

Clinical lectures on the physiological pathology and treatment of syphilis : together with a fasciculus of class-room lessons covering the initiatory period / by Fessenden N. Otis.

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WHITECHAPEL CLINIC



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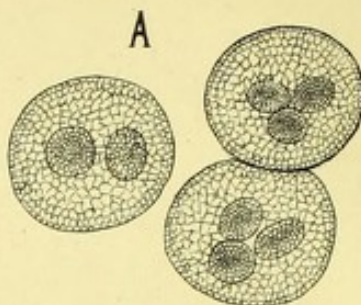
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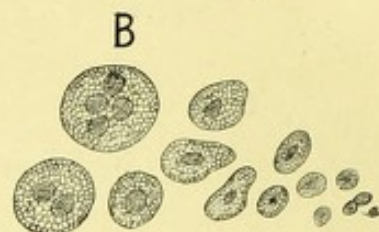
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with Compts of the
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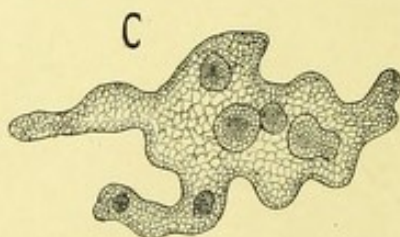
A
Healthy White Blood Corpuscles.
Diameter.
 $\frac{1}{2500}$ inch.



B
Degraded White Blood Corpuscles.
(Disease germs of Beale.)
Down to $\frac{1}{100000}$ inch.

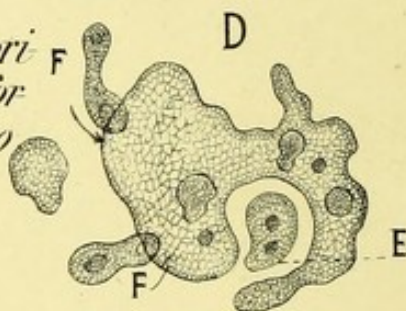


C
Normal White Blood Corpuscle
in motion.

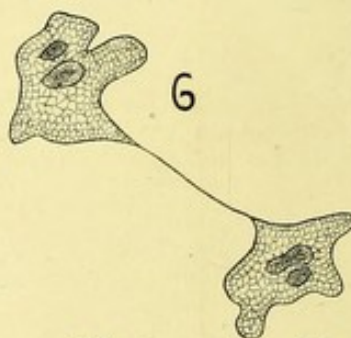


D
The same, showing mode of appropriating food and of incorporating foreign bodies; cells, corpuscles, etc. into its substance at E.

Degraded Corpuscles penetrating White Corpuscle by their power of amoeboid movement at F.F.



G
Proliferation, or division of the White Corpuscle, with its nuclei, by fission.



H
Increase of Cells by Budding.

I
Endogenous Cell Formation.

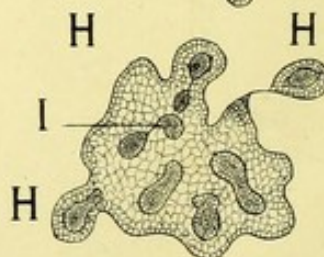


DIAGRAM.

Human White Blood Corpuscles, healthy and degraded, Illustrative of their connection with syphilitic infection as referred to in the following lectures. See views of authorities on page following title.

CLINICAL LECTURES

ON THE

PHYSIOLOGICAL PATHOLOGY AND TREATMENT

OF

SYPHILIS

TOGETHER WITH A

FASCICULUS OF CLASS-ROOM LESSONS COVERING
THE INITIATORY PERIOD

BY

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NEW YORK

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1881

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VIEWS OF AUTHORITIES CONCERNING SOME OF THE PROPERTIES AND POWERS OF EMBRYONAL OR WHITE BLOOD CELLS.

"All embryonic cells possess the property of giving origin to elements resembling themselves by the following process. The nucleolus enlarges, becomes constricted, and divides; soon the nucleus divides by a fissure, which separates the nucleus into two, or by a constriction which gives it an hour-glass shape. The mass of protoplasm surrounding the two nuclei, divides, and two cells are formed. The segmentation of the protoplasm does not always follow that of the nucleus, so that there may be many nuclei in one cell. Frequently a portion of the protoplasm is separated enclosing a nucleus." (Cornil and Ranvier's *Pathological Histology*, Am. ed., 1880, pages 21 and 22.)

MOVEMENTS OF WHITE BLOOD CORPUSCLES. Foster says (page 42, McMillan, ed. 1880, "A typical amœba (or white blood cell) may be regarded as spherical in form, and when it is executing its movements the pseudopodic bulging of its protoplasm may be seen now on this and now on that part of its circumference, and to take now this and now that direction."

"Each corpuscle changes its form continually, sending out quickly fine filamentous processes, singly or in groups, which processes thicken at their base and consist of a part of the substance of the cell-body. They again retract and disappear without leaving any traces of their existence behind. . . . The corpuscles exhibit these changes in form, as well in liquid connective substances, as in solid tissues, and consequently they wander in them for the most part in very circuitous routes. Migration is accomplished in the following manner: the cell mass shoots out into processes, then the round end opposite to the process advances with it in line, and then by a farther elongation of the body of the cell it moves on still further. This migration takes place, as already said, not merely through open spaces or cavities of the connective tissue but also through the walls of the capillaries and small veins." (Wagner, *General Pathology*, Am. ed., 1876, pages 152 and 153.)

"Colorless corpuscles by their contractibility are also able to TAKE UP and TRANSPORT FOREIGN SUBSTANCES (carmines, cinnabar, milk globules, red blood corpuscles, dust of every kind, etc.)." (Ibid. page 153.) "That the white globules absorb foreign substances into their interior was first made known by HAECKEL, then by COHNHEIM, RECKLINGHAUSEN," etc. (Ibid., page 154. Frontispiece, Figs. C, D, E, F.)

"The growth and multiplication of disease germs, their introduction into the body, their passage into the blood, and their subsequent wanderings are intimately connected with their capacity for vital movement." (Beale's *Disease Germs, their Nature and Origin*, London, 1872, page 100.)

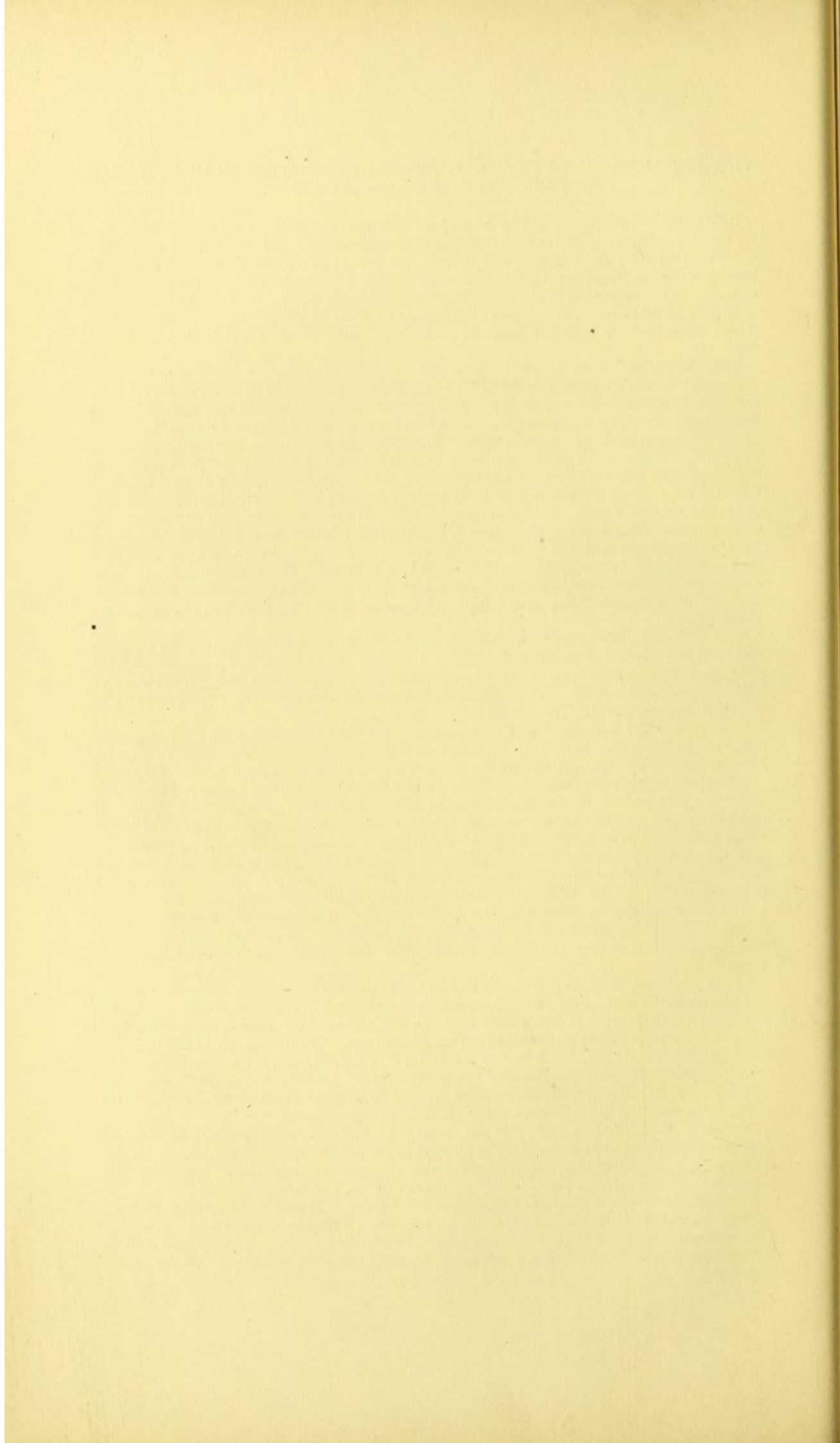
"Bioplasts (white blood corpuscles) which in health may slowly increase in size and divide and subdivide, grow perhaps ten or twenty times as fast as they should grow, and may produce as many descendants in twenty-four hours as, in the normal state, would have resulted in many weeks or months. The abnormal bioplasts have gained, as regards their rate of growth and multiplication, but they have deteriorated in formative power, if indeed they have not altogether lost it; and it is in formative power that the bioplasm of a tissue differs from the degraded forms of living matter." (The *Microscope in Medicine*, Lionel S. Beale, London, 1878, pages 136 and 137.)

"NEW FORMATION OF PATHOLOGICAL CELLS takes place from preëxisting normal or pathological cells, either by division or by endogenous cell formation. The origin of the cell always precedes that of the nucleus. In almost all cases there is a simultaneous increase of the protoplasm."

"CELL DIVISION affects the cell in toto, that is, all the parts of it (membrane, contents, nucleus, and nucleolus). It takes place for the most part in the long, rarely in the transverse, axis of the cell. By division there are at first, usually, only two cells formed, rarely three or more at the same time; they are for the most part smaller than the original cell. The division itself affects first the nucleolus, then the nucleus, which become elongated, then constricted in the middle and divided; the protoplasm at the same time increases in quantity. Division of cells, and especially that of the nucleus, is accomplished quickly, within a few seconds, so far as observations have demonstrated this in living cells and on the warmed object plate." . . . (Frontispiece, Fig. G.)

"Budding, so-called, is a variety of cell increase by division. After a single or manifold division of the nucleus one or many nuclei advance to the periphery of the cell. The latter protrudes at these points like buds, and at the same time a nucleus enters each bud. Finally the bud separates and becomes a free nuclear cell." . . . (Frontispiece, Fig. H.)

"ENDOGENOUS CELL FORMATION (endogenous cell-division at I) consists in this: the nucleus, after previous division of the nucleolus, divides into two, rarely into many, nuclei. With the simultaneous enlargement of the cell the new-formed nuclei divide, etc., — so that finally a cell is formed with 4-8, and more nuclei." (Wagner, *Manual of General Pathology*, Am. ed., 1876 page 358.)



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INTRODUCTION.

It is now nearly ten years since the attention of the medical profession was first invited to my views on the Physiology of Syphilitic Infection. This was in a paper read before the New York County Medical Society, in June, 1871, and published in the *New York Medical Gazette* and in the *American Journal of Syphilography and Dermatology*, in July, 1871. Again, attention was called to the subject, in another paper, before the same society, in May, 1872, on the Physiology of Syphilitic Infection as applied to the successive Manifestations of the Disease, and published in the *New York Medical Journal* of July, 1872. In the first paper it was shown, by citations from leading authorities throughout the world, that there was, at that time, an entire lack of harmony, in regard to their views as to the nature of syphilis and the manner in which the human system was infected by it; that, in regard to the leading doctrinal points involved in a consideration of this disease, almost an equal number of distinguished authorities were diametrically opposed to each other.

The virulent nature of the disease was agreed upon. Inoculation of the secretions of one suffering from syphilis, was accepted, by all, as a necessity for its production. Unanimity on this latter point had resulted from extended and studious clinical observation. Here, however, unanimity ceased, and at the first approach to a consideration of the physiology and pathology of the disease, division of opinions ensued. Two great parties arose: one asserting that on the instant of contact between the so-called virus of syphilis and an abraded surface on a healthy human subject, the entire organism became pervaded, permeated, with the disease, not only independently of all known physiological processes, but in defiance of all known physical laws; while the other party insisted that a distinct interval, one of several days, always elapsed between inoculation and constitutional infection. The initial lesion of syphilis, or chancre, was claimed by the first party to be the result of the general infection, manifesting itself by a local reaction at the point of original contact or inoculation, while the second held that the chancre was the first and only direct result of the application of the virus, and that the constitutional infection resulted through a gradual invasion, proceeding from this point: the one claiming (as with Auspitz and Kölliker, in 1879), as a result of

clinical experience, that excision of the chancre may wholly prevent the occurrence of constitutional infection ; while the other insisting (with Diday, Berkeley, Hill, Bumstead, and others), from the most positive personal experiments, that destruction of the lesion of inoculation, no matter how recent, is wholly useless in preventing general syphilitic infection. The fact that these parties and their representatives were then, and are to-day, thus opposed, on vital practical issues, is a sufficient commentary on the value of purely clinical experience, in the decision of questions involving observations on important physiological and pathological processes. These differences can never be harmonized until some other and more philosophic mode of arriving at conclusions shall be adopted than that offered by clinical observation alone.¹ Instruments of precision have become essential in every department of science, whether in the organic or in the inorganic world. What the telescope has done for astronomy, the microscope has done, and must continue to do, for physiological, histological, and pathological science. The names of Virchow, of Stricker, Billroth, and Rindfleisch ; of Beisiadecki, Cornil, Ranvier, Cohnheim, Beale, Chauveau, Burdon-Sanderson, and a score of other distinguished scientific workers with the microscope have, during the last quarter of a century, thrown floods of light into the mysterious processes of the human organism in health and disease ; but we look in vain through the numerous works on venereal disorders which have been issued during that time to find the advances in pathology and physiology applied to the adjustment of the great and much-vexed questions of syphilis and the allied diseases.

It was with the avowed object of bringing such knowledge, scattered through the literature of that period, to bear upon this matter that the physiology of syphilitic infection became a subject of study, and subsequently of the papers referred to as having been presented to the profession by me, eight and nine years ago. Since that time I have neglected no known opportunity of availing myself of every personal clinical experience, and of all advances in physiology, histology, and pathology, which might promise support to, or which might tend to overthrow, the materialistic position I had been impelled to assume, as against the supernatural views held by accepted authorities.

My effort was made in the direction of placing the question of syphilitic infection upon a rational footing, and was at first based chiefly upon the published investigations of Beale, Burdon-Sanderson, and Chauveau in regard to small-pox, the cattle plague, and relapsing fever. These gentlemen claimed to have demonstrated, through microscopic examination, that a living germinal cell was the

¹ See page 2.

starting-point of those diseases in each case; that this cell possessed the powers and properties of the human white blood corpuscle, in so far as growth, movement, and proliferation were concerned; that it was much smaller, more active, more short-lived, and yet was still capable of maintaining its vitality and exerting its powers after being removed from its seat of development and deposited in another locality, so only that it was furnished with suitable pabulum. Beale also claimed that another cell, with similar properties and powers, and *directly descended from degraded cell elements of human origin*, was the starting-point of syphilis.

The well-known fact, that all efforts made previously to this time, (and they were numerous) had failed to discover the physical entity or representative of the so-called syphilitic *virus* did not then, and does not now, militate against it, for the reason that only something foreign to the normal cell and tissue elements had been sought. This depraved human germinal cell of Beale was represented in size as varying from that of the normal white blood corpuscle, *in proportion to the degree of its degradation*, with nothing in its composition, or in its physical proportions, to distinguish it from the nuclei or the nucleoli of the normal white blood corpuscle. Hence, with nothing but its morbid activity, its increased capacity for proliferation, to distinguish it from the normal cell elements, being itself, in point of fact, a diminutive white blood corpuscle, it is not surprising that such a cell, as a disturbing element in the blood, in the nutritive fluids, and in the lesions of persons affected with syphilis, should have eluded microscopic research. The signal failure, of Lestorfer and others, to discover any peculiar or substantial virus, had left the subject of syphilitic infection in the same obscurity as when Fernel, in the middle of the sixteenth century, classed its poison with that of the plague and of hydrophobia, as possessing "a mysterious power to enter and vitiate the blood." In all the works on syphilis I was able to consult, there was no evidence that any distinct connection had been recognized, between the initial lesion and the subsequent manifestations of the disease. Each one of these stood separate and distinct from every other. The simple clinical fact that the initial lesion was the first tangible evidence of syphilis, and in certain instances possessed certain marked physical characteristics, was noted, and that, after a mysterious period, called the period of *incubation*, enlargement, and induration of adjacent lymphatic glands succeeded; that after another unexplained interval a cutaneous efflorescence occurred, accompanied, perhaps, by a pharyngeal congestion, — possibly, by ulceration of the tonsils; then, possibly, after another mysterious interval, a papular eruption of the skin and mucous membranes appeared, — possibly falling of the hair, inflammation of the iris, periosteal pains, swellings of

bone, etc. ; again, after another and a much longer mysterious interval, deposits, of an anomalous material, called "gumma" (from its viscid and gelatinous appearance), in the skin, in the testes, in the tongue, in the bones, in the brain and nervous system, and in the viscera, — producing trouble sometimes, apparently only by mechanical pressure, and again giving rise to extensive and unexplained deterioration or absolute destruction of tissue : but beyond a physical description of the various lesions of this period, and the information that all were in some way associated with the mysterious "gumma," no explanation was afforded. These, with all the preceding lesions, were summed up as syphilitic manifestations of the primary, secondary, tertiary, and quaternary periods, without any attempt at exposition on a basis of known physiological or pathological processes. Therefore, any new view of the subject, which could afford even a plausible explanation of the various processes and manifestations of syphilis, in accordance with the recognized laws of physiological and pathological science, could not fail to constitute an advance upon this position of acknowledged ignorance in regard to the nature and behavior of syphilis.

Soon after the first publication, of my views on this subject a reference to them appeared in the editorial columns of the *London Lancet* of November 9, 1872, in the course of which the following passage occurs : " We may then say that these new views on the physiology of syphilitic infection, are not based upon the results of any experiments, or new facts, or on the unraveling of observations. *They consist, mainly, of deductions drawn from a close and elaborate reasoning on the acknowledged features of syphilis, in connection with the latest doctrines and hypotheses of certain pathological teachers.*" This criticism very amiably expressed the exact position claimed by me in the whole matter.

The teachers referred to were Chauveau, Beale, Willis, Recklinghausen, Mialhe, Schweigger-Seidel, Stricker, Kölliker, Cohnheim, Virchow, His, Frey, Teichman, Rindfleisch, Tilbury Fox, Kohn, Ludwig, Gross, Sappey, Soemmering, and Bonamy ; and it appears to me proper now to state, that, in not a single instance, have the teachings of these authorities, to which reference was then made, been controverted. On the contrary, they have been confirmed by more recent investigations by the same and other authorities. This has been especially the case in regard to points of chief importance, such as the nature and powers of the white and red blood corpuscles, and the distribution and functions of the lymphatic system.

To the arguments drawn from the foregoing distinguished scientists, the microscopical investigations of Beisiadecki and Verson have been added,¹ affording a practical substantiation of the claims as to the

¹ See page 4.

minute anatomy of the initial lesion of syphilis, advanced by me in the first paper on the Physiology of Syphilitic Infection (previously referred to) independently of any knowledge of such investigation. Bäumler, one of the most recent authorities on syphilis, also offers his testimony in favor of this view of the initial lesion.¹ He also claims that all the lesions of active syphilis have for their basis "a cellular infiltration proceeding from the blood-vessels,"² in accordance with the advancing steps of the same views of syphilitic infection, as presented to the profession by me eight and nine years ago. At that time, only the so-called primary and secondary stages of the disease were considered. Since then, the same views have been extended over the later stages of syphilis, and have been shown to afford an explanation of the mysterious lesions of the tertiary and quaternary periods, apparently in harmony with known physiological and pathological processes, as investigated and explained by the distinguished authorities on such matters, previously referred to, and others equally distinguished, who represent the most recent advances in medical science.

The *treatment* of syphilis, in its various stages, has also been considered in its relation to a rational or physiological view of the disease.

In point of fact, the positions originally taken in explanation of the different lesions of syphilis, during the various periods, forced attention to the question of treatment at an early period in their discussion. The complete harmony between the treatment made a logical necessity by the acceptance of known physiological pathological premises, and that based upon clinical observation alone, afforded circumstantial evidence of great weight, in favor of the rational and material view of syphilis. The following lectures contain the practical results of more than ten years' consideration of the subject, and of the application of that view in teaching and in practice. They have been reported from the regular course of clinical teaching in the department of genito-urinary diseases at the College of Physicians and Surgeons, and carefully revised by me for publication in the columns of the *Boston Medical and Surgical Journal*, where they have appeared from time to time during the past year.

These lectures are now placed before the medical profession, in this more permanent form, with the hope that such attention will be secured to them, as will lead to an impartial examination into the evidences therein adduced in favor of the view of syphilitic disease based upon purely scientific grounds; — a view, through which, I firmly believe, every phase of syphilis may be legitimately explained, in its varied aspects, in complete accordance with known physiological and pathological laws.

¹ Ziemssen's Cyclopædia, vol. iii., p. 112, Am. ed.

² Ibid., page 131.

The appended Class-Room Lessons, commencing at page 91, have grown out of the necessity of having some medium of communication between teacher and pupil, which should not be liable to misinterpretation on important points. For the last three years it has been my habit to distribute, from time to time, during each session, to the students of the College of the Physicians and Surgeons, these lessons of three or four pages each, containing the salient features of syphilis and the allied diseases, especially including those not fully treated of in the ordinary text-books. The lessons covering the initiatory period of syphilis have appeared to me so intimately connected with the following lectures that it has seemed desirable to include them in the present volume, with the expectation, at some future time, of adding lessons on the later periods of syphilis and on chancroid.

FESSENDEN N. OTIS.

NEW YORK, *January 1, 1881.*

CLINICAL LECTURES

ON THE PHYSIOLOGICAL PATHOLOGY OF SYPHILIS.¹

DELIVERED AT THE COLLEGE OF PHYSICIANS AND SURGEONS, NEW YORK,
SESSION OF 1878-79.

BY FESSENDEN N. OTIS, M. D.,

Clinical Professor of Genito-Urinary Diseases, etc.

LECTURE I.

HISTORY AND NATURE OF SYPHILIS.

GENTLEMEN, — In entering to-day upon the systematic clinical study of syphilis, it will be worth our while to review briefly the teachings in regard to its history and nature, as presented to you somewhat in detail on a previous occasion. By citations from our most valued authorities it was made plain that the disease was of very ancient origin, antedating the Christian era by many centuries. It was made equally evident that while syphilis had been the subject of much and careful study during a long period, great differences of opinion existed in regard to its nature and the manner in which it affected the human organism. By the earliest writers accepted as a punishment inflicted upon the human race through some offended mythological deity, it was treated by prayers and sacrifices. But as the medical profession grew more observant and less superstitious, it came to be considered the result of a venereal miasm, which might be modified, possibly cured, by medical measures. The miasmatic doctrine in its turn gave way to farther observation and closer study of the matter, until we found, at about the middle of the sixteenth century, that contact with a person suffering from syphilis was held to be essential for the acquirement of this disease. From this fact it was assumed that a mysterious contagious element resided in the secretions of the syphilitic lesions, and thus the doctrine of a *virus* was first established. These lesions were, however, often so complicated with certain simple venereal diseases that a very long period elapsed before the separation was effected. Even now it can scarcely be said that syphilis has been absolutely separated from the local disease called the chancroid. This matter, as you know, has been much discussed, for the last quarter of a century, under

¹ Reported by P. Brynberg Porter, M. D.

the title of the unity or duality of syphilis. A vast amount of clinical evidence has been adduced in favor of each: one party claiming that syphilis is the only parent of chancreoid, — the local venereal ulcer, — and that, while the latter is *usually* a local disease, it may under certain circumstances acquire the power of communicating syphilis: the opposing party denying that power under all circumstances, and asserting the individual and unchangeable nature of each. Notwithstanding the profusion of clinical evidence always available in these discussions, this important question still figures as the "tug of war" in all general syphilitic discussions. It may be well at this point to call your attention to the fact that clinical observations, which have been thus far almost solely relied upon for the solution of the disputed questions in regard to venereal diseases, are, as a rule, made under such peculiar embarrassments — moral, mental, physical, and circumstantial — that the same apparent conditions falling under the notice of one observer often present phases and peculiarities in the experience of another that warrant entirely different conclusions. Hence it is that notwithstanding syphilitic disease has been studied by numerous earnest, honest, and competent observers, wide and sincere differences of opinion still exist in matters of great practical importance, aside from unity and duality. Thus, as has been seen, in regard to immediate and gradual infection in syphilis, the profession are still about equally divided: one side claiming that the virus of syphilis infects the entire system at the moment of inoculation, while the other claims that the initial lesion is purely local for a time, and that the organism is gradually affected.

Also in regard to the question of hereditary influence: one party claiming that syphilis may be communicated to the embryo through the spermatozoön furnished by a syphilitic father; the other holding, by virtue of an equal amount of clinical evidence, that this is never the case, but that the male parent can only infect his offspring through the medium of the maternal influence, that is to say, by first infecting the mother.

Nor is it alone in regard to such points of doctrine as have been cited that unsettled questions confront the student of syphilitic disease. Deductions from clinical observations continue to give us the most varied and discordant views and opinions, even in regard to the nature of the disease and its mode of affecting the system. Thus among those figuring in the history of syphilis, previously narrated, we may recall the views of the more modern authorities. Erasmus Wilson,¹ in 1832, gave it as his opinion that when the poison of syphilis is once admitted into the system, it has a tendency to accumulate until the entire system is saturated with it. As soon as this point is

¹ Page 7.

reached, he says, "an outburst of fever occurs, which results in the elimination of the excess of the collected poison." Acton,¹ in 1860, in regard to syphilitic infection, rejects this and all other attempts at explanation. He says, in so many words: "Clinical observation teaches only the facts, the *modus operandi* remains undiscovered; the real explanation of the matter we do not know."

Virchow,² Vidal, Billroth, and Sigmund each give us different opinions based upon clinical observation, no one of which sheds any new light upon the practical features of the disease. Lancereaux, in 1869, expressed the opinion that "syphilis affects the system like alcohol, contained in the blood and acting upon the net-work of organs, in which it occasions at the same time with hyperæmia the development of the elements of new formation." As regards the manner of absorption of the virus, he says "it is a matter that ill bears discussion." Mr. Hutchinson, of London, in 1871, gave it as his opinion — the result of a large clinical experience — that syphilis was a "specific fever, like small-pox, measles, and scarlet fever. . . . Like them," says Mr. Hutchinson, "it has its stage of incubation, efflorescence, relapse, and decline, . . . but that the stages are more protracted; instead of counting its duration by days we have to count by weeks or months."

We shall find it difficult to believe, however, that Mr. Hutchinson now attaches much importance to this alleged similarity between the specific eruptive fevers and syphilis when we recall, in the great discussion before the Hunterian Society of London in 1874, the announcement of his conviction that "*mercury* is the true vital and physiological antidote of the syphilitic virus."

It is true at this time that, through clinical observations, syphilis has come now to be appreciated in its varied manifestations, — that each of its lesions has been accurately studied and described; but clinical research has never solved the problem of its nature, or mode of development, or explained the connection between the different lesions and stages of syphilis. It has elucidated no mystery, nor led to any philosophical mode of treatment. Thus to-day, while recognized in its physical appearances, in its pathological results, while successfully combated in its protean developments, its position in medical literature is without scientific basis. It is yet unconnected with any ascertained physiological or pathological laws; explanations of its nature are but unsupported and contradictory opinions; methods of treatment purely experimental or empirical.

Hitherto we have studied but the external evidences of the disease, each manifestation presenting as a distinct and unexplained problem,

¹ Acton. London Edition, 1860, pages 279 and 342.

² Otis. Physiology of Syphilitic Infection, pages 8 and 9. New York Journal of Syphilography and Dermatology, July, 1871.

and have treated it by medicines and by measures which experience and experiment have shown to be "good for syphilis." The advances in physiological science, the immense strides in knowledge of histology and pathology by means of the microscope during the last twenty years, have given insight into the causes of disease which clinical observation alone could never have effected. The discovery by Beale of the active principle of the cattle plague, small-pox, the vaccine, etc., — *the living animal disease germ*, — led to the inference that a similar living principle constituted the virus of syphilis, and this Beale claimed in 1866. Verson and Beisiadecki, in 1869, were the first, by careful microscopical examinations, to recognize a peculiar and excessive accumulation of lymph or white blood cells as the first effect of the syphilitic process, and as a cause of the induration of the initial lesion. This matter seems to me so important in establishing a starting-point for the physiological explanation of syphilis, in its various phases, that I shall quote entire the results of Beisiadecki's observations on this point, as published in the Archives of the Academy of Sciences of Vienna in 1867. He says: "I have studied the Hunterian chancre in twenty specimens. The *induration* consists in a cell infiltration of the papillæ of the corium and subcutaneous connective tissue. The infiltrated cells are similar to those of dermatitis. They are round, have one or two nuclei, have a finely granular protoplasm, and separate the connective tissue equally. These fibres retain the normal size, are not infiltrated as in dermatitis; they are apparently denser and more resistant to chemical reagents. But the arrangement of the cells differs from that in dermatitis. In those places where a rich cell proliferation has taken place, and in their vicinity still more, we find that the neighboring tissues of the vessels, as well as of their walls, are abundantly infiltrated with cells. The walls of the capillary vessels of the papillæ are thickened, have a shining and rigid appearance, and *inclose numerous nuclei which project even into the lumen of the vessels*. The adventitia of the arteries and veins is three times its normal thickness, *in consequence of the presence of numerous round, spindle-shaped, and branched cells*. The calibre of the vessels is diminished, but the vessels are permeable. If the induration still increases we find in its vicinity *an abundant proliferation in the adventitia of the vessels, and subsequently the adjoining connective tissue cells enlarge and proliferate*, and anastomose with those situated in the adventitia by means of their processes.¹ . . . The induration is explained" (however, he further remarks) "neither by the number of cells nor by their peculiar properties, but by the fact that while in *dermatitis* we have a proliferation of cells, and also a serous exudation which infiltrates the tissue cells and fibres, in the *induration* of syphilis we have a dry, anæmic tissue, resistant connect-

¹ Italics my own.

ive tissue fibres, considerably thickened walls of vessels. The dryness of the induration, which produces the hardness and also the anæmia, is caused by the *proliferation in the walls of the vessels*, which makes it difficult for the serum to leave the vessels, and also diminishes their calibre. And this," he says, "explains why the syphilitic induration breaks down into a molecular mass, and why resorption takes place so slowly. *This investigation*," says Beisiadecki, "*might give us a clue to the mode in which the organism is infected.*"

"In consequence of experiments on animals and man, we came to the conclusion that the blood capillaries are surrounded by perivascular spaces, and that the adventitia of the blood-vessels is in part to be regarded as belonging to the lymphatic system. We have seen that the cells of the adventitia are in a condition of proliferation; that this proliferation is in the walls of vessels distant from the induration. We also know that when the induration continues, the larger lymphatic vessels appear as thick cords on the dorsum penis, and that the corresponding glands take part in the process. These cells, formed in the lymphatic system, can easily enter the lymph current and the blood, and become the carrier of the contagium." From this he concludes that "*the infection of the organism is not caused by absorption of fluid or broken-down substances in an unknown way, but the progressing inflammation of the lymphatics and glands, the formation of cells in them, and the entrance of these cells into the lymph current as living elements may be regarded as the cause of the general infection.*"

Here, then, we have claimed, as a result of scientific investigation, the localized and abnormal proliferation and accumulation of germinal cells at the point of a syphilitic inoculation. If we are willing to accept the conclusions of Beale, that the germ of syphilis is a degraded human germinal cell, capable of uniting with the normal human germinal elements and modifying their nature and behavior, we shall find a reasonable cause for this excessive localized cell accumulation. Beale says that this disease germ is a living amœboid cell, possessing, like the white corpuscle of the blood, the vital movement, and a like power of multiplication; "it is a molecule of living matter, derived by direct descent from the living matter of man's organism, — living matter which retains its life after the death of the organism in which it was produced; living matter which has descended from the living matter of health, but which has acquired the property of retaining its life under new conditions; living matter destroyed with difficulty, and possessing such wonderful energy that it will grow and multiply when removed from its seat of development and transferred to another situation, provided only that it be furnished with suitable nutrient pabulum."¹

¹ Disease Germs, their Nature and Origin, Lionel Beale, M. B., F. R. S., London, 1872, page 143, etc.

When it comes to be remembered that, through its degradation, the disease germ may be reduced in size even to $\frac{1}{100,000}$ of an inch or less in diameter, while its powers of movement and proliferation are still retained, and that the normal white blood corpuscle is only $\frac{1}{300}$ of an inch in diameter, it will be readily seen that this disease germ might easily, through contact, become incorporated with the white corpuscle, and proliferate in its substance; again, with increased rapidity, proliferating *with it*, be carried *by it* through the natural physiological channels; thus finding its way to the most distant points of the human economy, to develop or deteriorate in accordance with the effect produced by the introduction of this degraded element into its substance.

Thus far, through microscopical examinations, we have seen the apparent effect of the syphilitic element in producing an excessive proliferation of cells at the point of inoculation. Verson, Beisiadecki, and Auspitz have recognized a local result of this in an obstruction of the vessels of nutrition of the part, and this producing an anæmic condition which finally results in a molecular necrosis of the indurated tissue.

Now this we observe as a clinical fact. Here, for instance, is a young man, Case I., who had a suspicious venereal connection about five weeks ago. He represents himself as having been in perfect health at the time. On the morning after the connection he noticed a slight abrasion just behind the fossæ glandis. This, however, healed without treatment during the next twenty-four hours. A week since, on the site of that abrasion, he found a little bunch about the size of a pea, but without tenderness. His general health was still perfect.

We have here, apparently, a classical initial lesion of syphilis, as determined by clinical observation. I would be glad to have you come forward and examine the physical characteristics of this lesion. You observe that, pressed between your thumb and finger, the papule is hard, almost like a nodule of cartilage; also that it is movable under the skin. Its color is deeper than the surrounding tissue. There is no tenderness, but as you make tense the tissue over it, thus, you observe that the papule shows a pale yellow color. Now let us examine the evidences which point to syphilis in this case. First, it has followed a suspicious venereal connection. The patient claims that this was his first and only connection, and this was five weeks since; second, that the abrasion consequent upon it immediately healed. We know as a clinical fact that the wound of an artificial inoculation of pure syphilitic material, such as may be found in the blood in active syphilis or the secretion of a mucous patch in the mouth, heals promptly, as if no such inoculation had taken place; third, that nearly four weeks after the healing of the abrasion, a hard nodule was found

on its site. This period or interval of apparent rest, between the inoculation and recognition of an induration at that point, is a well-ascertained clinical fact in the history of syphilis, and is known as the *period of incubation*. There is nothing to account for this nodule except an abnormal cell accumulation, and no apparent cause, inflammatory or otherwise, for this accumulation, except the local *proliferation* of cells. If not caused by the syphilitic influence, as claimed by Beale and confirmed by Verson, Auspitz, and Beisiadecki, we have no explanation of it. These cells, according to the same authorities, are formed in the lymph spaces, the connection of which with the lymph vessels would, if accepting their views, lead us to look for further evidences of the disease in the line of the lymphatic system rather than in the blood vascular system.¹

The nutritive fluids exuded by the blood-vessels into the tissues are said to be in constant movement, and that too in a direction towards the lymphatic vessels, through which the excess over and above the necessities of growth and repair is carried back into the general blood current through the subclavian veins. This tissue-fluid, or lymph current, then, would serve to carry the germ of syphilitic disease from the surface of inoculation towards and into a lymphatic, the nearest lymphatic vessel. Movement through the lymph spaces is said to be retarded by a coagulation of the tissue fluid from slight irritations, while this retardation is most favorable to cell proliferation. Here, then, we find sufficient reason for detention of the infective process at the point of inoculation for a period greater or less. In the many instances of short incubation, or interval between the date of inoculation and the occurrence of characteristic gland enlargement, which I have seen, in the very great majority of cases the initial lesion has been near the *frænum preputialis*; a point where, according to modern histologists,² lymphatic vessels come nearest to the surface. In a case quoted in my article on the Physiology of Syphilitic Infection, published in the *Journal of Syphilography* in July, 1871, it was shown that the syphilitic inoculation was through a punctured wound of the finger, and that axillary enlargement followed within twenty-four hours, and general constitutional infection within six weeks, from that time.

We have, then, a so-called period of incubation of about three weeks, in the presenting case. This is claimed as the result of extended clinical observation to be about the average, although cases are recorded of intervals as brief as twenty-four hours, and as long as seventy days. Once a characteristic induration is observed, however, it is rare not to find lymphatic glands in nearest connection with it also

¹ Sudoriparous and Lymphatic Systems, by Robert Willis, London, 1867. The Lymphatic System, by Professor Recklinghausen. Strecker's Human and Comparative Histology, Sydenham Ed., vol. i., page 267.

² Ballieff, etc.

indurated and enlarged. Examination in this case shows this enlargement to have occurred. Here we find them in both inguinal regions, as large as a buckshot, hard, movable, and insensitive; as I press upon them the patient makes no sign or expression of pain. Recent painless gland enlargement is strong clinical evidence of the presence of syphilis; taken, as here, in connection with an indurated nodule, appearing three to four weeks after a suspicious venereal connection, renders it exceedingly probable that the trouble is syphilitic. This view is also confirmed by the possibility of accounting for this physical manifestation through the view of abnormal cell proliferation set up by a syphilitic disease germ.

CASE II. This case, which you may designate as W. G., presents another form of local lesion, also on the reflection of the mucous membrane of the prepuce, where, by the way, venereal accidents are most common. His history is as follows: First, an impure connection, or rather several, occurring during a period of three or four weeks. Naturally dating from the last, he states that three or four days after he noticed an abrasion which he supposed to be a simple chafe. In this opinion a medical gentleman whom he consulted coincided, and gave him an astringent lotion to apply. The trouble, however, slowly increased. The lesion was cauterized without benefit, and has since been treated with various lotions. Here you see a raw surface, about the size of a three-cent piece, lying, as the touch at once reveals, on an indurated base. There is no apparent loss of tissue; on the contrary, the part is elevated above the healthy surrounding structure. There is no evidence of suppurative action. The scanty secretion which moistens the surface of this lesion is serous rather than purulent, showing, under the microscope, chiefly epithelial scales, instead of pus corpuscles. This is evidently an initial lesion of syphilis, differing from the former case in that the cell infiltration has here involved the more superficial layers of its covering, no longer movable over the induration, but broken down from what Beisiadecki has called *anæmia* of the tissue, but which Virchow has called a *necrobiosis*.

Here, also, we find enlarged and indurated inguinal glands on either side, and also a distinctly knotted cord, movable under the finger, about the size of a goose quill, running back from the induration, just underneath the integument of the dorsum penis, until it is lost in the tissues near the right crus penis. This is an enlarged and indurated lymphatic vessel, evidently connecting the initial induration with the nearest lymphatic gland. It is not unfrequently found if carefully looked for, and would seem to clear up any possible doubt as to the mode of connection between the trouble at the point of inoculation and the inguinal gland enlargements, and shows that these gland enlargements are not caused by any reaction from a general

constitutional infection, but are evidences of cell accumulation from appreciable causes, and through recognizable physiological channels. At our next session I hope to be able to present other forms of the initial lesion of syphilis, and to show, as in the two cases brought before you to-day, that variations in form are chiefly due to differences in the locality and extent of cell accumulation; to show also that syphilis is, *per se*, neither inflammatory nor destructive, but consists primarily in a process of cell growth and accumulation, and thus quite opposed in its nature and action to the venereal lesion called the chancre.

LECTURE II.

INITIATORY PERIOD OF SYPHILIS.

GENTLEMEN, — Two of the common forms of the initial lesion of syphilis were presented to you at our last session: (1) *the papule*; (2) *the abrasion*. Both were shown to be associated with well-marked induration, distinctly traceable to a cell development and accumulation in the tissues underlying the point of syphilitic inoculation. The character of the cells composing the induration was not found to be different, microscopically, from that of normal germinal cells; but in their crowding of the tissues, and more especially of the walls of the vessels, to the extent of obstructing to a greater or less degree the processes of nutrition, this induration was shown to be unlike the results of cell accumulation from ordinary inflammatory causes. Furthermore, this accident, taking place independently of any evidence of inflammatory action, seemed to warrant a conclusion that the cells of the syphilitic induration were, in great measure, if not wholly, the product of a local proliferation, and the result of an impetus given by the disease germ of syphilis.

If we accept the statements of authorities in regard to the nature and powers of human embryonal cells, and also those of the disease germs (which are claimed to be but degraded forms of these cells), we are furnished with an explanation of this local cell proliferation, as indicated (page 5) in the previous lecture.

In the cases presented it was claimed that this localized cell accumulation, and its legitimate sequences, caused the characteristic induration in the first case; and also, by interference as foreign or superfluous material, caused the disturbance of nutrition which resulted in the abrasion in the second case. This view is fully supported by clinical experience. The indurated papule in Case I. is the type of a large class, in which the initial lesion of syphilis appears at varying intervals after the healing of

the surface of inoculation. From its inception to its disappearance, either with or without treatment, it may be quite free from any evidence of inflammatory action, and yet it is followed by the consecutive evidences of constitutional syphilis as soon and as certainly as any other recognized form of initial lesion.

The second case, that of the *indurated abrasion*, was also typical, and showed the manner in which the open initial lesion of syphilis is formed, independently of any external influence, and simply through interference with the nutrition of the indurated tissue.

This process, which has previously been referred to as a *necrobiosis* (page 8), first recognized in the abrasion, may, if continued, result in a gradual loss of substance (chiefly confined, however, to the neoplasm), producing finally, in various degrees, the saucer-shaped, non-suppurating, indurated sore known as the typical *Hunterian chancre*.

The impression given by some authorities is, that this latter is the characteristic form in which the initial lesion of syphilis is usually met. This is an error. My own experience is in full accord with that of M. Bassereau (quoted by Dr. Bumstead¹), who states that out of one hundred and seventy cases of syphilitic erythema observed by him, the initial lesion preceding the eruption, appeared in the form of a *superficial erosion* in one hundred and forty-six cases.

It will, I think, become evident to you, as we proceed, that the initial lesion of syphilis has no arbitrary form, but takes its peculiar aspect from physical conditions and causes which vary greatly in different cases; dependent, when uncomplicated, upon a localized cell accumulation, free from any specific irritating property, as a basis of the local disturbance in every instance.

I am able to present to-day a typical case of the so-called Hunterian chancre, — the *saucer-shaped, non-suppurating, indurated* initial lesion of syphilis; one which will serve not only to illustrate the manner in which loss of tissue takes place in the uncomplicated initial lesion of syphilis, but also to emphasize certain other points of importance already briefly spoken of.

CASE III. This young man gives an account of a single venereal exposure in the early part of October last; none during the three months previous, none since. As you see, his penis presents no external evidence of inflammatory disease. The very redundant prepuce is free from œdema and normal in color. On the left side, however, corresponding to the sulcus behind the glans, you may observe quite a projection. To the touch it is about the size and shape of an almond, and almost as hard. The loose tissues of the prepuce move over it readily. On pressure between my fingers there is no complaint of pain. When first noticed, about a month after his exposure, it was about the size of

¹ Third edition, page 418.

a pea. Since that time, without treatment, as he states, and without any especial discomfort to him, it has been steadily increasing until the present. During the last month or so he has observed some "lumps in his groin," and within a few days some "reddish spots" on his body.

You have already made up your minds as to the character of the disease with which this patient is *afflicted*, — not with which he is *suffering*, for he asserts that he has had no pain at any time. This leads me to remark that pain is not an essential element in syphilis; even when thoroughly characteristic, it is often absent throughout the entire course of the disease.

The induration under the prepuce, in connection with the previous history, points squarely to the site of a syphilitic inoculation.

Turning back the redundant preputial tissue, I bring into view, not a destructive suppurating ulcer, but a deep red protuberance, an outgrowth from the sulcus at the base of the glans penis. Upon the summit of this is a depression a quarter of an inch in depth, sloping on all sides to the centre. This presents a raw granular surface, of a vermillion color, covered with a moist, transparent secretion. Pressure against the sides of this mass whitens the border of the excavation, very much as the same effect is produced upon a congested palpebral conjunctiva, pressed against by the tarsal cartilage when the eyelid is turned back.

It is very evident that the open condition of this lesion has not been brought about by external influences. It has been perfectly protected by the healthy and more than ample prepuce. There is not the slightest evidence of any suppurative action, or of any rapid destruction of tissue, as in chancroid or other pus-producing sore. It is true, there is an evident loss of substance, and yet this has not been at the expense of the normal structures. I could cut down the mass for a full quarter inch, and still not encroach upon the cavernous body with which it is in close contact. Thus intimately connected with the deep tissues, it is almost immovable, and as resilient as cartilage or an epithelioma, for which a cursory examination might have easily mistaken it.

The open lesion in this case can only be explained, by assuming for this loss of substance, the same process of dissolution which produced the abrasion in the former case, namely, a *necrobiosis*, — molecular disintegration from *innutrition*, or, according to Biesiadecki, *anæmia of tissue*, caused by obstruction of the vessels of nutrition through the accumulation of more or less vitiated cell material.

Various conditions and influences, local as well as general or constitutional, may give rise to complications in the progress of a simple necrobiosis. Thus it may be superseded by a slower or by a more actively destructive process.

Initial lesions, thus altered, have received names intended to express

the nature of the complication. Thus we have the *mucoid* form of initial lesion or chancre, from its resemblance to the so-called mucous papule; also the *inflamed* or *suppurating* chancre, the *phagedenic* or *gangrenous* chancre. These modifications will receive especial consideration later, when we have the opportunity of illustrating them by presenting cases. So great an amount and degree of induration in the initial lesion of syphilis as in the present case is quite exceptional, although we shall find that it varies from that which barely stiffens the base of an initial lesion to one even greater in extent than in the instance before us.

The date at which the induration of the initial lesion of syphilis makes its appearance and the time of its continuance are alike variable. The period intervening between the inoculation and the appreciable presence of the characteristic induration has already been alluded to. This is characterized by many authors as *the period of incubation*. The idea of an incubative period, however, is necessarily connected with the claim that the virus of syphilis, once introduced, spreads from the point of inoculation by a sort of mysterious fermentation through all the channels and tissues of the body until, infection thus becoming complete, this event is announced by a reaction, at the point of inoculation, in the shape of an induration. Hence, in accordance with this idea, the initial lesion is, of necessity, considered the evidence of *complete constitutional infection*, and not the localized commencement of it, according to a strictly physiological view of the case. Proposing, however, to adhere as strictly as possible to the latter method, we shall be obliged to discard the term incubation in this connection as incorrect, and shall speak of this interval, greater or less, which is known to occur between the date of inoculation and the appreciable presence of the localized induration as the first stage of the *Initiatory period* of syphilis. This interval, according to the weight of clinical authority, is fixed at from fifteen to twenty days as the average. Of the two hundred and sixty-one cases observed by Sigmund the average was seventeen, ranging from four to twenty-one. Forty-five cases, reported by Fournier, averaging thirty-one days, varying from four to seventy. Rollet presents the results of artificial inoculation with the syphilitic virus in twenty-six subjects; the shortest interval before the appearance of the characteristic initial lesion was ten days, the longest thirty-nine; average, twenty-five days. Dr. Bumstead reports an interval of fifty days, Dr. Hammond one of three. The late Dr. J. C. Nott reported his own case (referred to in the previous lecture), where but twenty-four hours elapsed between the wounding of his finger with a spicula of the bone of a syphilitic and well-pronounced axillary-gland enlargement, and this followed by a general syphilitic eruption within six weeks thereafter. Dr. R. W. Taylor reports two cases, in one of which the initial lesion

made its appearance within twenty-four hours after connection, followed by characteristic induration within four days, and in six weeks by general syphilis; in the other the induration was discovered within a week after exposure, and evidences of constitutional syphilis at the end of the fifth week. *In both these cases the initial lesion was situated at the junction of the frænum with the glans penis.*

On repeated occasions, within the last eight years, I have called the attention of the class to the presenting coincidence of a short incubation (so called) of a well marked initial lesion and its situation in the near vicinity of the frænum. This locality (previously referred to, page 7) is notable as a point where the lymph canals come nearest to the surface, — in fact, according to Ballieff, “to a point *just* underlying the epithelium.”

In the absence of any other satisfactory explanation, the conclusion appears to me inevitable that the syphilitic cell accumulation progresses in all directions, as has been proven, until an entrance of the vitiated cells into a lymphatic vessel is effected. The nidus of induration once formed, during this delay, may, under certain conditions, continue to increase, or it may remain stationary for a definite period; or, on the other hand, through the ordinary processes of tissue metamorphosis, it may soon disappear. Thus the varying interval between inoculation of syphilis and the appearance of the induration may be reasonably accounted for by the distance of the inoculated surface from the nearest lymphatic vessel, as the accumulation must necessarily progress until such vessel is reached. This distance is known to differ greatly in different localities. It is interesting to note a clinical fact, which I have often observed, namely, that indurations of the initial lesion at the frænum and glans, posterior to the meatus, are uniformly small in extent. In the prepuce, on the contrary, where, according to the researches of Dr. Isidor Neumann,¹ the lymphatics are much more deeply located, we find indurations more extensive. These vessels are represented as still more deeply seated in the base and body of the glans. These are also the known localities of occasional extensive indurations, while in the integument of the penis, where the lymphatic distribution is very superficial, forming loops near the apex of each papilla cutis, we have the most common occurrence of that thin induration which is termed the *parchment induration*.

Again, on the integument also, we meet most frequently the initial lesion as a small indurated papule, much resembling the indurated papule of a later syphilitic manifestation (secondary papular eruption), which, as it will hereafter be shown, is always associated with the lymph vessel of a papilla cutis. It is unfortunate that, in the large number of

¹ Zur Kenntniss der Lymphgefässe der Haut des Menschen und der Säugethiere, Wien, 1873, Taf. viii.

cases reported by authors to illustrate variations in the so-called period of incubation, the locality of the lesion should in no case have been reported. For, while various constitutional influences *may* be potent to cause variations in the interval between inoculation and induration, as well as in the amount and quality of the induration, the relative position of the surface of inoculation in regard to the nearest lymph canal, through which the vitiated cells are known to be carried directly to the nearest lymphatic gland, must be accepted as an important element in determining variations in date of appearance, as well as quality and amount of induration.

The continuance of the induration varies as much in different individuals as its amount. In cases like the one now under consideration, where it is extensive and characteristic, it may remain more or less salient for months. The same is also true of the indurated papule, even when no larger than a pea. The development of the newly deposited cells into connective tissue fibres, to a greater or less extent (as claimed by Biesiadecki), may be reasonably held responsible for the exceeding density and prolonged duration in such cases.

In his description of the progress of his case, you will recall the statement of our patient that about a month since he "noticed some lumps" in his groins. With the remembrance of examinations in previous cases, this does not surprise us. The inguinal glands in each of these were found enlarged and indurated, movable, painless, *evidently not the subject of inflammatory action*. Here, also, as I press upon the "lumps" referred to, I find them to be enlarged and indurated inguinal glands, painless also, and movable. There are no appreciable attachments to the surrounding tissues, although the patient has been conscious of their presence for more than a month, and we can believe that they have been enlarged for a much longer time. No pain; not the least evidence of inflammatory action any more than in the initial lesion. If we remove and examine a gland so enlarged and associated with the characteristic initial lesion of syphilis, we shall find it packed with cells similar to those we find in the indurated tissue of the initial lesion.

In Case II. (page 8) you will remember that I directed attention to an enlarged lymphatic vessel, evidently connecting the indurated initial lesion with a similarly enlarged lymphatic gland. This, though not appreciable in all cases, may be recognized with sufficient frequency and certainty to indicate, beyond doubt, the channels through which the infective process is transmitted to the glands thus connected with the initial lesion.

It has been noticed that all lymphatic glands adjacent to a syphilitic initial lesion are not the subject of abnormal cell accumulation; only those in direct connection by lymph canals are involved. Those in the inguinal region corresponding to the locality of the initial le-

sion are usually the first to enlarge, yet the reverse is sometimes the case. This may be readily explained by the frequent crossings of lymphatic vessels on the *dorsum penis*. In the present instance there appear to be nearly a dozen enlarged and indurated glands, in either groin, varying in size from one half to one eighth inch in diameter. Such glands never suppurate except under prolonged external irritation in connection with a highly scrofulous diathesis. This is still another proof of the non-inflammatory nature of syphilitic cell accumulations. It would be very natural for you, at this point, to ask for an explanation of the causes which determine the direction of the infective processes of syphilis in the line of the lymphatic channels. For this we must revert to the nature of the infection, as claimed, through an incorporation of the degraded germinal cell (disease germ) into the substance of the white blood cell, *and its proliferation with this cell*. Stimulated in this manner to unhealthy activity, cell proliferation would appear to be capable of producing the abnormal cell accumulations which we have thus far found characteristic of the progress of the syphilitic infection; and, beside this, we have no other way of accounting for them. Why it does not combine with and infect the red blood corpuscle, and at once enter the general blood current, would seem to be accounted for by the fact (claimed by Beale, especially) that the red corpuscle is *formed material*, and hence the disease germ cannot combine with and become incorporated into its substance, nor subsequently undergo the rapid proliferation which is necessary to the generation and accumulation of the vitiated cells, *the essential product of syphilitic action*. This is, however, fully within the province and power of the white blood corpuscle, as already described to you in a previous lecture. Again, the lymphatic vessels are the *especial channels* of the embryonal or white blood cells. Every surface of abrasion or inoculation may be said to be in direct communication with a lymphatic gland, not with an open blood-vessel.

The current of the fluids which everywhere permeate the tissues is not in the direction of the blood-vessels, but of the lymphatics, and thus we can understand why the progress of the syphilitic infection physiologically considered should be just as we have found it clinically, — not penetrating, pervading the tissues, instantaneously, at the moment of inoculation and in defiance of all natural laws, but progressing slowly, certainly, physiologically, from the surface of inoculation through the contiguous and pervious lymph spaces into the lymph channel nearest, and thence directly into the substance of the lymphatic gland with which it has direct connection.

Thus far, then, as you have seen, we have syphilis as a purely local disease. No evidence of it has been observed in the blood up to the time of its appearance in the glands. I challenge history to produce a

single proven instance where syphilis has been demonstrated in the blood *before* the enlargement of the lymphatic glands in direct connection with the surface of inoculation, *or for several weeks after*. For the infective process, after reaching the gland thus in connection, in order to pass through it, must follow the intricate windings of the lymph current, through the gland substance, more or less obstructed by the same or similar influences which delayed the entrance of the infected cells into the lymph canal nearest the point of inoculation.

It is a well-recognized clinical fact that not a single evidence of constitutional syphilis is ever present until after a period of *at least twenty-five days* after the occurrence of the induration and local gland enlargement. The average, as stated by numerous accepted authorities, is *over forty days*. If it is present at any point other than that included between the initial lesion and the glands in immediate connection, we seek in vain for the evidence of it. Such evidence cannot be produced from any reliable clinical records of the disease, nor from the results of any reported experimental inoculations.

This period, during which the diseased elements are making their toilsome way through the channels of the lymphatic glands (citadels established by nature to protect the general blood current from noxious invasion), has been termed *a second incubation*.

You have seen what the first incubation has been proven, namely, a *gradual cell growth and accumulation*. In the same way, is the second apparent interval, an incubation. When the gland channels have been fully traversed by the vitiated cells, and they, still following the lymph current, through possibly still other intervening glands, have been carried into the *receptaculum chyli*, and from thence ushered through the subclavian veins into the general blood current, then, *and not until then*, may it be reasonably claimed that the disease has lost its local character, and has become in a strict sense a constitutional disease.

The period of purely local action, namely, that which precedes the entrance of the infective syphilitic material into the general blood current, may, it appears to me, be appropriately termed the Initiatory Period of Syphilis.

LECTURE III.

III. PERIOD OF GENERAL INFECTION AND SUBSEQUENT LOCALIZED CELL ACCUMULATION.

GENTLEMEN, — In the previous lectures it has been claimed that the one great characteristic, in point of fact the sole evidence we have, of syphilitic infection, in its early stages, consists in an increased proliferation and localized accumulation of germinal or white blood cells. Thus it was shown that the induration of the initial lesion was produced, and also, by consequent interference with the nutrition of the part, the characteristic forms of the infecting chancre or initial lesion of syphilis resulted. Entire absence of any sign of syphilis at any other point, and a gradual advance of the abnormal cell accumulation through the lymph paths connecting with the point of inoculation, appeared to warrant the conclusion that the disease was progressing through the lymph channels alone. Its course was clearly recognized from its initiation, at the point of inoculation, to the entrance into and enlargement of the lymphatic glands in connection with it.

The so-called *period of incubation*, or interval between the date of inoculation and the appearance of the characteristic induration, was readily accounted for by the gradual accumulation of cells at the point of inoculation, antecedent to effecting an entrance into a lymphatic vessel. The period of rest which was said to occur between the appearance of the induration and any constitutional manifestation of syphilis was explained by referring it to the slow progress of the infected cells through the labyrinthine channels of the lymph glands. Bäumler, latest of the German authorities on syphilis, says of this matter, "Several weeks always elapse from the first appearance of the local affection before the point is reached where general symptoms break out; and this circumstance speaks also in favor of the theory that the poison advances *by way of the lymphatics*, and the slowness of this advance finds its explanation in the hindrance offered to the passage of the virus by the lymphatic glands."¹ The interval now accepted by all authorities as occurring between the date of inoculation and the appearance of the characteristic initial lesion was fixed at an average of twenty-one days; the interval between the occurrence of the induration and the earliest evidences of constitutional syphilis at an average of forty days. Having shown, as I believed, that neither of these intervals was in any sense an *incubation*, but the consequence of interference with the progress of the diseased cells through natural anatomical and physiological barriers, I discarded the term incubation, and instead of the conventional title of *primary syphilis*, usually applied to the period which intervenes between

¹ Ziemssen's Encyclopædia, vol. iii., Am. ed., page 124, 1875.

inoculation and recognized constitutional infection, I designated it *the initiatory period of syphilis*.

This initiatory period of syphilis may be said to terminate when the diseased cells or germs have passed through the lymph vessels and glands intervening between the point of inoculation and the *receptaculum chyli*. On entering this reservoir these "carriers of contagium" must of necessity be swept along in the lymph current, through the subclavian veins, into the general blood current, and with it find their way to the remotest ramifications of the blood vascular system. "These cells," says Beisiadecki, "formed in the lymphatic system, can easily enter the lymph current and the blood, and become the carriers of the contagium." Now, in the natural history of syphilis, the earliest manifestation of constitutional infection or secondary syphilis, as it is usually termed, is, according to observation and authority, a peculiar and general eruption of rose-colored blotches on the skin at about the sixth week after the occurrence of the initial lesion, and known as the "syphilitic roseola." Although not always recognized, it is conceded by our best observers that it is always present in greater or less degree, in some instances extremely transient, lasting perhaps only a few hours, while in other cases it may last for many weeks. Its appearance in point of time will be found to coincide with the alleged period of entrance of the vitiated cells or syphilitic disease germs into the general circulation.

I shall present for your observation and study to-day several cases of this earliest and most common of all the manifestations of syphilis. This young man, for instance (whom you may indicate in your notebooks as Case V.), is by occupation a waiter, age twenty-four years. He states that he has often suffered from sores on his penis, following connection, but that he had always been able to cure them by applications of caustic in a short time. About three months ago he had a connection, followed in three or four days by several little sores on his penis, which he treated in the usual way, and with his usual success, and to all appearance continued free from trouble until about a month after, when, without other connection, his penis again became sore. Notwithstanding the applications of caustic, it not only refused to heal, but gradually grew so much worse that he has applied at our clinic to-day for relief. Some time since it was promised that in each case presenting, where the initial lesion of syphilis was found to vary in any characteristic way from those already described, it would be made the subject of especial consideration. In the present instance we find occasion to raise a question as to the character of the lesion on the penis. It is certain that we have a condition here markedly different from any of the preceding cases of syphilitic initial lesion. Thus, instead of an unbroken papule, a simple erosion, an insensitive, indurated mass, free from any signs of suppurative action, we find at base of the glans, supe-

riorly, an angry-looking sore, about the size of a dime. The inflammation which surrounds it is also seen in the congested and swollen preputial tissues. The excavation, while somewhat superficial, presents an abrupt and irregular border and a yellowish, sloughy-looking floor, secreting pus freely. Contiguous to it, in the fossæ glandis, you may observe several little ulcers, and also two or three small, unbroken pustules. The gross appearance is such as we might expect to find in an inflamed venereal ulcer, entirely local in its nature, and usually termed *chancroid*. Now the chancroid, as I have previously told you, is the result of a process of destruction, while the initial lesion of syphilis is the result of excessive growth of germinal or tissue-building material. Whenever the initial lesion of syphilis occurs as an open lesion it is the result, not of a true ulceration, but of a *necrobiosis*, a mechanical interference with the processes of nutrition, and its characteristic secretion is epithelial and serous, and not purulent. On the contrary, the secretion of the chancroid is *always* purulent. I have also told you that the base of the *chancroid* was supple, quite free from the induration characteristic of the initial lesion of syphilis. In this case we find the salient features of the chancroid, and yet by farther examination we ascertain that it is situated upon a *distinctly indurated base*, although not so much so as in that presented at our last lecture as typical of the chancre or the initial lesion of syphilis.

It therefore would appear that the induration, being thus apparently associated with the chancroid, was not especially significant. But in this connection you will also recall a fact, repeatedly referred to in our examinations of chancroid, that a very distinct induration may be produced by applications of caustic, such as have been made use of in this case, as well as by other modes of irritation. This, as you will remember, was alluded to as a temporary condition, but one which, for the time, might prove a source of embarrassment in arriving at a diagnosis, and that we might be obliged to wait for the result of treatment, in order to come to a correct decision, unless other evidences or manifestations of disease were present. In looking for such, our attention is arrested by the presence of the small ulcers and pustules associated with the principal point of disease. The initial lesion of syphilis is known to be usually solitary. This patient distinctly states that he has had no connection within the last three months, and that the small ulcers have appeared within the last week and the pustules within the last twenty-four hours.

Now, it is an important fact in the natural history of the chancre, or initial lesion of syphilis, that given a characteristic, indurated, non-suppurating, open initial lesion, a typical infecting chancre, with smooth, sloping edge and granular floor, secreting a serous fluid of a perfectly transparent and unirritating quality, and subject it to violent or pro-

longed irritation by caustics, or friction of clothes, or otherwise, sufficiently to produce inflammation, a destructive action will be set up in it, which, engrafting upon it a true ulcerative process, will entirely alter its appearance and the character of its secretion, changing its physical aspect to that of the chancroid, and its bland secretion to a purulent fluid of distinctly contagious and destructive character.

With the knowledge of this fact we may now see how this lesion, originally solitary, may have become multiple by recent auto-inoculation of its secretion upon the mucous surface in its vicinity, and that while thus possessing in a general way the characteristic features of chancroid, the lesion before us may yet prove to be an initial lesion of syphilis, one of the variety which we term *the inflamed chancre*.

I may here, in passing, call your attention to the fact, now well substantiated, that all pus, the product of inflammatory action, acquires to a greater or less degree the contagious and necrotic property, and hence that this peculiarity is not confined to the inflammation of chancre. This point will be more fully considered as we come to treat upon the subject of chancroid.

We must now, however, in this case, seek for further evidences as to the true character of the sore before coming to a final decision; for if it be the initial lesion of syphilis, now at the end of the third month from the date of inoculation, further evidences should not be wanting.

We will first endeavor to detect the lymphatic induration, the knotted cord, which on a previous occasion was found extending from the initial lesion to and into the region of the inguinal glands. The integument of the penis is here so swollen, by the intercurrent inflammatory action, that a satisfactory examination on this point is impracticable; but we do find distinct enlargement of the inguinal glands, free from tenderness, hard to the touch, and movable under the integument. The patient states that he has occasionally felt a little stiffness in this region after much walking, but has experienced no sensation of pain. Recent painless enlargement of the lymphatic glands, taken in connection with the history and condition of this patient, render it almost certain that his trouble is syphilitic; and yet his general health, he claims, is excellent, and his appearance fails to indicate any constitutional disturbance. His condition is much like that of Case III. at our last clinique where, you will remember, casual reference was made to some reddish spots upon the body of the patient. I did not mention their significance at that time, but it was the eruption which then made the diagnosis of syphilis absolutely certain. On removal of this patient's clothes, you may now observe a similar eruption, — dull, rose-colored spots, thickly scattered over his back, and to a less degree and somewhat fainter on his breast and arms. I find, also, a few sprinkled over his palms. This exanthem, associated with his history, with the sore on his

penis, and his enlarged and painless inguinal glands, enables us to state confidently that the local lesion in this patient is the *inflamed chancre*, —the initial lesion of syphilis modified in appearance and local character by superimposed inflammatory action, —and that this eruption is the roseola of syphilis. In its general appearance this exanthem is, as you may see, not unlike a slight eruption of measles. Pressure with the finger in the syphilitic roseola causes the color to disappear completely when the eruption is recent, but when it has existed for some weeks a brownish or copper-colored stain is left. In this case it leaves a slight coppery stain, which is an evidence, although the patient has been entirely unconscious of the fact, that it is a syphilitic roseola, and has been present for some time. The longer the eruption remains the more likely it is to leave its characteristic trace, namely, a coppery stain, unaffected by pressure. The color of this stain here, as well as in other syphilitic eruptions, is usually considered valuable as a diagnostic mark of syphilis. With this exception, however, it is not materially different from an idiopathic roseola. Like the latter, it appears suddenly; often during or following any exercise which gives a violent impetus to the circulation of the blood, such as rowing, dancing, or running.

Pain or other premonitory symptom is not necessarily associated with it. Sometimes it is slight, consisting only of a few pale spots, while again it is profuse and highly colored, and occasionally slightly elevated. But it never develops into any other form of lesion. Beyond a reddish blotch, it is never more than a copper-colored stain, and even this stain, the only really salient point of difference between simple roseola and that which is thus seen to be associated with the advent of constitutional syphilis, will be shown to result from simple causes. It is true that this eruption is popularly accepted as syphilitic, in the sense that it is caused by the local presence of syphilitic material, and is to be gotten rid of through the same means by which the specific cell accumulations (forming papules in the skin and mucous membranes) at a later stage of the disease are eliminated. I believe, however, that this can be shown to be an error, and that this roseola, like all the other roseolas, is the result of a purely functional disturbance. Bäumler says of it, "In every syphilitic efflorescence there is a circumscribed dilatation of blood-vessels, together with a certain amount of exudation of white blood cells into the sheaths of the vessels merely, and into the surrounding tissue. The greater the degree of stasis the more abundant will the exudation of red corpuscles be; and *it is the alteration of the coloring matter in these red globules which imparts to the color of the syphilides, after they have remained for some time, their yellowish or brownish shades.* These shades are more distinct in proportion as the congestion of the vessels thereby occasioned recedes, and they are

more pronounced, the longer the stasis has continued. In the same way, any efflorescence, or its immediate vicinity, or scars following ulcers on the lower extremities, *not due to syphilis*, may assume this color. Long-continued dilatation of capillaries and stasis of the blood are all that is necessary to produce pigmentation."

In seeking an explanation of the occurrence of this roseolous eruption, we naturally ask, then, What can and is most likely to produce "*long-continued dilatation of capillaries and stasis of the blood?*" Inasmuch as it is known that the capillary vessels derive their nerve supply from the sympathetic nervous system, their loss of contractility, and consequent dilatation, could occur only through some impression upon the sympathetic system, which would cause a paresis, more or less pronounced, of the nerves supplying the walls of the capillaries.

In an article on the Physiology of Syphilitic Infection, published in 1872, I took occasion to discuss the evidences for and against the functional character of the roseola of syphilis. It now appears to me that I cannot do better than to quote the views of authorities on this subject, and my comments upon them at that time, which, after several years of further study and observation in this connection, I find no occasion to alter.

Thus Mr. Erasmus Wilson, a distinguished English authority on diseases of the skin and syphilis, says, "It is now (1871) well understood that the influence of the *vaso-motor nerves* is involved in the production of *roseolas*."

It is proper, however, to state here that while Mr. Wilson describes no less than eighteen varieties of roseola, he practically excludes the roseola of syphilis by attributing its occurrence to the presence of the syphilitic virus in process of expulsion from the system, and by assuming that it may subsequently be developed into other and later manifestations of syphilis. Inasmuch as this idea is, perhaps, the generally accepted one, it appears to me desirable to place the whole matter before you in such a way that we may, if possible, be able to determine whether the roseola of syphilis is a true roseola, dependent simply upon an impression made upon the sympathetic nerves, like other roseolas, or whether it is a form of syphilitic manifestation, and pathologically different from other roseolas, which, in some curious and hidden way, gradually develops into other manifestations of syphilis. Mr. Wilson describes it thus: "*Roseola syphilitica* commonly presents itself in the form of undefined patches, giving to the skin an appearance identical with that of the common idiopathic roseola, or measles, and is due, like the two latter, to the manner of distribution of the blood-vessels of the skin. It is preceded by a peculiar fever called the syphilitic, and bears a resemblance in its pathognomonic symptoms to measles, scarlet fever, and small-pox: (1) in 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 the 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 elimination of the syphilitic material (whatever, in his opinion, that may be) through the skin. This view, elaborated more fully by Mr. Wilson than by any other writer on syphilitic or cutaneous diseases, I do not find contradicted by any except M. Diday, of Lyons, but it is accepted directly or tacitly 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 in 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 farther augmented*, namely, as a large papule or tubercle." In an earlier work on syphilis he says, "A roseolous patch may be seen to develop papules ; . . . and I have furthermore seen the small papule of lichen converted into the larger elevation called *tubercle* by sudden aggravation of the syphilitic fever, or from exposure to cold." It will be remembered that he was previously quoted as saying that "it is now (1871) well understood that *the influence of the vaso-motor nerves is involved in the production of roseolas* ;" but it will be observed that for the syphilitic roseola Mr. Wilson, in the foregoing statement, 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 usually associated with the advent of constitutional syphilis in representative cases. They are numerous and varied, as follows : *general malaise, headache, rheumatoid pains*, irregular and chiefly nocturnal, *loss of appetite, indigestion, nausea, diarrhœa, giddiness, mental irritability, sleeplessness, great prostration, unnatural acceleration of breathing on slight exercise* ; in some cases *exacerbations of an intermitting fever*, temperature running up to 103° or 104° F., followed by profuse sweats, etc. These are among the most prominent of the prodromata

cited by authors, and are grouped together under the general title of *the syphilitic fever*. This title is then applied, not simply to an acceleration of the pulse, elevation of temperature, 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, occurring about the time of the appearance of the syphilitic roseola, 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, the 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 intimate connection between syphilitic fever and roseola is *not*, however, universally accepted. On the contrary, Ricord says that the syphilitic roseola 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 that 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) says that of sixty cases 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. In one of the cases already presented to you, the surprise of the patient on our discovery of the eruption, will be recalled, and this, in my experience, has been the rule rather than the exception. Besides the records of observations covering a period of nearly two years in the Blackwell's Island Venereal Hospital, in 1851 and 1852, and during subsequent years, noting frequent cases in hospital and private practice, I have called especial attention to this matter in every case presenting at my clinic in this college for several years past; and I do not hesitate now to express my entire accord with the views of M. Ricord, namely, that the syphilitic roseola is *never preceded by, nor associated with*, any fever, pain, 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 almost thirty years past Mr. Wilson has taught without qualification, and almost without contradiction, that syphilis, with roseola as its early exponent, was a mysterious, but 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 her forces, at a given stage, to expel it, and with the directness and urgency of a woman in labor, as he puts it in his climacteric in describing the syphilitic 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. From the fact that there occurs an apparent period of rest in its early development, that in certain cases it is associated with varied disturbances of the nutritive functions and of the nervous and vascular systems, that preceding, during, or succeeding these disturbances an exanthematous eruption occurs, it has been the fashion, for want of a better place, to class it among the exanthematous fevers; and further, inasmuch as it has been, to a greater or less extent, an accepted conclusion that these diseases are the result of an effort of nature to get rid of the peccant material causing them, a like interpretation has been seized upon to explain the significance and value of the syphilitic roseola."¹ But it may be urged that, if it is granted that the largest proportion of syphilitic roseolas are ushered in without marked constitutional disturbance, yet in two thirds of the cases reported by McCarthy and quoted by Lancereaux, pains in the head or bones, or both, were present. Was this a simple coincidence, and not the sign that the roseola was in process of development? If there was nothing else, at this stage of syphilitic disease, to account for the constitutional disturbance but the roseola, I should certainly look upon it as a coincidence, simply; first, because the fullest development of the roseola does not relieve the pains, and secondly, because the most profuse roseolas occur independently of them. But I think with a little care we may be able to find another and most important manifestation of syphilis present, with or soon following the advent of the roseola, and that is enlargement and induration of glands and groups of glands, to a greater or less degree, *throughout the entire lymphatic system*, especially prominent and most readily recognized in the cervical and epitrochlear regions.² I pass my fingers

¹ Physiology of Syphilitic Infection. Otis, 1872.

² "Its occurrence in the lymphatic glands in the interior of the body has also been verified in post-mortem examinations by Von Barenprung and Virchow." (Beaumler, Ziemssen's Encyc., vol. iii., p. 182.) Also, "In the collection of the Hôpital de Lourcine there are those preparations of women who died of intercurrent diseases, while affected with syphilitic sores on the vulva. In these preparations, not only the inguinal glands are swollen, but there is a hyperplastic enlargement of a number of glands above Poupart's ligament. In the second case, there occur in the fossæ iliacæ, along the blood-vessels, nine enlarged glands, arranged in three groups, one above the other, the uppermost at the origin of the art. hypogastrica. The enlargement of the glandulæ iliacæ had attained nearly the same degree as that of the gl. inguinalis, among which, one or two on each of the three preparations were distinguished, through their greater size, as the ones first attacked." (Ibid., page 122. 1875.)

along the posterior border of the sterno-cleido mastoid muscle of this patient, with the almost absolute certainty of finding well-marked enlargement of the group of lymphatic glands peculiar to this region, and not only do I find them, varying in size from a small shot to a pigeon's egg, but hard and movable, and also painless, as you may judge by the serene expression of countenance here preserved, under the by no means superficial examination which I am making. I find an enlarged gland, also, over each mastoid process; also in the post cervical region, at several points; also in the epitrochlear space, just above the bend of the elbow. Here they are most valuable, in a diagnostic point of view, being rarely present before, or absent after, the tenth or twelfth week succeeding inoculation of syphilis, whether any roseola can be detected or not. Sometimes only one gland is enlarged, sometimes it is found higher up, along the inner border of the biceps. I also call your attention to two other cases of syphilis, drawn from my service in Charity Hospital (which you may note as VI. and VII.), one in the fourth and the other in the sixth month of the disease, and this simply that you may examine them in regard to the matter of gland enlargements. In each you will find well marked and characteristic hyperplasia, not only of the inguinal glands but of those in the cervical and epitrochlear regions. In case VI. you will find absence of enlargement of the epitrochlear gland on the right side, while it is present and as large as a marrowfat pea on the left. What I desire now particularly to show in these cases, is the uniformity of the general gland enlargement, and this will be found to hold in all cases, to a greater or less degree. Where you do not find it after the third month of the disease, it will be because the examination has been interfered with by excessive accumulation of adipose tissue, or because the examination has been inefficiently conducted. It may be still held as an open question as to whether this gland enlargement, remote from the point of inoculation, takes place by means of cell elements, carried from the glands first affected directly to glands remote from the point of inoculation, by channels not yet fully demonstrated, or whether they receive the syphilitic infection primarily through cells carried out by the blood current at the period of general infection or dissemination of the diseased germs. The fact that general gland enlargement is sometimes present before the appearance of the roseola, is considered evidence in favor of the former view.¹ Of one thing, however, we are certain, namely, that at about the time, within a very few days, of the appearance of the roseola (sometimes before, sometimes after), this characteristic general gland hyperplasia takes place; that, in connection with this enlargement, a

¹ Beaumler says: "It is probable that the poison circulating in the blood may cause hyperplasia of the lymphatic glands directly, for sometimes we see these glands reacting to the poison before the skin or mucous membranes." (Zeimssen, vol. iii., page 181.)

marked proportional increase of the white blood cells over the red has also been observed.¹ Now we have arrived at a point where, perhaps, we may be able to account for some of the so-called prodromata of the syphilitic roseola, without the necessity of considering them the result of nature's effort to expel the unknown element, in opposition to all known physiological laws, through the skin and mucous membranes. We have here a well-marked disturbance in a system of important functional use, one now recognized as occupying a place of acknowledged value among the hæmatopoietic organs; we have a condition which admits of explanation through known physiological processes, fully competent to cause all the nutritive, nervous, and vascular disturbances which have been recited under the title of *syphilitic fever*, or the prodromas of syphilitic roseola.

And now as to the cause of the roseola. We may accept it as localized hyperæmia, due, as Mr. Wilson says, "to the manner of distribution of the blood vessels of the skin," as in the common idiopathic roseola, the single patch of the eruption of which "represents the ramifications of a single arterial trunk," or "the small district of skin, the circulation of which may be governed by the ultimate divisions of one small nervous twig," a branch of the great sympathetic nervous system. Virchow 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."²

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 a 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 is always a completely passive one." Belladonna is well known as a relaxing agent in nerve tissue, notably seen in its effect upon the iris, and also in the production of an eruption in some respects similar to the roseola of syphilis. Mental emotions are also recognized as the cause of contraction of the calibre of the blood capillaries, producing pallor, and dilatation producing the blush. Also, in producing an eruption similar to the roseola of syphilis. I had, some time since, under my care a lady

¹ Section of these hyperplastic glands is found under the microscope to present the same closely packed cell accumulation which has been seen in immediate connection with the initial lesion of syphilis, and in lymphatic glands in direct connection with it.

² Physiology of Syphilitic Infection. Otis, 1872.

upon whom an eruption, in no way to be distinguished in appearance from a classical recent syphilitic roseola, was brought out upon the breast, back, and arms, chiefly, however, upon the neck, whenever she was subjected to any unusual mental excitement, and which remained distinct for several hours. And another case, at the present time (1879) under my care, where the passion of anger, or a sudden pleasure, or sense of mortification, will bring out a roseolous eruption, while a paroxysm of grief, no matter how severe, will have no such effect. We know that similar roseolas are initiated by digestive derangements and other causes that can be referred only to impressions made upon the sympathetic nervous system. Is it then remarkable that a cause dependent upon actual and more or less sudden changes in the blood proportions and quality should be found capable of producing equally important effects? May we not then reasonably infer from the foregoing, and in the absence of any other explanation of it, and of any 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 special but limited paralyzing influence exerted upon the great sympathetic nerve, through positively recognized blood changes, immediately preceding, accompanying, or following an initiation of the so-called secondary or active period of syphilis? This period, from a physiological point of view, I have ventured to term **THE PERIOD OF GENERAL INFECTION AND SUBSEQUENT LOCALIZED CELL ACCUMULATION.**

LECTURE IV.

IV. PERIOD OF GENERAL INFECTION AND SUBSEQUENT LOCALIZED CELL ACCUMULATION.

GENTLEMEN, — We have been able, thus far, to trace the progress of syphilitic infection, from the moment that the disease germs were deposited upon the surface of inoculation to their general dissemination throughout the blood vascular system. This has, I believe, been accomplished in complete harmony with the present state of our anatomical and pathological knowledge, and in unison with recognized physiological laws. This course may also have been observed to accord completely with the *clinical* history and condition of the cases brought before you as representing the various characteristic stages in the march of the infection, during the entire initiatory period of syphilis. At the termination of this period we found the progress of the infection signaled by the appearance of a rose-colored exanthem. To

the immediate effect of the general dissemination of the diseased cells or virus throughout the organism was attributed the appearance of this so-called *roseola of syphilis*. Its accession was accepted as important only as announcing the constitutional infection. Very many cases occur where, either with or without treatment, no farther manifestation of syphilis takes place during the entire active period of the disease, and yet these apparently mild cases, when not efficiently treated, are sometimes sufferers in after years from grave forms of syphilitic sequelæ.

If, at this point, we take up again the natural history of syphilis, in typical cases, we shall find presenting, an inflammatory engorgement of the mucous membrane of the tonsils, the border of the soft palate, and often of the whole faucial region.

In this connection your attention is directed to the fact that the tonsils have been 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 gland and the adjacent lymphatic vessels, Frey has shown that "the surface of each follicle is invested by an extraordinarily close net-work of lymphatic vessels."¹ The investigations of His, Recklinghausen, and Teichman have confirmed this statement, and have further shown that the lymph vessels so investing a follicle are greatly dilated, so much so that the follicle is quite covered in by them, "leaving only that extremity or pole uncovered which is directed toward the surface of the mucous membrane."²

"The entire pharynx is much richer in lymphatics than the surrounding mucous membrane."³ Here, then, in common with the engorgement and hyperplasia which has been observed at about this period in the lymphatic system at other points, we should expect early manifestations of similar disturbance.

Reasoning *a priori*, we should expect that these lymphatic accessories, when implicated in obstructive trouble, would be more readily engaged in true inflammatory engorgement, as they are brought, by more superficial distribution into a more intimate connection with the blood vascular system than occurs in lymphoid glands of a higher order. This is just what we do find, leading in certain instances to quite extensive tissue loss through a consequent ulcerative process.

Now, also, at about this time, we begin to find, in a very considerable proportion of cases, a true papular eruption of the skin, — usually first observed along the borders of the hair, especially prominent and noticeable along the upper part of the forehead. It may also be seen scantily developed on the back, breast, and extremities. Again, it may

¹ Human and Comparative Histology, Stricker, Syd. Ed., vol. i., p. 328.

² Ibid., page 328.

³ Ibid., page 326.

be very thickly studded over the entire body. This eruption differs greatly in appearance as well as in quantity in different cases. Sometimes the papules are large and flat, from the size of a split pea up to that of a dime; again, small and pointed, and not larger than bird shot. The varieties which have been described by authors are numerous, and will be attended to later. It varies also as to the date of its advent. Occasionally it follows the roseola almost immediately; in some cases not making its appearance until several weeks or even months after. At first development it is of a bright color, more or less elevated, and hard to the touch. It is much more persistent than the roseola, remaining salient for several weeks, and not unfrequently for several months.

It gradually loses its bright hue, and assumes a dull red or ham color, and shows a tendency to shed thin epithelial scales, especially at the base of the papules. The color in fading assumes a brownish color, finally leaving, as the elevation disappears, a coppery stain. The papular eruption of syphilis, so called, is seldom purely papular, some of the original papules becoming pustular, or having little accumulations of serum at their summits, thus exhibiting, apparently, a polymorphous character.

Having now given you a general idea of the papular eruption of syphilis, I shall, before entering into an examination of the forces, material, and pathogenetic influences involved in its production, present several cases exhibiting this prominent and important manifestation of active syphilis for your observation and study.

CASE VII. Here I am able to show you a common form of the papular syphilide, not extensive, but very characteristic. You may see along the upper border of the forehead perhaps twenty or thirty small red elevations, — *papules*. They are hard to the touch, insensitive, chiefly annoying to the patient because of their unsightly appearance. Their arrangement in this especial locality is significant, as simple papular eruptions are rarely so grouped without the occurrence of similar papules on the face, which in this instance you see is entirely free from them. Ricord has termed this variety of papular lesion the *corona veneris*, — the venereal crown. Here and there, in the eruption, we find a pustule, or a papule surmounted by a scab. Most of the papules, however, are simply smooth, hard, red elevations, about the size of a split and flattened pepper-corn. The patient states that he has none on any other part of his body. Let us see. A marked characteristic of this, as well as of all the eruptions of syphilis, is *insensitiveness*. Unless in sight, there is nothing to call attention to their presence. Having removed the patient's clothing, we find a few papules sparsely scattered over the back and shoulders. Just upon the right scapula is one which shows a scaling of the epidermis, at its base. This is occasionally seen, and I allude to it especially,

because it is considered a valuable diagnostic mark. Biett, a distinguished French authority, first called attention to this, and it is now known as the *collarete of Biett*. I shall show you, later on, that, while its diagnostic value is accepted from a purely clinical point of view, it is one more of the many external evidences of lymphatic obstruction in the progress of syphilis, and that the scaling results from the same histo-genetic conditions that produced the abrasion in the papular initial lesion of syphilis.

It will be interesting now to observe the grounds upon which the diagnosis of papular syphilide is based in the present instance. Reversing the usual order of examination, we will retrace our study of the natural history of syphilis. Thus we have the roseola preceding the papular eruption. On turning the patient so that the light strikes fairly upon his breast and abdomen, I can see here and there a faint coppery stain. On the back, however, are several traces of a previous roseola, so distinct as to be unmistakable. This is evidence, aside from its bright color, that the papular eruption is recent. The patient's own statement in regard to the appearance of his eruption is that about a month since he began to suffer with headache and to be generally miserable, although he continued his work as a printer. Headache chiefly at night. The eruption on his forehead came out about a fortnight ago, but he has not ceased to suffer with an occasional headache. According to authorities, then, he has suffered from syphilitic fever, not ushered in with the roseola, which he had failed to observe, but apparently in connection with the later papular eruption.

Let us see, now, if we cannot find something in the condition of the lymphatic glands to account for his constitutional disturbance, independently both of the roseola and the papular eruption, and in accordance with views previously suggested. Here in the cervical region are well-marked enlargements of the glands, in all the places which I have mentioned as characteristic in this respect; also in the epitrochlear space of the left arm; none in the right. Now in the groins you can distinctly see, as well as feel, the enlarged and indurated glands. The free handling of these glands, without complaint on the patient's part, assures us that the enlargement is not inflammatory, but is the result of simple hyperplasia. We follow the line of gland enlargements, finding them, at last, most prominent and numerous in the inguinal regions. This naturally leads us to look for the initial lesion on the genitals. The earliest gland enlargements, you know, are always in immediate connection with the initial lesion, and this initial lesion may be, through direct or mediate contagion, at any point on the entire body. Thus, when it is on the finger or hand, the cubital and axillary glands will be first affected; when on the eyelid, the preauricular; when on the lips or in the mouth, the submaxillary re-

gion; when on the genitals, in the groin; when within the anus, above Poupart's ligament alone, etc.; hence, in cases where the locality of the initial lesion is unknown, these early gland hyperplasias may lead to its discovery.

Here the inguinal gland enlargements point to the genitals as the seat of the primary lesion. The patient admits occasional impure sexual exposures during a long period, but denies that he has had a sore of any sort, or any urethral discharge. Examining the usual localities for such lesions, namely, about the frænum, along the fossæ glandis and mucous reflection of the prepuce, we fail to detect any suspicious appearance or induration. On the integument of the right side of the penis we find a small, slightly indurated, brownish spot, about the size of a five-cent piece, covered with fine epidermic scales, much like a patch of psoriasis. The patient is quite unable to say how long this has been present. He noticed it several months ago (at least two or three), but inasmuch as it did not give him the slightest discomfort or inconvenience he paid no attention to it; thought it some skin trouble entirely unconnected with venereal disease. This apparently insignificant lesion, gentlemen, I present to you as a somewhat rare but characteristic variety of the *initial lesion* of syphilis, which may be termed *the dry, scaling patch*. It is not raised above the surface of the surrounding integument, and hence is not visibly a papule; yet its base is distinctly stiffened with a sort of parchment induration, as it is usually termed, due to a superficial cell deposit.

From the distribution of the lymph vessels of the skin (just underneath the epidermis, where this form of lesion is always found), we may understand the superficial character of the induration. This has not, as we can see, been sufficient to cause an erosion, nor even to prevent the evolution of the epidermis; but nutrition has been interfered with to the extent of producing the unhealthy desiccation of the epidermal layer, as observed in the present instance. This is but a simple and natural variation from the forms of initial lesion previously presented, and will help to impress upon you the important fact that the initial lesion of syphilis has no stereotyped form, but may assume any appearance, between a prominent and dense hyperplasia, either intact or excavated, and a minute cell aggregation in the skin or mucous membrane so small as to defy clinical observation.¹ In whatever degree present, the infection may go on, as in this case it has evidently done, through the various early stages, until the characteristic papular eruption of syphilis is developed, as here seen.

¹ Bäumler in speaking of variations in density, of the indurations associated with the initial lesion of syphilis, says: "From these cartilaginous indurations to the flat, paper-like thickenings of the mucous membrane, where the increased resistance is perceptible only in feeling of it sideways, all imaginable intermediate stages occur, *the one thing common to them all being the dense cellular infiltration of the tissue of the cutis or mucous membrane.*" (Ziemssen, vol. iii., p. 112.)

Having thus examined the syphilitic papular eruption through clinical observation, we are now prepared to consider the minute structure of the syphilitic papule as ascertained by scientific investigation; to consider, also, the physiological processes connected with its formation; and especially to trace the influence of the syphilitic disease germ (which we have already followed from the point of inoculation to the remote vascular ramifications of the body) into the syphilitic papule, and thus to aid in affording a rational explanation of this important manifestation of syphilis.

According to the observations of Kohn¹ upon the papular syphilides, "They are formed 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 layers around the vessels and 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 a section of the 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, it may be said, are in complete accord with previous though less extensive and minute investigations made by Auspitz,² Virchow,³ Neumann,⁴ and Taylor.⁵

Bäumler,⁶ the recent German authority, speaks of the syphilitic papular eruption as consisting of "*well-marked, circumscribed infiltrations of the papillary body of the cutis.*" Of its intimate structure he says "The minuter anatomy of the syphilitic papule has been given already in that of the primary affection. Indeed," he continues, "*it is often impossible to distinguish an isolated secondary papule from a commencing primary affection.*"⁷ In his description of the microscopical examination of the syphilitic primary affection, or initial lesion, he says it "shows the tissue of the cutis and mucous mem-

¹ Caractères cliniques et histologiques des Syphilides. Par Moritz Kohn. Wiener Wochenschrift. Caractères, 1870, No. 55. Archiv générales de Médecine, March, 1872.

² Auspitz, Ueber die zellen Infiltration der Leidehaut medizinische Jahrbücher, vol. ii. p. 208, 1864.

³ Virchow, Pathologie des Tumeurs, Tradebbranc, vol. ii., p. 361, et seq.

⁴ Neumann, Lehrbuch der Hautkrankheiten, page 240.

⁵ Taylor, Observations on the Papular Syphilides, American Journal, Syph. et Derm., April, 1870, page 108.

⁶ Ziemssen's Encyc., vol. iii., p. 137, 1875.

⁷ Ibid., page 141.

brane to be filled with great numbers of nucleated cells, which are very closely crowded together between the otherwise normally-appearing connective tissue bundles, and with especial density in the adventitia of the blood-vessels. The capillaries also show numerous cells in their markedly thickened walls."¹ It will thus be seen not only that Bäumler's views coincide completely with those of Beisia-decki, in regard to the histology of the initial lesion of syphilis (fully given on page 216, Lecture I.), but that he finds the syphilitic papule under consideration to be, in its composition, identical with it, namely, *composed wholly of germinal or white blood cells*, the excess presumably due, in great measure, if not entirely, to a proliferation *in loco*.

We have seen that the local proliferation in the initial lesion immediately follows the application of the disease germ of syphilis, and that this result *invariably* follows such application to an abraded surface in a healthy human organism. The conclusion, *that it is in consequence* of the influence communicated by the disease germs to the normal white blood cells (thus setting up this excessive cell proliferation), *is inevitable*. If, now, we can trace the progress of the unhealthy cells *into a papilla cutis*, under circumstances favorable for continued excessive proliferation, and at a time when, through clinical observation, this accumulation is known to occur (inasmuch as it has already been shown that the character of the cell accumulation in the syphilitic papule is identical with that composing the induration of the initial lesion), then I think we may logically claim that the same influence which produced the latter gave rise to the former, and this through processes in complete accordance with known pathological and physiological laws.

"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

Of the early development of the lymphatic system Rindfleisch says,³ "This is the third and (we say it with emphasis) the last chief constituent of the intermediate nutritive apparatus. Last, not according to importance, but according to time. Only when the development of the embryo ensues at a less rapid rate, when all the other organs have been founded and built up to a certain point, do we remark *lymphatic vessels*; still later, *lymphatic glands*. This doubtless is connected with the physiological significance of the lymphatic vessels *as drains for the*

¹ Ibid., page 110.

² Text-Book of Pathological Histology, Rindfleisch, American edition, page 181, 1872.

³ Ibid., page 92.

surplus nutritive material. As long as, upon the one side, no nutritive material is superfluous in all that is applied to the new formation, and as long as, upon the other side, the external coverings of the embryo are not too thick to hinder a free afflux toward without, so long we need no lymphatic vessels." And further he says, "We can say also the reverse, that *luxurious new formations, catarrhs and surface secretions of all kinds, must be produced where the lymph conveyance is hindered*; and we will find that this position in pathology is very frequently confirmed."

The blood, or "*medium of exchange of the material of the organism*," is, then, carried out by the arteries from the centre of the circulation, to the periphery of the body, and is returned to it by the veins. Intercalated between these two systems of vessels is that other distinct system of vessels called *the lymphatic*, which withdraws from the tissues such nutritive materials as are exuded, in excess, by the arteries into the tissues, and restores them again into the circulation at a given point. According to Willis¹ and also Von Recklinghausen,² while they do not distinctly claim with Rindfleisch that the office of the lymphatic system is especially to return the surplus nutritive material to the centre of circulation, yet they agree that there is a current of nutritive fluid which is constantly exuded by the blood capillaries traversing the tissues, and which is returned to the general circulation through the lymphatic vessels; in other words, that there is a tissue current from the blood capillaries always setting towards the lymphatic vessels. Now, *at the nearest points of contact* of these different systems of vessels, at the superficies of the body, we should expect to find collections of surplus nutritive or germinal material, which, after having been exuded by the blood-vessels, were unable, from any cause, to effect an entrance into the *under-drainage* vessels, the *lymphatics*. The relation of these vessels in the cutaneous envelope is described by Teichman.³ Of the lymphatics he says, "The capillaries of this system lie exactly in the centre of the papilla cutis, whilst the blood-vessels traverse its periphery," winding up, "corkscrew fashion," until they unite at its apex. Rindfleisch says,⁴ "All these vessels are strikingly winding. It is particularly striking that the roots of the simple capillary loops wind *corkscrew fashion* around one another, until they unite at the apex of a papilla. The points of *union* or of *curving* are *constantly dilated*. Everything indicates that a certain increase of the pressure and retard-

¹ The Sudoriparous and Lymphatic Systems, by Robert Willis, M. D., London, 1867, page 32, et seq.

² The Lymphatic System, by Prof. F. Von Recklinghausen; Stricker's Human and Comparative Histology, Sydenham edition, vol. i., p. 297, et seq.

³ F. Von Recklinghausen on the Lymphatic System; Stricker's Comparative Histology, vol. i., p. 303.

⁴ Rindfleisch, page 277.

ation of the circulation must occur in the papillæ of the skin." Wagner says,¹ "The resistance which affects the velocity of the blood stream lies in *friction*. . . . It is greatest in the arteries, less in the veins, and least in the capillaries." Consequently it is in this juxtaposition of the blood capillaries surrounding the papillæ cutis and the lymph capillaries passing up through their centres, that is to say, in the spaces intervening between these, that we should expect to find germinal or other materials, escaped from the blood capillaries, detained in their transit into the lymphatic capillaries. At this point the force of the circulation has been shown to be at the minimum, the condition most favorable for proliferation. "Contact with the tissue and relative rest of the emigrant cells induces them, as it appears, *first to essay their amœboid mobility, then to division.*"²

The act of proliferation, when excessive, becomes a morbid process, thus predisposing to the coagulation of the fibrin contained in the tissue fluid.

Carried by the outgoing blood current into the most distant capillary vessels, the syphilitic disease germ has found its way, directly and inevitably, into a papilla cutis. Its exudation into the tissue is favored both by the natural process of exudation and by the amœboid power of the disease germ or morbidly active white blood cell.³ For in the stasis incident to this locality these cells "*first essay their amœboid mobility, then to division.*" These predisposing forces and conditions, with the proliferation and accumulation of cell material, and a separation of the fibrin from the lymph, resulting in a distinctly recognized hyperplasia of the papillæ cutis, causes the papules of syphilis to appear as a logical sequence.

I think, then, that it may be reasonably claimed that the papule of syphilis, always found in a papilla cutis, always composed of a dense cell infiltration of the papillary body of the cutis, is reasonably accounted for, — is shown, in point of fact, to be the necessity of a *physiological syphilitic infection*.

These papules are seen to vary in size according as the hyperplastic papillæ are more or less abundant, appearing as fine lichenoid elevations in some cases, while, in the larger varieties, an aggregation of hyperplastic papillæ occurs, and may be consolidated, through the escape of the hyperplastic materials, into the surrounding tissue. We are thus enabled to account for the variations in the size of the papules, and also to explain the apparent development of the papular syphilide in sebaceous follicles and sweat glands, which are said not to be supplied with lymphatic vessels. We are thus led to conclude that when

¹ Wagner's Manual of General Pathology, American edition, page 148, 1876.

² Rindfleisch, Pathological Histology, American edition, page 94, § 77.

³ See Lecture, first page, on the properties and powers of the disease germ.

they are apparently engaged in the formation of a syphilitic papule, it is only by their being aggregated into the papules by exudation of the plastic and cell material which has originated in the papillæ cutis.

Again reverting to our patient, we inquire as to the condition of his hair. He replies that he has had no trouble.

I will now present another patient, No. VIII., in the same stage of syphilis, drawn this time from our extensive field at Charity Hospital. Here, also, is a marked papular eruption, much more extensive than in the previous patient. I call your attention to him chiefly, however, for the purpose of showing the marked *alopecia* which has occurred, falling of the hair, eyebrows, and a perceptible thinning of the beard. This, you will observe, may occur in one case and not in another. Determination of syphilitic influences to different parts you will find to vary in degree in every case. The influence which is believed to cause loss of hair in this stage of syphilis is derangement of nutrition, in the hair follicle, by a *cellular infiltration of the papillæ surrounding it*. The loss, however, is rarely permanent. Natural or artificially induced fatty degeneration will probably remove the obstructing cell accumulation, when restoration of the hair will take place. Sometimes associated with the alopecia we may find the nails of fingers or toes the subject of trouble from similar cell infiltration into the matrices. The nails in such cases lose their lustre, and become dry and friable, or from denser cell infiltration disturbance of the circulation result in various forms of onychia, known as *syphilitic*. In this case I will ask you to observe in the eruption on his back, that pustules and papules surmounted with little scabs (collections of dried sero-purulent material) are quite thickly intermingled with the papules. This will be seen to some extent in almost every case of papular syphilide. In some instances we shall meet with eruptions, at this stage of syphilitic disease, which may even present a general pustular character. These variations from the simple papular appearance are easily explained by reference to the minute structure and behavior of the syphilitic papule, as previously given by Kohn. Thus he says, "These cells [which make up the body of the papule] are not destined to become permanently organized, as they degenerate and disappear, or assume a dull granular appearance, undergo fatty degeneration; or, they may become heaped together in the form of detritus and become pus." Pustular and vesicular eruptions at this period of syphilitic infection, with our knowledge of the processes through which the papular eruptions are produced, would seem rather to result from lack of formative power in the lymph, and from the inability to form, or the easy liquefaction of, the hyperplastic materials evolved or exuded into the papillary layer of the cutis; this occurring probably from a low state of the system,

induced by general causes, or by some especial dyscrasia not necessarily dependent upon the syphilitic influence. In some rare cases — usually in debilitated youths — superficial ulcerations occur, involving large patches of the papillary layer of the cutis, varying from the size of a quarter dollar to that of one's palm, not unfrequently mistaken for a so-called tertiary manifestation, notwithstanding that they only appear in the usual period of the papular syphilide. With proper attention to the general health, they will always be found amenable to the treatment found most useful in the simple papular eruption.

The *locality* of the syphilitic papule is found to influence its development to a greater or less extent. Thus, when the papular eruption appears on the hairy scalp, it is usually sparse, and covered with serous scabs. When situated in the depending portions of the body, as about the ankles, the papules tend to become pustular, and occasionally present as ulcerations of considerable size. When occurring upon mucous membranes, the papular eruption assumes the peculiar and characteristic features usually described by authors as the *plaque muqueuse*, or the mucous patch, commonly and best seen in the mouth and upon the mucous membrane of the faucial regions. In appearance it is like superficial erosion, covered with, or bordered by, a diphtheritic exudation of a pale gray color. When on the borders of the lip, it approaches more to the papular form. Papules situated on integument in the *vicinity* of mucous membrane, as at the anus, when they are subjected to continued moisture, and also for the same reason when about the scrotum or between the fingers or toes, appear as broad papules, often considerably elevated, eroded, more or less covered with the diphtheritic deposit, and exuding a serous secretion which decomposes easily, and are commonly associated with a characteristic disagreeable odor. These moist papules, to distinguish them from the mucous patch, and from their greater elevation, are called *mucous tubercles*. In the presenting case, in addition to the *corona veneris* and the papules which we have seen scattered over his body, I now call your attention to a characteristic *mucous patch* on the inner surface of the cheek, just in apposition with the second and, in his case, last molar tooth. This suggests the clinical fact that any external source of irritation, as the edge of a tooth or the stem of a tobacco pipe, will often determine the locality of a mucous patch. The irritation of tobacco smoke, or its juice, not only tends towards the development of the mucous patch, but often prevents its healing, indefinitely, under the best treatment.

Exudation and accumulation of cells *into the structures of the eye* are occasionally associated with the papular period of syphilis, and from the sensitive character of these tissues, are prone to result in a greater or less degree of inflammatory action. Infiltration of cells and

plastic material into the iris sets up an iritis, which is termed syphilitic, but which is said by authorities to be in no way distinguishable from a simple or rheumatic iritis.

When it is remembered that it is the resistance, in other words, the *friction*, that affects the velocity of the blood stream; that the velocity "*is least in the capillaries*;" and, further, that "*contact with tissue and relative rest* of the white or tissue building cells induces *first* to essay their *mobility*, then to *division*;" when, still farther, we consider it is thus evidently the *anatomical hindrances* to the velocity of the circulation in the papillæ cutis that determines the abnormal cell proliferation and accumulation which results in the papular eruption of syphilis, we can then readily understand why the capillary vessels of the eye should become the occasional seat of localized cell accumulation at the time when it is going on in the papillæ cutis. Clinically, we find that this is the case, and that fifty per cent. of all the cases of iritis, from all causes, occur during this period of syphilis. In certain instances, in addition to the plastic exudation into the iris, producing its characteristic interferences with mobility and transparency, the exudation extends in the form of an irregular nodule into the anterior chamber of the eye, sometimes as large as a small pea. This is usually termed the "*syphilitic gummy tumor of the iris*." But this gummy tumor is virtually identical, microscopically, with that of the syphilitic papule of the papilla cutis. It is composed, according to Wagner and others, "of colorless blood corpuscles, for the most part cells with a single and large nucleus and free nuclei, which, single or few in number, are imbedded in a connective tissue, poor in vessels."¹ In short, the so-called gummy tumor of the iris would appear to be but a syphilitic papule developed in a locality imposing no restraint, and hence its loose texture and irregular nodular form. Its occurrence at the same period, and its amenability to the same treatment of the syphilitic papular eruption of the skin would seem to give further support to such a view.²

Plastic nodules scattered over the choroid are also occasionally met with in this period of syphilis, sometimes quite independently of iritis, and consisting, microscopically, of simple cell elements. A growth of cells, supposed to be of the same character, has been described by Von Hippel "as having been found in the choroidal and sclerotic coats, as well as in the ciliary body, during this period of

¹ Wagner's General Pathology, American edition, page 434.

² Bäumler, Ziemssen's Encyc., vol. iii., p. 224. Von Graefe and Colberg have shown that "punctate deposits occur in syphilitic iritis, — chiefly upon the inferior half of the posterior surface of the cornea, or else in the form of a yellowish red papule, from the size of a pin's head to that of a pea, which is usually situated at the margin of the pupil, and consists of a circumscribed proliferation of cells," in other words, it represents a papule.

syphilitic disease.”¹ In short, it will be seen that blood capillaries, *in any peripheral location*, may become the seat of the arrest and excessive proliferation of the morbid cell elements at this period of syphilitic infection. Even in the deeper structures, as the bones (and probably from the same causes), points of soreness, and sometimes of bony elevation, occur. Pains in the bones are so often met with in the papular stage of syphilis that they are considered characteristic of this stage of the disease. These, while usually complained of as general, will be found to proceed from certain limited points of tenderness, and will be recognized on those bones within easy reach, as the top of the skull and the inner surface of the tibia. Sometimes slight elevations will be discovered. Intra-osseous or sub-periosteal pressure, which would be caused by the deep-seated cell accumulation, will account for the pain, and also the inflammatory action, in the cases where it occurs. A simple swelling sometimes results, which may subsequently, through natural causes, become the seat of true bony deposit. It is then called *a node*.

When we consider that not alone are the syphilized or imperfect cells coursing through the ordinary channels of the blood and lymph circulation, but that a migration of individual cells may take place, independently of those channels, into any contiguous living structure, there to establish new foci of proliferation, we shall find but little difficulty in accounting for cell accumulations in curious and rare localities, and, from influences peculiar to such localities, resulting in a great variety of external manifestations. The tendency of all cell accumulations, not necessary to the growth or nutrition of a part, is normally toward spontaneous removal, and return into the general circulation, or by a natural process of fatty degeneration, to be subsequently eliminated. This is especially the case in syphilis, where the accumulations are made up of hastily generated and imperfectly developed cells. Consequently, we find that in the natural history of this disease the cell accumulations in the skin, lymphatic vessels and glands, bones, etc., may disappear entirely in the course of a few months, and if no ulceration has occurred, without leaving any cicatrix, although the site of the papular eruption may be marked by a coppery stain for some time after.

Relapses of the accumulations occasionally take place at irregular points, especially in the skin and mucous membranes, evidently from influences of local origin; for these manifestations are never symmetrical, as in the general papular eruption, thus indicating that the exciting causes do not come from the general circulation. It seems most probable that this accident is due to the liberation of still active disease cells from isolated points (inferentially lymphatic glands) which

¹ Bäumlér, Ziemssen's Encyc., vol. iii., p. 224.

have been for a time separated from the general lymph current by obstructions (in the interior, or of their efferent vessels), from accumulations in the earlier stages of the disease. Such accidents in cancerous disease have led Virchow to the statement that lymphatic glands act as depots for diseased cells, often retaining them for a considerable period without disturbance of the adjoining vessels or structures.¹

It is well for you to know that syphilitic eruptions of the skin have been elaborately classified by authorities, according to their real or supposed resemblance to the simple diseases of the skin. For purposes of differential diagnosis, it is well for you to be familiar with their similarities and their unlikenesses with such diseases. It is also well that numerous other lesions of syphilis are described by authors with great faithfulness and minuteness as to dates of appearance, locality, and physical peculiarities, etc.; and, as opportunity presents, I shall endeavor to make you familiar with all the phases so described. But I can say to you *now* that the fact of chief importance which concerns you, and which under no circumstances should be lost sight of, is that the manifestations of syphilis occurring throughout the active periods of the disease (which usually lasts from six to eighteen months) *are, without exception, dependent solely upon a localized cell accumulation*, and that the principle of treatment in each and every case must be precisely the same, namely, by the use of such measures, general and local, as are known to be best calculated to assist nature in producing fatty degeneration and elimination from the infected organism of this abnormal, excessive cell accumulation, and at the same time to preserve and improve the general health of the patient.

LECTURE V.

PERIOD OF LYMPHATIC OBSTRUCTION.

GENTLEMEN, —We have now followed the natural history of syphilis, in its clinical, physiological, and pathological aspects, from its assumed initiation (by contact of a degenerate amœboid corpuscle, or disease germ, with the healthy human white blood corpuscle) into and through the lymph spaces and channels; from the point of original contact, or inoculation, to and into the general blood current. From thence we have also traced its course through most of the manifestations characteristic of the active period of syphilis.

We have seen that, wherever the syphilitic influence was recognized, the underlying conditions, culminating in a syphilitic manifestation,

¹ Virchow's Cellular Pathology, second American edition, page 221.

were, in every instance, attributable only to excessive localized cell proliferation and accumulation; and, further, that this local proliferation and accumulation were favored by certain anatomical conditions, in localities long recognized, clinically, as the favorite seat of such manifestations.

The active period of syphilis, thus shown to be marked by excessive localized cell proliferation, was shown to be equally characterized by the contagious property attaching to cells thus generated. Inoculation of the blood, and of the secretion of all open lesions during the active period of syphilis, has been found capable of communicating syphilis promptly to healthy persons.

The physiological secretions — milk, saliva, urine, perspiration, tears, and spermatozoa — *have not been proven to be agents of syphilitic infection*. Where apparently so, in many cases, syphilitic lesions of the mouth or breast have been found, to account for the seeming inoculability of the saliva or of the milk. Repeated experiments¹ have been made by inoculation of the spermatic fluid of a person proven to be in the active stage of syphilis, upon healthy persons, with absolutely negative results. In this we find confirmation of our position that the contagious property of syphilis is not an entity, an independent virus, pervading all the tissues and fluids of the organism, but that it is confined to the white blood or tissue-building cells, and, in this view, we readily see how the physiological secretions above mentioned, which do not contain them, are found also to be free from the contagious property of syphilis.

Thus far the *only distinguishing feature* which has been recognized between normal embryonal cells and cells which make up the accumulations characteristic of the active stage of syphilis is the possession, by the latter, of the *contagious property*; in other words, a *contagium*, — the power of setting up in other cells, through simple contact, the same disposition to rapid proliferation which the so-called syphilitic cells are known to possess. The direct result of this hasty proliferation, as far as we have yet been able to discover, *is not a destructive action*. It is simply and only what we should naturally expect from hastily generated normal material in excess of the necessities of growth and repair. In representative, uncomplicated cases it remains for a time obstructing the tissues by its presence, and then through purely normal processes, often of necessity set into operation by crowding of the newly-formed cells, prolonged pressure, and consequent innutrition, and also, from general causes, it undergoes fatty degeneration, and is in this way finally eliminated from the affected organism.²

Bäumler virtually supports this view³ when he says of the active

¹ Dr. Mireur, of Marseilles. *Annales de Dermatologie et de Syphilographie*, No. 6, Tome viii., 1877.

² A fatty metamorphosis, entirely like that which occurs pathologically, occurs in the normal condition of the organism. Wagner, page 305.

³ Page 247 of Ziemssen's *Cyclopædia*, Am. ed., vol. iii.

stage of syphilis, "If there are only a few local deposits, the elimination of the virus may be so much in excess of its production that the organism is gradually freed from it. *This takes place in the majority of cases, and at the expiration of eighteen months, or two years, the infection is entirely exhausted.*"

Mr. Hutchinson, of London, in speaking of the contagious property which attaches to the emasculated white blood cell, which we call pus, says, "*All living pus is contagious.* . . . I mean," he further says, "that *all* pus cells possess the power of setting up, when transferred to another home, if that home be a suitable one, a kind of inflammatory action similar to that from whence they themselves had originated."¹ This, we know, results in the almost immediate death of cells in localities so contaminated. In the case of the germinal cells contaminated by contact with the syphilitic cells, however, this results only in a hasty genesis of cells, a too rapid production, which prevents their highest development; they fall by the way, are heaped up, undergo fatty degeneration, and are, or may be, eliminated. Nor is it alone in diseased cells that a contagious property is claimed to reside. Rindfleisch, an eminent German authority, in speaking of embryonal cells coming up from the tissue juices for the regeneration of mucous membranes, says of such cells that "*they become epithelial cells only by coming into contact with such.* We must believe," he continues, "in a kind of epithelial infection." This, he says also, "must of course just as well obtain when embryonal formative cells approach an existing epithelial stratum, as when, conversely, epithelial elements approach embryonal formative cells."² If this be true, it at once becomes evident that the contagious property is not of necessity a *virus*; and it must, I think, be suggested, in this view of the matter, as equally evident, that the so-called *virus* of syphilis is simply a manifestation of that property, or personal influence, inherent in all cells, whether healthy or degraded, and which is as subtle and intangible, — as incapable of material demonstration, as the influence which one mind exerts over another. Is it not then possible that the mischief which syphilis does is rather the result of an interference with the normal processes, through hasty development brought about by this influence, than of the action of a specific virus?

In any event, this contagious property of syphilis *ceases with the active period of the disease*. After this has passed, the secretions of open lesions, and the blood, no longer contaminate. It may also be said that, in by far the greater number of subjects of syphilis (and more especially those who have been systematically and judiciously treated), they remain free from any farther sign of the disease. If this be so, then we may legitimately claim that, at the termination of the

¹ London Lancet, September 18, 1875, page 409.

² Text-Book of Pathological Histology, Rindfleisch, Am. ed., 1871, page 100, § 83.

active period of syphilis, just described, all subsequent troubles must be looked upon as sequelæ, and not as a stage of syphilis, any more than we should look upon dropsy as a stage of scarlet fever, or stricture as a stage of gonorrhœa. Mr. Hutchinson, who is recognized as one of the most advanced of the English authorities on syphilis, says: "*What are called tertiary symptoms do not constitute a necessary stage, and are rather to be regarded in the light of sequelæ, which may or may not show themselves.*"¹ Mr. Henry Lee (also a valued authority), in his Hunterian Lectures delivered at the Royal College of Surgeons of England in 1875, presents the same view of so-called tertiary or late syphilis thus: "The pathological changes in this class occasionally, according to Mr. Lane's view, present themselves in patients *who have passed through the primary and secondary stages of syphilis, but in whom the venereal poison no longer exists, and therefore cannot be transmitted.*"

This is, I know, quite at variance with the usual teaching in this matter. The accidents following upon the active period of syphilis are usually represented, not as sequelæ, but as the direct result of the syphilitic virus, which had never been completely eliminated, but had remained in the system in a latent state. Authorities are quite agreed, however, in regard to the clinical fact that, after a varying interval of from one to forty or fifty years from the acquirement of syphilis, a new variety of lesions appears in certain cases. Sometimes within a few months an eruption appears similar to the one I now present to you.

CASE IX. This young man gives us the history of a sore on his penis fully three years since, coming on three or four weeks after a suspicious connection. It was followed, in a few weeks, by an eruption which his medical adviser told him was syphilitic; he also had sores in his mouth and throat, all of which disappeared after a mercurial course of a month or so. He had supposed himself entirely well, when, about a month ago, another eruption appeared on various parts of his body.

We are here at once struck with the deep wine color of a patch of papular elevations on the temporal region, irregular in form and extending somewhat upon the forehead. A casual observer might perhaps confound it with the papular eruption of syphilis, which has been so often before us. But you will, by a moment's inspection, find well-marked and important differences. First as to color: here we see a distinct purple hue, instead of the ham color of the papular syphilide. In the next place, instead of being symmetrically distributed, the eruption occurs in patches; here is quite a large one, the size of my palm, on the right scapula; another on the thigh; this is an indication that the cause of this trouble (unlike the papular syphilide) has not been free in the blood. Again, the induration is deeper, involving the whole

¹ London Lancet, page 88, January 17, 1874.

thickness of the skin. On the scapula, also, are seen a number of small cicatricial depressions, where resolution of the eruption has taken place, evidently *without ulceration*. I may here state that this is not an unusual course in the *tubercular eruption* of so-called *tertiary syphilis*.

CASE X. Here I show you another example, where the tubercles are much larger, only half a dozen in number, and are confined to the right side of the nose. In this case active syphilis occurred four years ago, and the present eruption appeared as small red elevations of the skin, about two months since.

In this lesion you see even more distinctly than in the other case the loss of tissue which has occurred, the site of which is marked by several small cicatrices. A large tubercle is here covered by a scab; on removing it we find only a superficial excoriation. Loss of tissue in these cases does not commonly result from ulceration, but from absorption of a material which has been infiltrated into the tissue. The scars here give the lesion the appearance of simple tubercular lupus, and mistakes of diagnosis on this account are very common. We find in the excellent work of Van Buren and Keyes an explanation of the manner in which *scarring without ulceration* occurs in these cases, thus: "The syphilitic tubercle is due to a diffuse hyperplasia of small cells in the substance of the true skin. These cells, which partake of the nature of the *so-called gummy* exudation, grow at the expense of the natural tissues, and cause the atrophy of more or less of the substance of the latter, even while there is apparently a hypertrophy, as evidenced by the little tumor called a tubercle. When, however, the adventitious newly-formed cells go into atrophy and are absorbed, during the progress of the eruption, then not only does the tubercular prominence disappear, but the scar left attests the atrophy and absorption of the true elements of skin tissue which took place during the deposit of the morbid material."¹

In the opening of this analysis of the syphilitic tubercle, it is said to be "due to a diffuse hyperplasia of small cells in the substance of the true skin;" at the close, it is characterized as a "deposit of the morbid material." A little further on I propose to bring evidence to show that this lesion, in common with all syphilitic sequelæ, is not due to a hyperplasia, such as we recognize in the papular syphilide and in all the new formations of the active stage of syphilis, but that it is due chiefly to a *deposit*, not of *morbid*, but of *arrested normal material*.

CASE XI. Again, here is an old man, sixty-five years of age. He has come to our clinic on account of an enlarged testicle. His attention, he states, was drawn to it about three months since, first by a sense of heaviness in the organ. He then noticed that it was double

¹ Genito-Urinary Diseases with Syphilis, Van Buren and Keyes, page 583, New York, 1874.

the usual size. Since that time it has progressed, without pain or any especial annoyance except the dragging sensation, to the present size. The right testicle now presents to us as an ovoid tumor, fully four inches in its vertical diameter and three in its horizontal, as the patient stands before you. To the touch it is hard, not sensitive. A small amount of fluid is present in the tunica vaginalis, but not enough to obscure the somewhat irregular outline of the tumor. There is no history of any urethral discharge, or injury to the urethra, or prostate, or testicle, but there is a pretty clear history of an occurrence of syphilis. At the age of twenty-four, and thus *over forty years ago*, a sore on the penis coming at a long time after connection; he cannot remember exactly, but estimates it at from three to four weeks. He took mercury for a while, until it healed, and no further trouble was noticed. He married a few years after, and has had several children, — four, — also grandchildren, not one of whom has had any recognized signs of hereditary taint. Notwithstanding this I do not hesitate to suspect that the difficulty of the testicle will prove to be a sequel of syphilis. The physical signs accord with such a view; the history is sufficiently complete to warrant such a conclusion (many persons pass through the active stage of syphilis without its recognition by themselves or others). The final test here will be the effect of treatment which we find so promptly curative in such cases as to be of great diagnostic value, namely, that by mercury and the iodide of potassium. This is another of the so-called *tertiary* manifestations of syphilis.

Do you ask me, Of what is this enlargement and induration made up? I answer (in accordance with the usual teaching), of “gummos material,” — the same that is found in the tubercular eruption in Cases IX. and X.

CASE XII. Again I present you a form of trouble which has followed an attack of syphilis after a very long interval of apparent good health. Fifteen years ago this man (who is now fifty), according to his very clear and intelligent statement, had unmistakable syphilis, characteristic initial lesion, early erythema, general papular eruption, mucous patches, etc. After several months among quacks, he was finally treated by a well-known surgeon of this city for about a year; then, being apparently well, he left off treatment. About six months ago, or some fourteen years from the date of the initial lesion, and after some months of dissipation, he began to suffer with a naso-pharyngeal catarrh which became fetid. It was not, however, until a characteristic perforation of the hard palate had occurred, that the source of his trouble was suspected, and he then went up to Charity Hospital for treatment. Here, as you can observe, is a distinct loss of structure involving a portion both of the hard and the soft palate. Repair is going on, in the soft parts, under appropriate treatment, which, I wish to remind you, is the

same which has been prescribed for the three cases preceding, namely, *mercury and the iodide of potassium*. Why? Simply because the source of the trouble has been shown in such cases to be dependent upon the "gumous" deposit in the soft palate and in the bony arch of the mouth, and in the vomer, in this case, and that mercury and the iodide of potassium, as in the previous cases, are our chief reliance in eliminating it from affected tissues.

CASE XIII. The patient is a man of forty, who presents several ulcers of the legs which we term characteristic of so-called "*tertiary syphilis*." They are abrupt losses of integument, as if some foreign substance had sloughed out; bluish thickened edge, undermined, and on pressure giving exit, not to pus, but to a thin, serous fluid. Here are also two or three points, higher up on the calf, slightly elevated, and to the touch giving a distinct sense of fluctuation. The physical appearances here are alone sufficient, even without a history of antecedent syphilis, to warrant the diagnosis of "gummy tumors;" although the patient claims to have had syphilis ten years since. I introduce a bistoury into one of the seemingly fluctuating points, and not pus, but a serous fluid, exudes. Both the secretions and the tumor will be found to consist of the same so-called "gumous" material which we recognized as constituting the tubercular eruption in Case IX.; which caused the induration and enlargement of the testicle in Case X.; which also caused the destruction of the soft palate and bony structures in Case XI., and this material has been proven, by repeated and exhaustive microscopical examinations, to be made up of gelatinous fluid containing normal cells and nuclei which do not differ in the least demonstrable degree from the white blood cells and nuclei of a healthy person. Wagner, perhaps the most recent standard authority, says of this gumous material (which he terms *syphiloma*), "Microscopically *syphiloma* consists of cells, or nuclei, or both at the same time, so that sometimes the former, sometimes the latter, exceed in number. Young *syphilomata*, as well as the peripheral parts of the older ones, contain for the most part only nuclei, or nuclei and isolated cells; the older *syphilomata*, not yet very atrophic, consists for the most part only of cells, or of cells with few nuclei. *The nuclei offer nothing characteristic*. They are from 0.01 to 0.02 mm., large, round or rounded, or somewhat angular, and contain for the most part a distinct nucleolus. *The cells resemble most uninucleate colorless blood corpuscles*; their size varies, however, sometimes between 0.01 and 0.03 mm.; some are even still larger."¹ Again Wagner (page 436) says: "The influence of *syphiloma* on the organism depends upon the fact that the affected portions of the membrane and parenchymata are more or less incapable of function; partly on the deposit of cells, and especially of nuclei, upon compression

¹ Wagner's Manual of General Pathology, Am. ed., 1876, page 435.

or secondary atrophy of the gland cells, nerve fibres, ganglion cells," etc.

Bäumler, who fully adopts Wagner's views, says: "From the fact of the close resemblance of the cells which pervade the tissues, or occur in the form of young tissue growths, with the white blood corpuscles, it is evident that, however much they [authors] may characterize syphilitic new formations, *they wholly lack specific microscopic characters.*" He also says: "Tumors of this sort [gummy], varying in consistency, may develop in any organ in consequence of syphilis, *but their favorite seats are in the subcutaneous cellular tissue, the skin, in and upon the bones, the liver, the testicles, the brain, the kidneys, and, especially in children, the lungs.* According to Wagner's description," he further says, "they present the appearance of a grayish-red, soft, homogeneous mass, either without fluid contents, or else yielding a scanty juice like mucus. They may occur as infiltrations of microscopic size scattered throughout the parenchyma of an organ; and even when they appear as sizable tumors, as large as a walnut or larger, *they are not encysted nor sharply defined, but merge directly into the surrounding tissue.*" "The effects of a gummy tumor," says Bäumler, "may extend to a great distance *in case it has caused contraction of the calibre of some vessel*, especially of a blood-vessel, which is particularly liable to occur when the tumor has its seat in the adventitia of a vessel. *Fatty degeneration and wide-spread processes of softening may be the consequences of a tumor in itself insignificant*, as occasionally happens in the brain. When situated in the skin, in the subcutaneous cellular tissue, upon mucous membranes and superficial bones, *the gumma often makes its way to the surface*, since in these situations it is not uniformly inclosed on all sides, but is exposed to unequal pressure. The entire infiltration then ulcerates." It is reasonable to conclude, from the foregoing views, that *contraction of vessels* often plays an important part in causing the lesions of so-called tertiary syphilis; a purely mechanical matter quite independent of the influence of any virus. In passing, I desire also to call your attention to the statement of Bäumler, that "gumma often makes its way to the surface." I hope to be able, subsequently, to show how this occurs, not *making its way*, but progressing by natural forces in line of the natural physiological channels.

Ricord claims that *tertiary lesions are not inoculable, and cannot be transmitted by hereditary descent.* Bumstead states, in his last edition, after reviewing this matter, "*Hence we consider the blood and the secretions in tertiary syphilis innocuous.*"¹ "Diday performed inoculations with the blood of persons in the tertiary stage of syphilis, and invariably with a negative result. Von Barenprung states that from observation as well as experiment he is persuaded that so soon as the syphilis

¹ Venereal Diseases, Bumstead and Taylor, page 443.

has passed into the destructive forms of its tertiary stage, *it ceases to generate an inoculable virus*," and, says Bäumlér, "clinical observation seems to confirm this view, both in respect to direct contagion and with reference to the inheritance of the disease."¹

These authorities, together with Lee, Hutchinson, Lancereaux, and many others of our best clinical and scientific observers, thus agree fully on this very important point. What, then, is there to show that the so-called "*period of gummy products*" (Lancereaux) is not simply a period of sequelæ, when they are found, practically, by competent observers, to be free from the contagious property, and when by scientific investigators it is shown that they are capable of producing, without a virus, all the lesions, without exception, which ever occur in the so-called tertiary or gummy stage of syphilis? — producing them, too, simply *by interference with function* of vessels and organs, not improbably through pressure occasioned by the presence of abnormal or excessive accumulations of material, which the most experienced and learned microscopists cannot distinguish from the normal elements of new formations.

If, then, we accept the lesions of the so-called tertiary stage (or the period of gummy products of Lancereaux) as sequelæ, where shall we look for the *causes* of the possible accumulations of normal germinal material at every point in the human organism? Naturally, it appears to me, *in interferences with the lymphatic circulation*, the natural channels, through which, according to Rindfleisch, the nutritive material exuded into the tissues, in excess of the necessities of growth and repair, is returned to the general circulation.²

According to the same distinguished authority,³ "*Luxurious new formations, catarrhs, and surface secretions of all kinds must be produced when the lymph conveyance is hindered*, and," he further says, "*we will find this position in pathology very frequently confirmed*." One thing is now admitted by all recent accepted authorities, namely, that all the surface secretions and new formations of the tertiary or gummy period, all the infiltrations and tumors, all the peccant elements which produce the varied lesions in the skin, in the cellular tissue, in the bones, in the viscera, by whatever name characterized, are but the various forms of infiltration or deposit of *gummy material*; and if this is, as it would appear by the results of scientific investigation to be, *nothing more nor less than normal germinal elements* thus retained at various points, then the only legitimate way of accounting for this retention would appear to be through obstructions, "*hindrances to the lymph conveyance*," which Rindfleisch insists, is of itself sufficient, independently of any question of syphilis, to produce just such results as are known to occur in the so-called tertiary stage or period of gummy products.

¹ Ziemssen's Cyclopædia, Am. ed., iii. 57.

² Rindfleisch, Pathological Histology, Am. ed., 1871, page 92.

³ Ibid., page 93.

And yet another circumstance would favor this view; clinical experience has shown conclusively that whatever the form or locality or name of a lesion, whether in the skin, as a scaling eruption, or as a tubercular eruption, or as a heaping up of gummous exudation in scabs, with or without ulceration, or as an ulcerative loss of tissue, or whether as a gummy tumor in the cellular tissue, in the bones, in the viscera, or in the brain and nervous system, *one and the same treatment is adopted* and found most efficacious and judicious for all, namely, *the administration of mercury and the iodide of potassium*. I have not heretofore objected to the term gummy period (so called only from the similarity of its products to the viscid material which it was believed to resemble), nor to the term *tertiary*, which is a purely arbitrary one; but it appears to me that we may now venture to substitute for these, *the period of lymphatic obstruction*, as more scientific, because expressing the localization of lymphatic elements, which is proven to occur, and as suggesting the lymphatic canal system as among the possible causes of that localization. It appears to me that, inasmuch as it has been shown that the lymphatic spaces and vessels are primarily and chiefly affected and obstructed during the active stage of syphilis, it is not unreasonable to infer that damage *might* have occurred to those spaces and vessels during the active period of syphilis, which, if properly investigated, would lead to the true explanation of the failure of that system to return to the general circulation the germinal material exuded or developed in the tissues, in excess of the necessities of growth and repair, such as is practically demonstrated to have occurred in the so-called tertiary or gummy period of syphilis. There are various known facts and analogies which afford strong presumptive and circumstantial evidence that this view is the correct one. Among these we have, first, the fact, generally recognized, that the more severe and prolonged the secondary or active stage of syphilis the more certain and severe are the so-called tertiary or gummous manifestations.¹ Second, the results of treatment show that the difficulty is not simply an aggregation or infiltration of material, which, when removed, restores the patient permanently, but that the conditions for its reproduction remain, and relapses occur.

Thus the iodide of potassium is recognized as capable of most rapidly removing the gummous material, and thus of relieving symptoms; but mercury is found requisite to produce permanent immunity. The iodide of potassium acts readily in removing recent new formations and cell accumulations, probably through the iodine it contains. The *fucus vesiculosus*, a remedy in use for obesity, and popularly known as "anti-fat," owes its virtues to the same ingredient. But mercury is known not only to hasten dissolution and elimination of fatty matters and new

¹ Hutchinson, London Lancet, January 31, 1874, page 159.

formations; it is, besides, the only agent with which we can expect to disintegrate more or less long-standing fibrous obstructions.

In the gummy accumulations of so-called tertiary syphilis, we are obliged to infer that *some* condition remains, after the removal of this material, which predisposes to, or causes, subsequent reaccumulation. What is more likely, as such condition, than *obstruction of lymphatic vessels*, the office of which is to carry just such material as we find producing the difficulty; vessels, too, that have been, more than any other structures, involved in recognized troubles during the active stage of the disease? More or less inflammatory action, usually of a very low grade, is recognized at different superficial points in the lymphatic system during this period. The well-known tendency of all such action is to the deposit of fibrous material, — the very material through which cicatricial contractions of other tissues are brought about. Analogous, in a degree, are the conditions which result in stricture of the urethral canal, ten, twenty, or even forty years after the original inflammation; conditions which set in motion a process which culminates, finally, in obstruction to the passage of urine.

It has been claimed that much of the trouble, in so-called tertiary syphilis, may be the result of wide-spread fatty degeneration caused by contractions of vessels.

It is well known that fatty metamorphosis occurs more easily in some subjects than in others, — that purulent degeneration is most readily set up in the debilitated and diseased. It is also claimed by Hutchinson and others that the liability to and severity of the lesions of the so-called tertiary period of syphilis "is in proportion to the duration of the secondary stage."

Hence we may conclude that the varied degrees and forms of so-called tertiary manifestations depend upon, first, the damage caused during the "duration of the secondary stage," and inferentially in consequence of it; and, secondly, upon the condition of the individual affected, and this quite independently of any specific virus.

It may be objected to this view of lymphatic obstruction as a cause of the sequelæ of syphilis, that, while all the known physiological and pathological processes favor it, it lacks actual demonstration.

It is unfortunately true that the investigation of these matters requires an amount of special training, knowledge, and experience with the use of the microscope, which puts it practically beyond the province of the general physician or surgeon, and also that experts have paid no systematic attention to the pathological processes associated with syphilitic sequelæ, but have rather wasted their labors in the vain endeavor to find a specific virus to which all these pathological conditions could be directly attributed, — a sort of philosopher's stone, which when found would suggest an antidote, with properties as marvelous as

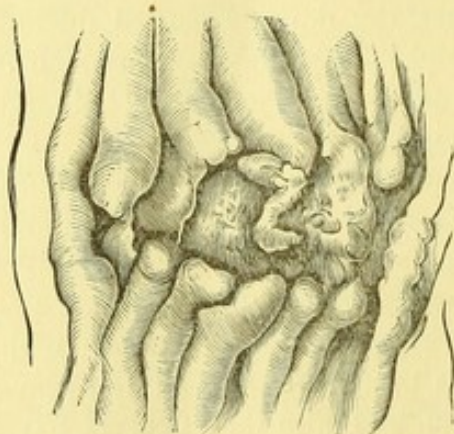
those attributed to the virus, and of universal application for cure of every form and result of syphilis. But a single case has rewarded my search in the literature of microscopic investigations of syphilitic lesions, which, presented simply as a record of pathological appearances, independently of any theory, appears to confirm my views in regard to the presence and importance of obstructions of the lymph channels in the sequelæ of syphilis.

TERTIARY SYPHILITIC ULCERATION OF THE ILEUM.¹

F., fifty-one years old (counselor), had been healthy, with the exception of syphilis, until six months before his entrance into the hospital. At about that time he felt a weakness in the lower extremities, especially the right, and fatigue in walking. The appearance of locomotor ataxia developed more and more, and this caused him to go into the hospital. At his entrance he was found to be robust, well nourished, with scars of mucous patches on the lips, psoriasis palmaris, and in the right groin scars from ulcerations of the glands.

The digestion was pretty good, stools not bad, no pains in the intestines. On the whole, the case appeared like one of locomotor ataxia.

The treatment against the syphilis was decided, and iodide of potassium and Zittmann's decoction were prescribed; but the patient was scarcely put upon this treatment when he suddenly died. The post-mortem examination showed the following condition of the intestines: "All the layers of the intestines, from the lower part of the jejunum up to the ileo-cæcal valve, corresponding to Peyer's plates, were pervaded by a gray, reddish mass, which had on these parts a parchment-like feeling; the folds of mucous membrane were broader than normal, stiff,



not expansible. In the middle of this infiltration an ulcer was found, of polygonal shape, and of the size of a small silver three-cent piece (kreutzer), parallel to the longitudinal axis of the intestine. The base of this ulcer is formed of the thickened, smooth, fatty-looking submucous layer, the borders of which are flat but sharply marked. The peritonæum is here covered with a tender pseudo-membrane and pervaded by enlarged lymphatic vessels,

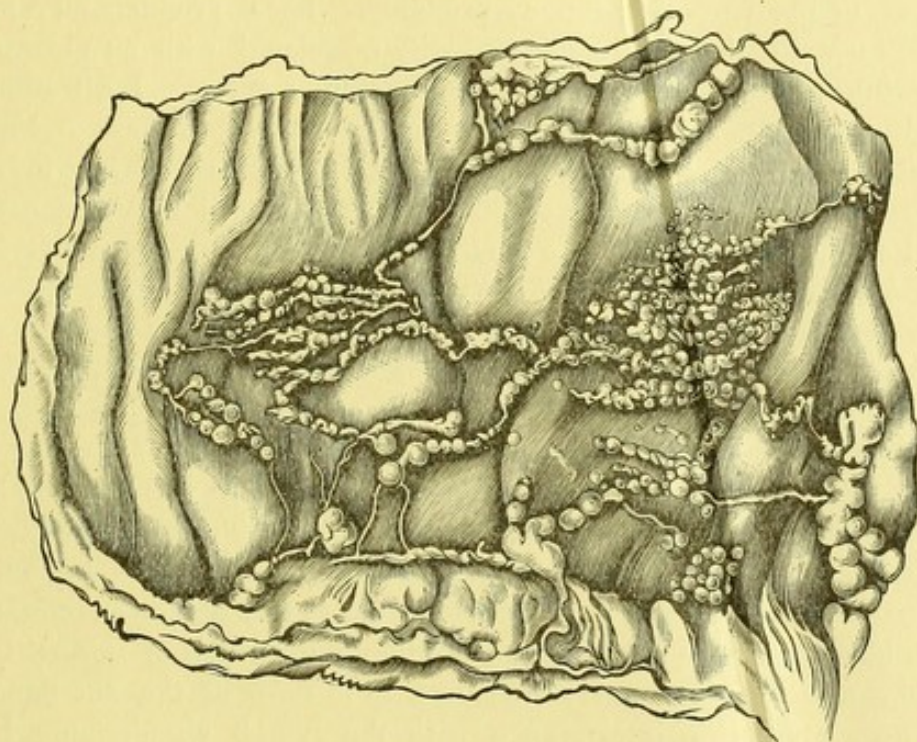
filled with thick yellowish-white lymph.

¹ Untersuchungen aus dem pathologisch-anatomischen Institute in Krakau. Von Dr. Alfred Biesiadecki, Professor an der K. K. Universität in Krakau. Mit 11 Holzschnitten. Wien. 1872. Page 84, Die Fälle von Enteritis Syphilitica aus dem Archiv für Dermatologie und Syphilis, 1871. Von Dr. Oser.

"Between the vessels were to be seen numerous little knots, of different sizes, which were in communication with the lymph vessels. The lymphatic glands of the mesentery were slightly rough and swollen. In the cavity of the intestine were bile-colored pulpy fæces."

MICROSCOPIC APPEARANCES.

"We found a very abundant growth of round, tender cells, which were partly filled with fat; these, after the addition of acetic acid, showed several granules. The growths embrace the normal mucous membrane, extend through all the layers, especially the submucous connective tissues, and these, as well as the crypts of Lieberkuhn, well preserved, were filled with detached epithelium."



"On the ulcer found in the centre of the infiltration the intestinal villi were very imperfect or missing entirely."

"On the smooth, fatty base of the ulcer *we saw numerous round cells imbedded in the tissues. The same growth of cells was also present in the muscular structure*, in which the cells were imbedded between the muscle fibres which separated them."

"On some parts of the preparation (microscopic) aggregations of cells which had separated the muscle fibres had changed to a molecular mass."

"Upon a cross-cutting of the thickened peritonæum, besides enlargements of the thick-walled vessels and round cells, distributed especially around the vessels, we found also heaps of cells which seemed to be surrounded by a firm membrane."

"The cross-cut of such groups of cells were mostly circular and showed a space filled with round cells of the same size, which space was marked off from its surroundings by a sharp line. *These were taken to be sections of lymphatic vessels.*"

"Upon the longitudinal cut (especially in places where the enlarged lymphatic vessels and the small knots above described could be seen with the naked eye) were seen frequently *heaps of cells surrounded by a sharp line. These heaps of cells took in the whole field of the microscope and were in connection with the lymph vessels. We saw both afferent and efferent vessels, filled with the same cells which formed the contents of the little knots visible to the naked eye.*" Here we have the history of a well-marked example of the so-called tertiary period of syphilis, or the period of gummy products. These products on a post-mortem examination are found distinctly associated with an ulceration in the intestinal canal, characteristic of syphilitic action. Infiltration of round cells (gummy products) into the mucous, submucous, and muscular tissues, stiffening the structures so as to produce distinct induration, separating the bundles of muscular fibres until they become reduced to the appearance of a molecular mass, practically a necrosis. *Lymph vessels so distended with cells that a knotted appearance indicates the pressure to which they have been subjected* and reveals the fact that a localized obstruction to the return of lymph through its natural channels has occurred, — vessels filled almost to bursting with a yellowish fluid lymph, and cells (gummy material?); and why? What has caused this obstruction of lymph channels and evident loss of substance, by interference with the nutrition of the parts? The microscopic examination fell short of an inquiry into the *causes* of the obstruction. The tissues of the vessels were not subjected to any test or examination to see how the structure of the walls differed from that of normal lymphatic canals. The observer was content to show us that the damage was associated with interference with the lymph circulation. It is evident that if these vessels (whose office is to return to the general circulation the lymphatic elements exuded in excess of the necessities for growth and repair) had been patent, the accumulation could never have occurred. It is known that obstruction of lymph vessels often results in pressure upon blood-vessels and such interference with the circulation as to induce extensive loss of tissue by ulceration or fatty degeneration. This case carefully and ably investigated, in its gross as well as in its microscopical features, with no possible suspicion attaching which could indicate on the part of the distinguished narrator of the case the endeavor to form or bolster up a theory, has been shown to be a case of lymphatic obstruction, so associated with a lesion of tertiary syphilis (so called) that it will be difficult to resist the conclusion that the characteristic lesion was caused by that obstruction.

With these palpable indications of the manner in which the so-called gummy products have been localized in the present instance, shall we fall back upon the local presence of the traditional *virus* to account for the gummy accumulation? Shall we not rather claim of the renowned scientists who have already accomplished so much in the philosophical interpretation of general pathological and physiological processes, that they shall afford us a reasonable explanation of the gummous material (a material which is known not to differ in the least degree from normal germinal material), and a reasonable explanation for the manner of its accumulation in the tissues, in so-called tertiary syphilis? In the absence of other cases, similar to the one just presented (and with the probabilities that absence is to be accounted for simply by neglect to look for and investigate), this case, presented by a competent and presumably honest observer, must be accepted as representing facts, which may be significant as to what occurs in all collections of "gummous material," — facts which are important as possibly affording an explanation of the hitherto mysterious lesions of so-called tertiary syphilis.

It appears to me that a review of the foregoing facts and arguments will show that the lesions of the so-called tertiary period of syphilis are not the results of the local action of a virus, but are caused through damage to lymph channels, in the active period of syphilis, which finally results in their contraction, thus causing obstruction to the passage of lymph and cells, and their undue accumulation at various points; producing disturbance of function and nutrition which will account philosophically for all the losses of tissue, by necrosis and fatty degeneration, which are known to occur in tertiary or late syphilis: these, together with the case cited, I think, warrant me in terming the period above referred to the PERIOD OF LYMPHATIC OBSTRUCTION.

LECTURE VI.

PERIOD OF LYMPHATIC OBSTRUCTION (CONTINUED).

GENTLEMEN, — In resuming the consideration of the so-called tertiary or late manifestations of syphilis, it may be well to recall an important advance in the systematic study of this subject, brought prominently before you at our last session, namely: that while, as a rule, authorities treat of these manifestations as implying the influence and actual presence of a *virus*, a so-called "syphilitic taint" in the blood, yet clinical observers and authorities, such as Hutchinson, Lancereaux, Von Barenprung, Bumstead, and others, have, somewhat recently, drawn a broad line of separation between the earlier

and later lesions due to syphilis, by accepting the former as specific and always associated with a contagious element, and characterizing the latter as "sequelæ;" lesions free from any contagious property, and thus strictly personal; incapable of transmission either by inoculation or hereditary influence; not an essential, but merely an accidental, result of syphilis. This, it will be seen, has a tendency to lift the late lesions due to syphilis out of the realm of the supernatural, and lead us to a study of cause and effect through known physiological and pathological processes.

The first positive step in this direction was recognized in the acceptance by authorities of the "gummy material," the "syphiloma" of Virchow and Wagner, as *uniformly* if not *necessarily* associated with all the late lesions due to an antecedent syphilis.

Whether in the skin as a diffuse infiltration of its superficial layers, and resulting in a so-called *scaling syphilide*, or localized in the deeper layers as a *tubercular syphilide*, or in the cellular tissue, in the muscles, in the bones, or in the viscera, as the *gummy tumor*, the constant presence of this still mysterious material was recognized, and always suggested its importance as a prime factor in effecting the mischief with which it was associated. But the most searching analyses had failed to find in it any mischievous property, or to show that it was anything more or less than an aggregation of normal nutritive elements.

It was at this point that I called your attention to the significant fact that during the active stage of syphilis the vessels and organs of the lymphatic system (whose uses, as far as known, are confined to the normal nutritive elements of the organism), were prominently affected, and that, too, in such a way as to suggest the possibility of subsequent pathological changes in the walls of the lymph channels, and an interference with the lymphatic circulation as a legitimate consequence.

If then we accept the *gummy material* for what scientists have proved it, simply an aggregation of normal germinal elements in various localities and degrees, its exact localization of necessity must be referred to spaces, vessels, and organs of the lymphatic system, as the recognized habitat of those elements. In order, however, to account for the localized accumulation of this material in such degree as to constitute a pathological condition, obstruction of the lymphatic channels becomes essential. Now it is that the preëxistence of the syphilitic disease, prominently affecting this especial system, becomes important, and furnishes us with the only logical and legitimate explanation of the cause of obstructed lymphatics, and of accumulated normal germinal elements; in point of fact, now for the first time we are in possession of a reasonable solution of the origin and nature of the mysterious *gummy material* of late syphilis.

In the first of the five cases (Case IX.) presented as typical of as many different phases of syphilitic sequelæ, the damage to the tissues implicated in the tubercular eruption was recognized as an atrophy resulting from mechanical pressure. It was seen that loss of substance had not occurred through the ulcerative process. Authority was cited to prove that ulceration was not the necessity in such cases, but that the accumulation of the gummy material, "a diffuse hyperplasia of small cells," was the cause of the "atrophy and absorption of the true elements of the skin tissue." In the remaining four cases the behavior of the accumulation was not so easily appreciated. I propose, however, to-day to continue the consideration of the lesions then presented, and shall endeavor to show among other things that the damage resulting is still (as in the tubercular eruption) independent of any destructive property, or constitutional taint, *per se*, but that the sources of trouble are purely local, and that the losses of tissue which do occur result from arrest of the processes of nutrition through *mechanical* disturbance; primarily of the lymph channels, and secondarily of the blood-vessels, with which they are associated.

CASE XIV. This patient gives a tolerably clear history of active syphilis occurring about twenty years ago, and of eruptions more or less ulcerative during two or three years subsequently. Since that time he had enjoyed good health up to five years ago, when his right testicle became enlarged to the size of his fist. He states that under occasional treatment by the iodide of potassium, the testicle grew very much smaller. In fact, he thought the difficulty almost cured; but within the last few months the swelling had returned and had again become troublesome from its increased size. We find here the right scrotum greatly enlarged; not at all sensitive to the touch; and so far like Case XI. of syphilitic testicle, previously examined. But the tumor, while quite heavy, fluctuates very perceptibly, and it is only by firm pressure that a solid material can be felt through the fluid, and this apparently not much larger than the testicle in its normal condition. Application of the light test, in this instance, is not altogether satisfactory, but as no impulse is transmitted to the tumor through the inguinal canal in coughing, we may venture to aspirate it. And now, after introducing the needle, as I draw back the piston of the instrument, the straw-colored fluid, characteristic of hydrocele, flows into the glass barrel of the aspirator, in quantity sufficient to show that the mass of the tumor was fluid, just filling the receptacle, which registers a capacity of a little more than four ounces. Having removed the fluid, it at once becomes evident that the tumor, while not larger than a normal testicle, is irregular, somewhat nodulated in shape, and, especially at the lower portion, is very hard, quite like cartilage. As I press it between my thumb and finger there is

no complaint of pain until reaching the very top of the organ, where, as you have seen, the patient shrinks and makes some complaint. This remaining sensitiveness is an evidence that the normal structure of the testicle is not entirely destroyed.

In the post mortem examination of similar cases, it is found that two forms of trouble, frequently (and always in long standing cases), unite in the so-called chronic orchitis of late syphilis, the one usually earliest to manifest itself being a localized tumor at one or more points in the substance of the organ. This is found to be made up of materials characteristic of the "*gummy tumor*" occurring in other localities. Subsequently to the occurrence of these tumors a marked growth of fibrous tissue is found to take place, *apparently commencing in the lobular spaces*, and gradually encroaching upon the seminal lobules until they are destroyed. The elements of new formation, traversing in this same way the substance of the entire organ with a cicatricial net-work, the contraction which naturally follows, often results in the total destruction and almost complete disappearance of the organ. This explains what we find in the present instance. The history points to a general so-called gummy infiltration, involving, probably, the epididymis and the body of the testicle, and a later development of fibrous tissue, which has, by its subsequent contraction, reduced the organ to its present indurated and atrophied condition. It is interesting here to recall the fact, made prominent by all authorities on syphilis, that cicatricial deposit and its subsequent contraction and strangulation of the parenchyma of the testicle, resulting in true atrophy, is characteristic of the influence of late syphilis, and occurs not alone in the testicle, but notably also in the liver and the kidneys. The tendency to formation of fibrous tissue has also been recognized (from apparently the same causes) at other points, as in the larynx, intestine, etc. Ranvier and Cornil significantly remark¹ that all profound syphilitic lesions of the mucous membrane occasion a proliferation and a production of connective tissue usually much greater than in diseases due to other causes. It is a well ascertained clinical fact that gummy infiltration precedes the stage of cicatricial deposit, and that while both the gummy tumor and cicatricial atrophy are often met with in the same testicle, general enlargement *first occurs*; then comes the recognition of localized deposits of gummy material, and later, often several years after, compression, due to contraction of cicatricial deposit, finally takes place, and atrophy of the testicle results. The clinical evidences are strongly in favor of considering the gummy exudation as the *basis* of the cicatricial deposit, and the different subsequent conditions as but stages of the same pathological process, terminating finally in atrophy, through cicatricial contraction. In favor

¹ Patholog. Histol., page 399, 1880.

also of this view, and as affording a possible explanation of the cause and mode of formation of the cicatricial deposits in other organs, due to late syphilis, we may recall the statement of Rindfleisch in regard to the most favorable conditions for the development of new cell formations, namely, "Contact with tissue and *relative rest* of the emigrant cells induces them first to essay their amœboid mobility, and then to division."¹ But *absolute rest*, *stasis* of such cells, or of any cells, is necessary for their *development into tissue*. All fibrous or connective tissue is said to be made up of the spindle-shaped or connective-tissue cells and fibrillæ which are simply a higher stage of development of the lymphoid cells and corpuscles, evolved from and circulating in and through the lymphatic organs, spaces, and vessels. This is exactly the essential material of which *cicatricial tissue*, wherever found, is made up, and this is exactly the sort of tissue which has caused the mischief in this testicle, and which by authorities is accepted simply as one of the many mysterious phases of the so-called tertiary period of the disease. Only a single condition is lacking, however, in order to place this cicatricial deposit, due to syphilis, in the line of ordinary pathological conditions, and that is, one which will account satisfactorily for the presence and quantity of embryonal or formative cells in the localities where the cicatricial tissue is subsequently developed, and the causes of their enforced accumulation and stasis in those localities, during a period sufficient for the formation of such tissue.

His and Thomsa² claim to have demonstrated a very generous distribution of lymphatic channels in the testicle, the liver, and the kidneys, organs in which the cicatricial contraction due to the influence of late syphilis is chiefly found. Especially are the lymphatics claimed to be numerous and ample in the testicle, where injections performed upon dogs have shown that lobular spaces are simply lymph sacs or lacunæ. In point of fact, the seminal lobules are literally inclosed in lymph chambers, and the reticulation of lymph channels not only surrounds, but permeates, every portion of the testicle and its appendages. The same rich distribution is shown also in the liver and kidneys. Having, then, the material necessary for the formation of cicatricial tissue, and in localities where it is known to develop, the essential condition to produce it is an enforced stasis of cell elements through interference with the lymph circulation of these organs; in short, *obstruction of the lymph channels* at various points.

The possible damage to these channels, — to the walls of lymphatic vessels and sacs and spaces, through development of fibrous tissue in the active stage of syphilis, has already been explained to you. The coincidence of antecedent syphilis, of the development of this cica-

¹ Rindfleisch, Path. Hist., page 94, section 77.

² Stricker.

tricial tissue in the line of the lymphatic distribution, and apparently in proportion to its richness; the coincidence of the aggregation of purely lymphatic elements as the condition preceding the cicatricial formation (as in the testicle); the coincidence also of the entire absence of any injury to the affected organ except that which results from purely mechanical causes, will, I think, warrant us in claiming, at least as far as syphilitic degeneration of the testicle is concerned, that there is no necessity to invoke the influence of a taint in the blood in order to obtain an explanation of its occurrence. When at a later period we come to consider the treatment of this and allied affections, it will be found that the only agents which are accepted as most efficient, or which are at all efficient in preventing their occurrence, or of arresting their progress, are just and only those which are known most potent to prevent, arrest, or dissipate new formations, normal or abnormal, which occur independently of the syphilitic influence.

In support of the views just advanced in regard to the formation and behavior of the gummy and cicatricial deposits in the testicle resulting from syphilis, I will quote from a recent authority¹ an account and opinion of similar pathological conditions occurring in the liver.

DEVELOPMENT OF THE GUMMA OF SYPHILIS.

"*The first phase* consists in the proliferation of connective tissue or of an analogous tissue. . . . In syphilitic interstitial hepatitis the proliferation of cells of the connective tissue takes place not only between the hepatic islands, but also in their interior, along the capillaries, and up to their entrance into the central vein. . . . This formation of embryonal tissue takes place either throughout the organ or in limited points. . . . The new tissue, which accumulates in masses, becomes riddled with numerous vessels. *Then commences the second stage of the development of gummata.* The cells multiply, diminish in size, are compressed against each other, and there are thus produced little nodules or irregular islands, in which the *central* cells are atrophied and granular (from pressure?), while the *peripheral* cells are more voluminous and *present the character* of embryonal cells (because freed from pressure?). . . . Then in regard to "gummatous nodules which have undergone degeneration:"² "One might at first sight believe that these groups of fatty granules correspond entirely to the *plasmatic cells*, but, studying more closely, we see that many belong to *spaces*, more or less lengthy and sometimes wide, *which represent the disposition of the lymph canals* in the fibrous tissue, and we are right in concluding that the spaces filled with these groups of fatty granules are *lymph vessels* stuffed with the fat result-

¹ Cornil and Ranvier, American edition, 1880, page 110.

² Ibid, page 112.

ing from the decomposition of the morbid mass. . . . It is by means of the *lymph vessels* that the products of the decomposition of the nodules are absorbed, when, after yielding to *proper treatment* or to the *processes of nature*, the gumma diminishes."¹

I shall now call your attention to another variety of lesion, also characteristic of the influence of late syphilis.

CASE XV. This patient's age is fifty years. He has a clear history of syphilis of twenty years ago. His appearance indicates a generally bad condition. Somewhat emaciated, his dusky complexion and his anxious expression, and a previous history of syphilis, would lead us to look for syphilitic degeneration of the liver or kidneys or both. When we find such a condition as his associated with visceral disease due to syphilis, we call it *syphilitic cachexia: innutrition* occurring, not from any *virus* circulating in the blood, but from functional incapacity of the organs affected, and due to the so-called gummy deposit, or infiltration, in various stages of its development. This man's health and habits have, by his own account, been bad for several years. He has suffered from no local pain except occasionally in his back, and this he is not able to localize sufficiently to indicate any special trouble. Examination by percussion and palpation, over the right hypochondrium, shows that the liver is diminished in size. I cannot positively make out any irregularity in its form or consistence. Gummy tumors may be present for years, in similar cases, without creating any marked local or constitutional disturbance, and even subsequent cicatricial contraction may go on to a considerable extent without much constitutional suffering. Again, in a case like this the contraction of the liver may be due to alcoholism. If the trouble in the liver is, in considerable measure, due to gummy infiltration or localized deposits, which have not yet undergone the cicatricial change, we may hope for improvement by use of remedies, previously spoken of as appropriate for removal of new formations. If, however, cicatricial tissue has formed, *from whatever cause*, the probabilities are greatly against any marked improvement.

This patient is presented, however, chiefly to illustrate the behavior of "gummy deposits" in bony structures. He shows us here, on the right parietal protuberance, a swelling or tumor about the size of half a pullet's egg, very dense in structure and resistant to the touch, like other parts of the cranium. Besides this, at the vertex, on removal of the carbolated dressing, you may observe that complete destruction of the scalp has occurred, for the space of a full square inch. The external table of the skull is also gone, as well as the diploe, and as I pass my probe under the overhanging edge of the scalp, I find that the bone is destroyed for a half inch beyond the

¹ Italics are my own. — F. N. O.

apparent size of the ulcer; yet, as you see by its rosy, sloping edge, it is healing. About a month since, when this patient first came under observation, the ulcer was at least twice its present size, and presented an abrupt and ragged edge, and the cavity filled with fetid pus. This improvement has apparently resulted from treatment which I will explain to you later.

According to the patient's account, his bone lesion came almost imperceptibly, as a swelling, without tenderness, about three years ago, and remained unchanged until a few months since, when, after a heavy drinking bout, it began to be sensitive, and finally softened down and discharged a quantity of matter.

We may reasonably infer that this destructive process was preceded by a condition similar to the swelling on the adjacent bone, to which attention was first directed, and that the insensitive bony swelling and the destructive bony lesion are but stages of the same trouble. These inferences are in complete accord with what is known in such cases. It is furthermore shown that, in similar cases, true bony material is exuded, or accumulated, and organized, under the influence of mysterious conditions following syphilis (anywhere from one to fifty or more years), and that such overgrowth may occur at any point in the osseous system, or it may rise up under the periosteum of one of the long bones, as the tibia or the humerus, and appear as a distinct bony tumor, and remain as such, for years, without causing great inconvenience; or it may originate in the substance of the bone as in the present instance, and after a long quiescence break down into a bony abscess within a few weeks or even days. Examinations of these lesions in every stage have shown that they are made up in the first place of simple collections of germinal material, identical in nature with that forming the gummy tumor of the soft tissues. The cells become organized, in some instances, into solid bony material, especially when external pressure is slight; in others, where the "gummy material," that is, "*accumulated germinal material*," is deep seated, the pressure causes atrophy of bone, bony loss taking place just as loss of cellular tissue was explained in the tubercular syphilide, *without ulceration*. Again, in others the material breaks down from irritation caused by the pressure, and under influences such as lower the resisting powers of the patient, and the newly organized material melts away into pus and the débris of disorganized tissue.

It will be seen, then, that in these three modes of action of the gummy deposit in bone, we have nothing to suggest any destructive property or virus *per se*; nothing to militate against the application of the same explanation that was offered to account for the gummy tumor and other forms of gummy deposit in the soft tissues, namely, simple obstruction of the lymphatic vessels of bones in this case, the

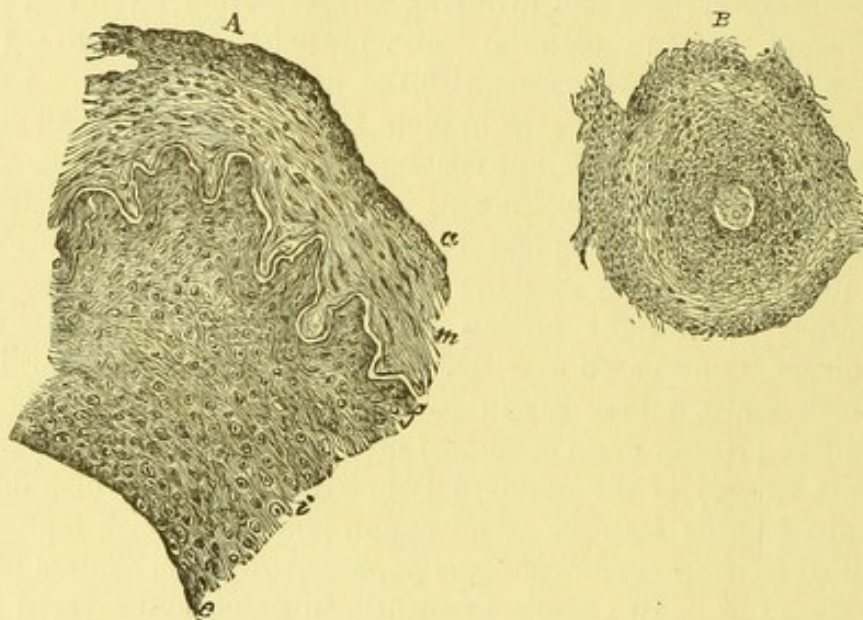
results varying, from circumstances of location and from condition of the subject. Destruction of the tissues implicated, in such cases, never occurring except from mechanical pressure, either acting as an interference to nutrition directly, through *pressure*, or through pressure upon blood-vessels supplying the part. The fact that the same treatment which has been found successful in *treatment* of gummy tumors and infiltrations of the soft tissues is equally efficient in lesions of bones, due to late syphilis, is in support of such a view.

It will be seen that the affections of the so-called tertiary or late stage of syphilis affect various structures, and that their destruction, as far as we have found any explanation for it, has been the result of purely mechanical causes. The cases, however, which have been presented up to this time have not been characterized by the extensive losses of substance, rapid and involving various tissues, often met with. Infiltrations of "gummy material" may indeed be invoked to explain such losses through interferences with the nutrition of parts. Examples of such destruction are seen in plate 16 on my right, which represents the serpiginous ulcerations characteristic of late syphilis, where the entire thickness of the integument is shown to have been destroyed from knee to ankle. In plate 17 — representing what are called *rupetic* ulcers, some fully as large as a silver dollar, and presenting an appearance as if some foreign body had sloughed out — several smaller ulcers are also seen near by, covered with thick sienna-colored scabs, which scabs, I may say in passing, apparently the product of the ulcerative process, when examined under the microscope, are found to be made up only of disorganized lymphatic elements which do not present any specific feature. And again, plate 18, which represents the so-called *tertiary syphilitic impetigo*, a superficial ulceration of the skin the size of your two hands, crescentic in shape and covered here and there with a thick, crust-like scab, while alongside of it is represented an ulcer which has destroyed the integument and the underlying cellular tissue to a considerable depth. Here, again, at plate 19, is an ulceration with profound loss of substance at the ankle, and still another, No. 20, which represents loss of the soft and hard palate, and implicates the fauces.

Now I want not only to show you, by these and other examples, that destruction from the influence of syphilis, occurs at any point where lymphatic vessels are present, — in other words, at any point to which nutritive material is carried; not only to the skin, the cellular, muscular, bony, and even cartilaginous structures, but to every part of the brain and nervous system. I want also to say at this point, that the behavior of tissues and structures infiltrated with the so-called gummy material of syphilis, in all forms in which it presents a destructive result, shows nothing, either by inoculation or by any

physical property, which proves it capable of acting except by the mechanical influence of its presence, by interfering with function and cutting off nutrition, through diminishing the calibre of blood-vessels, or possibly effecting entire obliteration of such vessels.

In this connection the statements of Cornil and Ranvier in regard to what is termed *tertiary* degeneration of arteries — certain changes recently described by Huebner as characteristic of syphilis — may be introduced in illustration of the foregoing statements: "These changes have been recently brought prominently before English pathologists by Drs. Greenfield and Barlow and others, and the investigations of the first named of these observers would tend to render it probable that similar changes occur in arteries in other situations. In the cere-

FIG. 182.¹

Syphilitic Disease of Cerebral Arteries. A, segment of middle cerebral artery, transverse section; *i*, thickened inner coat; *e*, endothelium; *f*, membrana fenestrata; *m*, muscular coat; *a*, adventitia. $\times 200$, reduced $\frac{1}{2}$. B, small artery of pia mater, transverse section, showing thickened inner coat, diminished lumen of vessel, and considerable infiltration of adventitia. The cavity of the vessel is occupied by a clot (? thrombus). $\times 100$, reduced $\frac{1}{3}$.

bral arteries the changes produce *opacity* and *marked thickening of the vessel, with considerable diminution in its calibre*. It is this diminution in the lumen of the vessel which is especially characteristic.

"When transverse sections of the vessels are examined microscopically the principal change is seen to be in the inner coat. This coat is considerably thickened by a cellular growth. The growth, which is limited internally by the endothelium of the vessel (Figure 182, A C) and externally by the membrana fenestra (Figure 182, A f),

¹ Cornil and Ranvier, *Pathological Histology*, American edition, page 331. Electrotypes through favor of Mr. Henry C. Lea, publisher American edition.

closely resembles ordinary granulation tissue, *consisting of numerous small round and spindle-shaped cells*. This tissue appears gradually to undergo partial development into an imperfectly fibrillated structure. In addition to this change in the *intima*, the *outer coat* is unusually vascular and *infiltrated with small cells*, and *this cellular infiltration usually also invades the muscular layer* (Figure 182, A m). The result of these changes in the inner coat is to diminish very considerably the lumen of the vessel (Figure 182, B), and the consequent interference with the circulation *frequently leads to coagulation of the blood, thrombosis, and cerebral softening.*¹

Dr. Greenfield's observations, as already stated, tend to show that similar arterial changes occur in other parts, and that they account for the degeneration of the syphilitic gummata.

A case of syphilitic intercranial disease, with cerebral softening, is reported in the *American Journal of Medical Sciences*, 1875, vol. ii., page 432, by Dr. Stedman, of Boston. Prof. Robert T. Edes describes the microscopical appearances of the diseased cerebral arteries in this case on page 435 of the above-named journal, as follows:—

"Sections were made of the thickened arteries. . . . The best starting-point in the examination of these sections is the muscular coat, which presents a normal appearance. Externally we find a layer of many cells, mostly round or oval, but in many places surrounding the muscularis, and evidently replacing or representing the adventitia. There is, however, no distinct limitation; but the accumulation of cells spreads out upon both sides into the pia mater, and sometimes embraces many smaller vessels. At the point of contact with the artery with the cerebral surface, and opposite to this, the cellular layer is less thick, and probably here represents, pretty accurately, quantitatively, the adventitia.

"Internally to the muscular coat, joining sometimes a ring of uniform thickness, and sometimes much thicker on one side than another, we find the intima composed of parallel bundles of tissue with circular and oval spaces. Many or most of these spaces are occupied by a body which probably represents a nucleus. The spaces are more abundant and larger at the edge nearest the lumen of the artery, and farthest from the muscularis. In some places these spaces or cells present very much the appearance of several irregular layers of epithelium lining the artery. The inner portion of the intima is stained with blood. Where the intima is most hypertrophied *the lumen of the artery* (if we regard the circular fibres of the muscularis as occupying the normal position) cannot exceed one half its former diameter or one fourth of its former area. Immediately beneath, the artery, imbedded in the cerebral substance, appeared, as it were, crowded,

¹ Italics my own.—F. N. O.

the outer layer being no longer distinguishable at this point, and the cellular elements being increased in number.”¹

Thus it will be seen that the *degeneration of arteries* from syphilitic influences, according to recent eminent authorities, consists in an antecedent accumulation of cells and growth of new fibrous tissue *at the points of degeneration*, — fibrous tissue not distinguishable, either in its cell elements, or the fibrillæ developed from such elements, from normal productions, and that, through this, of necessity, the blood supply is diminished, and that the occurrence of thrombus is favored at the contracted points. There can scarcely be a question that, occurring as a recognized sequence of the same trouble and in the same period which produced in the liver a similar cell development, resulting in cicatricial contractions of that organ, the fibrous tissue thus developed in the coats of the arteries had a similar origin. It is true that the lymphatic channels in the coats of arteries have not yet been practically demonstrated, and yet it will be remembered that Recklinghausen says (page 5) that “*the adventitia of the blood-vessels is in part to be regarded as belonging to the lymphatic system* ;” but if, as claimed by Rindfleisch, the office of the lymphatic system is to return from the tissues nutritive material, tissue-fluid, and white blood cells, exuded by the blood-vessels in excess of the necessities of growth and nutrition, then we must admit the existence of lymphatic channels *in every tissue*. It is scarcely ten years since their existence in bones was denied by all histological authorities, but since then Ludwig and Schweigger-Seidel² have demonstrated their presence in cartilage, and Thin,³ has furnished a chart of lymphatics of the cornea.

It may be now claimed, I think, that the evidences which have been adduced in proof of the important part played by the lymphatic system in the early and late periods of syphilis will warrant further investigations into the histology and pathology of that system. With newer discoveries we shall, I believe, find the demonstration of causes of syphilitic trouble, in regard to which, at present, we are obliged to depend for solution upon analogy, treatment, and the lack of any other way of accounting for them. Syphilitic disease of the brain, for instance, is now usually considered as resulting from the deposit of gummy material in its substance, and so it may be proven by plenty of post-mortem evidence ; but softening of the brain, independently of the recognized presence of gummata in that organ, would not suggest a syphilitic cause. By analogy, however, the disease — first the gummous,

¹ In a recent note from Professor Edes (August 20, 1880), he says : “The section from a cerebral artery described by Dr. Stedman and myself in the *Journal of American Sciences*, 1875, shows the proliferation, not only of the *endothelium*, but of the *adventitia*. . . . My description was printed before I had seen or heard of Heubner's work on the syphilitic diseases of the cerebral arteries.” — F. N. O.

² Leipsic, 1872.

³ London Lancet, February 14, 1874, page 225.

then the fibrous deposit — might be in the coats of an artery supplying a large tract of brain substance, interference with the calibre of which, and consequent innutrition of the tissues it was designed to nourish, would eventuate in a case of as extensive cerebral *ramollissement* as could be met from any other cause. In the same way loss of every kind of tissue might be reasonably accounted for, wherever gummy deposits are located in the coats of vessels. A destructive agent of the most positive character and wide-spread influence, is thus added to the simple processes of atrophy, and localized strangulation of vessels of nutrition, from mechanical pressure, resulting in more or less rapid local necrosis of tissue.

The measures for relief and cure of syphilis, logically suggested by the foregoing views of its nature and behavior, in its various stages and phases, will next be considered.

LECTURE VII.

TREATMENT OF SYPHILIS.

GENTLEMEN, — Having illustrated the development and progress of syphilis through the clinical cases presented, from the initial lesion, in its varieties, through the active or so-called secondary stage of the disease, in all its typical manifestations; having, still farther, studied with you its influence in connection with the so-called tertiary or later effects of the disease, I desire now to recall the significant fact, that, in regard to clinical history, physical appearances, and pathological conditions, as far as we have been able to appreciate them, all have been found in complete accord with the position heretofore taken by me, claiming the simple nature of the syphilis. Simple, in that it is the result of causes and conditions arising chiefly, if not solely, from undue activity of natural processes; in short, a hypergenesis of germinal matter. The varied lesions of syphilis occur, in this view of the case, as the natural mechanical sequences of a localized accumulation of the superabundant germinal material in the affected organism. This, it will be seen, is wholly opposed to the supernatural view of syphilis, heretofore and at present supported, or tacitly admitted, by all writers on the subject, up to the present time. With them, the so-called SYPHILITIC VIRUS, plays the leading rôle from first to last; its origin enshrouded in mystery; its action miraculous. It is accepted, by weight of authority, as pervading the entire physical organism at the instant of contact, independently of all known physiological laws, and often not seriously implicating the general health of the person affected. Unappreciable

to the senses, and eluding the most skilled and painstaking microscopical research, it is yet accepted as a vicious physical entity, a sort of corpuscular devil, which speeds through any and every tissue, depositing seeds of the multiform lesions of syphilis, warranted to bear fruit in due time, and unmistakably branded with the cloven-foot. This is the conventional idea of syphilis, — practically if not literally — and the theory of the treatment of the disease (when any theory is claimed), is based upon grounds not less unphilosophical, not less unscientific, than the popular conception of the syphilitic virus. The theory of the *virus* once accepted, *antidotes* are naturally in demand. Every remedy which aids to cure, or favorably modify, an attack of syphilis, becomes an antidote of greater or less efficiency. The mode of its operation is not important, the result alone is of interest. This was the case in the fifteenth century, when mercury was first claimed as an antidote to syphilis. It is of historical interest to know it was so vigorously used, as an antidote, then, and from time to time since, that, while often recognized as producing beneficial results in the treatment of syphilis, it was alleged by many distinguished contemporaneous writers to have done more harm than good. But with all the abuse which has been heaped upon it, much of it well deserved, we find as late as 1874, in the great discussion on syphilis which took place before the Clinical Society of London, in January of that year, Mr. Jonathan Hutchinson, senior surgeon of the London Hospital and one of the most distinguished of living authorities on syphilis, distinctly claiming that "mercury is a true antidote to syphilis." Thus he says:¹ "I will at once express my belief that the drug is a real antidote for the poison, and that, if it is carefully and fully employed, it is capable of procuring the complete extinction of the malady." Mr. Hutchinson then goes on to explain what he means by the term *antidote* in this connection. "By an antidote we mean something which not merely conceals but which counteracts and neutralizes. A chemical antidote effects a combination and produces a harmless compound. A vital or physiological antidote in all probability kills. It is in this sense that I wish to use the term as applicable to mercury in its relation to the living syphilitic virus." He then goes on to say: "The facts that we possess seem to warrant a belief that it (mercury) really destroys *it* (the syphilitic virus). That *it* prevents *its* breeding in the blood, if that process have not already taken place, and, if *it* have, cuts short *its* life in the tissues."² I have thus quoted Mr. Hutchinson's views on the treatment of syphilis, because he is accepted at home and abroad as a great clinical authority; one who, perhaps, more than any other English-speaking

¹ London Lancet, January 17, 1874, page 87.

² Italics my own. — F. N. O.

writer, is claimed to represent the present status of syphilitic science.

Mr. Hutchinson's conclusions in regard to the action of mercury as a "real antidote to the poison" of syphilis, it is proper here to state, are based upon purely *clinical* grounds. He accepts the virus of syphilis as a distinct entity, on traditional evidence, and without comment. *Clinically*, in his experience, mercury "*prevents it (syphilis) from breeding in the blood, if that process have not already taken place, and if it have, cuts short its life in the tissues,*" and yet Mr. Hutchinson does not attempt to explain or even to suggest what is the "it" which he calls syphilis, except that it is a *living virus*. Mr. Hutchinson speaks of mercury "preventing syphilis breeding in the blood," and by the same means "its life is cut short in the tissues." The virus is then at times in the blood and in the tissues, but whether as an independent, living animal organism, *sui generis*, or a vegetable spore, we are left to conjecture. We are only told that whatever it is, mercury is its antidote. In his able and extended clinical observations Mr. Hutchinson has recognized the fact "that in practice a good many cases are really cured by mercury; the cure being proved by the restoration to good health, and in some cases by renewed susceptibility to contagion." We are also told "that many cases of indurated chancre, treated early by mercury, never show any of the characteristic symptoms of the secondary stage." "That when mercury does not wholly abrogate the secondary stage, it exhibits a remarkable power in delaying it," etc.

These conclusions, with others, resulting from his clinical experience, have induced Mr. Hutchinson to claim and to teach that "mercury is a true antidote to syphilis." It is evident, however, that it is not an antidote in any true sense, and for the reason, among others, that (as claimed by Mr. Lucas, of London, also an authority in such matters)¹ "in most known antidotes the remedy bears some definite relation to the poison it modifies, or at least if added in quantity to the virus it may be expected completely to destroy it; but in syphilis, the continuous administration of mercury for months fails to destroy the poison, so that some consider it desirable to continue the drug for two years after infection." Mr. Hutchinson himself says² that "in order to secure the antidotal efficacy of mercury against syphilis, it is desirable to introduce a considerable quantity into the system, and to protract its use over a very long time," and "that ptyalism and other evidences of the physiological action of mercury, so far from being beneficial, are, if possible, to be carefully avoided, since they prevent the sufficiently prolonged use of the remedy." In any case, it is quite clear that no

¹ London Medical Times and Gazette, January 31, 1874.

² London Lancet, January 31, 1874, page 159.

advantage has been gained by the assumption of Mr. Hutchinson that "mercury is a true antidote to syphilis." No indication of any practical value is suggested by it, in the treatment of the disease, that had not already been acquired from clinical experience. On a previous occasion, the venerable and renowned syphilographer, M. Philip Ricord, announced before the Clinical Society of London the conclusions to which his clinical experience had then brought him, namely, that *the cure of syphilis was possible ; but only through the systematic administration of small doses of mercury, always falling short of ptyalism, and continued for at least one year.* This without any suggestion of the manner in which the mercury was supposed to act. He had found out this plan by careful experiment and intelligent observation. Mr. Hutchinson was led to the same conclusion and plan through the same or similar influences. The suggestion, or claim, that mercury acts as an antidote to syphilis was, then, without value in a practical point of view, and was objectionable, inasmuch as, under the influence of such an idea, the temptation to over-dose with mercurials would always present itself, unless the practitioner had been chastened by a long and intelligent practical experience. Bäumler, a distinguished and recent German authority, is inclined to accept the antidotal view. Thus he asks,¹ Are there remedies which act as direct antagonists to the virus of syphilis ? and he answers, "in accordance with the experience of the last three centuries in the treatment of syphilis, the answer to this question must be, that *mercury appears to be such a remedy ;*" but a little further on ² he says "the intimate nature of its action is still veiled in obscurity."

My object in calling your attention thus specifically to the teachings of these recent eminent authorities, is twofold ; first, to bring you to appreciate the great value in which the mercurial treatment, first begun over three centuries ago, is still held ; second, to show that this valuation has resulted from clinical observation alone, and not from any real knowledge or appreciation either of the true nature of the syphilitic virus, or the manner in which the curative changes, recognized as following its judicious use, were effected. In other words, the present mode of its use, as determined most judicious, and commended for general adoption, by M. Ricord, Mr. Hutchinson, Herr Bäumler, and all who accept their teachings, is still experimental and thus without scientific basis. *Mercury is administered because experience has shown that it cures syphilis.*

What we require now, in order to make this knowledge scientific, is an explanation of its action, based upon the known powers of mercury in its relations to living organisms and tissues, and an appreciation of the true nature and composition of the material which constitutes

¹ Ziemssen's Encyclopædia, American edition, 1875, vol. iii., p. 275. ² Ibid, page 278.

what we call syphilis. After a varied experience of over three centuries, clinical experience has failed, eminently, in affording us this knowledge. Every clinical effort to penetrate the mysteries of syphilis, through the assumption of a virus, has proved futile. Modern science has applied the microscope in search of a syphilitic virus, and has become weary with its failures to discover a specific material or organism as its representative. Occasional suggestions that syphilis might, possibly, exist independently of any specific property or virus, may be found in medical history. Broussais, the founder of what was known as "the physiological school," in France, made a profound impression upon the profession at large, by denying (in accordance with the doctrines of his school) the existence of a virus in syphilis, and claiming that the treatment suitable for ordinary inflammatory affections was sufficient for the treatment of syphilis. Eminent medical men in Germany and England have also, from time to time, practically supported this view, and condemned the use of mercury in the treatment of syphilis. But the denial of the existence of a specific virus by Broussais and his followers was based upon purely theoretical grounds, and did not furnish any logical explanation of the nature or peculiar characteristics of the disease. The only practical result attained by this school was (through elimination of mercury from the treatment) to demonstrate that persons affected with syphilis might recover without the use of mercury. Mercury, as a power to aid in curing the disease, although in abeyance at times to some extent (by reason of injudicious use of the drug, and the fact that in accordance with Broussais's claim the disease would sometimes go on to recovery under simple treatment), has nevertheless retained its reputation, and as a remedial agent is, at the present day, esteemed by the most experienced and judicious surgeons and medical men, throughout the world, as the remedy of greatest value in the treatment of syphilis. At this point, gentlemen, I would like to suggest, that, in full agreement with what has been said in regard to the nature and behavior of syphilis, it appears to me quite possible to accept the foregoing statement as to the value of mercury in the treatment of syphilis, and this, too, without accepting the assumption that mercury, in its curative effect on syphilitic disease, acts as an antidote to the so-called syphilitic virus.

A pregnant suggestion, in regard to the mode in which mercury may act in curing syphilis, is made by Mr. Clement Lucas, in the *London Medical Times and Gazette*, of January 31, 1874, in a reply to Mr. Hutchinson's claim that mercury acts as an antidote in syphilis. After remarking that even Mr. Hutchinson considered that the continuance of the mercurial treatment for a year might be necessary to obtain security against a relapse, he says: "During all this time the remedy circulates through the tissues containing the poison, yet fails to eradi-

cate it, so that on omitting the remedy the symptoms again appear." "Surely," says Mr. Lucas, "the facts are far more consistent with the hypothesis that mercury attacks only the effects of the syphilitic virus which in time exhausts itself upon the tissues: that, in fact, the action of the drug is to *disencumber the tissues of the products of a specific inflammation*, and in this way to bring about an apparent and perhaps a permanent cure."

We have a work here suggested, which is eminently in the line of the recognized power and influence of mercury, namely, to *relieve tissues encumbered with superfluous and obstructive material*. The question as to whether this material may be properly designated as "the products of a specific inflammation" is not important for us to raise at this time; or whether it is, strictly speaking, the effect of a virus or not is not now at issue. Of one thing we are certain, and that is, of the power of mercury in hastening metamorphosis of tissue, of bringing about a fatty degeneration, and thus favoring the elimination of living animal material, normal and abnormal. We know that while tissue change is favored by various conditions — by various medicines — mercury stands at the head of the list as an agent in effecting it. Consequently, if we had the tissues in syphilis encumbered with superfluous and obstructive living material, of whatever character, the only way known to science whereby it could be physiologically eliminated would be through a tissue metamorphosis which mercury in various forms is best capable of inducing. In such case the mercury would still remain the remedy *par excellence* in the treatment of syphilis; not with the purpose of antidoting a virus, which may or may not have produced the difficulty, but with the legitimate and scientific object of adapting the best known means to the accomplishment of an intelligent purpose.

It is hardly necessary for me to remind those of you who have followed this course of lectures from their commencement, that the first evidence of syphilitic action, in all cases, is the accumulation of superfluous living material in the tissues; that the first evidence of its effect, as shown you in repeated clinical instances, is in *encumbering the tissues*; producing in the initial lesion, by simple, mechanical pressure caused by its presence, the various interferences with nutrition which result in the different appearances, and grades of necrosis, which are found characteristic of the initial lesion of syphilis. What has been presented to you clinically has been illustrated and enforced by the results of microscopic examination by able and distinguished scientists. I propose, now, to put a practical point upon this view of syphilis, by directing your attention to an uncomplicated initial lesion in this young man, whom you may indicate in your note books as —

CASE XIV. The exposure in this instance was about four weeks

ago. On the morning following he noticed a slight chafe just within a somewhat redundant prepuce. This healed promptly under the use of a little simple dressing, and no further attention was paid to it until yesterday, when this little hard lump, about the size of a small pea, was discovered. It is, as you see, quite free from inflammation; insensitive to the touch; movable in the loose cellular tissue of the prepuce. This, in connection with a suspicious exposure a month ago and several enlarged and painless glands in either groin, warrants us in considering the nodule, although entirely free from tissue necrosis, an initial lesion of syphilis; here we again see that the process of ulceration is not essential to the initial lesion of syphilis. Having settled this point, the next is the question of treatment.

In the first place, we can assume that there is not the least doubt of the sort of material making up this nodule. The microscope has settled that. It is made up of cells closely packed in the tissue, so that with the development of perhaps a few of the best of them, into connective tissue, the mass is indurated in a characteristic way. The bulk of the little tumor is composed of cells which are possessed of the capacity to infect with the peculiar syphilitic influence. I have alluded on a previous occasion to the fact that all cells are capable of a sort of infection, an influence which may be exerted favorably or unfavorably when brought into contact with other cells.¹ In this case the cells have proliferated hastily and in excess of the necessities of nutrition of the part — hence the accumulation; hence, also, the induration. The effect, then, of contact of the hastily generated cells composing this nodule, with healthy white blood cells, such as they would always come into contact with, when applied to any living human tissue, is found to be to induce them to a similar hasty proliferation. This, I desire distinctly to be understood as claiming, is all there is of the so-called virus of syphilis. It is an *influence* and not a material substance. Cells *degenerated*, impressed in some unknown way with the tendency to hasty development: living too fast, they lose, in greater or less degree, their formative capacity — their ability to develop into useful tissue; their natural infective power is increased with their degradation, and this power or influence is no more a material virus than that through which a vicious human being exerts a pernicious influence upon those with whom he is brought into contact. This position is amply fortified by the results of microscopical and clinical observation. As a natural consequence of the proliferation of such degraded cells, we find them heaped up in the tissues at the point of first introduction, what we term the point of *inoculation*; and the first result, capable of clinical appreciation, is a nodule like the one under consideration. We call it the *initial lesion*

¹ See page 43.

of syphilis. If there is anything more of this initial lesion than what I have just told you, it has not been demonstrated, and the claim to it is based upon the purest conjecture. What we have now to deal with, practically, is the accumulated mass of cells composing the initial lesion. This view of the case has been virtually supported by Auspitz, in 1877, and Kölliker, during the last year (1878), who claim to have prevented systemic infection by excision of the initial induration, in some cases, and modified the course of the disease in others. This Auspitz very naturally regards as a proof that "*the initial sclerosis is not a pathological result of a preëxisting general systemic infection, but a starting point, or an original depot for the infective material by which syphilis is transmitted.*"

The number of cases reported by Auspitz and Kölliker, some forty in all, do not, however, seem to me to be sufficient to warrant any positive claim to the prevention of general infection, by excision of the initial lesion of syphilis. The manner in which infection takes place (any moment after which, might carry an infected or degraded cell into a lymph vessel and thus out of reach) would appear to render it, at the least, highly improbable that every infecting cell could be removed by removal of the initial lesion. But the procedure is in complete harmony with our view of the case, and it is what I practice, when agreeable to the patient, and advise, in all cases when the initial lesion is situated upon, or in, loose tissue, as in the present case. Under favorable circumstances, as in this instance, the operation is a very simple one. Thus: the indurated mass is raised between the thumb and finger and encircled with a bit of fine silver or malleable iron wire, being careful to include the entire induration. Now, with a narrow, sharp-pointed bistoury, pierce the tissues at the centre, beneath the compressing wire, and cut well under and out, including all the induration and a little of the sound tissue. Then, reversing the knife, the remaining half of the nodule is excised, again also carefully including a little sound tissue, so as to make sure of getting rid of all the indurated material. Three or four interrupted silk sutures secure perfect coaptation of the edges of the wound, and we may confidently expect union by first intention. In about a dozen operations of this sort, I have never failed to obtain union by first intention. Under similar conditions, the operation is equally applicable to *open* initial lesions. As illustrative of one of the collateral advantages of this mode of treatment, I will cite the case of a gentleman who came to my office some time since, presenting a typical initial lesion, on the loose tissue, just behind the *fossæ glandis*. The induration was as large as an almond, and the tissue necrosis had excavated a space in it the size of my thumb nail, and a quarter of an inch in depth. He had been under local treatment for this nearly

three months. His constitutional symptoms had been progressing favorably under a mild mercurial course, but the sore refused to heal. A cable despatch received from his wife, the day previous, announcing her intention to take that day's steamer for home, had occasioned a somewhat sudden determination to solicit change of treatment. After thoroughly cleansing the lesion and bathing it with a five per cent. solution of carbolic acid, I excised the entire mass, closed the wound with half a dozen sutures, applied a simple carbolated dressing, and sent him home, with directions to keep the recumbent position for three days. At the end of that time I removed the stitches and found union by first intention throughout. By the time of the arrival of the steamer there was not the slightest trace of ulceration or induration, and a faint red line alone indicated the site of the former trouble.

Now, if the syphilitic material were always within reach of the surgeon's knife, the treatment of it would be greatly simplified. Unfortunately, in even the cases where we can remove the initial lesion *en masse*, the same degenerated cell material, which alone constitutes it, has found its way, in the manner previously described to you, into the adjacent lymphatic channels and glands, inevitably destined to gain access to the general system in quantity, greater or less, according to the peculiar circumstances and idiosyncrasies of each individual case. Notwithstanding, then, that we may successfully remove the initial lesion of syphilis with the knife, and by this means, as I believe, favorably modify the subsequent course of the disease, it is still necessary to use other measures in order to eliminate the remaining degenerate cell elements from the system.

With the acceptance of the material views of syphilis as here taught, every manifestation during the active stage of the disease, excepting the syphilitic roseola (which has been claimed as a physiological phenomenon), is just as much the result of the mechanical presence of a vitiated cell accumulation as is the induration, and the consequent different grades of necrosis of the initial lesion, in its varieties. What we want then for the treatment, — for reducing, in the first place, these enlarged inguinal glands, for instance, — is some means or measures capable of breaking down and eliminating this newly-formed germinal material which makes up the enlargement; in other words, we require some agent capable of hastening the tissue metamorphosis, by which means alone it can be removed from the affected system.

Mercury has been shown to be such an agent, and we administer it here, not in an empirical way, as an antidote to a hypothetical virus, but, in accordance with known scientific principles, for the distinct purpose of effecting the disintegration and elimination of the cell ele-

ments, which alone have been recognized as the source of trouble. Clinical experience has taught us that small doses of mercury, administered for a long period, is the mode of treatment which has proved most effective and harmless. Scientific deduction from the conditions, presenting in every lesion during active syphilis, *as shown by the microscope*, and the known nature and powers of the proposed remedy, bring us logically and inevitably to the same conclusion. We have, for instance, an excess of living cell material encumbering the tissues. Material hastily generated, and hence holding its life by a feebleness of tenure than healthy living cell and tissue material. We have also an agent acknowledged to stand first in its power to hasten tissue metamorphosis, to bring about the fatty degeneration of healthy tissue. Paris, in his *Pharmacologia*, informs us that the characteristic effect of mercurialization upon a healthy person is an excessive flow of saliva of a peculiarly fetid character, and that this fœtor is due to the decomposing fat, which has resulted from the rapid tissue metamorphosis which the mercury has induced. If, then, mercury is recognized as effecting the fatty degeneration and decomposition of *healthy* structures, we may readily accept it as in a higher degree capable of effecting the same result in material of similar nature, but degenerated, and hence with less power of resistance. It is at once seen, that such an amount of mercurial as would effect the metamorphosis of the hastily generated and weaker material, might fail to affect the normal healthy structures in any appreciable degree. And it must also be equally apparent, that such an administration of the agent as would strike just this happy medium, would constitute a treatment of the highest excellence. We are led thus, at once, and logically, to precisely that method of prescribing mercury, in the treatment of syphilis, which the most experienced and wisest of our profession have been years in arriving at. It only remains to test by actual experience the amount of mercury which can be borne without damage, in a given case, to know the most judicious and effective way of curing the disease.

Again, by arriving at this plan of treatment not empirically, but as the legitimate result of scientific deduction, we are not tied to a single remedy which experience has shown to be beneficial, or which is warranted to act as a specific, an antidote, or a tonic in the cure of syphilis. It is the principle which guides us, and upon this principle we make legitimate use of other agents which are of known power in inducing tissue metamorphosis, such, for instance, as the iodide of potassium, which by a curious coincidence, second only to mercury in its known power of setting up fatty degeneration, is also second only to it, in the estimation of the highest authorities, in its curative influence on syphilis; and again, when, on account of condition or idiosyncrasy, the system of the patient is found to be wholly intolerant of the use of

mercury, or the iodide of potassium, other medicines and means, which are known to act more or less efficiently in hastening tissue metamorphosis, are naturally suggested.

It is a significant fact, and one which gives great strength to our position in this matter, that every medicine or mode of treatment, which during the last three centuries has found even temporary favor in the treatment of syphilis, is now recognized as of value, greater or less, in hastening tissue metamorphosis.

Thus the ancient sweating cure by use of decoctions, which was in vogue during the whole of the sixteenth century,¹ and is still esteemed in various countries; and also by baths in conjunction with other remedies, as at the Hot Springs of Arkansas; so justly famed at the present day; the starvation cure and treatment by laxatives; greatly employed by the Portuguese to the exclusion of mercury; in fact, the treatment chiefly by purgatives, as the "Zittman's decoction," is esteemed by the Germans. Then the *syphilization* cure, of which Professor Böck was the great exponent—and in opposition to this, the tartar emetic or so-called *tartarization* cure,—pustules in the former produced by inoculation of unhealthy (syphilitic or chancroidal) pus, and in the latter by the application of the potassio-tartrate of antimony. All these remedies and measures will at once be recognized as chiefly capable of inducing or hastening fatty metamorphosis, and hence, to a greater or less degree, would promise to be curative in syphilis.

In view of the weight of evidence, then, which has been brought to show the value of the mercurial treatment of syphilis, we shall find it advisable to prescribe it in the present instance. The evidence of syphilitic action is here distinctly present in the glands of the groin. At present there are no characteristic gland enlargements in the cervical region. While we can scarcely hope to prevent these, we can at least hope to modify favorably any subsequent manifestations of the disease, by the judicious use of mercury. Our usual formula in these cases is the one originally recommended by the late Professor Bumstead, namely, two grains of mass hydrarg., with one grain of the exsiccated sulphate of iron, made into a pill, three to be taken each day, one after each meal. At the end of a week we may find some evidence of the mercurial action in a slight sponginess of the gums. The patient will be directed to note such occurrence, and if it occur before that time, to omit the pills until we see him. Simple nutritious diet and avoidance of spirituous drinks and tobacco are advisable in all cases of syphilis, from the commencement to the termination of the active stage of the disease.

CASE XV. In this young man we have a clear history of a suspi-

¹ Bäumlér, Ziemssen's Encyc., vol. iii., page 279.

cious exposure four months since. He presents an open initial lesion, occupying the central part of the corona glandis; the induration, about the size of a half filbert, is perfectly characteristic; the inguinal glands are distinctly enlarged and painless, also those in the cervical and epitrochlean regions. He has here on his forehead, as you can see, and also on his breast and shoulders, papules, varying in size and of a coppery color, very much like Case VII. This is the papular syphilide previously described. As we examine his mouth we find several distinct mucous patches; simply a variety of papule before described. This patient may be said to be in the midst of the active period of syphilis. His treatment, according to his own account, has been very irregular and inefficient. The initial lesion, the gland enlargement, and the eruption are all well marked, also the mucous patches. It is of common occurrence to find these lesions present together and yet you will see many cases, where, in this stage, only the gland induration is present, as in Case XIV. Here I show you the initial lesion equally well marked, also the enlargements of the groin and cervical region. I also discover, in this case, a small mucous patch inside the mouth, near the left labial commissure. Now, in regard to treatment; with the exception of the local measures especially necessary in regard to the mucous patches, we shall prescribe just the same pill as ordered for the first patient, and for reasons that you probably already appreciate, but which I will again call your attention to on another occasion. The local treatment of the open initial lesions here, is not important, as there appears to be no inflammatory complication in either case; keeping them dry by dusting calomel over them, and protecting from friction of the clothes by application of a little lint, is all that will be required. Only when inflamed do such lesions require special attention, rest, poultices, and sedative dressings. The real cause of the persistence of these open lesions is the *induration*, dependent upon the cell accumulation; this we can only hope to reach by our internal remedies. The mucous patches we will touch thoroughly with a solution of nitrate of silver $\mathfrak{z}\text{i}$ to the ounce of distilled water, and reserve the especial reasons for this until our next session.

LECTURE VIII.

TREATMENT OF SYPHILIS.

GENTLEMEN, — At the close of the previous lecture, it was intimated that there were some especially important reasons, why the mucous patches present in Case XVI. (which I again present for your con-

sideration) should be subjected to the application of a strong solution of the nitrate of silver. The first of these is the fact, well ascertained, that the secretions of these, as well as of all open lesions, during the entire active period of syphilis, and the blood, furnish a contagious element. That cells, which have become degraded by contact with other degraded cells, in the process of infection going on in the general circulation, find their way through the walls of superficial vessels, and are exuded with the fluid secretions of all moist lesions in syphilitic subjects.

They are the *disease germs* of syphilis, and contact of these, with any abraded surface, on a healthy person, will communicate syphilis to that person, just as certainly and speedily, as contact with an open initial lesion resulting from venereal contact. Disease germs, from a mucous patch in the mouth or throat, suspended in the saliva, are thus readily transferred to a cup or tumbler, a spoon, a pencil, the mouth-piece of a tobacco pipe, and a great variety of other articles. These, again, accidentally coming in contact with an abrasion on the lips of a healthy person (and thus inevitably into practical relations with normal white blood cells), constitute that mode of communication of the disease which is termed *mediate contagion*.¹ For this reason we look carefully for such lesions, and when found make prompt application of a solution of the nitrate of silver, of a strength of thirty to sixty grains to the ounce of distilled water, and repeat daily until they are healed.

The effect of this treatment in the present instance has not been as satisfactory as could have been desired, probably owing to the continued use of tobacco, to which the patient confesses. This leads me to remark, that, under such circumstances, the use of tobacco is especially pernicious, not only because it delays healing of open syphilitic lesions of the mouth and throat, but because the local irritation of the mucous membrane which it occasions, frequently induces such lesions, at points where, independently of the tobacco habit, they would never have occurred. This patient has taken a mercurial pill (containing two grains of mass. hydrarg. and one of the exsiccated sulphate of iron) morning and night, for one week, and yet we see no evidence of mercurialization either in the breath or in the gums, nor has he, apparently, experienced, from its use, any effect upon the digestive tract. This is the usual tolerance to the remedy, given in this form and quantity. We shall now increase the medicine to three pills daily, the object being to bring the system gradually under the mercurial influence.

What we desire, is, to fix upon such an amount of mercurial as may be borne without irritating the digestive tract, or producing any recognizable damage to the healthy tissues, or the blood, and yet such an amount as will be sufficient to effect our purpose, namely, the metamor-

¹ See Class-Room Lessons, page 102.

phosis and elimination of the material which has been found forming his gland enlargements, and the papules of his eruption. These manifestations, as you may see, have not changed appreciably since we began the treatment. We must not look for rapid changes. We must bear in mind the fact that the syphilitic processes, somewhat like the processes of normal growth, though less in degree, are still very deliberate. Experience has taught us that complete metamorphosis and elimination of the superfluous material encumbering the tissues in syphilis, and which has been shown to be the sole appreciable cause of every possible lesion, throughout the active period of the disease, cannot be effected in less than a year in the great majority of cases, and many require a much longer time. This, in regard to the time demanded, is the plain statement of the case as made by M. Ricord before the Clinical Society of London,¹ and it is a statement which should be made to every patient who presents himself to you for treatment during the early active stage of syphilis. This must be the same whether he has for his initial lesion only a little insensitive nodule, without fracture of the skin, and a few innocent-looking, enlarged lymphatic glands, like Case XV., or a classical open chancre in connection with a distinct papular eruption and mucous patches in his mouth, like Case XVI. This treatment or its equivalent must be conscientiously carried out, if you would secure to your patient the best results in the present and the greatest immunity from trouble in the future.

We propose to watch the effect of the mercurial in these patients, and as soon as any intestinal irritation occurs, or any tenderness of the gums, or any mercurial fœtor in the breath (not common when using the amount we ordinarily prescribe), to reduce the quantity to two, or even one pill per day, gradually pushing it, however, as the irritation subsides, until some slight but well-recognized sponginess or tenderness of the gums takes place, or slight fœtor of the breath or metallic taste in the mouth occurs; then, by graduation of the dose, to keep the patient habitually a little short of this point throughout the progress of the case. No absolute rules as to the amount required to effect this can be laid down. Nor can any one preparation be relied upon for all cases. Some will be best treated with granules from one fourth to one half of the proto-iodide; others, again, with a solution of the bichloride; others you will find who cannot take any mercurial preparation internally, and who will require treatment by fumigations with the vapor of sublimating calomel, or by inunctions of the oleate or the ung. hyd. mit.; and still another class of highly scrofulous tendencies, who cannot bear mercury in any form, and who must be treated by other agents, less powerful in effecting the necessary tissue metamorphosis, such as the iodide of potassium and iodine in different forms, decoctions of sarsaparilla, etc., baths of various kinds, etc.

¹ See page 70.

A few words at this point in regard to the probable mode of action of mercury, based upon some of its known properties and effects, local and general, may not be inappropriate, especially in view of the claims which have been made as to its power as an antidote and a specific, and also as a tonic in syphilis. In any soluble and concentrated form, as, for instance, a saturated solution of the bichloride, mercury is promptly destructive to any living tissue. The proto-chloride, on the contrary, insoluble in water and only very sparingly so in the digestive fluids, when locally applied, is found quite free from any destructive property or local irritant action.

Administered internally, the bichloride in any considerable quantity, as a grain or more, acts promptly as a corrosive poison.

The proto-chloride, on the other hand, may be given in quantity without producing any such effect.

Used externally, or internally, preparations of mercury are found to be active in proportion to their solubility, and, whatever action the proto-chloride may produce, it is claimed by Mialhe, and others, to result from the transformation of a certain portion into the bichloride, probably at the expense of the chloride of sodium in the blood.

In minute quantity, the bichloride may be given (as one twentieth to one twelfth of a grain) to a person in health without setting up any marked local irritation, but, when absorbed into the general circulation, it soon exercises a stimulating effect, first upon the mucous, lymphatic, and salivary glands, producing undue functional activity, and, if continued, inducing in the latter a characteristic excessive flow of the salivary secretion, which soon comes to be of an exceedingly fetid character. The breath is also tainted by the same fetor, and this *precedes* the excessive salivary secretion, thus showing that the cause is not confined to the salivary system, but that it is in the general circulation. The cause of the fetor (alluded to in a previous lecture) is claimed to be from the *decomposition of fat produced by the rapid fatty degeneration of cell and tissue elements throughout the organism*, induced by the characteristic influence or action of mercury.¹ This effect results not only from the excessive administration of mercury in the form of the bichloride, but from the introduction into the system of the mercurial principle in excess, whether in this form or any other form, — whether administered internally, through the digestive apparatus, or externally through the skin by inunction, or through the respiratory apparatus by inhalation of the mercurial vapor. It has been detected, by chemical analyses, in the blood, in the viscera, in all the secretions, in the muscles,

¹ Under such circumstances, according to the analyses of Dr. Wright, the *blood* is also materially changed; "the fibrin, albumen, and red globules are diminished in amount, and very fetid fatty matter is present in large quantity." Headland on the Action of Medicines, London, 1867, page 382.

and in the bones, in the serous membranes, and in the cartilages, of persons to whom it has been administered.¹ Its capacity for diffusion throughout the system, therefore, and of reaching, through its material influence, every tissue and fluid of the entire organism, has been amply demonstrated. It would appear, like oxygen, to be taken up by the blood and carried throughout the system, and like it, or in a manner equivalent to it, to produce a special influence on the material with which it comes into actual contact, — a species of oxidation, which, in its feeblest action, hastens the natural evolution of living elements, and promotes their retrograde metamorphosis by its solvent property. Increasing the amount, its effect is seen in the solution and elimination of the products of new formation. Lancereaux says, "The action of mercury on the general economy is opposed to the increase and development of new tissues;" and, according to Headland and, others it "diminishes the amount of fibrin and corpuscles in the blood."

In syphilis, we have seen that the chief feature of the disease is the increase, through excessive proliferation, of the white or earliest form of blood corpuscles. The proportion over the red corpuscles (which are now known to be a higher form of development), is hence greatly increased. Foster, in speaking of the origin of the red blood corpuscles, says, "From these several facts, it is concluded that the red corpuscles take origin from colorless nucleated corpuscles, similar to, if not identical with, the ordinary white corpuscles of the blood."² Mercury acts, first, in hastening the dissolution of the white corpuscles, and, then, in reducing their number. An apparent increase of the red corpuscles results. The relief to a circulation overburdened with white cells, through the removal of such as are superfluous would also, and of necessity, tend to favor the normal development of red corpuscles out of the white. Such a result of the use of mercury might be attributed to a *tonic* property in the drug, as first claimed by Dr. Billing, and quoted by Headland in 1867,³ and more recently by Dr. Keyes, of New York, in his so-called "Tonic Treatment of Syphilis."⁴

Tonics, says Headland, are remedies, but not poisons, and it is certainly not among the least of their recommendations that we can seldom or never do harm by their use. It is scarcely necessary to suggest that, with such an explanation of the term, the acceptance of mercury as a tonic would lead to mischievous results. The acceptance of mercury as a tonic is based upon grounds no more tenable than those which are advanced to prove its power as a specific or as an antidote; the manner of its action in all these ways is accepted as a mystery, independent of any supposition even, of the nature of syphilis, and equally in-

¹ Headland, page 376.

² Text-Book on Physiology, London, 1880, page 37.

³ Headland, on the Action of Medicines, London, 1867, page 161.

⁴ Keyes on Syphilis, Wood & Co., New York, page 117.

dependent of any demonstrable property which mercury is known to possess.

Given in diseases not syphilitic, but characterized by the exudation of plastic lymph, — as in inflammation of serous membranes, — mercury acts as a solvent. Its influence in preventing organization of plastic material, as well as in breaking up and removing it, apart from any syphilitic complication, is distinctly recognized and appreciated. This, it is well understood, occurs through the tissue metamorphosis or fatty degeneration, especially of new cell or tissue formations, which mercury is recognized as the most efficient agent in promoting; likewise aiding in the elimination of the products of such metamorphosis through the increased action of the mucous, lymphatic, and salivary glands, which its influence is known to affect.¹ The action of mercury upon the various systems of glands can only be explained by attributing it to the highly diffusible and peculiar irritant property of the drug, always positively recognized when this remedy is pushed to the least degree beyond a point of healthy stimulation. In just what this stimulation consists, lacking the results of scientific investigation on this point, we are not able now to state. There is, however, good reason to suppose that this stimulation is due to the *corrosive* power of mercury, which produces rapid destruction of living tissue, subjected to any soluble concentrated form of this mineral, and which produces irritation of the skin and mucous membranes in less concentrated solution, — which decreases in proportion as the strength of the solution is diminished, until it serves simply to stimulate the mucous surface in contact with it, to slightly increased secretion. There is good reason, also, to suppose that the effect of the mercury absorbed into the system, acts in precisely the same manner as when applied locally to parts within reach of observation, namely, to stimulate up to a certain point, and when the mercurial influence is increased beyond that point, to produce death of tissue; first of the weaker, newly formed tissues, or any imperfect, hastily generated tissue, or cell material; and then, if in increased strength, to destroy normal healthy cell material and tissue. We know, from an extended clinical experience, that mercury introduced into the system, in quantity so small as not to interfere in the least appreciable degree with the processes of healthy growth and nutrition, is yet capable of bringing about the death and fatty degeneration of new cell and tissue materials distributed throughout the system. We know, furthermore,

¹ "Probably mercury acts upon the lymphatic system directly, standing in that respect next to iodine. But mercury has another action with which we are acquainted, and that is its destructive action upon new growths." John Hunter, of old, taught "that mercury acted upon abnormal and diseased parts with much energy, while it affected but little the healthy structures." Fothergill says: "There is a great deal in this, really and actually; mercury does break down such growths, and the detritus is removed by the lymphatics." Fothergill's Principles of Therapeutics, Am. ed., 1877, page 449.

that this effect is not produced through any antidotal or specific or tonic property which it possesses in its relations to syphilitic disease, but that it is produced through the power which mercury is known to exert in effecting the death of new cell and tissue formations, when brought into contact with them in its soluble forms. If, now, it can be shown that there is anything more of syphilitic disease than new cell and tissue formations, — anything more than imperfect and superfluous cell and tissue material; in other words, if there is any substance *sui generis* which constitutes the so-called syphilitic virus, — then it may perhaps be claimed that mercury acts upon that substance or virus, or whatever it may prove to be, as an antidote, or a specific, or a tonic; but no such substance has yet been found. Until, therefore, such substance has been practically demonstrated, the cure of syphilis, through the action of mercurials, must be attributed to properties which mercurials are known to possess, acting upon materials which have been scientifically proven to exist, and which, moreover, have been shown to be sufficient, in kind and in degree, to produce all the recognized lesions and manifestations of syphilis, during the active period of the disease.

In consideration of the foregoing views and facts it may then be said, that, whether the presenting trouble is a well-marked initial lesion, with enlarged lymphatic glands in connection with it, alone, or whether the initial lesion has disappeared, and there are only a few mucous patches in the mouth; or if there is a papular eruption alone; or an iritis, or an alopecia, — whether these are present singly or all together, in the same case, — the treatment is the same, and must be continued until all have disappeared, and the enlarged lymphatic glands in the groin, in the cervical regions, in the epitrochlear spaces, are reduced to their normal dimensions; then, and only then (unless through some idiosyncrasy, tolerance of the remedy has not been secured), is it considered warrantable to discontinue the treatment.

Again I call your attention to the fact that this treatment is now virtually approved and recommended by all accepted authorities, as a result of clinical experience. Forms of mercury may vary, modes of introduction may differ, but the acknowledged object of treatment is to continue a mercurial impression until all traces of the disease have disappeared. The last traces of the disease are seen in the continued enlargement of the lymphatic glands, — an enlargement demonstrated to consist of the tangible cells and tissue elements, which have caused and characterized all the recognized lesions of the active stage of syphilis. These glands being restored to their normal condition, the disease has no longer recognized existence. The whole aim of the treatment, at least the whole force of it, has been to promote tissue metamorphosis, to induce fatty degeneration and elimination of recognized obstructive material. What becomes of the virus during this time? What evi-

dences have we seen of the antidotal power of mercury independently of its capacity to induce tissue metamorphosis? With just as much reason might we admit a claim that its effect in producing the solution of a plastic effusion in pleurisy was from its power as an antidote to pleurisy, as that the same effect is evidence that it acts (by breaking up and removing the obstructions in the tissues during syphilis) as an antidote to the syphilitic virus.

The highest type of treatment, then, during the active period of syphilis, in accordance with the material views advanced in these lectures, would be such an administration of mercury, or any other agent capable of producing or hastening tissue metamorphosis, as will act efficiently upon the unhealthy cell and tissue formations producing syphilis, and at the same time fall short of any unfavorable effect upon the healthy fluids or structures of the affected organism. This accords fully with the results obtained by clinical observation, and as cases present from time to time during the present college term I hope to have an opportunity of demonstrating the soundness of this plan, and of giving you a practical knowledge of the characteristics of the various phases of the active period of the disease, and of the varied forms and modes of administration of remedial measures best adapted to their cure.

Thus far, mercury alone has been suggested in the cure of syphilis. This is simply because it is now conceded by all recent accepted authorities to be, when judiciously administered, the most *certain* — in point of fact, the only certain — means at our command for hastening and establishing the cure of syphilis during the active period of the disease. Given, according to the principles which have been previously insisted on, and to persons, otherwise healthy, who have acquired syphilis, it constitutes a perfectly safe remedy, — the most speedy in its effects and most easy of administration. Through its persistent and intelligent use by far the largest proportion of cases of syphilis may be carried to a complete and satisfactory cure. And yet it is not because mercury aids in the cure of the *initial lesion* or of the *eruptions* of the active stage that it is chiefly valuable; it is because better than any other known remedy, it prevents the later manifestations, — the sequelæ of syphilis; compared with which the temporary inconveniences and sufferings of the early manifestations of the disease are insignificant. These will pass off in time, often in a very short time, and frequently with so little inconvenience or annoyance as to escape observation, — and this with any sort of treatment, or with no treatment: but without a thorough mercurial treatment, the liability to trouble from late lesions (the lesions of so-called tertiary syphilis) constitutes an ever-present peril throughout the life-time of the patient; *with it he may rest in comparative security.*

There are certain cases, however, where mercury is not well borne;

where even the smallest quantity sets up serious irritation in the mucous surfaces, or in the lymphatic and salivary glands ; where it aggravates the suppurative processes when present, and *predisposes* every manifestation of syphilis to suppuration. Some one of, or even all, these accidents, may be found resulting from the persistent use of mercury in persons of a highly scrofulous temperament. There are also rare cases where the susceptibility to the influence of this medicine, independently of any marked scrofulous tendencies, is abnormal.¹ The occurrence of syphilis in such constitutions is especially unfortunate, and must always occasion great solicitude, not only on account of the liability of the disease to pursue a more unfavorable course in such cases, but from the fact that the destruction and elimination of the syphilitic products (absolutely necessary to a cure of syphilis) are rendered difficult by reason of the lack of means to hasten tissue metamorphosis in such cases without including the healthy cell and tissue material ; — material which, though capable of laudable development and stability, under favoring circumstances, yet, when deteriorated by the invasion of the syphilitic influence, is prone to break down under the stimulation required to set up fatty metamorphosis of the syphilitic products. Under such circumstances, if, with judicious general care and the use of tonic and supporting treatment, we shall find that tolerance of the remedy, in any form, is not attainable, we are then obliged to make use of other means or measures of recognized value in hastening transformation of tissue. We must, however, recognize the fact that, without mercury, we have no prompt and reliable agent in combating the earliest manifestations of the disease.

Iodine and its compounds are found to be remedial agents of recognized value in hastening tissue metamorphosis. Iodine has been long celebrated for its influence in scrofulous hyperplasias, and especially in the treatment of bronchocele or goitre ; but Dr. Wallace, of Dublin, was the first, in 1832, to present the iodide of potassium to the profession as of especial value in the treatment of syphilis. It was at once accepted as the best and readiest form of introducing iodine into the system, and soon came to be considered by many as a substitute for mercury, — fully equal in its curative power in all stages of syphilis, while comparatively innocuous in its effects upon the general organism.

Headland² has credited Dr. Williams, of London, with being the first, in 1834, to claim that its chief value was in the treatment of the *late* lesions due to syphilis. It was then suggested that this value was partly, if not wholly, due to the power of the iodide of potassium to unite

¹ Bäumlér says : "Mercurial treatment is contra-indicated in but few cases of syphilis, and chiefly when the disease is met with in patients who are already seriously affected by some other disease." Ziemssen's Encyc., vol. iii., p. 294.

² Headland on the Action of Medicines, 4th ed., London, 1867, page 204.

with certain insoluble forms of mercury, forming a soluble salt, through the absorption of which the mercury previously administered, but not completely absorbed, was rendered efficacious. Dr. Headland says: "It may sometimes fail to effect a cure, — a failure which is often due to the *omission of mercury in the primary disease.*"¹

Notwithstanding these teachings, which were widely accepted, the iodide of potassium continued to be used in the early stages of syphilis, as well as in the later, as a substitute for mercury; and especially so on account of strong prejudices against that remedy, occasioned by its injudicious administration in syphilis and its indiscriminate use in all forms of venereal disease.

To this same cause may be attributed the fact that, up to the present time, the iodide of potassium has continued to be used by many physicians in the treatment of the early lesions of syphilis, to the exclusion of mercury; but the results of careful and extended clinical observation by our leading authorities in such matters have shown that its curative influence, in the early stages of syphilis, is small, and that *its power to prevent the later lesions of the disease* (in cases when no mercurials have been used) *is so insignificant as to be scarcely recognizable.* Its curative influence in the *later* manifestations due to syphilis, namely, in the true sequelæ of the disease, is of a high order, and will be presently considered; but for all the active period, covering the initial lesion, from its commencement and through the so-called secondary stage, including all lesions incident to it, we have no well-settled testimony of the value of iodine, or any of its compounds, in interfering materially with the natural course of the disease.

In the absence, however, of any better means, we may use the iodide of potassium in the early stage of syphilis in doses of from five to ten grains, three times a day, in combination with a strong decoction of the fluid extract of sarsaparilla, using also such other measures and medicines as are of known or probable use in hastening tissue metamorphosis, as may be deemed judicious and found practicable in any given case.

We must not forget that the very *crowding* of the superfluous cells, which constitute the active element in syphilis, is highly conducive to their fatty degeneration, and that hence the tendency of the active lesions of syphilis is always toward recovery, *sua sponte*; that, in all probability, nine tenths of all the cases would recover completely in a year or two, if left to the unaided resources of nature. The importance of active interference lies, as has been before impressed upon you, chiefly in the fact that it is during this active period that, without efficient

¹ "The mercury salts, like those of most other metals, form insoluble compounds with albuminous substances:" in this form it is claimed that mercury is deposited in the tissues, and remains until, coming in contact with chlorides, bromides, or iodides, it is re-dissolved, and again brought into the circulation in an influential form. *Ibid.*, page 204.

treatment, the damage to the lymphatic system which results in the late or so-called tertiary manifestations of syphilis, is claimed to occur. The manner in which such manifestations are brought about was thoroughly discussed during Lectures V. and VI., devoted to the Period of Lymphatic Obstruction, page 41 *et sequitur*. The so-called "gummy material," there shown to constitute the substantial basis of every lesion of late syphilis, was demonstrated to be simply a collection of lymphatic elements, in no way differing from normal cell and tissue growth, confined *in loco* by obstruction to the lymphatic circulation at the points where the lesions occurred. The manner in which, through disturbances of nutrition, destruction of every kind of tissue occurred, was shown. Cases (page 44 *et seq.*) were brought before you illustrating the peculiar appearances and conditions associated with late syphilitic lesions of the skin, the cellular tissue, and the bones. One point was made especially prominent in connection with all these cases, and in carefully executed plates, representing lesions of the brain, the nervous system, and the viscera, namely, *the presence of accumulations of the so-called gummy material in various conditions and stages of development*. Two prime necessities were shown to be essential to cure in every case: first, the disintegration, absorption, and elimination of a material, the presence of which was claimed to produce by mechanical pressure the various forms of disturbed nutrition and tissue necrosis, presenting; second, to break up and remove the fibrous material upon which the constriction of the lymph channels was claimed to depend. The so-called "gummos material" was shown to be a simple collection of germinal elements and their débris. The administration of iodine and the iodide of potassium was repeatedly alluded to as a potent agent in inducing fatty degeneration and elimination of such material; to be, in fact, as essential in the successful treatment of these late or tertiary lesions, due to syphilis, as mercury was shown to be in the earlier manifestations and conditions of the disease. This is, and has long been, the reputation possessed by iodine and its compounds throughout the civilized world, and *it is based entirely upon the results of clinical observation*. What I propose now, is to examine into the properties and powers of iodine and its compounds, to see if we cannot find, in their highly curative action upon the lesions due to syphilis, a confirmation of our position in regard to the causes of these lesions, and the manner of their improvement and cure under the influence of measures clinically proved to be efficient; and thus to substitute a scientific reason for the administration of an approved class of remedies, in place of the heretofore empirical assumption that they act as antidotes, or specifics, or tonics in the cure of the late lesions of syphilis.

In the first place, iodine is unequivocally one of the most diffusible of all known remedies. It volatilizes with promptness, and is highly sol-

uble. It is readily taken up by the blood, and thus carried to every portion of the human organism. It has been found by chemical analysis, in the blood, saliva, milk, urine, and, according to Ringer, even in the urine of a sucking child whose mother was taking the iodide of potassium. This, then, fully establishes the capacity of iodine to come into actual contact with the products of syphilitic action in any subject of the disease. In the second place, its capacity to modify the products of new formation both in health and disease are well recognized. Fothergill says: "By means of iodine in its various forms (the most distinct and powerful absorbent with which we are acquainted) we excite the lymphatics into greater activity, and so reduce certain tissue enlargements, especially such as consist of certain forms of connective tissue."¹

Lancereaux says: "The salt of iodine is met with in the blood, with all its chemical qualities; . . . it does not modify the blood globules in form or number, but it has the property of acting upon the albumen of the blood. Like mercury, iodine would thus exert a modifying, *solvent* action upon the albumen, and to this action are due, according to Overbeck, the therapeutic effects of the preparations of iodine in syphilis."²

Headland says: "When given for some time it has the effect of impoverishing the blood and diminishing the quantity of fibrine."³ According to Mialhe, "iodine is one of the most energetic of the class of fluidifiants,"⁴ or agents which promote fluidity. Bartholow says that "the iodides increase waste and the elimination of the products of waste."⁵ Thus, according to the best and most recent authorities, we have, in iodine and the iodide of potassium, remedial agents of the highest value in stimulating the functions of absorption and secretion, and of reducing albumen and fibrine in the system, — remedies, also, possessing highly solvent properties when brought into contact with cells and tissues of new formation, — in short, of promoting in well-known ways the process of tissue metamorphosis, through which alone the so-called *gummy material* (which as far as known, is the only material causing the lesions of late syphilis) can be dissolved and eliminated. In the acknowledged absence of any demonstrable virus we are forced to accept a material explanation of these lesions due to syphilis. They have been shown to consist simply of normal germinal elements, accumulated at points where such lesions have occurred, and in sufficient degree to cause by the mechanical obstruction the disturbance associated with their presence. To a contraction or obstruction of the lymphatic channels at such points, alone, can we refer the localized ac-

¹ Fothergill on Treatment, page 448.

² Lancereaux on Syphilis, vol. ii., p. 330.

³ Headland on the Action of Medicines, page 207.

⁴ Headland, foot-note, page 393.

⁵ Treatise on Therapeutics, 1879, page 188.

cumulation of this superfluous germinal material. Contractions can only occur through antecedent deposit of fibrous or connective tissue material, such as has been shown to result, to greater or less degree, throughout the lymphatic system, in the active stage of syphilis.

We have, then, in the treatment of all the late lesions due to syphilis, according to these views, two pathological conditions which legitimately demand consideration: first, the accumulated material, which produces damage to the various structures involved by mechanical pressure; and second, the fibrous material, causing the contraction or obliteration of the lymphatic channels. In the first condition we should expect prompt and efficient relief to the accumulated germinal material through the influence of iodine and the iodide of potassium. Iodide of potassium, says Ringer, is the most soluble of all forms of iodine. It has been found also to be a form the most convenient for administration, and the one most usually acceptable in its effects upon the digestive apparatus. It has, therefore, been most generally used in the treatment of the so-called tertiary stage of syphilis.

Of the practical results of its use, simply as expressing the accepted status of this remedy in the late lesions due to syphilis, I will quote from the most recent authorities on therapeutics in this country, and whose views will be recognized as but the reflection of the teachings of distinguished syphilographers throughout the world at the present day: "No therapeutical fact is more conspicuous than the cure of syphilis of the nervous system by the iodides. Mental disorders, epileptiform seizures, paralytic states, etc., *dependent upon gummata, nodes*, etc., are usually removed (by their use) in a manner little short of magical. Syphilitic paraplegia is equally amenable to the same means. The various neuralgias of syphilitic origin (that is to say, caused by the presence of gummata), *occurring in any situation*, are usually very promptly cured by the iodide of potassium. . . . There is no therapeutical fact more conclusively established than the power of iodide of potassa, in large doses, to arrest destructive syphilitic ulceration of the nares, palate, tonsils and larynx."¹ Through their solvent or fluidifiant properties; through their action in stimulating the function of the mucous, lymphatic, and salivary glands; through their power to hasten tissue metamorphosis, iodine and its compounds constitute just the remedies which, from a purely scientific stand-point, we should select as best calculated to remove the elements of new formation which are demonstrated in the constitution of the so-called "*gummy material*." We have prescribed the iodide of potassium to arrest the progress of disease in the cases hitherto brought before you (pages 44 *et seq.*), and it is just the remedy which we shall find it judicious to prescribe in every

¹ Treatise on Therapeutics, page 188. By Roberts Bartholow. Appleton & Co., New York, 1879.

case of late trouble due to syphilis, of whatever appearance, or in whatever locality, unless through some personal idiosyncrasy this form of iodine is not well borne.

The second condition alluded to, as calling for attention, in the treatment of the late lesions due to syphilis, is contraction of the lymphatic channels. We have shown that there is reason for believing that obstructions are present, and due to deposit and organization, more or less complete, of plastic material, deposited during the active stage of syphilis. Here we often find, as might have been inferred *a priori*, that the iodides are not sufficient; that, while competent to cause the removal of the gummous material, in the great majority of cases (as previously suggested at page 50), the conditions for its reproduction remain, and relapses occur. This is a well-established clinical fact. It is also as well established, that, through administration of a mercurial, in addition to or in combination with the iodide of potassium, cures are more speedy and permanent; hence it has come to be considered requisite for the successful management of lesions of all kinds, due to late syphilis, to combine mercury with the iodide of potassium. Fothergill says: "By the combination, then, of mercury, to break down structurally, the neoplastic growths, and iodine to stimulate the lymphatics, we can remove the products of excessive or perverted nutrition."¹

It has, I think, been conclusively shown that the so-called gummy material of syphilis in the broadest view which can be scientifically taken of it, is nothing more than "the product of excessive or perverted nutrition." As such, then, we treat it with mercury and the iodide of potassium. Not with the intention of neutralizing a virus, but upon principles which enable us, in case of intolerance of these medicines (from idiosyncrasy of the patient or from any other cause), to supply other remedial agents and measures. These, though less efficient, will yet be in the direction of intelligent effort to remove, not alone the immediate results of syphilitic action, but to combat the conditions upon which the persistent recurrence of the lesions due to late syphilis has been shown to depend.

¹ Fothergill on Treatment, page 449.

CLASS-ROOM LESSONS.

LESSON I.

THE INITIAL LESION OF SYPHILIS, OR CHANCER.

(1.) The initial lesion of syphilis begins by a process of **UNDUE GROWTH** and **MULTIPLICATION** of normal germinal cells, induced by contact (through a lesion of mucous membrane or integument) with **DISEASED** or **DEGRADED** cells, derived from a person suffering from **SYPHILIS**.

(2.) Cells, thus generated, accumulate at the point of initiation, in a circumscribed portion of the surrounding and underlying tissue, and also in the walls, and interior, of the blood and lymph vessels of the tissue so implicated, and thus form a characteristic neoplasm, which is termed the *Initial Lesion of Syphilis*—of which there are five characteristic forms, namely:—

(1.) The Indurated Papule.

(2.) The Dry Scaling Patch.

(3.) The Chancrous Abrasion.

(4.) The Saucer-Shaped Non-Suppurating Chancre, with indurated base and edge.

(5.) The Elevated, Moist, Velvety Papule.

And, as modifications, —

The Mucoid Form.

The Inflamed or Suppurating.

The Phagedenic or Gangrenous.

Also modifications arising from implantation of the *Virus of Chancroid*, or other *Vicious Secretion*, upon the Initial Lesion of Syphilis, of any one of the above named forms.

The initial lesion of syphilis may be situated at any point on the surface of the body, or it may be concealed within the orifice of the meatus urinarius, the anus, or the mouth.

INITIAL LESIONS OF SYPHILIS.

The differences in form of the initial lesion of syphilis, are the legitimate and direct results of interference, to a greater or less degree, with the circulation of the tissues, at or beneath the point of initiation, of the abnormal cell growth. Thus, in regard to the first named form,

(1.) THE INDURATED PAPULE

is a dense neoplasm, in the cellular tissue: *movable* under the skin, and hence not materially impeding its functions. Complete absorption of this morbid growth may take place, and the organism become thoroughly contaminated with syphilis, without the occurrence of any open lesion.

(2.) THE DRY SCALING PATCH.

This always occurs upon integument, and the cell accumulation is diffused and quite superficial, producing an induration which, to the touch, is like *parchment*; hence the term, "*parchment induration*," applied to this lesion. Interference with the circulation, in this case, is not sufficient to prevent the evolution of the epidermis, but its development is impeded, and layers of dry epidermic scales cling to its surface, giving it a characteristic scaly appearance.

(3.) THE CHANCROUS ABRASION

occurs upon an indurated papule, which, by peripheral cell growth, has come to involve the circulation of the cutaneous or epithelial structures, to the extent of rendering them friable and easily abraded. Imperfect evolution of the underlying cell elements results in a free shedding of the superficial layers from the moist surface of the lesion. Under the microscope these are seen to be like laminated epithelial scales, and constitute a significant mark of *chancreous abrasion*.

(4.) THE SAUCER-SHAPED NON-SUPPURATING CHANCER, WITH INDURATED BASE AND EDGE.

In this form a characteristic loss of tissue has taken place (almost entirely at the expense of the adventitious cell growth), through the continuance and extension of the causes which produce the *chancreous abrasion*; loss of tissue, as in that case, also occurring, not through the suppurative or ulcerative process, but by that which Virchow has termed a *necrobiosis* (death from altered life), that is, from a gradual obstruction to the processes of nutrition of the affected part. The secretion of this form of initial lesion is scanty, free from pus, and presents under the microscope the squamous epithelial elements found in the secretion of the chancreous abrasion.

(5.) THE ELEVATED MOIST VELVETY PAPULE

is neither more nor less than the previously described lesion, "*The saucer-shaped, non-suppurating chancre, with indurated base and edge*," upon which the *granulation tissue* of Billroth has been devel-

oped. This tissue is described in Billroth's Pathology, Am. ed., page 93, under the head of "*Proliferating fungous granulations*." He says, "The most frequent cause of the development of such granulations is, *any local impediment to healing, such as rigidity of the surrounding skin*, so that the contraction of the cicatrix is difficult." This rigidity, in the case of the moist velvety papule, is caused by the characteristic induration of syphilis, always associated with this form of initial lesion.

We shall consider next the *modifications* to which the different forms of initial lesions are subject.

(1.) THE MUCOID CHANCRE.

The mucoid form is that modification of the *moist velvety papule* which arises from the occurrence of a diphtheritic membrane, or deposit, upon its surface, giving it the appearance of that secondary or constitutional manifestation of syphilis known as the *mucous papule*. This modification usually takes place coincidently with the appearance of mucous papules, or patches, in other localities. The *induration* associated with the *initial lesion*, thus modified, and its entire absence in the *mucous papule*, will constitute the distinguishing difference between these lesions.

(2.) THE INFLAMED OR SUPPURATING CHANCRE.

In any of the open initial lesions subjected to persistent irritation, from friction of clothes, repeated coition, application of caustics, alcoholic excess (especially in the scrofulous and debilitated), an inflammatory action may be set up. This soon results in pus formation, and a more or less active necrosis, so like in character to that occurring in chancroid that errors in diagnosis are easy. The now purulent secretion of the chancre is found to be contagious, producing, by auto-inoculation, a sore identical with true chancroid, thus farther obscuring the differential diagnosis. Previous history, and the induration more or less distinctly marked, will usually be sufficient to establish the true character of this lesion.

(3.) THE PHAGEDENIC OR GANGRENOUS CHANCRE.

In certain cases of the inflamed or suppurating initial lesion the indurated tissue becomes livid in color, quite suddenly, and exhales a peculiar sickening odor, announcing the occurrence of gangrene. This results from arrest of the vascular supply to the induration, through an aggravation of the causes which led to the antecedent *necrobiosis*. This view is sustained by the known influence of mercury in staying or arresting the destructive process thus set up in the initial lesion, while in any other form of gangrene the influence of this drug is

known to be pernicious; and also, from the fact that the loss of tissue is usually limited to the induration. When the death of tissue occurs, by molecular continuity, the lesion is said to be PHAGEDENIC; when the induration sloughs out *en masse*, it is called GANGRENOUS. The influences which tend to convert the inflamed or suppurating initial lesion into the phagedenic or gangrenous are, *predisposition to suppuration from any cause*, constitutional dyscrasia, alcoholic excess, low, irregular life, etc.

MODIFICATIONS FROM IMPLANTATION OF THE VIRUS OF CHANCROID, OR OTHER VICIOUS SECRETION, UPON THE INITIAL LESION OF SYPHILIS.

All forms of the initial lesion in syphilis may be modified and more or less obscured by the occurrence of ulceration, from any cause, upon the site of syphilitic inoculation.

No surface changes at the point of entry of the syphilitic virus, or principle, can affect the course of the syphilitic infection, after the disease germ has passed into lymph channels (spaces or vessels) below that surface. The characteristic local evidences of syphilitic infection may, however, be modified, and more or less completely obscured by accidental lesions, such as herpes, resulting from contact with vicious vaginal and uterine secretions, or by contact of the lesion of syphilitic inoculation, with the virus of chancroid.

Such lesions pursue their course, uninfluenced by the syphilitic cell-proliferation previously inaugurated, and may thus obscure diagnosis until evidences of constitutional infection are manifest.

Hence, wherever the *possibility* of a syphilitic infection is present, any breach of tissue, whether a simple abrasion or fracture of mucous membrane or integument, or any vesicle or pustule, whether from general or venereal causes, whether healing as if simple, or pursuing the characteristic course of the chancroid, then, in such case, opinions in regard to the *presence*, or *absence*, of the *initial lesion of syphilis* must be reserved, until such time, from the date of latest exposure, *as will equal the longest period known to obtain between inoculation and syphilitic infection*, as indicated by induration of the local lesion and enlargement and induration of the adjacent lymphatic glands. This is not less than forty days.

LESSON II.

THE INCUBATION OF SYPHILIS.

This is a term usually applied to the period which elapses from the date of inoculation to the appearance of the characteristic initial lesion, and may vary in different cases, according to different authorities, from one to seventy days, the usual time being from ten to twenty-five days. Strictly speaking, syphilis has no period of true incubation, inasmuch as the process of cell-proliferation is undoubtedly established at the moment the virus (disease cell or germ) comes in contact with the germinal or white blood cell of the human organism.

The immediate effect of such contact seems to be a rapid increase in the process of proliferation of such of the normal white blood cells as have become contaminated or degraded by the influence of the disease germ (virus) of syphilis. Through accumulation of this degraded product, the tissue (including the vessels of nutrition) at the point of initiation of this process, becomes densely packed, forming a neoplasm of greater or less extent.¹ The process of degradation or infection is confined to the immediate locality of the inoculation, until the degraded cells have gained access to the interior of a lymphatic vessel. Through this channel the diseased cells are carried to the nearest lymphatic gland (the *gland of connection*, as it may be termed), and here are arrested, by the peculiar conformation of the gland structure, for a longer or shorter period (usually about six weeks), during which time there is no further evidence of constitutional infection.

This period of *apparent* rest is usually termed the *second* incubation of syphilis.

NOTE. — It is probable that the interval between the date of inoculation and appreciable gland enlargement is dependent upon the facility or difficulty with which the diseased cells gain access to the lymphatic vessel connecting the point of inoculation with the adjacent gland. Hence, at points where the distribution of lymphatic vessels is most liberal and most superficial we should expect to find the *shortest interval* between inoculation and gland implication. This view is supported by the clinical fact that, in cases when the shortest interval occurs, the initial lesion (in the male) is located at the frenum, or the anterior-inferior surface of the glans penis. From this point, chiefly, the superficial lymphatic vessels radiate, and are (according to Balaieff) "most *superficial*, rising, in this especial locality, until they lie just *underneath the epithelium*" (see pages 12 and 13, where it is shown that, by direct introduction of the syphilitic element into the *interior* of a lymphatic vessel, diseased action, in the gland of connection, is inaugurated at once).

TREATMENT OF THE INITIAL LESION OF SYPHILIS.

First, by *Excision*. Whenever a well-determined initial lesion is situated in loose tissue (integument or folds of prepuce in males, or

¹ See Beisiadecki's account, page 4.

of the vulva in females), the earlier removal, by excision, is accomplished the better. Not with the expectation of preventing constitutional infection (which, as a rule, is inevitable before the local lesion is discovered), but, as far as possible, to remove a focus of dissemination for diseased elements, and to diminish the danger of conveying disease to others.

The infective neoplasm, whether under sound skin or appearing in any one of the forms or modifications previously described (except the inflamed or suppurating), should be removed *entire*. The resulting wound heals, as a rule, by first intention. Even when the induration is large, little, if any, deformity remains after cicatrization. Practically the indurated tissue is a foreign body, and its thorough removal requires the sacrifice of but little of the surrounding healthy structure. Favorably situated open initial lesions, of long standing, may be promptly cured in this way.

For the performance of this operation — First cleanse the parts thoroughly, by gentle bathing in warm water; in all open lesions apply a solution of carbolic acid of a strength of one part of the acid to forty parts of water, after which raise the mass of induration between the fore-finger and thumb, and encircle it firmly at the base with a bit of fine silver, or malleable iron wire. The indurated part may be separated from the normal tissue, in the same way, by compression between the arms of a bent probe, being careful to include the entire induration.

Now with a narrow, sharp-pointed bistoury, pierce the tissues at the centre, beneath the compressing wire probe, and cut well under and out, including all the indurated and a little of the sound tissue of that side. This effected, from the place of beginning, cut out in the same way on the opposite side. Be assured by careful examination that every portion of the neoplasm is removed, then introduce interrupted sutures of silk or silver wire at intervals of a quarter of an inch.

The patient should be kept in the recumbent position, the parts constantly wet with carbolated water, until the third day, when, on removal of the sutures, union by first intention will, as a rule, be found to have taken place.

The resulting cicatrix may indurate, to a greater or less degree, but rarely, if ever, to the extent of inducing a solution of continuity.

In no case does this procedure lessen the necessity for *Constitutional Treatment*. The indurated papule, when so located that excision is unadvisable (as on the *glans penis*, or involving the tissues of the *corpora*), may be subjected to applications of the oleate of mercury (six per cent. solution), or any correspondingly mild mercurial ointment. When the mucous membrane, or cuticle, covering the induration, is abraded, or at any stage of simple *necrobiosis*, dusting the

surface with dry calomel, and protecting it with a thin layer of dry lint, is often serviceable. Calomel, in combination with lime water, in the proportion of a drachm to the pint (*lotio nigra*), or bichloride of mercury, half a drachm to the pint of lime water (*lotio flava*), are also much esteemed as applications to the open initial lesion. The tissue metamorphosis and absorption, which are requisite for the removal of the syphilitic neoplasm, are most readily induced by the internal administration of some one of the various mercurial preparations. In all forms of the initial lesion, the chief obstacle to resolution or healing is the *mechanical* interference to nutrition, occasioned by accumulated cell growth. Its removal must occur through the process known as *fatty degeneration*. The most active and reliable agent in effecting this, and in promoting the necessary subsequent absorption and elimination, is mercury; hence the internal administration of some mercurial preparation is *essential* in all well-determined initial lesions. The proto-iodide (so-called *green iodide*) of mercury, in pill, one quarter grain to one grain, three times a day. The biniodide in one thirtieth to one twelfth. The bichloride, in doses of from one thirtieth to one twelfth of a grain. The mass. hydrargyrum, from two to four grains, and may be judiciously combined with iron. A favorite formula, and one which I usually prescribe, consists of two grains mass. hydrarg. with one of the exsiccated sulphate of iron. This may be made into a pill, and if intestinal irritation ensue one fourth grain of the watery extract of opium may be added. This pill was first suggested to me by the late Dr. Bumstead, and is sometimes known as pil. *Duo* or *Duplex*. Any of these forms of mercury may be administered (in suitable vehicles) in the dose deemed judicious for the presenting case, three times a day (increasing the dose if necessary to the limit as above indicated) until the constitutional influence of the drug is manifested by a spongy and sensitive condition of the gums, or a slight mercurial odor in the breath.

The mercurial impression should be maintained as nearly as possible at this point *until complete absorption of the local neoplasm has been effected*. Its further employment will be considered in the Lessons on treatment of General or Constitutional Syphilis.

Cleanliness, freedom from friction, and irritation from all other causes, simple diet, and abstinence from alcoholic stimuli are necessary to the most favorable results in treatment of the INITIAL LESION, as well as all other forms of syphilis.

In regard to the modifications of the initial lesion of syphilis:—

THE MUCOID FORM

requires, in addition to the constitutional treatment previously described, the application of the solid *argentum nitratis* (or some other

caustic), sufficient *only* to destroy and subsequently to repress the exuberant granulations.

THE INFLAMED OR SUPPURATING INITIAL LESION

requires rest and opiate, or sedative dressing, as the *lotio plumbi et opii*, in the proportion of five grains each to the ounce of water; or the powdered *iodoform*, simple, or with an equal part of *tannic acid*, which seems to deodorize in some degree, and, possibly, increases the efficiency of the *iodoform*.

IN THE GANGRENOUS FORM

the powdered *iodoform* is efficient as an antiseptic.

Poultices of powdered charcoal are also of value, but the internal administration of mercury must not be neglected *while the gangrenous action is limited to the induration*. Passing beyond this point, prompt and thorough cauterization under ether, with the fuming nitric acid, or the galvano or the gas cautery, should be done so as completely to destroy the tissues involved in the destructive action. Opium is of great value in subduing pain in these cases as well as on account of its bracing effect on the nervous system. Occurring in debilitated or highly scrofulous subjects, as is usually the case, attention should be given to general support, by generous diet, quinine, and iron. The *potassio-tartrate of iron*, in fifteen to twenty grain doses every three or four hours (as recommended by Ricord), seems to exert a specific influence over gangrenous conditions.

It must not be forgotten that healing and apparent cure of the initial lesion does not mean *cure of syphilis*. After disappearance more or less complete the induration may return. Not unfrequently, it may be observed to increase or diminish in apparent sympathy with the progress or abatement of the constitutional disease. From this fact the local induration has come to be considered by some as a reliable barometer, by which the effect of general treatment may be appreciated. The duration of the initial lesion varies greatly in different cases, sometimes disappearing within a few weeks, and with it every trace of induration; at others, it continues as an induration, more or less distinctly marked, throughout the active stage of the constitutional infection. Enlargement and induration of the lymphatic glands, nearest in connection with the initial lesion, constitute the first positive evidence of the progress of constitutional infection.

Concealed initial lesions (as within the meatus urinarius or the anus) may be treated with bougies, or suppositories, medicated with opium, salicylic acid, or *iodoform*.

LESSON III.

CONTAGION OF SYPHILIS.

Recent investigations in regard to the disease germs of contagious diseases warrant the assumption of Dr. Lionel Beale (*Disease Germs, their Nature and Origin*, London, 1872, page 143, 21 *seq.*) that they are degraded cells (bioplasts), originally derived from the healthy elements of the human organism.

Having lost, by degradation, the capacity for development into useful tissue, they still retain the power of amœboid movement, proliferation, and vital sustenance.

This view affords a starting point for the rational explanation of syphilitic disease, which, so far as known, is confined to the human *germinal* elements. It is distinctly appreciable only in the lymphatic organs and channels, and in lesions which can be directly traced to disturbances of structure or function in the lymphatic system.

In complete accord with all that is known in regard to syphilis, we may assume that contact of normal germinal cells (white blood corpuscles) with those which have been degraded through the syphilitic influence brings about a similar degradation in them: and these, again, in the same way, acquire the power to degrade other normal germinal cells with which they may be brought into contact, whether in the same or in another person.

Thus the syphilitic influence, at the point of original inoculation, in varying intensity, is transferred from cell to cell, until its vitiating power is lost by attenuation or dilution, or until the entire organism is profoundly affected. Thus it is that we shall meet with syphilis in varying degrees of severity: from that where the subject passes through it with scarcely a single characteristic manifestation, to one, who, in its various periods, will present a classical picture of every phase of the disease.

Germinal cells from one source or organism cannot come in contact with those of an independent organism without a breach of tissue.

Experiments by inoculation of syphilitic blood, and of the unmixed secretions of unirritated syphilitic lesions, have demonstrated the complete absence of any erosive property in the so-called *virus* of syphilis. In the wounds of such inoculations healing was as rapid and perfect as in similar wounds where no inoculation had been made.

All the secretions of syphilitic lesions, and of the blood, during the active stage of syphilis (usually from one to two years) contain degraded germinal cells or disease germs, and are thus capable of communicating syphilis.

The modes of transference of syphilis from the diseased to the healthy are three: —

(1.) By DIRECT CONTACT of the diseased surface with an abrasion, or other breach of tissue, on a healthy person.

(2.) By MEDIATE CONTAGION.

(3.) By HEREDITARY TRANSMISSION.

Communication of syphilis by DIRECT CONTACT (as under the circumstances peculiar to the venereal act) is the most frequent mode of the acquirement of syphilis. In the female, initial lesions from this source are most common in the vicinity of the *ostium vaginæ*; especially so in the folds of mucous membrane about the *fourchette*; between the greater and lesser *labiæ*; under the sheath of the *clitoris*; upon, and even within, the *meatus urinarius*. They are also found to occur, not unfrequently, about the *anus*; they are rarely found on the *os uteri*, and still more rarely on the *vaginal rugæ*.

In the male, the most frequent sites are upon the *glans penis* and *prepuce*, occurring with especial frequency in the *sulci* by the side of the *frenum*, at the *meatus urinarius*, and in the *fossæ glandis*, and occasionally on the integument of the *penis*.

In both sexes the initial lesion is sometimes found upon either *lip*, in the angles of the *mouth*, or even within it, and also near, or within, the *anus*; all as a result of direct contagion. Communication of syphilis by direct contact, through the act of *kissing*, is an accident of occasional occurrence. There is also a danger that it may be transferred, through the act of nursing, from syphilitic infants to healthy wet nurses, or from syphilitic nurses to healthy infants. Relations between nurses and children should never be entered into without a careful consideration of this fact. In these cases, the inoculating secretion may be furnished, either by an *Initial Lesion*, or by one of the common manifestations of active syphilis, known as the *Mucous Patch*.

Initial lesions are also found in various other localities, as solutions of continuity, at any point, may become the accidental recipients of the syphilitic *contagium*. Usually, they are rare in proportion to their distance from the genitalia. Surgeons, accoucheurs, and gynecologists, are especially exposed to the peril of an innocent inoculation of syphilis by direct contact. Within the circle of my city acquaintance, at the present time, are three medical gentlemen who acquired syphilis through an initial lesion on the right forefinger. In another case, a surgeon, also an acquaintance, received the syphilitic inoculation in the end of his right forefinger, through accidental puncture, by a spicula of bone, while amputating the leg of a syphilitic subject.

INOCULATION OF SYPHILIS THROUGH MEDIATE CONTAGION.
Cells diseased by the syphilitic influence (or what is usually termed

the syphilitic *virus*) may cling to substances with which they are brought into contact. All degraded animal cells, or disease germs, have the power of maintaining their vitality for some time after removal from the organism in which they have been developed. (Beale.) Any material, therefore, which has been in contact with the secretions of syphilitic lesions, or the blood of a syphilitic, during the active stage of syphilis, may prove the medium of communication of syphilis to a healthy person, provided, only, that the substance so contaminated is brought into contact with a *lesion*, however slight, of the skin or mucous membrane.

The most common source of the *contagium*, in cases of *MEDIATE CONTAGION*, is the *Mucous Patch*, a constitutional syphilitic lesion, frequent upon the mucous membrane of the lips, mouth, and facial region in persons passing through the active stages of syphilis. The *saliva* is thus impregnated with the syphilitic disease germs, and, through it, a variety of domestic utensils have been the known medium of syphilitic inoculation, by contact with abrasions upon the lips of healthy persons, without regard to age or sex. In the same way, pipes, passed from syphilitic mouths, cigars, from syphilitic cigar-makers, canes, pencils, and even sticks of candy, contaminated by syphilitic saliva, have effected a syphilitic inoculation. Within the last eighteen months I have met with four cases where there was undoubted proof of the acquirement of syphilis through mediate contagion. One, of a young lady, with the initial lesion on the lower lip, acquired from her lover's kiss. The second, a physician, with the initial lesion just within the angle (on the right side) of the mouth, from a syphilitic friend's pipe. The third, in the same locality, appearing, characteristically, about three weeks after a morning spent in a dentist's chair. The fourth, a worthy merchant, with his initial lesion (well marked) on his lower lip, with mucous patches in his mouth, and an accompanying syphilitic iritis. In this latter case the only clue to the mode of acquirement of syphilis was the habit of passing among numerous clerks and occasionally transferring a lead pencil from their desks to his mouth.

Well marked constitutional syphilis, with complete absence of any genital lesion, was present in each case cited.

The foregoing typical cases, illustrative of the modes through which syphilis may be contracted by *Mediate Contagion* (with the exception of the last), were seen in consultation with physicians from neighboring states. Such accidents, however, are of more likely occurrence in great cities, where moral restraint is least stringent and opportunity for acquiring venereal diseases most favorable. It becomes necessary, therefore, in connection with cases of obscure disease, simulating syphilis, to make a searching scrutiny of all incidents, con-

ditions, and exposures which may, in the light of possible accidents, point to opportunity of syphilitic infection through mediate contagion. The third case cited is of especial value, as conveying a lesson on the necessity of scrupulous care of instruments used in operations about the mouth.

So simple a procedure as the depression of a patient's tongue with a spatula, in examinations of the mouth and throat, may easily become the means of carrying the syphilitic disease germ to an abraded surface in a healthy person.

In all cases, therefore, where the same instruments are in use for different persons, after thorough cleansing their passage *through the flame of an alcohol lamp* should be systematically practiced after every operation. The same procedure is equally indicated in regard to instruments used upon other mucous membranes, as those lining the urethra, the bladder, the rectum, the eye. It is also essential in all instruments used in cutting operations at any point. Not the least important among the modes of conveying syphilis by mediate contagion is that by *vaccination*. Numerous well-authenticated cases of this disaster may be found recorded in any modern systematic work on syphilis. Inoculation of syphilis by vaccination may be effected either by an impure virus, or an unclean knife. Use of the bovine virus, by means of a clean instrument, relieves this beneficent operation from the stigma of being considered a possible means of communicating syphilis.

LESSON IV.

SYPHILIS BY HEREDITARY TRANSMISSION.

Heretofore, in considering the modes of transmission of syphilis, we have accepted the probable fact that this disease is communicated by contact of a diseased with a healthy human germinal cell. We have now to consider how diseased cells in the adult, male or female, suffering with syphilis, may be brought in contact with those of the embryo, or of the foetal organism. It is claimed that the foetus, through the natural processes of growth and development, may be built up from a syphilitic seminal animalculæ (*spermatozoid*) furnished by the male, in conjunction with an ovum furnished by a healthy, or even by a syphilitic, female, and may thus come to comparative maturity. Much clinical material has been adduced to prove this. On the other hand it is claimed, with equal proof of a similar character, that this is *never* the case; but that the syphilitic influence is *always* furnished by the *female*; presumedly communicated to the embryo or

fœtus through contact with the nutritive elements furnished by a mother in whose organism the degraded cells or disease germs of syphilis are present.

Like most important questions in which syphilis is involved, a solution of the foregoing, based on clinical evidence alone, is most difficult. The best proof of this statement is, that, on either side of all such questions, the most experienced and competent observers are ranged in nearly equal force. To constitute *Hereditary* syphilis either the embryo or the fœtus must be infected. All infection during or subsequent to birth must be classed with one or other of the modes of transmission of syphilis previously considered.

If we accept the syphilitic influence to be, as previously claimed, a degraded formative cell, we may also accept, as a legitimate sequence, that, through this degradation, there is a loss of formative power—an inability to develop into any useful tissue.

The contagion of syphilis, as claimed, is always effected by contact of a *degraded* with a *healthy* germinal cell. In a strict sense, therefore, it is always localized. Cells thus degraded are practically emasculated, their capacity for usefulness is lost. Of necessity, then, growth of living tissue occurring, it must take place through the normal cell elements, that is, through those which have escaped this degradation. It is thus plain that only a portion of the germinal material of a living organism can be affected by syphilis. Sufficient germinal material to carry on the processes of life and growth must escape, or growth would be at once arrested and life would cease. The possibility of involving in the syphilitic dyscrasia so infinitesimal a fraction of a spermatogenic organism as would still enable it, in conjunction with the ovum, to play an efficient part in the growth and development of the human embryo, is scarcely conceivable. Especially difficult shall we find it to accept such a view when we consider that, once in connection with the ovum the syphilitic influence would be rapidly imparted to the germinal elements furnished by it. We may, then, consistently throw the great improbability of continued growth (or indeed of any growth), under such an unfavorable influence, into the scale with the clinical claims of those who *deny the possibility* of the embryo or fœtus being infected with syphilis by the *spermatazoids*. With this view of the subject, the onus of hereditary transmission of syphilis is necessarily thrown upon the MOTHER, under all, even under apparently contradictory clinical circumstances. Hence, when an embryo or fœtus is the subject of syphilitic infection, we may conclude that it is the result of *contact* of its normal formative or germinal cells, with cells degraded through the syphilitic influence, furnished by the nutritive fluids of *the mother*; either directly through the circulation, or through degraded cells from her organism, gaining access to that of the embryo or fœtus by their amœboid power.

Hence, to make the syphilitic infection of an embryo or a fœtus possible, the organism of the mother must *first* be infected with syphilis. The previous acquirement of syphilis *by the mother* from the father, or through the secretion of a syphilitic lesion, or from the blood of one suffering from active syphilis (by direct or mediate contagion), is necessary to the syphilitic infection of a fœtus or an embryo.

It is only during the active stages of syphilis (primary and secondary periods) that the contagious element of the different lesions of syphilis and of the blood is present. Therefore hereditary transmission of this disease is only possible during this time (*usually* from one to two years). The sequelæ of syphilis (tertiary and quaternary periods) contain no *discovered* elements of contagion. The most careful microscopical examinations have failed to demonstrate in the products of *Tertiary Syphilis* (various forms of *gummata*, including eruptions) anything besides the débris of normal germinal elements. Repeated inoculations of these products have failed to disclose any contagious principle. *Without contagium there is no Syphilis.* Hence we may reasonably conclude that hereditary syphilis is only acquired during the active periods of the disease, and that in order to effect syphilitic contamination of the embryo or fœtus the female organism must first be infected.

With this view of the maternal influence in syphilitic infection of the fœtus or embryo, cases reported, claiming such infection to have occurred through the sole agency of the father suffering with syphilis (the mother, up to this time, free from the disease), must be classed either among those instances where the characteristic features of the disease are absent, or where they are so imperfectly developed as to have escaped detection.

The difficulty of instituting a through examination, under circumstances where it is necessary to avoid suspicion of its object, the want of tact, care, and experience in detecting obscure evidences of this disease, have, without doubt, too often led to the acceptance of syphilis acquired through the paternal influence, where, under other conditions, and in other hands, infection of the mother would have been recognized.

The following case will serve to indicate some of the various ways in which syphilis may be overlooked, and further, to show important variations in time and manner of development of syphilis from a similar source. Some three months since, Dr. W., a naval surgeon, consulted me in regard to a small nodule on the *frenum preputialis*. An abrasion was discovered, after a suspicious exposure, some four weeks previous. This healed at once, as if simple, and nothing farther was noticed, until the nodule, about the size of a kernel of

pearl-barley, was observed. Its surface was abraded, probably during a recent connection. Its scanty secretion was found under the microscope to consist chiefly of laminated epithelial scales. On account of the obesity of the patient, a satisfactory examination of the inguinal glands was impracticable. No enlargement could be felt. I advised excision of the neoplasm. This was done at once, and healing by first intention was complete within forty-eight hours.

A few days ago (December 15th) the doctor called to say that the operation had evidently been efficacious in saving him from a general syphilitic infection; that he had positive proof of having, himself, communicated syphilis to a young lady the night previous to the excision. In her case an initial lesion followed, in due time after the connection, accompanied by inguinal gland enlargement and succeeded by general gland hyperplasia. She now had, in addition, a characteristic papular syphilide, and yet he claimed to be absolutely free from the least evidence of syphilis.

A cursory examination appeared to confirm the doctor's statement. This, however, appeared so improbable, that I at once instituted a more thorough examination, which resulted in the discovery, under a deep layer of adipose, of small but characteristic gland enlargements in connection with the initial lesion. The cicatrix on its former site was slightly indurated. Glands at a distance—epitrochlean and post cervical regions—perceptibly enlarged. Slight, but positive, congestion of the fauces and a narrow, but characteristic, *mucous patch* hidden behind the anterior pillar on either side. These proofs of syphilitic infection had escaped the anxious search and skill of the patient, also of a professional associate, who was a competent and experienced general surgeon.

Through evidence furnished by clinical cases, it has been claimed that syphilis once acquired is never fully eliminated from the system, but that it exists as a possible infecting agent, after the stages which furnish *known* contagious elements are past. During more than twenty years of observation and especial interest in regard to this point I had been unable to find a single undoubted instance, where a person in the known *Tertiary* period of syphilis (and so demonstrated by the absence of the glandular enlargements characteristic of the active stages of the disease) had been the proven carrier of syphilis to a healthy person. I came to believe fully, in regard to persons who had passed successfully through the so-called *primary* and *secondary* periods, and so proven by complete absence of *primary* and *secondary hyperplasias* that treatment was no longer necessary, that such persons might, if desirable, even, be permitted to marry, with the assurance that, through them, transmission of syphilis to wife or child was impossible. This doctrine I had taught and practiced for a very

long period, when a case came under my observation which, but for a mere chance, had unsettled me on this vital point forever. The important lesson, which it enforced, namely, *to distrust the value of purely clinical evidence*, may be profitably transmitted by the brief extract from my note book, which follows : —

Mr. Q., a young lawyer, twenty-five years of age, had acquired a well marked initial lesion of syphilis on the *glans penis*. His gland enlargements in the epitrochlean, cervical, and post cervical regions were characteristic — his roseola escaped observation, but a classical papular syphilide appeared about the fourth month, and continued for several weeks. Ulcerations of the tonsils and *mucous patches* on the soft palate and inner surface of the cheeks followed, but yielded satisfactorily to treatment.

The gentle but persistent use of mercury internally and by inunction had been pursued from the first and through a period of twelve months, occasionally combined with the iodide of potassium. At this time all glandular enlargements had disappeared, except a small one, the size of a pea, in the right *post cervical* region. Treatment suspended for three months, when a thin diphtheric patch appeared on the right side of the tongue, with slight induration.¹ Treatment resumed, mercury, with iodide of potash. Patch on the tongue faded slowly out in about a month, but was replaced by another, on the opposite side, which continued about the same time, *cervical gland* not perceptibly changed. A series of mercurial baths, and a course of Zittman's decoction, covering nearly three months longer : gland now scarcely felt. Patient very anxious to marry, but was advised to wait a full year. The next six months passed without any new development. *Gland* very small, but still recognizable, when the patient, now in good general health, married on his own responsibility.

One year after marriage the wife gave birth to a fine, healthy-looking boy. During the fifth month of lactation, the wife had scrofulous abscess of the neck (inherited tendency), which alarmed the husband (fearing syphilis) exceedingly. She recovered under simple treatment, and relief from nursing. Child healthy up to third year, when it died from tubercular meningitis, following scarlet fever. No salient evidences of syphilitic taint. Fear that his old trouble had been in some way connected with his child's death, made the husband very unhappy, and he frequently expressed the fear that he had contaminated or might yet contaminate his wife, to whom he was tenderly attached.

In November, 1870, Mr. Q. complained of some swelling and soreness over the right tibia. A gummy tumor was found presenting, the

¹ I have known patches similar in appearance to result, in certain cases, *from the use of the iodide of potassium*, to pass off when the remedy was discontinued, and again to return when it was resumed. I have also seen patches of the same appearance in the mouths of persons habituated to the use of tobacco, where no history of syphilis could be ascertained.

size of half a horse chestnut. The nature of it explained, he was put on a mild mercurial, with large doses of the iodide of potassium, which resulted in its entire disappearance within a month. Both husband and wife continued healthy up to October, 1871, when one morning he called, in great distress, to say that his wife had some sores in her mouth, resembling those of his early syphilitic trouble. I did not hesitate to assure him that this was simply impossible; that his disease, if any trace of it remained, was beyond the fear of contagion. The spotless character and chaste deportment of his wife, made me sure there could be no other danger, and I comforted him accordingly.

What was my surprise, on seeing her, to find, not only several characteristic mucous patches in her mouth, but, on further examination, to discover four or five mucous tubercles; one on the inner border of the thighs, and the others on the right labium. I was forced to acknowledge to the unhappy husband that he was right, and we could only conclude, contrary to all my assurance and belief, that his old taint had been the cause.

Here was a dilemma. I could not suspect the wife. I could not accept the contagion from a source which stultified all my conclusions, teaching, and experience. I was wretched. Husband was wretched, but resigned, desiring only, if the knowledge of it was not necessary to her recovery, that I should keep the secret from his wife. *She was serene.* After a few weeks medication, and not unfrequent painful applications of caustic to the mucous tubercles, I thought she was *too serene.* I asked and received permission from the husband to tell his wife what her trouble was, if I thought it best. My manner to her was changed; from being sympathetic and considerate, it became brusque and reserved. An explanation was finally demanded. I evaded the issue. After a little dexterous fencing, the source of her troubles was flatly claimed. Ignorance of my meaning was feigned.

I explained the only possible causes of her disease, and said she had been married too long to suspect her husband. She promptly replied that he was "as pure as the sun." I then told her if she would give me her confidence, I would protect her, — if not, would lay the matter before her husband (who was not supposed to be aware of the nature of the disease). Then came tears — reproaches — and finally, in a tempest of womanly indignation, she bade me leave, *forever.* I left, disheartened and in disgrace, — but, before I was well on my way down stairs, I was recalled, and amid tears and sobs she confessed. A yachting excursion, — an unexpected night at sea; exposure with an old lover; and all this about three months before. A letter was subsequently received from him full of regret that he had discovered himself syphilitic, and inquiring if he had been so unfortunate as to have communicated the disease to her.

The subsequent progress of this instructive case was not peculiar. The lady made an apparently complete recovery in about a year. After another year she again became pregnant, — was delivered of a healthy child, now living, but died of puerperal fever the third week after her confinement.

In carefully reviewing this history it will be observed that while it is seen to be no exception to the rule that *tertiary lesions* are not contagious — it will show how easily they may achieve the credit due to the *active* manifestations of syphilis.

LESSON V.

EARLY DIFFERENTIAL DIAGNOSIS.

The characteristic, and only constant, feature, of all lesions, during the active stages of syphilis, is shown by microscopic examination to consist in a localized cell accumulation.

Consideration of the nature and behavior of this material will afford intelligent aid, in a differential diagnosis, between the initial lesion of syphilis, in its early period, and solutions of continuity from other causes. As far as shown, syphilis is primarily a process of cell growth and accumulation, so rapid that it interferes with healthy *tissue* growth, by obstructing the processes of nutrition and development. Not of necessity interfering to the extent of causing death of tissue, but of impairing its vitality, and thus causing it to break down more rapidly under influences which favor solutions of continuity. Hence we have presenting, as *characteristic* initial lesions of syphilis, either a neoplasm, dense, insensitive, and covered with unbroken and apparently normal cuticle or mucous membrane, or, from the causes above mentioned, some one of the various characteristic *solutions of continuity* described at page 93.

In addition to the foregoing *characteristic* lesions, we may also find early local disturbance, in various forms and from various causes, associated with the beginnings of syphilitic cell accumulation, but presenting no features *characteristic* of syphilitic inoculation.

The known fact, however; that syphilitic infection not unfrequently follows a wound of inoculation, which heals promptly, and with no subsequent solution of continuity, is sufficient to prove that *neither* INFLAMMATION *nor* ULCERATION *are essential features in a syphilitic inoculation.*

Thus, wounds, abrasions, broken vesicles, pustules, or ulcers *may* receive a syphilitic inoculation and progress or heal as if no such inoculation had taken place.

It is then evident that no *positive* differential diagnosis can be made *at once* between lesions which *will* be followed by syphilitic infection and those which *will not*. A positive decision cannot be rendered until after such *interval*, from latest exposure, as may be required to develop some characteristic cell accumulation, either on the site of the lesion or in the adjacent lymphatic channels and glands.

This *interval* is recognized by all authorities as a clinical fact and is characterized as "*The Period of Incubation of Syphilis.*"

The term was invented in accordance with a belief (formerly prevalent) that the *virus* of syphilis was a mysterious impalpable influence. That this, having entered the system at a given point, instantly permeated the fluids and solids of the entire organism. It then accumulated by "a kind of germination" until the point of "*saturation*," or extreme limit of tolerance, was reached. This event was announced by a peculiar and characteristic action, at the point of entrance of the virus, which was termed the *Chancre*.

It is plain, however, that such a view of syphilitic infection can have no support, if we accept the view of a cell degradation, and a systemic syphilitic infection, in accordance with known histological, physiological, and pathological laws.

It is then to the local conditions, at the point of inoculation, that we must look for the earliest evidences of syphilitic action. This is afforded, at first, through the microscope, by discovery of a densely packed *non-inflammatory* cell accumulation which steadily increases until it is appreciable to the ordinary touch. The same cell accumulation is also seen to occur in the lymphatic vessels connecting the initial lesion with the adjacent lymphatic glands. These vessels are not unfrequently found obstructed and indurated, and, like knotted cords, the size of a crow's quill or larger, often easily traceable to their gland termination. The associated blood-vessels are never narrowed or interrupted from this cause.¹

The local induration of a suspected lesion, however, is not *positive* evidence of syphilitic action. Cell accumulation sufficient in degree to produce well pronounced induration may result from *irritation* of a *simple* lesion. Thus, an herpetic vesicle, or pustule, even a simple abrasion, through friction from clothes, or from applications of caustics or astringents, may become indurated sufficiently to raise grave suspicions of syphilis.

Induration, in such cases, is always the result of *inflammatory* action.

¹ The only recognizable cell accumulation in syphilis is confined to the lymphatic system. If, during the period of so-called incubation, the syphilitic influence has found access to the general circulation, no evidence of it has ever been discovered in the condition of blood-vessels, or of the blood, or in the conditions or sensations of the person so affected.

The induration of *syphilis* is essentially *non-inflammatory*. The differential diagnosis is aided by means used to combat the inflammatory condition. Under the influence of rest and local sedatives the *incidental* induration is promptly dissipated; *in the initial lesion of syphilis* the induration is made more salient. Sometimes, though rarely, the induration is quite obscured by a slight localized serous effusion, which gives it a bluish appearance. This I have observed in several cases, where the lesion was on a finger. The same condition, quite frequently, succeeds well marked indurations, near the *fossa glandis*, and is so persistent as to become a valuable diagnostic mark.

The induration may be said to be *characteristic* when insensitive, dense, and resistant, like cartilage. If pressed between the thumb and finger it becomes exsanguinated, and like in appearance to the tarsal cartilage, when the eyelid is turned back.

Even this most positive evidence of syphilis cannot be accepted as conclusive. The induration of a commencing *epithelioma* simulates it very perfectly, and, if an open lesion, its secretion under the microscope presents appearances almost identical. In summing up the whole matter, we are forced to confess that a final decision in any given case is not warranted, until some other evidence is present besides the appearance and character of the *local* lesion.

In all cases, where possible, *the person from whom syphilis may have been acquired* should be carefully examined.

In making such examination, search not only for the initial lesion, but for each of the possible *secondary* manifestations. Even when such are found, it must be borne in mind that *a breach of surface on the person exposed* is essential to the acquirement of syphilis, and that this surface must be brought into CONTACT with the syphilitic secretion, either *directly* or *mediately*. So that while the presumptive evidence furnished by *confrontation* is often strong, it is not *necessarily* conclusive.

The following cases will serve to illustrate the importance of caution in arriving at conclusions in regard to the true nature of venereal lesions:—

CASE I. Mr. T., aged twenty-three, on the fourteenth day after his first and only connection, noticed a slight urethral discharge. Under the microscope this was found to be distinctly purulent. No pain on urination. Meatoscope showed the mucous lining of the urethra deeply congested for half an inch. Beyond this there was no purulent secretion; appearances normal. The difficulty was, evidently, not *gonorrhœal*. A *syphilitic inoculation* was suspected. Examination of the woman with whom he had connection *showed her to be passing through the active stages of syphilis*. No initial lesion was found; but the inguinal, epitrochlean, and cervical glands were characteristically en-

larged. Several *mucous tubercles* were discovered within the vulva; one in the *cervical sulcus*, and three on the *os tincae*. Besides these there was a double row around the *anus*, eroded and secreting pus freely. In the presence of such evidences of syphilis, it seemed impossible that the young man could have escaped infection. The urethral discharge was probably caused by a syphilitic inoculation which had not yet produced a well defined initial lesion. Inguinal glands of both sides slightly enlarged. Treatment for syphilis deferred (much against the patient's wish) until evidence of syphilis should become more positive. *The urethral discharge gradually declined and disappeared entirely in about a month.* Up to the present time (four years from date of exposure) patient has not had the slightest evidence of syphilitic trouble.

CASE II. Mr. H., aged thirty, had a suspicious connection in May last. On the third day following he noticed several small pimples on his prepuce. Fearing venereal disease, he consulted his family physician, who, at once, pronounced the trouble a simple *herpes*. A mild lotion was recommended. Under its use all evidences of disease disappeared within a few days, and the patient was assured, in the most positive manner, that he was free from disease. June 10th, four weeks after the suspicious connection (and more than two after he had been pronounced free from disease), the patient was brought to me by his physician for an opinion in regard to a small, hard, eroded nodule on the former site of the *herpes*. Inguinal glands, on corresponding (right) side, characteristically enlarged. My belief that the nodule was an initial lesion of syphilis was strongly expressed, and the gentleman was put upon a mercurial course. A month later he called, presenting a well marked roseola, with the usual secondary gland enlargements. His wife, who accompanied him, had an indurated initial lesion on the lower border of the meatus urinarius and well marked inguinal enlargement.

CASE III. Mr. W. V. No unusual trouble until two and one half months ago, when ten days after a suspicious connection he noticed a small sore on the right side of the penis. He consulted a surgeon, by whom he was informed that he had a "*soft chancre*;" that he would quickly destroy it by application of nitric acid, and further, that *there need be no fear of subsequent trouble.* The cauterization was made, was repeated several times, at intervals of three or four days; healing finally taking place in about three weeks. Patient had connection with his wife the night previous to receiving the surgeon's opinion that he had a *chancroid*; no connection since.

This gentleman called upon me to ascertain the cause of a papulopustular eruption which was confined to the face and neck. I at once recognized it as syphilitic; examined the cicatrix of the so-called

chancreoid, and found it distinctly indurated. Gland enlargements of elbow and neck, all well pronounced and characteristic.

In answer to an anxious inquiry, as to the possible infection of the wife, I was obliged to admit the possibility of such a calamity. He assured me that she had been, and was then, perfectly well in every respect — “*except that she had some little swellings in the right groin; not the least pain.*” An examination of the lady, on the following day, disclosed characteristic gland enlargements, not only in the groin, but in the arm and neck. No search was made for the initial lesion. She was put upon constitutional treatment for “*a form of leucocythemia,*” and remained in blissful ignorance as to the nature of her own and her husband’s trouble.

LESSON VI.

PROGRESS OF THE SYPHILITIC INFECTION.

The term *CONTAGION* has been used to designate the act by which, through cell contact, the syphilitic influence is conveyed from a diseased to a healthy person.

By means of the influence thus communicated, proliferation and accumulation of degraded cells, at the point of original contact (or inoculation), are claimed to result in the establishment of the initial lesion of syphilis, or *chancre*, in its various forms.

The course of the disease beyond this point is indicated, *a priori*, by the known fact¹ that all integumentary and cellular tissue are pervaded by lymph spaces and channels, which lead, more or less directly, into lymphatic vessels; and that the lymph current is constantly flowing *from* the tissues *toward* the lymphatic vessels and the glands in which they terminate.

Therefore a degraded germinal cell (syphilitic) introduced into the tissues (as by an inoculation), unless carried directly into the interior of a blood vessel, must (itself, or its vitiated descendants), of necessity, sooner or later be carried along by the lymph current to and into the gland of connection.² All clinical observations confirm this view. First, in the discovery of indurated lymphatic vessels, leading from the point of inoculation to the gland in connection. Second, by the subsequent enlargement and induration of such glands. Third, their

¹ Stricker’s Human and Comparative Histology, Sydenham ed., vol. i., pp. 307, et seq.

² “The wandering red blood globules mostly again return into the circulation through the lymphatics. The wandering white blood corpuscles probably return into the circulation in the same way.” Wagner’s Manual of General Pathology, Am. ed., p. 151.

acceptance as a necessary sequence of the inoculation, and as positive proof of the nature of the disease.

The process through which the syphilitic influence thus gradually advances and finally invades the general system is termed the process of **SYPHILITIC INFECTION**.

The progress of the *syphilitic infection*, from the date of its *genesis* at the point of inoculation to its characteristic appearance in the glands nearest the point of inoculation (the glands of connection), varies in different persons, from causes not thoroughly settled, but which are indicated in note on page 96.

The degraded cell elements, then, effecting an entrance into the substance of the lymphatic gland, are here detained by the peculiarities of the gland structure, and perhaps by other inhibitory influences, for a period, varying, in different instances, from twenty to sixty days. This period is recognized by all clinical observers, and has been described as the second incubation of syphilis. It is certain, however, that no syphilitic influence has yet been discovered, in the general blood current, during this period, and there is sufficient reason to suppose that the diseased elements are confined to the glands of connection, and those intervening more deeply between these and the thoracic duct.¹

The glands of connection become gradually enlarged, apparently through the proliferation and accumulation of cells in their interior.

When the initial lesion is located upon the genital apparatus, on the glans or on the body of the penis in the male, or on the labiæ or within the vulva in the female, the lymphatic glands of the groin become enlarged, so that, as a rule, several may be distinctly recognized by the touch, varying from the size of a small pea to that of a large

¹ A similar inhibitory influence, exerted by the lymphatic glands in cancerous diseases, is cited by Virchow, in his *Cellular Pathology*, Am. ed., p. 221, with the following explanation. "We can account for this by 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."

It has been suggested that if the disease were really so localized, prompt *enucleation* of the initial lesion, and of the affected glands, might prevent general infection. It must be remembered that the infective cells, each of which is potent to act as a starting-point for systemic infection, are not only present in untold numbers at the point of inoculation, but that (as shown by Beisiadecki's microscopic researches) the walls of the intervening lymphatic vessels are lined if not packed with them. Hence any proposed surgical extirpation of the disease must imply the entire removal of all the lymphatic connections of the initial lesion and the glands of connection. A procedure not only without sufficient promise of benefit at this stage of the infection, but even at the earliest date after inoculation, the necessary ignorance as to the degree of implication of the lymph spaces and vessels in the vicinity of the inoculation would in all probability render all such means of preventing the spread of the infective processes of uncertain value.

Early excision of the initial lesion may, however, be found to modify the intensity of the subsequent general infection. My own experience in twelve cases of excision, during the past eight years, would warrant this inference.

bean. Sometimes these enlargements are apparently confined to the side corresponding with the initial lesion, — sometimes to the opposite side; usually, however, the glands of both sides are more or less enlarged. Hard, nearly or quite painless, and movable, their *gradual accession within two or three weeks after a suspicious venereal exposure* is strongly indicative of syphilitic origin, without regard to the character of the *local lesion*. If this is present and indurated, the syphilitic character of the trouble is no longer doubtful. It must, however, be borne in mind that glands enlarged through the influence of scrofula cannot be with certainty distinguished from those of syphilitic origin.

They are found in the same locations, and though usually less positively indurated, are still sufficiently so to prevent certain diagnosis. When the initial lesion is on the lips, or in the mouth, the submaxillary gland is affected. Wherever situated, it is always the *glands of connection* (*i. e.*, those nearest to the seat of inoculation) which are involved. Such enlargements are called syphilitic *buboes*.

The complete freedom from true inflammatory action, which has been shown to characterize the induration of the initial lesion of syphilis, and the lymphatic vessels in connection with it, is equally characteristic of the enlargement and induration of the associated lymphatic glands. When attaining sufficient size to interfere with freedom of motion of a part, or where, from any cause, they are subjected to undue pressure, a degree of tenderness may result. From the same cause inflammation, and even suppuration, may occur in highly scrofulous subjects. Such accidents, however, are exceptional, and do not materially lessen the diagnostic value which attaches to *recent and painless* enlargement of lymphatic glands.

The progress of the syphilitic infection, which has been steady and persistent from the moment of inoculation to the engagement of the nearest lymphatic glands, appears now to be arrested. Gradual increase in their size and density alone indicates the activity of the infective process, until, after a period (varying in different instances from twenty to forty days), evidences of constitutional infection may appear.

Access from the surface to the general blood current, through the lymphatic spaces and vessels, *necessitates* passage, 1st, through the gland in immediate connection; 2d, through any other glands or vessels which may intervene between them and the great lymph channels; passage from thence into the general blood mass is immediate.

Thus, the delay between appreciable implication of the glands of connection and earliest evidences of constitutional syphilis is explained in accordance with known histological and physiological laws. Hence, it is only *after* a time sufficient for the passage of the diseased elements

through the natural barriers, the lymphatic glands, to the general blood channels, that systemic infection can take place.

With this view of the *progress of the syphilitic infection*, the interval between the date of inoculation and the introduction of the diseased elements into the general circulation may be appropriately termed the INITIATORY PERIOD OF SYPHILIS.

