enabled them to be partially or wholly eliminated from the system. In this way, the occurrence of cases of syphilis presenting marked deviations from the usual course of the disease may be accounted for. In classical cases, however, there seems to be no reason to doubt but that the vitiated germinal material passes into the blood along with the normal lymphatic elements.

The earliest evidence that this occurrence has taken place appears in the very great majority of cases in the development of a papular eruption—symmetrical and more or less general—and usually preceded by or ushered in with an increase of temperature, an acceleration of the pulse, and variable degrees of nervous and functional disturbance. This eruption is usually composed more or less from distinct eleva-

tions of the skin, varying in different cases from the size of a pin's-head to half a dime, or even larger. Mr. Wilson, consistently with his teaching in regard to the syphilitic roseola, remarks that "when the eruptive force is sufficiently powerful, the case is one of lichen.[1] In this form there sometimes appears a tendency to aggregation into small groups or clusters; this is known as the *lichen corymbosus*. Other varieties present, dependent upon size or arrangement, as the lenticular, the papular, the annular, as described by different authors. The seat of origin of these papular eruptions appears to be still in dispute. Zeissl thinks that the sebaceous or the hair-follicles are the principal seat. Mr. Wilson, in describing a case of the lichenoid form observed by him, says: "The aperture of a follicle was apparent at the summit of each papule, marking the seat of the inflammatory congestion to be the capillary plexus of the follicle." Lancereaux believes that the papillæ of the dermis are also sometimes the starting-point of this affection. Rindfleisch says of the simple papulous exanthemata that "the exudation is seated in the papilla itself." According to Mr. Tilbury Fox, "the true papule is due to a plastic exudation into the skin, especially of the papillary layer." Possibly it can be shown that the origin of the papule is *always*, and of *necessity*, in the *papillæ cutis*.

"The blood," says Rindfleisch, "is the medium of exchange of the material of the organism. It is the nutritive fluid which conveys to each individual portion of the body the nutritive ingredients necessary for its existence, and instead, carries away from the parts the useless and injurious products of the chemical processes associated with nutrition."[2] This circulating medium is carried out, from the centre of the circulation to the periphery, by the arteries and returned by the veins. Intercalated between these two sets of vessels is the lymphatic system, which withdraws from the tissues such nutritive materials as are exuded in excess by the arteries into the tissues, and returns them again into the cir-

[1] Wilson on "Diseases of the Skin," 1866, p. 474.

[2] Ripnfleisch, p. 181.

culation at a given point. Now at the nearest points of contact of these systems of vessels, at the superficies of the body, we should expect to find collections of surplus material, which, after having escaped from the arteries, were unable from any cause to effect an entrance into the under-drainage vessels, the lymphatics. The relation of these vessels in the cutaneous envelop, as described by Teichman, is as follows: "The blood-vessels lie around the circumference of the papillæ[1] (winding up, corkscrew fashion, around the papilla until they unite at its apex); while the lymphatic vessels lie exactly in the centre of the papillæ, and no lymphatics are found in the sebaceous follicles, the sweat-glands, or the hair-bulbs. Consequently, it is in this juxtaposition of the blood-capillaries surrounding the papillæ, and the lymphatic capillaries passing up through their centres, that is to say, in the interval between these, that we should expect to find materials escaped from the blood-capillaries, detained in their transit into the lymphatic capillaries. At this point, the force of the circulation is at the minimum, the condition most favorable for proliferation. The act of proliferation is a vital one, one predisposing to the coagulation of the fibrine contained in the tissue-fluid.

With these predisposing forces and conditions, it is natural to expect an accumulation of cell-material and a separation of the fibrine of the lymph, and these resulting in a hyperplasia of the papillary layer of the cutis. This, too, most prominent, in the interval between the blood-capillaries distributed around the summit of the papilla and the lymph-capillary which passes up through its centre, necessarily giving rise to the abnormal elevations termed syphilitic papules. These papules vary in size, as the hyperplasic papillæ are more or less abundant—appearing in lichen as quite discrete, while in the larger varieties an aggregation of papillæ occurs, and is consolidated through the escape of the hyperplasic materials into the adjacent surrounding tissue. We are thus enabled to account for the variations in the size of papules, occurring as a result of the proliferation of cell-elements in the papillary layer of the cutis.

[1] Rindfleisch, p. 277.

The recent observations of Kohn, 1870,[1] in regard to the histological constituents concerned in the formation of the papular syphilides, confirm the foregoing views: "They are formed," he says, "uniform and dense, limited clearly by infiltrations into the papillæ and corium. These infiltrations are constituted by an accumulation of cells, which are piled up in dense and regular layer, around the vessels in the interstices of the connective tissue. The cells are not destined to be permanently organized, as they degenerate and disappear, or assume a dull granular appearance, undergo fatty degeneration and are absorbed, or they may become heaped together in the form of detritus and form pus. Upon the section of a papule, it is seen that it is limited by two lines formed of cells which are accumulated in the corium and on a level with the papillæ. The latter two structures are glued together, while the epidermis is stretched. The papule is resistant, in consequence of the accumulation of the cell-elements, and its color is due to the capillary stasis, to any effusion of the coloring-matter, and perhaps to the color of the new formation." These observations of Dr. Kohn are in complete accord with the previous statements made by Auspitz,[2] Virchow,[3] Neumann,[4] and Taylor.[5]

The syphilitic papule, then, whether occurring as a local or a general eruption, may be considered as the result of a proliferation of the cell-element, and an organization of the fibrine, separated from the tissue-fluid, and which has usually, if not always, a papilla cutis as its seat of origin. Here we find the point of nearest circumscribed contact or closest relation, viz., between the blood-capillaries and the intercalated lymph-vessel of the papilla, and *not* in the sebaceous follicle, or in

[1] "Caractères cliniques et histologiques des Syphilides," par Moritz Kohn. Wiener Med. Wochenschrift, 1870, No. 55. Archives Générales de Médecine, March, 1872.

[2] Auspitz, "Ueber die Zellen Infiltration der Leiderhaut," Medizinische Jahrbücher, vol. ii., p. 208, 1864.

[3] Virchow, "Pathologie des Tumeurs." Trad. Franc., vol. ii., p. 361, *et seq.*

[4] Neumann, "Lehrbuch der Hautkrankheiten," p. 240.

[5] Taylor, "Observations on the Papular Syphilides." *American Jour. of Syphilography and Dermatology*, April, 1870, p. 108.

the hair-bulbs, or in the sweat-glands, with which lymphatic vessels have not been found to be so associated. In regard, therefore, to these latter, we are led to conclude that when they are apparently engaged in the formation of a syphilitic papule, it is only by their being aggregated into the papule by the exudation of cell-material which has originated within the papilla cutis. It is not now, perhaps, too much to assert that the syphilitic papule is always an evidence of an abnormal proliferation, excited by the influence of the syphilitic disease-germ, or corpuscle which has escaped from a blood capillary in a papilla cutis, and occurs separately or in groups, the arrangement differing in different cases, from influences not yet determined.

We have, besides the well-marked papular syphilide, pustular and vesicular eruptions associated with the early period of syphilis, and from the manner in which the papular syphilide has been claimed to originate, it is easy to understand why the pustular and vesicular forms of eruption, occurring at a similar period in the progress of the disease, often mingled with and visibly originating from the syphilitic papule, should be considered simply as abortive papular syphilides. Kohn, it will be remembered, remarks of the syphilitic papule, that "the cells composing it are not destined to be permanently organized, as they degenerate and disappear, undergo fatty degeneration, and are absorbed, or are heaped together as detritus, and form pus."

The pustular and vesicular syphilitic eruptions, then, would seem to result from a lack of formative power in the lymph, and from the inability to form, or the easy liquefaction of, the hyperplasic materials, this occurring probably from a low state of the system, produced either by general causes or by some especial dyscrasia, *not necessarily dependent upon the syphilitic influence.*

Prominent among the manifestations of early constitutional syphilis is the mucous patch. This consists of an erosion of the surface or a complete destruction of mucous membrane upon which this peculiar lesion is always situated. The erosion or entire disintegration of the mucous membrane is followed by the exudation of lymph from the denuded

surface and its rapid organization, thus producing a white fibrinous pellicle which is a constant accompaniment of this lesion.

Virchow[1] says of *hyperinoses:* "I do not think that we are enabled to conclude that, in a person who has an excess of fibrine in his blood, there is, on that account, also a greater tendency to fibrinous transudation, on the contrary, I should rather expect that, in a patient who produces at a certain point a large quantity of fibrine-forming substance, much of it would pass from that point into the lymph and finally into the blood. The exudation, therefore, in such cases, may be regarded as the *surplus* of fibrine formed *in loco*, for the removal of which the lymphatic circulation did not suffice. In accordance with this view, then, the mucous patch may be considered the accidental focus of development of the syphilitic corpuscle, resulting from superficial lymphatic capillary obstruction caused through a hyperplasia excited by the presence and usual influence of the syphilitic disease-germs. Mucous patches always occur upon mucous membranes richly endowed with lymphatic vessels, as upon the soft palate, the tonsils, the gums, the inner surfaces of the cheeks, the tongue, the walls of the pharynx, etc.

The mucous tubercle, which is the analogue of the mucous patch, occurs upon the integument at points also of unusually abundant lymphatic distribution, as about the vulva, the anus, on the scrotum, about the nails of the fingers and toes, etc.

A specific exudative inflammation of the eye is a not infrequent occurrence in early constitutional syphilis. The late Prof. Von Graefe made the statement that, according to statistics collected by him, about sixty per cent. of all cases of iritis occur in persons affected with syphilis. Dr. Bumstead[2] says: "We have no certain means of distinguishing syphilitic iritis from that dependent upon injury, rheumatism, or other causes," and thus describes the pathological changes which occur in the course of this affection in syphilis:

"At an early stage of the disease, the pupil assumes a dull appearance, owing to commencing changes in the anterior

[1] "Cellular Pathology," p. 199.

[2] Bumstead on "Venereal Diseases," third edition, p. 660, 1870.

capsule of the lens; it may also be somewhat irregular. This irregularity of outline due to adhesion between its margins and the capsule of the lens, or to exudation into its substance, becomes more marked as the disease progresses, and is especially evident if the pupil be dilated by belladonna or atropine. When its margin is found to be scolloped, owing to its being attached at some points and drawn out in others, in some cases the adhesions become continuous around the whole circumference, and the capsule of the lens is covered with a layer of lymph which completely blocks up the pupil."

This inflammation may be serous instead of plastic, or it may assume a suppurative form. It is associated with the period of roseolous or papular eruptions, mucous patches, etc. Carmichael states that the eruption usually associated with it is the papular.

Recent observations have shown the presence of an extensive distribution of lymphatic vessels in every structure and tissue in the human organism. Everywhere that blood-vessels are present, an accompanying system of lymph-vessels is also found, thus going far to confirm the recent views of Willis, Recklinghausen, and others, of the office of the lymphatic system as a necessary adjunct to the blood vascular system, for the purpose of gathering in and returning to the general circulation the excess of lymph exuded for purposes of nutrition. With this view of the office of the lymphatic system, it is easy to account for many diseased conditions heretofore considered anomalous, to appreciate the causes of the multiform lesions in syphilis which have hitherto puzzled acute clinical observers, and conveyed to them the impression that the disease was developed through no fixed laws, but resulted from a general and almost necessarily permanent vitiation of the entire affected organism.

The structures of the eye, especially the more delicate, as the iris, the retina, the conjunctiva, etc., have hitherto been considered as entirely deficient in a lymphatic circulation. Schwalbe [1] has, nevertheless, fully demonstrated their presence

[1] "Handbuch der Lehre von den Geweben der Menschen und der Thiere," by Stricker, Leipsic, 1872.

in all these structures, and has shown an especially generous distribution to the iris, and in excess of the neighboring tissues. With the presence of the vitiated germinal element free in the general circulation, with its known power to cause obstruction to the lymph circulation, and a consequent hyperplasia, what should we expect to find? As a natural sequence, we should expect what we find in the advance and course of syphilitic disease, viz., that this delicate structure often suffers, and through the same causes that result in hyperplasias, in other parts richly endowed with lymphatic vessels.

A very general impression prevails that there is an entire absence of the lymphatic distribution in the osseous structures. Cruikshank, many years since, claimed to have discovered the entrance of a lymph-vessel into a dorsal vertebra. More recently, this observation has been confirmed by Soemmering and Bonamy. Sappey and Gross have demonstrated the presence of lymphatic vessels in the marrow of the tibia. Bonamy states that he injected the lymphatics which arise from bones by little foramina which are found on the side of the internal condyle of the femur. Accepting these statements, we find a reasonable explanation of the occurrence of ostitis and periostitis, and the formation of nodes, which are found associated with the early or active period of syphilis.

Not alone in the structures of the eye, and in the bones, in the muscles, and in the serous membranes generally conceded to be outside the track of the lymphatic distribution, are these essential vessels now ascertained to be present. Even in the fibrous and cartilaginous tissues—those most scantily supplied with blood-vessels of all the normal structures—these vessels have been absolutely demonstrated. The recent work of Ludwig and Schweigger-Seidel, published in Leipsic, 1872, is rich in illustrations of the presence and distribution of lymph-vessels in cartilages and fasciæ. Through the kindness of the President of this Society, Dr. Jacobi, I am now able to exhibit to you this very admirable and elaborate work, received during the last month from Leipsic.

Time does not, at present, allow me to extend the consideration of the subject of the evening further, but on a future occasion I confidently expect to be able to demonstrate the

intimation conveyed to you at the close of my previous paper on syphilitic infection, viz., that many if not all of the later manifestations of syphilis may be satisfactorily explained through causes wholly dependent upon interference with the lymphatic circulation, and that it is to deposits of fibrine, organized through the syphilitic influence, in and around lymph-vessels and lymph-sacs, in the earlier stages of the disease, and its subsequent contraction, that the various external and internal lesions occurring in the later stages of syphilis are chiefly due.

And, still further, I believe that the management of this disease is capable of being established upon an intelligent and philosophical basis; not necessarily changing the present recognized methods of treatment, but by affording a reasonable explanation of the manner in which known, effective, remedial measures, result in the alleviation and cure of syphilis, and thus aid, to some degree, in extricating the *prophylaxis* and the *therapeutics* of this disease, from the slough of empiricism in which it has hitherto been submerged.

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