SYNTHETIC PRODUCTS, POISONING BY.—Out of the large number of synthetics obtained from the hydrocarbons of coal-tar a few have come into general medical use, and one of these, acetanilid, is a common ingredient of the headache cures sold by druggists. Antipyrin and phenacetin are also much used, but, being more expensive, are less common in proprietary articles. All these bodies are antipyretics, and when taken in overdose, produce depression of the heart, with slow respiration and lowered temperature. Marked cyanosis is also observed. Nausea and vomiting may occur. The effects of the drugs are much influenced by idiosyncrasy. The treatment should be free washing out of the stomach, artificial warmth to counteract the antipyretic action, and stimulants, alcohol and coffee, to counteract collapse. Inhalations of oxygen have been suggested; also the hypodermic use of strychnine.

Sulfonal, trional, and tetronal are members of a group of synthetics that have hypnotic action, and have been used as substitutes for morphine. Sulfonal has been much used. These agents may cause vomiting and purging, but not usually. In fact, the bowels are often constipated. Sometimes the most marked symptom is depression, but the typical effect is sleepiness which deepens into coma, and may last for a long while. The urine is diminished and becomes very dark, owing to excess of a coloring matter. This symptom, known as hæmatoporphyrinuria, is generally early developed. In a case of trional poisoning recently reported, the patient, a woman aged twenty-eight, had well-marked hallucinations with dizziness, staggering, and loss of reflexes. The change in the urine came on late. The patient was in bad health when she took the drug. She died from the effects.

Treatment of this class will be carried on along somewhat the same lines as those given above. The stomach should be washed out well. As the drugs are eliminated by the kidneys in unchanged form when the dose is large, it is deemed advisable to use warm water freely as a diuretic. Constipation will be, of course, met by mild purgatives or enemata. *Henry Leffmann.*

SYPHILIS.—The word syphilis was probably first suggested by *Syphilus*, the name of one of the characters in a pastoral poem composed by Fracastor in 1530. This name was unquestionably coined by the poet for his fictitious character, by a combination of σῦς, hog, and φίλος, fond of—a not uncomplimentary designation for swineherd.

Definition.—Syphilis is a specific, infectious, and chronic disorder, resulting either from inheritance or from immediate or mediate transference of the disease from an infected to a sound individual, beginning always, in the latter event, after the lapse of a characteristic incubative period, by the appearance of an initial lesion, at the site of infection, commonly termed a chancre; and followed after an interval of time by symptoms of systemic derangement, often evolved in a determinate order, which eventually may affect any organ of the body, one attack usually conferring upon the subject of the disease immunity against subsequent infection.

Synonyms.—Many of the names which have been employed to designate the disease seem to have originated in attempts to shift the reproach of its origin and existence from the people of one nation to those of another. It has been called morbus gallicus, the French disease, lues venerea, mal vénérien, vérole (in France), sifilide (in Italy), French pox, chronic pox, "bad disorder," "bad disease," Lustseuche, Krankheit der Franzosen, radezyge (in Sweden), and other names. The discovery of the micro-organisms responsible for the production of frambœsia and yaws has differentiated completely the three affections.

History.—Toward the close of the fifteenth century—soon after, in fact, the discovery of a new continent—syphilis made its appearance among Europeans and became the subject of discussion in medical literature. By many it was then supposed to have originated in consequence of the relations newly established between the inhabitants of the Old and those of the New World, and it was therefore often termed the "American disease." Later investigation, however, makes it appear possible that syphilis appeared among the races of men at a more remote period of antiquity. Evidence of supposed syphilitic disease of the bones has been recognized in the skeletons of prehistoric man.

Interest has been revived in the questions relating to the supposed American origin of syphilis by fresh studies of original documents, and by discoveries, in different portions of the continent, of bones supposed to exhibit changes due to the disease. Papers touching on the theme originally well elucidated by Joseph Jones, of New Orleans, have appeared from the pen of Bruehl and others, throwing further light upon both sides of the problem. The writings of Sahagun, Torquemada, Roman, Mendieta, Pane, and others have been found to show, as to New Spain, that the bodies of those affected with syphilis were interred, as distinguished from those dead of other disorders, which were cremated; that the infected were not deemed fit for religious sacrifices; that they were not represented at the festivals; and that the disease was counted a punishment sent from the gods for the nonperformance of religious rites and for other offences. The Mexicans not only recognized the connection between the earliest and later manifestations of the disorder, but distinguished between several types of the former, understanding also its remedial treatment far better than the Spaniards, and even seeking thermal resorts for the purpose of securing relief. In seventeen Indian dialects, each of which has a primitive and native term for designating the disease, none of the terms thus employed suggests confrontation with a new malady, although soon after contact with the whites the natives were compelled to apply new names to many novel objects with which they were to become familiar. These new names either bear witness to the impression on their ears made by the speech of the Castilians, or describe some prominent feature of the object to be newly named, a rule distinctly observed by them in the case of diseases known to have been imported from Europe to America, as, for example, measles and smallpox. The singular confusion, existing in the Mexican language of the sixteenth century respecting the terms employed to indicate ideas of power, divinity, and the special disease here under discussion, possesses an interest in view of the fact that this is recognized in the dialects of Quechua and Aymeras, three hundred years before Pizarro conquered the capital of the Incas.

Symptoms scarcely to be distinguished in their description from those of syphilis are described in the ancient literatures of China, Mexico, Peru, Arabia, Greece, Rome, and in the sacred writings of the Hebrews. It is probable that, at the periods which have been assigned for the origin of the disease in the fifteenth century, its rapid extension was largely due to the awakened activities of mankind in the direction of geographical discovery and international traffic. It is a well-known fact that epidemics of infectious diseases are usually most severe in communities which have long been virgin of such accidents.

The literature of syphilis may almost be said to date from the period so long assigned as that of its first appearance among the races of men. It has since been adorned by the names of such eminent medical authors as Astruc, Van Swieten, Boerhaave, Bell, Sydenham, Colles, Hunter, Ricord, Gross, and Bumstead. The contributions to the subject made by contemporary authors have been as voluminous as valuable. The evolution and involution of the syphilitic process in every organ and tissue of the body have been observed and described with as much detail and accuracy as have been bestowed upon any of the problems in medicine.

Geographical Distribution.—Syphilis exists to-day in almost every country to which commerce has pushed its ventures. The degree of its depredations in any province may be wellnigh regarded as a measure of the extent of the intercourse of the inhabitants of such a country with the world at large. It exists in Great Britain,

Russia, France, Italy, Norway, Sweden, Denmark, Prussia, Austria, Portugal, Switzerland, and in every other country of Europe. Its victims are usually more numerous in the larger centres of population where the activities of trade are greatest. England, for example, with her enormous maritime traffic, pays a heavier price of this character for her commercial profits than France, which is popularly supposed to suffer in larger measure. In a few of these countries, Italy, for example, where many of the people are densely ignorant, filthy, and poor, epidemics of the disease have occurred with disastrous results. On the African coasts, in Egypt, Madagascar, and Abyssinia; in all countries of Asia with which Europeans sustain commercial relations; in Japan, where the disease is reported to be both widely prevalent and virulent; in the Levant; in all parts of Asia Minor, and throughout all districts lying upon the shores of the Black Sea, syphilis is found, varying both in types of intensity and in preponderance. The same is true of all the countries of North and South America, Oceanica, and the Hawaiian Islands. In the United States of America, syphilis may be recognized in every hospital and in the practice of almost every physician of repute. It is fortunately, however, much more common in the large cities, the rural populations escaping to a happy extent. It is found here among those who are native to the soil, including the negroes and Indians, as well as among the Chinese and other individuals of foreign birth who have immigrated hither.

It appears, in brief, that the extent and severity of the disease are not related to climate, isothermal lines, or degrees of latitude and longitude. They are intimately related, rather, to certain social traits in mankind, distinguished in their commercial, military, and religious excursions, trading ventures, pilgrimages, wars, fairs (*e.g.*, that of Nijni-Novgorod), and encampments of armies; their hygienic and medicinal methods; and, more or less in consequence of what precedes, to the density of population and the degree of intelligence possessed by infected classes as displayed in their management of the malady.

Nature of the Disease.—Syphilis is a specific infectious disease, always occurring in consequence of transmission from a diseased to a sound individual, and always transmitted as such. It does not sustain etiological relations with scrofulosis, tuberculosis, leprosy, or any other known disorder. It is capable of transmission by inheritance, and also by the medium of fluids furnished by the pathological tissues of diseased individuals. These fluids when isolated may be said to embody all the power and potency of the disease, and hence are described as virulent, or containing the virus of syphilis.

This virus, or contagious element of the secretion, which may be removed from one individual and artificially introduced into another with the result of thus assuring the complete evolution of the symptoms of the disease, has been the theme of much discussion. Its very existence has been doubted by Bru, Jourdan, and others.

The Bacillus of Syphilis.—After years of research and experimentation, the special micro-organism of syphilis would seem at last to be discovered, though there is yet lacking the production of the disease in man by inoculation with pure cultures.

Max Joseph and Piorkowski, of Berlin (*Berl. klin. Wochenschrift*, Nos. 13 and 14, 1902), discovered in the spermatic fluid of a male subject, twenty-two years of age, a bacillus 4–8 microns in length and 0.2–0.3 micron in thickness. These were cultivated on sterilized placentæ; they closely resembled in size and other features the diphtheria-bacillus. Transferred to artificial media, there promptly appeared, in twenty-four hours after inoculation, a colony of micro-organisms scarcely visible to the naked eye, producing later a grayish, confluent, agglomerated mass in which, with the aid of the microscope, bacilli were recognized resembling the bacillus subtilis, staining readily with carbol-fuchsin and gentian-violet. They were blunt-pointed; usually knobbed at one extremity; and were cultivated on artificial media for three generations; the last produced colonies showing diminution in the size, frequency, and vigor of the bacilli, all of which was materially changed by reinoculation upon blood-serum.

These experiments were verified by examination of the sperm of twenty-two male patients, control experiments with no recognition of the same elements having also been made on sound male subjects. The introduction of pure cultures of this bacillus into a sow was followed by morbid results which, however, might have been possibly due to swine cholera.

Claims to the discovery of a bacillus of syphilis have been made also by Lustgarten, Pisarevski, Klebs, Birch-Hirschfeld, and others.

Syphilis without question belongs to the class of infectious granulomata, and is the result of the introduction of a parasite into the human economy. The disease should be classed to-day with tuberculosis and leprosy, the etiological bases of which are now beyond question.

Neisser believes that the bacteria may be transmitted by intra-uterine inheritance or extra-uterine infection at a given point where multiplication of the germs occurs. Whether instantaneous general infection follows by the sudden admission of these micro-organisms into the circulating fluid, or by the slower process of invasion of the lymph-channels and extension through the lymph-glands to the general economy, it seems clear that the initial sclerosis of the disease, a "chancre," becomes a focus of infection which only gradually participates in the same process of distributing the germs of the disease throughout the general economy. Later, the lodgment of these germs in various parts of the body determines the development there of the specific products of the disease; possibly also exercises there that specific local modification which renders the tissue then capable of reacting in a certain characteristic morbid behavior, after the operation of external irritants (mucous patches in the mouth of the smoker, etc.). Neisser believes that the nearer the date of infection, the larger the number of bacteria present at any one moment in the body; and, as a corollary from the above, the more numerous, symmetrical, and superficial the lesions. But in later periods, with a smaller number of bacteria and a gradual decrease in capacity for infection and hereditary transmissibility, there are fewer, deeper, more asymmetrically disposed, and more malignant manifestations of the disease.

Evolution of the Disease.—Between the moment of infection and the earliest appearance of a chancre to the unaided eye, there is usually a delay of from fifteen to thirty-five or forty days, a period of twenty-one days for the average of cases. This is usually called the first incubation. There is, however, neither an incubation, a "hatching," a delay, nor an arrest. If our methods were without flaw, we should be able to detect the movement toward general infection from its very first to its completed step. In the attempt to study the evolution of syphilis, questions of time, the crude hypothesis of an incubation, and all really artificial distinctions, should be, for the purposes of critical investigation, set aside.

By the late eminent Philip Ricord, the evolution of syphilis was divided into three stages, the primary, the secondary, and the tertiary. The primary included the symptoms concerning the chancre and its accompanying multiganglionic adenopathy. The secondary period included the symptoms displayed during the succeeding term, in which systemic infection occurs, with usually symmetrical and superficial cutaneous and other manifestations. This was loosely estimated at about one year in duration. Lastly, following this stage of efflorescence, came the tertiary period, that in which the deeper structures of the body are involved; that in which the disease commonly ceases to be transmissible, in which it may produce its most destructive effects, or pass into a complete innocuousness and decline. The influence of this doctrine of periods has been incalculably great and valuable. It once marked a revolution in the history, in the study, and in the treatment of the disease. It has dominated the minds of the medical men of all lands

since it was first completely grasped by the intellect of its master.

But it has served its day. To thoroughly grasp the problems of syphilis, it is now needful, for the time being, to emancipate the mind wholly from the ingenious suggestiveness of this doctrine. It must be clearly seen to be nothing but an artificial device for classifying in a clumsy way the clinical phenomena of the disease.

As a matter of fact, there is no line of demarcation between the successive phenomena of syphilis as they appear in the evolution of the disease in any given case. From the moment when infection has been wrought to that of the gravest injury, or of the mildest efflorescence, there is, when no arrest occurs, a gradual but continuous progression of the disease. This advance is commonly marked by interludes as striking as they are salutary. They may be due to the intervention of treatment, or to changes in the general health of the infected due to other causes. Apparently capricious cessation of the advance of the disease may occur, since even the cutaneous symptoms of marked cases may wholly disappear without treatment. If we were in position to view with keenest scrutiny the unmodified progress of syphilis in cell and vessel, no one can doubt that the so-called period of incubation would disappear and the microscopic eye of the observer would be as busily occupied during that as throughout any other period of the disease. Similarly, there would be no sharp distinction possible between primary and secondary syphilis. One could scarcely note the hour when, from the first to the last, there was not in progress a slow and gradual progression, from point to point, of the toxæmic product originating in the changes wrought at the site and at the time of infection.

These suggestions are needed for a clear comprehension of the phenomena following the stage of so-called "primary syphilis." The "primary" hypothesis made it absolutely necessary to assume that after the primary came a secondary; and after a secondary, an inevitable tertiary stage. More, the mind thus habituated to a study of the evolution of the disease in periods looked to an evolution of symptoms in these periods in due order and line of procession. One was thus educated to expect in a typical and uninterrupted attack of syphilis (could such be observed) each and every one of the several manifestations of the disease. After macules, papules should appear and, in course, pustules, gummata, ulcers, and successive involvement of organ after organ of the body. Some such definiteness of order is, in point of fact, to be recognized in the evolution of variola, with which, unfortunately, syphilis has been too often and too closely compared.

But no such syphilitic history has ever been observed. It is the artificial manikin of the schools, the figment required by the domination of the medical mind by the time-rules of the French school. It was this once useful and ingenious time-schedule which made it equally imperative for the French to coin for some of the manifestations of syphilis the striking terms "precocious," "galloping," and "tardy," words which embody a confession of the weakness of the schedule to explain all the exact clinical pictures of the disease.

Almost immediately after lymphatic adenopathy has declared to the eye and the finger of the observer that the toxic product of the chancre site is finding its way into the vascular channels of the body, the phenomena of the disease are evolved, not in the order of a time-card, but, to employ a different figure, in radii from a pathological centre. Early indeed, in many cases, can it be seen that the future of the malady is to be sought along one or another line toward exceedingly variant results. The complexus of these results may be conveniently classified in four divisions, which are named later.

Toward these the advance is either slow or rapid. The gravest may be imminent when the chancre is yet unhealed, the adenopathy unrelieved, the lymphangitis discernible. The mildest may be attained when months have passed, the early accidents are wellnigh imperceptible or forgotten, and the general health of the infected individual meanwhile not manifestly impaired.

Whether this apparent interval (the so-called "secondary period of incubation") be brief or protracted, none can doubt that when an ultimate evolution of the disease occurs there is a continuous progress toward complete or partial systemic intoxication. When well marked, this apparent interval occupies from forty to fifty days, but it has been noted as brief as twenty days and as prolonged as a twelvemonth. Its limits are usually defined between the date of the chancre's appearance on the one hand, and the date of the first cutaneous exanthem on the other. That this is a purely artificial distinction becomes at once apparent when one of these dates of limitation is questioned. There is nothing in a cutaneous exanthem which entitles it to pre-eminence above other symptoms of syphilitic invasion perfectly evident during the so-called second incubative stage. From the date first assigned to the last arbitrarily selected there is no real pause, no conspicuous absence of invasion signs. On the contrary, the symptoms of this period are often more suggestive and significant than when, for example, the skin of the patient's belly is beset with a macular syphiloderm.

The merest enumeration of symptoms possibly occurring in this period of apparent pause is sufficient to indicate that no real incubation can be observed. Yet here again it is important to note that not all of the enumerated symptoms are to be observed in one individual, and further, that they observe no definite order when two or more chance to be parts of one syphilitic history. Rather are they different surface-indications of the several lines along one or another of which the disease may advance toward its ultimate results.

After the chancre appears, and before the first exanthem of general syphilis follows, the condition of the average patient is far from in apparently sound health. The blood-globules commonly decrease, while the leucocytes by actual enumeration increase in number. The glands of the body elsewhere than those in the region of adenopathy near the chancre site, slowly or suddenly enlarge, become tumid, painless, much less indurated than those first noted in the disease, and are often symmetrically, rather than, as in the other instance, asymmetrically involved. The spleen, so intimately is it concerned with the fluids traversing the vascular channels, becomes tumid and at times tender. The liver function is often disturbed, as shown by an icteroid skin with muddy conjunctivæ and the appearance of bile-products in the urine. The functions of the stomach, of the bladder, of the suprarenal capsules, and of other viscera, may be seriously impaired. Continuous or interrupted febrile temperatures may be reached ("syphilitic fever"), the thermometer rising at times even to 105° F., the patient being not rarely treated by a physician ignorant of the nature of the effective poison for an intermittent or relapsing fever. The nervous system may seriously suffer. Atrocious neuralgias, substernal and periosteal pains, pains in the bones and joints, osteoscopic sensations, and even synovial effusions, may be the protest of the system against the advent of the recently introduced poison. Often there are signs of mischief even of a severer type. The lassitude and depression are profound; a condition of mental hebetude gives place to partial syncope; a headache results in a temporary strabismus, a pain in the upper or lower limbs is followed by muscular contracture. None can doubt that in a carefully studied case where the evolution of syphilis is actually in progress, however mild its future is to be, a skilled diagnostician could recognize, at one point or another of the body presumed to be in the stage of this so called secondary incubation, unmistakable evidences of an insidious advance of the malady.

The term "explosion" has been repeatedly employed, with other metaphorical phrases, to describe the moment when the first cutaneous exanthem appears. Its use is an index of the extravagant importance attributed to the onset of skin-symptoms in early syphilis. As a

matter of fact, the latter are surface indications of more serious and deeper processes (probably involving the nervous centres) and are all-important to the eye only of the vulgar. As a matter of fact, too, they never occur by explosion. The first efflorescence of the disease may be as gradual as the dawn of a day and as impossible to define. Before the human eye traces its first expression, the camera of the photograph can produce with fidelity the faint mottlings of a skin that is to be later visibly the seat of a syphilitic efflorescence. No one who has with minute care watched the oncoming of the cutaneous manifestations of the disease, can have failed to note how insidiously the approach is made to the eye. An accident may change all. The excessive heating of the body in a bath or by dancing may simply precipitate the blushing of the first rash.

This once apparent, and let it be noted even without this, syphilis exposes its advance in numberless directions, probably in no two cases exactly the same. These advances may be, however, for practical purposes, classified in four principal directions, as previously suggested in these pages. They may be named and briefly sketched as follows:

1. Benign syphilis with mild and transitory symptoms.

Every vacciniculturist has recognized the fact that a few heifers fail to respond to all efforts to inoculate the udder with vaccinia. The reason is not explained; the system of a few individuals in every thousand simply refuses to react against the introduction of the poison. No expert of wide experience can fail to have been impressed with the fact of the existence of this exceptional class of human subjects with respect to syphilis.

There are persons who exhibit typical chancres with characteristic adenopathy of the vicinage, who never after exhibit the slightest signs of systemic disease. The objection to this statement is suggested at once to the mind of the profane. It is, that an error was made in the diagnosis of the initial sclerosis. That which seemed to be a syphilitic chancre was really not such, but spurious, an imitation of the genuine lesion. But, it is responded, such chancres have been not carelessly, but with exquisite skill, studied by experts, and found not different from others followed by grave syphilis. Further, the persons enjoying this immunity have failed later to contract the disease when exposed to it; and, more important than all else, individuals of this class correspond to others of the same class who, having actually exhibited such chancres, do later have systemic symptoms of such mild type as to astonish those unfamilar with these singular exceptions to the rule.

These interesting exceptions are either the triumphant proofs of the skill of the physician, or (what is far more probable) proofs that some of the phenomena of natural law defy ultimate analysis by the human mind. Persons of this class have typical, severe or mild, premonitory chancres. In due time they have also slight ganglionic engorgement, post-occipital, along the nucha, or in the line of the sterno-cleido-mastoid muscle. An exanthem occurs, of macular type, upon the belly, over the chest, slightly upon the face, or perhaps limited to the trunk. When this fades, with or even without medical treatment, the disease is absolutely at an end. These cases are annually observed in every extensive syphilitic practice. They are not rarely seen in women who have been infected without their knowledge by a husband, or through the innocent contacts of daily life.

2. Benign syphilis with relapsing or persistent superficial symptoms.

Cases assignable to this category are those in which typical chancres are followed by typical early manifestations of general syphilis, the patient continuing, for months or even years after, to be annoyed by intractably persistent or relapsing, but wholly superficial syphilitic symptoms. If described according to the former phraseology, these would be classed with the subjects of prolonged secondary syphilis, never proceeding to tertiary stages. Two, three, and four years after infection, such subjects are found with an infiltrated patch of scaling papules on buttock or back; with mucous patches of lips, tongue, or fauces; with a squamous scrotal, palmar, or plantar syphiloderm; or with a cluster of superficial and crusted papulo-pustules over the occiput or temple in the pilary region. After alternately trying and tiring of all methods of treatment, the disease at last yields. Throughout all, from first to last, there is no sign of a formidable malady. When recovery has at last occurred, no trace is left on the body of the infective process. There has been no deep ulcer, no cicatrix, no permanent impairment of any organ or tissue. The disease, viewed in retrospect, has been perhaps a long but always rather an annoying than a dangerous affection. It may never have for a day prevented attention to the routine work of the sufferer. Had it not been for the incidental apprehension of the future, it would not have attracted serious attention nor demanded assiduous care.

Such, without any question, is the course of the majority of all cases of syphilis. It is claimed that, however mild these histories, each is liable to result in the graver forms of the disease, and that which determines the difference is treatment, always of highest importance. The most superficial study of syphilitic statistics, however, demonstrates that the majority of all patients, with the best, with the poorest, and without treatment, escape what has long been termed tertiary syphilis; in other words, do not exhibit the destructive types of the disease. The percentage of the latter to the former, in both hospital and private practice, has been estimated at the lowest at about seven per cent., at the highest at nearly thirty per cent. The corollary, therefore, is trustworthy that at the least two-thirds of all patients in all countries, and subjected to all methods of treatment or none (homœopathy, ignored cases, expectant treatment, "mind cure," etc.), escape the destructive ravages of the disease. It is upon this issue in the majority, and not upon the dreaded results in the minority, that the evolution of syphilis in the average of cases is to be predicated. Nothing that is here set down is to be interpreted in denial of the equally palpable fact that the mildest case of syphilis at the outset may become the severest in the end; that the patient fairly launched in the direction of benignancy may be mischievously turned in a different and more dangerous course; that scientific treatment of the disease furnishes one of the greatest triumphs of human ingenuity and skill. It is here intended merely to look at the results of the evolution of the disease, among all classes of men and in all countries, from the broadest point of view.

3. Malignant syphilis with relapsing or persistent profound symptoms.

A recent French writer has well distinguished between the syphiloma that resolves and that which degenerates. In this third category are included all patients exhibiting gummatous lesions that are either resolved and do not return, but leave serious consequences behind; or that are resolved and return later with serious consequences after either or all outbreaks; or that persist with no less harmful results. Here, too, are variations from the less to the more dangerous grades.

Any one of these conditions may develop after the patient has exhibited only such lesions as would justify his being classed in the category just considered. But it is highly important to note that all the symptoms here described and catalogued may succeed the chancre-stage without intervention of milder symptoms, and also without an important interval of time. Early, indeed, after the chancre has healed, often before this last is completed, there are indications of the evolution of the disease toward a malignant type.

The "malignancy" of this class of cases is seen in the deterioration of the general system and the production of a syphilitic cachexia, without absolute destruction of the tissues of the body. Gummata that never ulcerate or degenerate may form in the skin, subcutaneous tissue, bones, periosteum, periarticular and articular tissues, mammary gland, testis, or other organ. By the production of pain; by displacement or mechanical effects; by

a subtle influence, that is difficult of analysis, on chylopoësis, sanguification, or nutrition, and by interference with other functions, a disastrous influence is exerted that justifies the term malignancy in describing the course of the disease. Its effect is most striking when the structural lesions are few and not in themselves grave. A patient with merely a submaxillary lymphoma or periosteal gumma, or with an obstinate pachymeningitis producing injury by pressure-effects rather than by destructive action, may be in a graver physical state than another with a profound ulcer of the leg or of the throat.

In this category are to be found the smaller number of all cases of syphilis. It is pre-eminently the category of the transitory. They who have suffered from a syphilis trending along these lines, either by force of good management or as a result of the self-limiting energy of the disease, or the reverse of these, are readily transferred to the class just described or to that which is considered below.

4. Malignant syphilis with relapsing or persistent and profound lesions that are ultimately destructive.

In this category are classed all those patients who exhibit the worst phases of what is called by the French "tertiarisme," the symptoms which have made the disease to be dreaded as much as any of the pestilences that have visited destruction upon the human family, the histories which have engendered the popular and quasi-professional belief in the non-curability of the disease, those which have led philosophers to wish that the disease were one that kills, rather than one that can so frightfully mutilate without killing.

Here the resolving or disintegrating gumma opens an avenue to ulceration that pierces through connective tissue, cartilage, periosteum, and bone; to resorptive results which, when the gumma has disappeared, leave in its site shrivelled secreting cells, nervous, hepatic, renal, osteoid; that leave the testicle a shrunken miniature of its former self; that leave a sclerotic tissue in the place of brain cells or spinal cells, whereby one-half of the body loses its motor function, or a portion of the brain its ability to preside over the function of speech. Here, too, remote as are these formidable consequences on the time-schedule of the French school, all are obliged to admit that but a few weeks may intervene between the chancre evolution and the worst ruin. In a few days, while yet the induration of the chancre persists, the hard palate may be perforated as readily as the finger may be pushed through a sheet of wet paper; or a liver may be stuffed with ominous nodules; or the surface of the body ploughed here and there with deep and even gangrenous excavations where a gummatous infiltration has rapidly melted to destruction. It is true that for the most part these grave results occur between the third and fourth years after infection; but the facts of early appearance of so-called late symptoms in syphilis are by none better attested than by the French themselves. It is they who have coined for science the phrases "malignant precocious syphilides" and those of similar import. It is they who freely admit that the malignancy and precocity are in these cases intimately associated. It may even be asserted as a fact that the majority of all truly malignant manifestations of syphilis are precocious to the extent of violating the old rule of tertiary syphilis as a sequel of an orderly and classically developed secondary stage. It is the characteristic of these dreaded devastations of the malady that they are early declared and rapidly evolved as extremely formidable types rather than as dangerous complications or perilous sequels of lues. Even with the chancre unhealed, the surface of the body may be in these cases riddled with sloughing cavities.

Between the four main lines of evolution briefly delineated above, there are to be recognized clinically innumerable variations in the direction of both mild and severe symptoms. That these types mutually merge and are to a degree interchangeable by the accidents of environment, constitutional influences, and treatment cannot be questioned.

An examination of the symptomatology in 96 cases reveals several points of interest. The organs affected were, in 47 cases, the derma, subcutaneous, and adjacent tissues; in 11, the bones and periosteum; in 11, the brain and cord; in 7, the soft and hard palate; in 6, the tongue; in 7, the testes; and in one each, the vulva, the eye, the kidney, the rectum, the muscles, the lungs, and the joints. Fournier, of Paris, reported before the International Congress of Syphilography and Dermatology in Paris, in the year 1889, the fruits of twenty-nine years of private practice in the French capital. In these twenty-nine years he had been able to study 2,600 cases of tertiary syphilis occurring in private patients. Some of his results were in the highest degree confirmatory of the important data of tertiarisme given above. But he also demonstrated that among 3,429 instances of tertiary manifestations, he had tabulated 1,085, or nearly 32 per cent. of cases, in which there was some involvement of the brain and cord. Haslund, of Copenhagen, has studied patients treated in the Communal Hospital of his city. Of 514 cases of tertiary syphilis observed by him there, there were 133 in which there was involvement of the nervous and other systems, or a percentage of the latter to the entire number of cases of 25; while the derma was implicated in 290 cases, a percentage to the whole of nearly 60. Among Americans the statistics of private practice indicate that the nervous system is involved in but a trifle more than 13 per cent. of all forms of tertiary syphilitic manifestations under observation; while the derma and its connections were implicated in about 60 per cent. of all cases.

The recognized elements of importance in grave syphilis are, first, the constitutional condition of the patient. Malnutrition from whatever cause produces a marked decrease in the weight of the subject; and it is also true of the excessive weight of patients who are more fleshy than the average, a class in private practice decidedly outnumbering the others.

Second in importance, and often indeed co-operating with the cause already named, may be named the agencies producing debilitating effects upon the system, including among men alcoholism and excessive tobacco usage. All other debilitating agencies (anxiety, affliction, overwork in business or profession), all that engender anæmia, loss of vigor, neurasthenia, are here properly included.

At the foot of the list should be placed complete absence of treatment, insufficient or injudicious treatment, and even intolerance by the patient of mercury.

Syphilitic Chancre (Initial sclerosis of syphilis; Hard chancre; Infecting chancre).—After exposure to the active virus of syphilis there is commonly a period of delay before the first perceptible symptoms of local infection occur. This period, usually described as the first "incubation stage," extends on an average from about sixteen to thirty days, but it is claimed that exceptional cases occur in which it may be as brief as two or three days only, or prolonged beyond the larger number days named above.

The resulting chancre which therefore, in acquired syphilis, points to an infection occurring within the month preceding its appearance, develops at the site of introduction of the germ of the disease, and may occur in many types according to its location and the accidents of its environment. There is no single lesion, the appearance of which invariably signifies that a chancre is present.

Every chancre is characterized: First, by the delay after infection before it appears (described above); second, by a characteristic induration, or hardness, of its base; third, by a coincident or succeeding enlargement of the glands in proximity to its site, the "syphilitic bubo."

A chancre may be either a modification of the normal tissue of the skin or mucous membrane, or a modification of any possible morbid condition, such as a cigarette burn of the lip, an excoriation of the mucous membrane of the genital or progenital region of either sex, etc.

In general, the clinical features of chancres correspond more or less closely to the following types:

1. *Erosions*, or superficial roundish or irregularly outlined macules, shallow losses of the superficial layers of the skin or mucous membrane, reposing on delicate beds of induration. The type of the latter is that often described as "parchment induration," the sensation it produces to the fingers of the surgeon, suggesting that a thin sheet of parchment has been let in under the excoriated surface. These may be pin-head- to bean-sized lesions, dry, or scantily secreting and slightly moistened, very rarely indeed, unless greatly irritated, degenerating into ulcers. For the reason that they may have an innocent aspect, they are often misinterpreted, but they should always be regarded as the precursors of syphilis when accompanied by the characteristic bubo of that disease.

They may be complicated by the occurrence of very considerable induration or may be transformed into large flat elevations of the surface, suggesting condylomata, but readily differentiated from the latter by their exceedingly dense induration; and when cauterized or otherwise improperly treated, they may even ulcerate, a change for which they have no aptitude when pursuing their usual career. They are occasionally represented by odd-looking ridges (along the corona glandis or at the rim of the labia minora in women); by thickenings of the membrane at the tip of the glans (urethral chancre); or by a firm and circumscribed thickening of a limited part of the upper or lower lip of the mouth.

2. The *dry papule* is of commoner occurrence on the skin of the body elsewhere than that of the genital region, as of the arm after intentional or accidental inoculation. The chancre is then a pea- to lentil-sized, dry, scaling, and indurated papule or papulo-tubercle, with dirty-grayish scales at apex or base. It is at times seen over the pubes, near the anus, on the integument of the pendulous portion of the penis, in the groin, etc.

3. The *ulcer* is decidedly the rarer type of chancre, and may be said to result invariably from some accidental interference with the normal evolution of the process occurring at the site of inoculation, such as pus infection, admixture with the virus of "soft chancre" (*q.v.*) or improper treatment. Both shallow and deep ulcers may form, each with sloping edges, never exhibiting the clean-cut, sharply defined edge of the chancroid. These ulcers are at times represented by indurated fissures or cracks. The so-called "Hunterian chancre" is a huge crateriform excavation of a densely indurated mass of sclerosis. This sore, which Mr. Hunter supposed to be the sole precursor of syphilis, is merely an altered lesion of one of the types already described. Other chancres of unusual type and appearance have been described as "diphtheroid," "herpetiform," umbilicated, "silvery spots," diffuse infiltrations, indurated nodules, annular and encrusted lesions, all these terms describing merely accidental modifications of the lesion occurring always with the three invariable characteristics already enumerated.

The "mixed" chancre is that in which the virus of both syphilis and the chancroid are commingled in the production of a lesion which at first assumes the aspect of the chancroid without the lapse of the usual incubative period of the infecting chancre; and later, after that period has lapsed, takes on the usual characters of the initial sclerosis.

The Stage of Invasion of Systemic Syphilis.—After the appearance of a chancre, from forty to fifty days usually elapse before the appearance of the first syphilitic eruption. This period may be shortened to three weeks; and, in exceptional cases, prolonged to several months. There is strong reason to believe that it may be prolonged under the influence of mercury. In it the chancre commonly progresses from complete evolution to involution; and, when there has been ulceration of that lesion, to cicatrization. Usually, also, when ten or fifteen days only of this period have elapsed, the adenopathy connected with the chancre has appeared and reached its full development. With the chancre healing or cicatrized, and with one or several of the neighboring glands, possibly their lymphatics also, in a state of painless induration, the concluding three-fifths of this period is one of apparent inactivity of the disease. It has been called for that reason a second incubative period of the disease. In the view of the inexperienced, the subject of the disease at this time may be possibly regarded as in a condition of health. Careful examination, however, reveals usually the following significant symptoms:

(*a*) *The Chancre Features.*—If the chancre be examined it will be found, if recognized at all near the conclusion of the period, either ulcerated, cicatrized, represented by a sclerosis, or preparing for transformation to a lesion of secondary syphilis. Sometimes a deeply ulcerated and formidable chancre persists as such till the complete evolution of secondary syphilis; oftener, before the date of such evolution, a previous ulceration has resulted in a tender cicatrix surmounting one of the several grades of induration which characterize the primary lesion. In yet other cases, without any distinct ulceration, the characteristic sclerosis of the disease persists (upon the genital region, finger, lip, etc.), ranging in bulk from a parchment-like thickening to a large nut-sized semi-solid mass usually freely movable upon the tissues beneath. Careful search for this sclerosis in every suspected region should be made in all first examinations of a patient at this period. In yet other cases the chancre is represented by an erosive lesion capping any form of sclerosis which, participating in the process of systemic evolution of symptoms, soon exhibits an elevated floor which may be covered with a whitish pellicle resembling the surface of a mucous patch, and be thus in fact changed to a true granulating mucous patch, the so-called transformation of chancre *in situ*. In all or any of such events, just prior to the evolution of secondary syphilis, there is often a marked, pathological activity of some sort in the chancre-site, the sclerosis becoming larger, the declining maculo-papule more vivid, the ulcer deepening or reopening, or the superficial erosion becoming a smooth, granulating surface with an opalescent pellicle spread over its area.

(*b*) *The Lymphatic Glands and Vessels.*—With very few exceptions one or more, usually several, of the lymphatic ganglia nearest the site of the chancre are found enlarged and indurated in this invasion period. From the tenth day after the appearance of the primary lesion to the conclusion of the invasion stage (that is, the date of appearance of the first syphiloderm) these symptoms persist. In general, it may be said that the first half of this period is required for complete evolution of the local adenopathy which in the latter half may be somewhat less conspicuous, but which yet often, at the termination of this stage, exhibits the evidence of pathological activity described above. In some cases the glands become swollen, tumid, and tender at the onset of general symptoms. The induration of the glands may persist afterward for months, the duration of the syphilitic bubo depending somewhat upon the treatment pursued. Suppuration of these indurated glands is very rare. The lymphatic vessels in anatomical connection with such glands may also undergo this specific induration, and be represented by dense quill-sized cords, single or multiple, reaching from the site of the chancre to the single lymphatic gland or cluster of glands which are superficially involved.

Besides this persistent indurated condition of one or several of the glands near the chancre site, noticeable in the invasion stage of general syphilis, there is usually appreciable toward its conclusion a remarkable and often suddenly occurring engorgement of the superficial ganglia. This symptom is not of local but of systemic importance. It is related less to the chancre than to the general oncoming syphilis. It is an early and almost constant symptom of general infection, often, as just described, particularly conspicuous prior to the evolution of the first syphiloderm; at other times, not fully developed till such early symptoms have been declared, and in