

SUPPLEMENTARY TREATMENT

It has been so well established that patients may be apparently well and remain so even up to five years, only to succumb to an acute, explosive recrudescence, that there is positive indication for prolonged after-treatment, periodically repeated. The exceeding importance of protecting the general health cannot be overstated. Periods of even slight mental and physical depression have preceded, if they have not introduced, recrudescences. Except in two cases, in which the blood picture returned to normal and has remained there, we have not seen a single instance in which this evidence of a persistence of the infection was eliminated. Routine blood examinations are made as the patients report for observation, either at stated intervals of a few months or whenever untoward symptoms are suspected. The blood count has been found to give the earliest and surest evidence of an impending recrudescence or of the persistence of some focus of infection that had escaped detection. Apparently, recurrences of the disease, if taken very early, may be controlled by appropriate measures, whereas, if the infection increases to any extent in virulence the characteristic rapid fatal progress is to be expected.

REEXCISIONS

Glandular recurrences have shown two types. One that follows soon after incomplete excision is of the softer, more cellular and acute variety. The other appears at a longer interval, perhaps more than a year after complete excision and repeated courses of the Roentgen ray, and is more chronic in every way, yet reexcisions usually done under local anesthesia have produced improvement, local and general, otherwise unobtainable. Removal of early recurrences is at times justifiable, but seldom is to be expected to help materially and has led to the opinion expressed by Fischer that reexcisions are always unwarranted.

During the period of quiescence, when there is no longer any external evidence of the disease, should be the time, hypothetically at least, when the administration of vaccine virtually prophylactically might be expected to be of the greatest benefit. Under such conditions the only judgment as to immediate improvement would have to be based on blood changes, and as the vaccine itself affects the blood picture nothing definite can as yet be stated. There has been no improvement noted in the return toward normal; either there has been no change or there was evidence of some degree of unfavorable variation.

One must constantly bear in mind that the safety of these patients lies in unremitting watchfulness and attention to details. The fact that otherwise there must be a certain fatality should lead to persistence to find the therapeutic measures indicated and give one courage to put them to practice.

RESULTS

A cure or, better, a recovery can be considered as established only when there is no trace of the disease, including a normal blood picture, at least five years after the last manifestation of the infection. Recrudescence has occurred after a shorter period of apparent freedom. A case recorded by Eve,³⁰ had an interval of six years between a primary operation and the first recurrence but the diagnosis was not established.

30. Eve: *Brit. Med. Jour.*, 1897, i, 584.

THE BEGINNING OF SYPHILIS*

W. A. PUSEY, M.D.

CHICAGO

"By the historical method alone can many problems in medicine be approached properly. For example, the student who dates his knowledge of tuberculosis from Koch may have a very correct, but a very incomplete, appreciation of the subject. Within a quarter of a century our libraries will have certain alcoves devoted to the historical consideration of the great diseases, which will give to the student that mental perspective which is so valuable an equipment in life."—Osler.

The history of syphilis is unique among the records of great diseases. For, unlike most diseases, it does not gradually emerge into the historical records of medicine as its characters become recognized, but appears on the stage of history with a dramatic suddenness in keeping with the tragic reputation it has made—as a great plague sweeping within a few years over the known world. Syphilis is the one disease whose history begins with a definite date. That date is the date of the discovery of America. It happens also that the ten years from 1903 to 1913 were fruitful of discoveries of such fundamental importance in syphilis that they represent an epoch—the most important epoch—in the history of our knowledge of the disease.

LACK OF KNOWLEDGE OF SYPHILIS AMONG
THE ANCIENTS

Local genital diseases have been recognized from ancient times; references to them are numerous in both Occidental and Oriental literature. It is, however, a very striking fact that in all medieval and ancient literature, although sexual matters are favorite topics and are considered frequently and with freedom, there is no reference to a disease of the genitals which is followed by constitutional symptoms. Many diseases involving the skin are easily recognized in the descriptions of medieval and classical literature, but in spite of the most painstaking and zealous searching of all literary evidence, no single authentic document has been found in ancient literature in which a description of syphilis can be recognized. Prior to the last years of the fifteenth century no description of the syphilitic syndrome existed.

THE EPIDEMIC OF SYPHILIS AT THE END OF
THE FIFTEENTH CENTURY

In the autumn of 1494, Charles VIII of France, with an army composed of mercenaries from all parts of western Europe, invaded Italy for the conquest of Naples. Italy, which at this time had reached the height of effeminate luxury and was weakened by the rivalries of her numerous states, was able to make no effective resistance to the well-organized forces of Charles; and the progress of his army through the peninsula was more of a triumphal march of debauchery than a serious military campaign. Charles was able to make good his claims to the throne of Naples and to set up his court for permanent occupation. In a short time, however, his army became so

* This article is the first chapter of a monograph on "Syphilis," being one part of a volume, now on the press of the American Medical Association, commemorating the completion of the Panama Canal and reflecting what medicine has done to make the canal possible. The article on Typhus Fever by Vaughan, published May 29, 1915, was part of a monograph on "Infection and Immunity," also to be included in this book. The other articles contained in this "Commemoration Volume" are by Drs. W. J. Mayo, Simon Flexner, E. O. Jordan, Major General Gorgas and Mr. F. L. Hoffman. The book, of some 380 pages, will be issued about July 1. Price, \$2.50.

weakened through disease and dissipation that the Neapolitans were able to assert themselves and drive it out. The retreat of Charles and his soldiers from Italy in the summer of 1495 was little better than a rout, and the various troops were left ultimately to return to their countries in their own disorganized way.

THE BEGINNING OF THE EPIDEMIC

All contemporaneous records are at one in attributing the epidemic of syphilis which began in Italy at this time to Charles' army, and the quick spread of the disease over Europe to the scattering of his troops. Syphilis, if it existed before this time, was unrecognized. It was at the appearance of this great epidemic that physicians and laymen alike became aware of a disease of the genitals, which was followed by constitutional symptoms and of which they had no previous experience.

THE SPREAD OF SYPHILIS OVER EUROPE

The development of syphilis in Italy can be traced in the local chronicles of the time step by step with the progress of Charles' army, and with the scattering of his soldiers it went over western Europe in a rapid-spreading epidemic. It appeared in France and Germany and Switzerland in 1495, in Holland and Greece in 1496. It spread to England and Scotland in 1497; to Hungary and Russia in 1499.

Iwan Bloch, to whom all students are indebted for bringing together the known facts concerning the early history of syphilis, gives many contemporaneous references testifying to the interest excited by the new disease and to the importance attached to it. Thus, in 1496, the Parliament of Paris decreed that all persons infected with the disease should leave the city within twenty-four hours. In 1496-1497 prophylactic measures against the disease were attempted at Nürnberg. On April 21, 1497, the town council of Aberdeen, Scotland, ordered that, for protection from the disease which had come out of France and strange parts, all light women desist from their vice and sin of venery and work for their support, on pain, else, of being branded with a hot iron on their cheek and banished from the town. Six months after the Aberdeen order, the Scottish Privy Council passed an edict ordering all inhabitants of Edinburgh afflicted with syphilis into banishment to the island of Inchkeith near Leith. In 1496, Grünpeck, a German writer, mentions that English soldiers in Italy had acquired syphilis. The archives of Bristol indicate that the disease was introduced there in 1498 from Bordeaux, and hence was called the Bordeaux disease. In the *Breviarie of Health*, by Andrew Boorde, published in 1575, it is stated that "In English Morbus Gallicus is called the French pocks, and when that I was young they were named the Spanish pocks."

Indeed this tendency to shift the responsibility for the disease on others by giving it their name, appears all through the early references to it. The Italians called it the Spanish or the French disease; the French called it the Italian disease; the English called it the French disease; the Russians called it the Polish disease; the Turks called it the French disease; the Indians and the Japanese called it the Portuguese disease. And, as we shall see, the first Spaniards who recognized the disease called it the disease of Española, which meant at that time the disease of Haiti.

ITS SPREAD TO THE ORIENT

In quick sequence the disease spread over the rest of the known world, carried by the great voyagers of that period. The Portuguese soon carried it to Africa and the Orient. The researches of Okamura and Susuki for Japan and China, and those of Jolly and others for India, show the introduction of syphilis into these countries only after contact with Europe. The Indian, Chinese and Japanese languages had no native names for the disease, and, like the Europeans, the Orientals gave it names indicating its foreign origin. In India the disease was first recognized in 1498, after the arrival of Vasco de Gama, who had left Portugal in 1497. It appeared in Canton, China, in 1905, after the visit of Europeans. It was not recognized in Japan until 1569, when its appearance at Nagasaki was attributed to Chinese or Portuguese sailors.

There is thus an accurate historic record of the startling spread of syphilis over the known world in a few years after 1495; and from that time it has everywhere been endemic. No similar record exists of the sudden establishment of any other great disease among the larger part of the earth's inhabitants.

THE SEVERITY OF THE FIRST EPIDEMIC

The early recognition of syphilis and the prompt record of its spread over the civilized world are to be accounted for not so much by its newness, although it was everywhere recognized as a new disease, as by its severity. It amounts almost to an axiom in pathology that when an infectious disease first appears among a people—finds lodgment in a virgin soil—it rages with unwonted severity. This has been noted many times—with measles, scarlet fever, smallpox, and with syphilis in modern epidemics among isolated peoples. And this was a characteristic of the great epidemic of syphilis which occurred at the end of the fifteenth century.

In syphilis as ordinarily seen, its early manifestations are trivial in character, so trivial in fact that they are dangerously deceptive to the careless. The symptoms are mild and the patients are not acutely ill. All evidence, however, points to the severe character of the disease during this first epidemic. The cases ran an acute febrile course accompanied by symptoms of such severity as are now seen only in very unusual cases. There were high fever, intense headache and bone and joint pains; early skin symptoms so severe that they simulated smallpox; great prostration, and very frequently a fatal ending early in the disease, a result that is the rarest occurrence at present. This epidemic had all the characteristics of a virulent plague. With the loose morals of the time, however, syphilization of the world was rapid, and contemporaneous evidence, Fracastoro for example, indicates that the severity of the symptoms of early syphilis rapidly diminished; and within fifty years the disease had assumed the character with which the world has since been familiar.

EARLY SPECULATION AS TO ITS ORIGIN

The origin of syphilis was, at the time of this great epidemic and until recently has still been, a subject of much speculation and discussion. In keeping with man's superstitions, particularly at the time of the appearance of syphilis, it has been attributed to every imaginable source; to vice and sin, and the anger of

Providence; to dirt and beasts; to the elements and the influence of the heavenly bodies. Much unsuccessful effort was made to demonstrate its presence in Europe in the middle ages and earlier, although contemporaneous opinion pointed to the Spaniards and Americans for its origin. Later, as the disease became familiar and men lost sight of its sudden appearance, opinion veered round to the view that it had always existed in Europe. It is only within the last thirty years that its American origin has been practically demonstrated.

THE EVIDENCE OF ITS AMERICAN ORIGIN

The bald fact of the sudden appearance of syphilis shortly after the return of Columbus from his first voyage might easily suggest and lend plausibility to the theory of the American origin of the disease. The presence of Spanish adventurers in Charles' army would furnish the connecting link between Barcelona and Seville and Columbus' crew and the Italian epidemic. But in addition to the chronologic sequence of Columbus' return from America and the first recognized epidemic of syphilis in Europe, there are numerous other facts which confirm the American theory of its origin.

As we have seen, certain of these facts stand out prominently in the great epidemic:

The disease at the time was recognized as a new disease.

Names for it did not exist, and as it spread over Europe, men were hard put to give it a designation. The same was true on its appearance in the Orient.

The development of the great epidemic was definitely associated with the Italian campaign of Charles VIII, and its rapid spread over Europe was associated with the breaking up of his army. Its origin was recognized as being southwestern Europe. Even with the first outbreak in Italy, Spain was pointed to as the country whence it came, and the Spanish soldiers of Charles' army were incriminated as the authors of its distribution.

The disease pursued a course of unusual severity and spread over Europe with the rapidity of an infectious disease among people unprotected by any previous infection with it.

ABSENCE OF EVIDENCE IN EARLY EUROPEAN BONES

Parallel with the absence of any pre-Columbian documentary evidence of the existence of syphilis, is the absence of any evidence of syphilis in pre-Columbian European or Oriental bones. Bones withstand time, and the ravages of many diseases can be clearly traced in ancient bones that have come down to us. Syphilis is one of the diseases which leaves frequent, unmistakable evidence of its existence in bones; and if syphilis existed in Europe before the discovery of America it would be expected that evidence of it would be abundantly found in the great collections of prehistoric, ancient and medieval bones that exist. With the licentiousness of Rome and of the Dark Ages, syphilis would have been expected to leave a broad trail in the bony remains of those times; and yet careful scrutiny of those bones has failed to reveal any evidence of it. Most of the great European collections of human skeletons of pre-Columbian times have been carefully examined with

this point in view, without the finding of a single syphilitic bone, and no less an authority than Virchow, one of the world's greatest anthropologists and probably its greatest pathologist, has declared that no pre-Columbian bone has been produced presenting evidence of syphilis. On the other hand, human skeletons of later date showing syphilitic changes have been found in all parts of the world.

AMERICAN PREHISTORIC BONES

On the other side it must be said that we have no unquestionable evidence of syphilis in pre-Columbian bones in America. Syphilitic bones have been found in North and South and Central America, and the presumption is strong that some of these bones are of pre-Columbian origin. Nevertheless, the difficulty in establishing the antiquity of Indian remains is so great that the pre-Columbian origin of these bones cannot be demonstrated.

SPANISH DOCUMENTARY EVIDENCE

But quite apart from this circumstantial evidence of the American origin of syphilis, there has been discovered in recent times definite documentary evidence indicating the introduction of syphilis into Spain by the sailors of Columbus' first voyage. For the unearthing of this evidence we are indebted to Montejó y Robledo, a Spanish army surgeon, who critically examined all the early Spanish sources and reported his findings at the fourth Congreso internacional de Americanistas, at Madrid in 1882. The importance of Montejó's work was overlooked until attention was called to it by Seler in 1895.

Ruy Dias de Isla.—The most important evidence produced by Montejó—and surprisingly definite evidence it is—is the account of syphilis of Ruy Dias de Isla. To paraphrase Bloch: at the time of the first appearance of syphilis in Europe, Dias de Isla was a physician of note, who for ten years held the position of surgeon at the Hospital of All Saints in Lisbon. There he had a large experience in syphilis, which he incorporated in a special work which was published between 1510 and 1520, and was fortunately discovered by Montejó in the National Library of Madrid. Dias de Isla is known to have been in practice in 1493 in Barcelona, and he was thus in a position to be a witness to the very landing of syphilis in Europe. The title of Dias' book put into English is: "Treatise, entitled, Fruit of All Saints against the Disease of the Island Española, by Master Rodrigo de Isla, Surgeon and Citizen of Lisbon, to the Common and General Good of those Suffering from the Disease in Question, Commonly Called Bubas." The contents of the book are, briefly, as follows: Syphilis was unknown before the year 1493. It was brought by the crew of Columbus on his first voyage from Española, or Haiti. Dias called it the disease of the Island of Española, but also gave a number of native names for the disease. A majority of Columbus' crew returned to Spain infected with syphilis, and Dias himself treated several syphilitic sailors from this squadron, among them the pilot, Pinzon of Palos.

Oviedo, Las Casas, and the Spanish Chroniclers.—This record of Dias de Isla is corroborated by other contemporary Spanish chroniclers; particularly by the important works of Oviedo, and of the great Las Casas, both of whom were in America within a few years after its discovery. Oviedo was in Barcelona

at the return of Columbus in 1493, and knew Columbus and members of his crew. In his "Historia general y natural de las Indias," and in a report drawn up at the command of Charles V of Spain, he recites: That the disease was contracted from Indian women by the Spaniards with Columbus; that it was brought by them to Spain and thus transmitted to the army of Charles VIII by Spanish soldiers; and that syphilis should be called the West Indian disease, rather than the French or Neapolitan disease. He also mentions in independent corroboration of Dias de Isla, that one of the brothers, Pinzon, contracted the disease, and that it "is common among the Indians, but in those regions is not so dangerous as with us."

Oviedo was an advocate for Spain, and it has been urged that the theory of the Indian origin of syphilis may have been readily adopted by him in his attempts to palliate the cruelty of the Spaniards toward the Indians. No such charge, however, will stand against Las Casas, whose efforts were all in behalf of the Indians, but who, nevertheless, did not hesitate to give in detail the facts of syphilis among them.

The father of Las Casas accompanied Columbus on his second voyage, and Las Casas himself was in Haiti in 1498, where he lived many years and wrote his "Historia general de las Indias." He records: "There were, and still are, two things which at the beginning were very dangerous to the Spaniards. One is the disease syphilis, which in Italy is known as the French evil. . . ."

"It is, however, known for certain that it came from this island, either when, with the return of the Admiral Don Christóbal Colón with the news of the discovery of the West Indies, the first Indians arrived, whom I saw myself in Seville, or it may be that certain Spaniards were already tainted with this disease at the time of their first return to Castile. . . ."

"I took the trouble on several occasions to interrogate the Indians of this island as to whether this disease was of great antiquity, and they answered, 'Yes.' . . ."

"It is also an undoubted fact that all Spaniards addicted to sexual excess, who did not in this island observe the virtue of continence, were attacked by the disease, not one in a hundred escaping, unless the woman was healthy." He too emphasizes the greater severity of the disease among the Spaniards than among the natives.

In addition to Oviedo and Las Casas, numerous others of the early chroniclers of Spanish America (Panc, Sahagun, Hernandez), testify as shown by the researches of Montejó, to the pre-Columbian existence of syphilis in America. They show not only that the disease was known to the Indians, but that the Indians had numerous names for it; that they were fairly familiar with its symptoms and course, and had well-worked-out methods of treatment for it; and that the disease was much milder in its course among the Indians than among the Spaniards, who contracted it from them.

This brief summary of the discoveries of Montejó y Robledo from his researches among original Spanish authorities, furnishes the final link connecting the origin of syphilis with America, and, it would seem, compels us to conclude that syphilis was introduced into Europe from Haiti by the sailors of Columbus on their return in 1493 from his first voyage to America.

THE LANDAU IODIN SERUM TEST FOR SYPHILIS *

ARTHUR W. STILLIANS, M.D.

Associate Professor of Dermatology, Chicago College of Medicine and Surgery; Attending Dermatologist, Cook County Hospital; Consulting Dermatologist, Chicago Lying-In Hospital

CHICAGO

A good deal of interest has been aroused lately in the new serum test for syphilis proposed by Landau.¹ It is declared that this test is more sensitive than the Wassermann reaction and that its simplicity makes it available for every one. Among the many tests said to have these qualities, the Landau demands attention because of the popular interest shown in it and the possibility that it may come into more or less general use. Any new test for deciding so important a diagnosis as that of syphilis must be subjected to the sharpest scrutiny, and tried in many thousand cases.

Landau at first used as a reagent a 0.05 per cent. solution of iodine in liquid petrolatum. The composition of various samples of this solvent varied enough, however, to make it difficult to obtain a reliable reagent, so that he later adopted carbon tetrachloride (CCl₄) as a solvent. In this he dissolves 1 per cent. of iodine (a saturated solution which requires trituration to complete it); and uses 0.1 c.c. of this reagent to 0.2 c.c. of the serum to be tested. These are shaken together in a test tube 12 mm. in diameter, and allowed to stand at room temperature for four hours. If, at the end of this time, the serum above the decolorized reagent is a clear yellow, the reaction is recorded as positive. If the serum is an opaque grayish-white, it is recorded as negative. Only fresh serum, obtained not more than six hours before, and free from any cloudiness or hemoglobin stain, can be used. If the result is not easy to determine, 0.2 c.c. of ammonia solution may be added to clear up the doubt.

Landau, with his first technic, reported that he obtained, in a series of 122 cases, only one result that did not agree with the clinical diagnosis. This was a positive test in a case of a leg ulcer, clinically and serologically nonsyphilitic. He reported also that the reaction gave fifty-five positive readings in a series of ninety syphilitics, in whom only forty-nine positive Wassermann reactions were obtained.

These results have not been substantiated by others. Golay,² using the carbon tetrachloride reagent, obtained forty-one positive, eleven doubtful, and eleven negative reactions in a series of sixty-three syphilitics, in which only thirty-seven positive Wassermann reactions were obtained. But he also reports in seventeen nonsyphilitics, all of whom had negative Wassermann reactions, a positive Landau test in eight cases. One of these was a case of gonorrhea, three cases of soft ulcer, two of tuberculosis and two of malignant tumor: 47 per cent. positive in nonsyphilitics! He concludes that the test is positive in a large percentage of cases of systemic disease, but reports negative reactions in all of three cases of "skin disease of external origin" and three healthy persons.

Villaret and Pierret³ report agreement with the Wassermann reaction in thirty-two cases of thirty-nine

* From the Dermatological Department of Cook County Hospital.

1. Landau, Wilhelm: Untersuchungen über eine Reaktion luetischer Sera mit einem Jodöl-Reagens, Wien. klin. Wchnschr., 1913, xxvi, 1702.

2. Golay, J.: La réaction de Landau, Rev. méd. de la Suisse romande, 1914, xxxiv, 571.

3. Villaret and Pierret, R.: Tr. Soc. biol. de Paris, Presse méd., July 29, 1914, p. 582.