Similar testimony is give by Bassereau,[1] Victor de Méric,[2] Fournier,[3] MacCarthy,[4] Sigmund,[5] Ricord,[6] and others.

The testimony derived from artificial inoculation (which has the advantage that all the steps of the process are under the direct observation of the surgeon) is essentially the same. Thus in 12 cases of inoculation of the secretion of a chancre, the mean length of the second period of incubation was 48 days; in 14 cases, in which the secretion of various lesions of the skin and mucous membranes was employed, it was 45 days; in 4 cases, however, in which the matter was taken from pustules, it was 82 days.

In my own practice, I have learned to regard the appearance of secondary symptoms between the fortieth and fiftieth day after the development of the chancre as almost certain, and I have never seen a case which was carefully watched, in which they failed to show themselves within three months. Ricord's limit of "six months" will certainly include the most extreme cases.

The conclusion at which we have arrived furnishes the strongest inducement in all ulcers of a doubtful character to defer general treatment, and keep the patient under careful observation until the time for secondary symptoms to appear is passed.

To sum up this whole matter:

A venereal ulcer which is not subjected to specific treatment (so called) *will usually, if at all, be followed by secondary symptoms within fifty days, and always within six months.*

It follows as a corollary from this proposition that

The earliest symptoms of general syphilis (except in cases of hereditary origin) *have been preceded by a chancre, probably within fifty days, and certainly within six months.*

I will merely add that the development of general syphilis is hastened by an elevated temperature, and by those causes which tend to depress the vital powers, as excessive or prolonged exertion, or a dissipated course of life; and that it is, on the other hand, retarded by the contrary influences, and also by the supervention of an acute disease, as continued fever, inflammation of the lungs, etc. It also appears to be earlier in women, in whom mucous patches are developed with great rapidity, sometimes even three weeks after the chancre.

[1] Op. cit., p. 176.
[2] Lettsomian Lectures, 1858, p. 31.
[3] Notes to Ricord's Leçons sur le chancre, 2d ed. p. 466.
[4] Thèse de Paris, 1844.
[5] Wien. Wochenschrift, 1856.
[6] Lettres sur la syphilis, 2d ed., p. 300.

CHAPTER II.

THE NATURE OF SYPHILIS.

In its nosological relations syphilis has been called a contagious and a virulent disease, a specific fever allied to the exanthemata, a disease of the lymphatics, a disease originating in a fungus, a purulent diathesis (Després), and a blood disorder.

Although these appellations, with the exception of the purulent diathesis, are applicable in a restricted sense, they are all of them more or less incorrect and unsatisfactory. It is true that acquired syphilis is communicable through the blood and certain secretions which are contagious, but this is only a comparatively minor feature of the disease.

The same remarks apply with even more force to the term virulent, since the only reason for using it is that virulent diseases, like glanders, farcy, and hydrophobia, are transmitted by means of a morbid secretion termed *virus*, and have periods of incubation. There is, however, no pathological resemblance, much less a relation, between syphilis and these diseases.

Though the adoption of the term "specific fever" in classifying syphilis is urged even by celebrated syphilographers, a careful examination and comparison of the course of syphilis and of the exanthemata shows only certain resemblances in prominent, but from a pathological view merely accessory features. Syphilis originates in a fixed contagion; the exanthemata likewise in a volatile or fixed contagion; they have periods of incubation; syphilis two, the exanthemata one, which are followed by constitutional disturbance and fever; syphilis in this feature being comparatively mild. Further, they all have extensive integumentary and mucous membrane lesions, which in the exanthemata are always inflammatory during their whole course, while in syphilis they are moderately hyperæmic and essentially proliferative. Here is a radical point of difference; the exanthematous eruptions are simply inflammatory, and if cell-proliferation occurs it is of a simple nature, a mere increase of the normal cells. The opposite occurs in syphilis; the inflammatory process is less active and always results in infiltration of new cells entirely foreign in their nature.

In order to complete the comparison which places syphilis in the group of specific fevers, it is urged by the chief advocate of this view, Mr. Hutchinson, of London, that the late or tertiary lesions of syphilis have their analogue in the sequelæ which sometimes follow the exanthemata, and, instead of calling them tertiary lesions, he would call them sequelæ. According to this view, syphilis ends with the

secondary period and all subsequent lesions are not, as we believe them to be, new pathological processes originating in the one virus, but they are simply non-specific tissue changes induced by the previous ones in the secondary stage. Not only is this comparison false, but it is founded on false assumptions. The sequelæ of the exanthemata are simple tissue changes, resulting without doubt from inflammatory processes; they are in fact true sequelæ, and are etiologically related to the acute stage of the disease. Now tertiary lesions are simply a late series of specific pathological processes following, at varying intervals, somewhat similar processes, called secondary lesions, which are etiologically related to the same morbid cause, the syphilitic diathesis. We can scarcely imagine a greater difference. The one is a simple, chronic, inflammatory process depending on acute antecedent inflammation; the other is the definite and late expression of a diathesis, which manifests itself by a series of proliferative lesions separated by varying periods of time.

Although the lymphatic vessels and ganglia are largely affected by syphilis, and although they are the means of its diffusion and probably its occasional depots of deposit, this relationship, though intimate, is but transitory, since the full development of syphilis takes place not in the tissues of either vessels or ganglia but in the connective tissue to which these are freely distributed. Syphilis cannot therefore be classed among diseases of the lymphatics.

It would be a waste of time to entertain the probability of syphilis being caused by a fungus. It was claimed by Salisbury, some years ago, that the disease had its origin in a certain fungus, the "*crypta syphilitica*," which he said he found in the blood during the activity of the diathesis, and which he did not see when the disease was cured. Since no one else has been able to find this source of the disease, we conclude that it does not exist, and that the specimens, upon the study of which the theory was based, were those of syphilitic blood, into which, owing perhaps to carelessness of preparation and exposure, fungus growths had permeated and fructified.

Perhaps the most remarkable theory of the nature of syphilis is that of Després, who, in a work of over 500 pages, elaborates the assertion that syphilis is a purulent diathesis; that the blood is contaminated by an animal poison containing the syphilitic elements; that it is altered little by little by contact of the débris of syphilitic pus with its globules, thus infecting them, and multiplying the poison, which seeks to escape by the skin in the form of eruptions. Among humoralists, this author goes to an absurd extreme. His work need only be mentioned to condemn it as a piece of theorizing, utterly at variance with facts, and not supported by any tenable simile. The truth is, that of all diseases, syphilis is essentially the least purulent. It is not so in its origin, since the unirritated secretion of the initial lesion never contains pus; its most extensive lesions are peculiar in the fact that pus is rarely present, and then only

accidentally. Further, the course of purulent infection is widely different from that of syphilis.

Lastly, syphilis, according to the views of humoral pathology, is a blood disease. The main fact in support of this opinion is that its contagion is in some stages transmissible through this fluid, yet we must admit the qualification that this is true *only at certain times*. In order to prove that it is not in its essence a blood disease, we must show what form of disease it is. We have found that it originates in the secretion of active lesions and in the blood during an active stage of syphilis. These fluids inserted upon or beneath the integument probably do not at once pass into the circulation but cause a local cell-increase, which forms a peculiar circumscribed tissue entirely foreign to the parts. We then have a local new growth which is limited but exuberant. Remaining in all probability local until mature, this tissue or initial lesion passes away, having been accompanied by markedly indurated enlargement of neighboring lymphatics. Such being the facts, the presumption is that these new cells have, like those of cancer and sarcoma, passed into and infected the lymphatic ganglia. That here, owing to the profusion of lymphatic elements, which we know to be protoplasm, or living matter of the most active kind, this new tissue, or rather these new cells, undergo a great change, increasing in numbers according to the susceptibility of the patient. Having been thus proliferated, these cells are now taken into the blood, either gradually or suddenly, and by it are carried over the body, chiefly, however, at first to the periphery, where they are deposited.

Being deposited in the connective tissue, they take root in this soil, which is peculiarly susceptible to the influence of the syphilitic diathesis. Here they luxuriate, and are still further developed, not attacking primarily other tissues. Inducing, in scattered, circumscribed spots, cell-proliferation in the middle layer of the blastoderm, they cause increase of the cells of this connective tissue itself, as well as the development of a new tissue, the granulation tissue, also called gummatous tissue, gumma, and syphiloma. This is a young transitory tissue composed of cells, sometimes called *cytoblastômes* and *cytoblastions*, which resemble white corpuscles. In describing their development, Virchow says: "The process begins by a proliferation of cells, which augment in volume (hypertrophy), and of which the nuclei are multiplied, often in an astonishing manner. Then follows segmentation of these cells, and finally the veritable development, ordinarily, the production of numerous cells, which in general are very small and usually contain nuclei, these latter being large and for the most part round. They have a certain resemblance to the lymphatic globules, and have been heretofore called lymph-corpuscles or exudation-corpuscles, as they were thought to be due directly to this process. On cutting such a tissue, we find a great number of free nuclei, which are round or oblong, pale, slightly granular, and containing one or more nucleoli. In short, it is essentially a young production,

but slightly advanced in development, and especially indifferent in its cellular nature." This description applies to a gummy tumor of recent date. Such a tissue is not always sharply limited and compact, but is infiltrated; its shape being moulded by the surrounding parts. In old cases, however, there is often a collection of fully developed cells, with but few free nuclei. Among them may be stellate and fusiform cells, and, frequently, Baumgarten has clearly shown that giant cells, formerly considered distinctive of tuberculous infiltration, are found also in these tumors.

These stellate and fusiform cells are distributed through the tumor, which is frequently traversed by an intercellular substance, which is sometimes fibrous. In some instances these tumors merge gradually into the surrounding parts, while in others they are encapsulated. Their structure varies in compactness; they may be firm and fibrous, or they may have a gelatinous consistence, resembling mucous tissue. Such is the general formation of syphilitic tumors; it must be remembered, however, that their structure depends largely upon the configuration of the region in which they are developed and the arrangement of its anatomical elements. In the development of these tumors, as well as of syphilitic papules and tubercles, the first morbid change is in the adventitia of the vessels.

The description here given applies to the fully developed gummy tumor. The cells of the earlier stages are mainly similar. Those of the initial lesion are mingled with molecules of fibrin, showing a more inflammatory process, while those of tubercles form infiltrations rather than distinct tumors. All of these cell changes are similar and etiologically related. The cells, being immature, are liable to fatty degeneration, and for this reason syphilitic lesions often disappear spontaneously. These cells belong to the group called by Virchow *granuloma*, which also includes the tumors of lupus and leprosy. The cells of each of these diseases are similar and resemble those of granulation tissue. Those of syphilis are peculiar in their arrangement, mode of development and course, and in being absorbed under the influence of mercury. An important and almost unanswerable question is, whether these cells of syphilis are specific. They are so regarded by Wagner, who gives the name "*syphiloma*" to the tissue which they form. Virchow, on the contrary, denies their specific nature, and prefers the terms "*gumma*" and "*granuloma*." Although the appearance of these tumors is almost identical, it must be acknowledged that the property of contagiousness is peculiar to the cells of the syphilitic tumors.

We now come to the consideration of hyperæmia. Chronic congestion is an important feature in the pathology of syphilis. It is especially noticeable in the early stage, and is best exemplified in the exanthematous syphilide and in the hyperæmia of the fauces. Many other secondary symptoms have a similar nature, and hyperæmia of the viscera probably occurs in this stage, yet generally it altogether escapes observation. Early in syphilis, this hyperæmia precedes and

accompanies the extensive lesions, though it may exist merely as capillary stasis without cell change. In the late stages, the hyperæmia is milder and more localized. It is probably always a forerunner of gummy tumors.

An additional phenomenon of syphilis is the production of connective tissue, either without gummatous cells or accompanying gummy tumors. This tissue increase is the result of mild hyperæmia, and occurs in firm, fibrous tissues, such as the periosteum and the capsules of the viscera. It is best seen in syphilitic periostitis and in the fibrous bands observed in the liver, spleen, lungs, and testicles.

It is noticeable that suppuration rarely accompanies syphilitic lesions; when it does, as in the early pustular eruptions, it is a secondary result or an accidental occurrence, and is not an essential part of the syphilitic process.

Although it was long since claimed that the lymphatics were the active agents in syphilitic infection, and although Virchow has for years insisted upon a similar theory, the question has never been properly studied, and modern authors are vague and uncertain in their opinions. The majority, however, regard the blood rather than the lymphatics as the vehicle of contagion.[1]

Our own conclusion is that syphilis is a disease of the connective tissue, and not primarily of the lymphatics or of the bloodvessels, although the blood may be temporarily modified and may be the vehicle of contagion.

The secretions of syphilitic lesions are found to consist of a serous

[1] In the year 1871, Dr. F. N. Otis published two articles, endeavoring to explain the periods of incubation and the course of syphilis upon the theory that infection occurs only through the lymphatics. Assuming the syphilitic virus to consist of disease germs, the author thinks that the first period of incubation is occupied in their passage through the tissues, the process varying in duration in proportion to the depth of the lymphatics and the resistance of the tissues. He believes that the syphilitic virus coagulates the superficial tissue-fluids, causing obstruction to the circulation and attraction to the spot of wandering white corpuscles, which by their amœboid movement entrap the specific disease germs. The latter are developed and increase within the white corpuscles, which themselves multiply. According to this view, the initial nodule is simply an aggregation of diseased white corpuscles. These latter pass into the ganglia and there again multiply, passing finally from the lymphatics into the circulation. Though Dr. Otis has on many occasions recently advocated this theory, which by the way is not original to him, since it was first advanced by Nisbet, in 1788, and again in 1863 by Sperino, I am to-day as much opposed to it as in years gone by. Dr. Otis asks us to assume certain fancies in the absence of definite facts, and to felicitate ourselves with the idea that we know how syphilis works in the system, when the truth is that we do not. We know that the lymphatics have something to do with the entry of the syphilitic virus, but it is not at all clearly established that the bloodvessels do not also participate in the process. Further, when syphilis is ripe we find its activity is expended upon the connective tissue framework of the body and secondarily upon other tissues. I think that the true way to study the disease is in the clinic-room and dead-house, and that its essence will never be clearly understood by presenting a mosaic of incongruous pathological facts blended together by a sophistical and specious argument. I feel that I must here enter a solemn protest against the acceptance of this unsubstantiated theory.

fluid containing numerous shining granules or molecules, which are masses of protoplasm or germinal matter, holding the contagious properties of syphilis. These microscopic bodies are probably taken into the circulation by the lymphatics and conveyed over the body. Possibly they are absorbed by the blood-corpuscles, or the latter are infected in some mysterious manner by these actively increasing morbid cells. The fact that serum alone does not convey the syphilitic poison goes to prove that the corpuscles hold the contagious material.

In the secondary period of syphilis these cells are very numerous, and the body may be covered with papules and tubercles composed of them. As the disease wanes, these lesions become more localized and fewer in number, and the blood is less contagious. Finally these cells may be limited to a few gummous tumors; the blood no longer carries the molecules, and it loses its contagious properties. The cells no longer have a tendency to reproduction, which characterizes them in the early stages, but rather degenerate. Hence we consider the blood and the secretions in tertiary syphilis innocuous. Even if cells are present, they are old and inactive, and are incapable of reproducing themselves. Lancereaux states that he has often punctured himself in making autopsies on subjects with gummy tumors, and has never seen any bad result.

The periods of latency observed in the course of syphilis are of interest, and may perhaps be explained in the following way. Each outburst is attended by the development and multiplication of the peculiar cells, which run their course and are finally absorbed. Some remain and after a time are excited by unknown causes to activity. Thus repeated exacerbations may occur, each one depending upon the multiplication of cells remaining from a previous outburst. But each relapse is less active and less prolonged than its predecessor, until perhaps only one nodule, and that composed of effete cells, may remain. The disease is then cured. This explanation may seem to apply imperfectly to those cases of prolonged latency in which no lesion whatever has been perceptible. Virchow thinks that in these cases the lymphatic ganglia have been the places of deposit of the syphilitic cells, which, at the expiration of the period of latency, undergo the changes mentioned. In any case, the specific cells must be hidden away somewhere in the system, since the continuance of the disease depends upon their existence.

With this view of the nature of syphilis, its effect upon the health and upon the organs and tissues may be readily comprehended. In the early active stage of proliferation the red globules are diminished and the white increased in number. The depressing influence of syphilis is thus fully accounted for. Digestion is impaired and the tissues are poorly nourished. Finally, the functions of vital organs may be perverted or destroyed by the cell-changes produced.

It seems probable that Hunter's dictum that syphilis is the sole

appanage of man, and that the tissues of animals are not susceptible to its influence, may, as time passes, be more or less generally disproved. Though Turnbull, Hunter, Babington, Ricord, and Castelnau and others, had failed to inoculate animals with the syphilitic virus, and the vaunted results of Auzias-Turenne upon the monkey were finally declared failures, and that the experiments of Cullerier, Robert de Weltz, Diday, Sigmund, Bassett, Ricord and others, though inducing chancroids by the inoculation of syphilitic matter, had failed in producing syphilis in dogs, cats, rats, guinea-pigs, and rabbits, and that Lancereaux, though seemingly successful, was in doubt as to whether the disease he had produced in a guinea-pig was syphilis or tuberculosis, and finally that the results claimed as successful by Messenger-Bradley, Vernois, Depaul and Lichtenstein, were vulnerable in many particulars, later observers have not been deterred from further experimental investigation. Thus Klebs has published two striking cases.[1] He injected a small quantity of a solution of isinglass, in which pieces of hard chancre had been macerated for a few days, under the skin of a monkey. Five weeks later, ulcers of the gums and tongue, resembling, in all particulars, those of syphilis of the human subject, were observed. The animal was killed fifty-five days after the inoculation, and cheesy nodules which, in Klebs's opinion, resembled gummata, were found between the skull and dura mater, and in the lungs and kidneys. In the next experiment, small pieces of hard chancre were inserted under the skin. No local reaction followed, but later on, the lymphatic glands became enlarged, and in six weeks a tubercular eruption appeared, accompanied with slight fever. The tubercles underwent spontaneous involution. In five months the monkey died of marasmus, and at the autopsy a worm-eaten appearance of the skull and cheesy deposits in the lungs and kidneys were found. The skeptical may claim that these were cases of tubercular inoculation. The latest claimant to success in this direction is Martineau,[2] who thinks that Klebs and Anfrecht, who first discovered the bacillus of syphilis, should have pushed their observations further in cultivating the micro-organism, and with the germs thus developed inoculated animals. This, Martineau, with his assistant Harmonic, claims he has done successfully. They proceeded as follows: "They cultivated (*sic*) a chancre, and placed it in a close vessel previously heated to a red heat, then, having prepared a concentrated *bouillon* (Liebig) kept at the boiling-point for about two hours, they placed the *bouillon* in a flask with a long neck, then introduced the chancre quickly and corked and sealed it with wax. This liquid, when examined the next day (April 30th), contained numerous bacteria of a peculiar form. On the 1st of May

[1] Ueber Syphilis-Impfung bei Thieren und über die Natur des Syph. Contagiums. Prag. Med. Wochenschrift, No. 41, 1878, and Beiträge zur Path. Anat., 11 Heft, 1880.

[2] La France Médicale, Sept. 7, 1882.