The history and epidemiology of syphilis ... / by Wm. Allen Pusey.

The History and Epidemiology of Syphilis

Pusey

THE
HISTORY AND EPIDEMIOLOGY
OF
SYPHILIS

By Wm. Allen Pusey:

Principles and Practices of Dermatology	Appleton
The Care of the Skin and Hair	Appleton
The Wilderness Road to Kentucky	Doran
A Doctor of the 1870's and 80's	Thomas
The History of Dermatology	Thomas
The History and Epidemiology of Syphilis	Thomas

THE HISTORY AND EPIDEMIOLOGY OF SYPHILIS

THE GEHRMANN LECTURES
UNIVERSITY OF ILLINOIS
MDCCCCXXXIII

BY

WM. ALLEN PUSEY, A.M., M.D., LL.D.

PROFESSOR OF DERMATOLOGY EMERITUS, UNIVERSITY OF ILLINOIS
SOMETIME PRESIDENT OF THE AMERICAN DERMATOLOGICAL
ASSOCIATION AND OF THE AMERICAN
MEDICAL ASSOCIATION

SPRINGFIELD, ILLINOIS BALTIMORE, MARYLAND

CHARLES C THOMAS

1933

PRINTED IN THE UNITED STATES OF AMERICA

LECTURES

delivered under the

ADOLPH GEHRMANN

ENDOWMENT

University of Illinois, College of Medicine,

Chicago

March 1, 2 and 3, 1933

PREFACE

These lectures are an elaboration of certain chapters in my monograph Syphilis as a Modern Problem, which was one of several contributions that made up the Commemoration Volume of the American Medical Association issued as part of the celebration of the Panama-Pacific Exposition at San Francisco in 1915. For permission to use this material I am indebted to the American Medical Association.

The justification for presenting the same subjects again lies in the fact that much has been added to our knowledge of them in the last eighteen years. In the history of syphilis, we have important new information. In the epidemiology of syphilis, the experience of the Great War and the more exact knowledge of the epidemiological facts of syphilis which have come from the intensive study of the disease in the last eighteen years have given us a firmer standpoint from which to consider its sanitary problem. I welcomed the opportunity, therefore, to traverse the field again, particularly as the subject seemed appropriate to the occasion, Dr. Adolph Gehrmann, in whose honor these lectures were endowed, having been a pioneer bacteriologist and student of epidemiological problems.

Chicago.

July 1, 1933.

LIST OF ILLUSTRATIONS

THE
HISTORY AND EPIDEMIOLOGY
OF
SYPHILIS

Lecture I

THE BEGINNING OF SYPHILIS

IT has seemed to me fitting for several reasons to choose for the topic of my lectures on this occasion the history and epidemiology of syphilis. Syphilis is a part of every branch of medicine. It is an epitome of pathology, and the history of its progress since the beginning of the sixteenth century is the best illustration that we have of the evolution of the modern knowledge of medicine. At the same time its history is the most dramatic story in the history of disease, and its control is one of the most important sanitary problems. I have hoped also by its consideration to give you young men some intimation of the interest and importance of the history of medicine. As the great pathologist Rokitansky said, "Younger physicians should light their torches at the fires of the Ancients."

Syphilis is strictly a disease of man, and it is one of the most important diseases that afflict him. It has the tragic human interest of being hereditary as no other important disease is. It is one of the most difficult diseases from the social standpoint, for it is inextricably involved in one of the great unsolved problems of modern civilization—the problem of the relation of the sexes. And with all this, the history of syphilis is unique among the records of great diseases in that it does not gradually emerge into the his-

torical records of medicine as its character became 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.

THE IMPEDIMENTA (of the army)

Triumph of the high and mighty Dame Syphilis, Queen of the Fountain of Love. *Le Triumphe de treshaulte et puissante Dame Verolle.* Lyons, 1539. (Anon.). (Jeanselme)

Let us consider first its history. At the end of the fifteenth century a new disease of devastating character spread rapidly over Europe. In the autumn of 1494 Charles VIII of France invaded Italy to make good his claims to the throne of Naples. Italy, weakened by luxury and the rivalries of her numerous states, was able to make no effective resistance, and the progress through the peninsula of Charles' army, composed of mercenaries from all parts of Western

Europe, was more a triumphal march of debauchery than a serious military campaign. Charles captured Naples on February 22, 1495, and prepared for its permanent occupation. But dissipation and disease did what the Italians could not; a plague attacked his troops which compelled the evacuation of the city and in the spring of 1495 the army was in undisciplined retreat from Italy. Ultimately the various disorganized troops scattered over Europe and returned to their own countries, carrying with them the new disease which thirty-five years later became known as syphilis. This was the historical beginning of syphilis.

All contemporary records agree 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. The spread of syphilis from Italy can be traced in the local chronicles of the time, step by step with the dispersal of Charles' army. It appeared in France and Germany and Switzerland early 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 contemporary 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 1496–97 prophy-

lactic measures against it were attempted at Nürnberg. On April 21, 1497, the town council of Aberdeen, Scotland, ordered that, "for protection from

SYPHILIS. 1496. ALBERT DÜRER.
(Bloch)

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 Inch-

Title Page from Bartholomew Steber's *Syphilis*, 1497 or 1498. Probably the earliest illustration of syphilis. (Bloch)

keith 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 *Breviairie 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." These early records of syphilis, all taken from Bloch, have been confirmed and greatly enlarged by Haustein, to whose work I shall refer more fully later in this lecture.

There was no name for the disease and this tendency to shift the responsibility for it to 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 or Neapolitan disease; the English called it the French disease; the Russians called it the Polish disease; the Turks called it the French 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.

The spread of the disease can be traced in chronological sequence not only through Europe, but through all the parts of the world which at that time came in contact with Europe. 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.

Professor Dohi, of the University of Tokyo[1] in elaborate studies has confirmed these facts for Asia.

He gives an interesting map that traces the distribution of syphilis throughout the world by the discoverers who, beginning with Columbus, opened up the world.

The East 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 1505, 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 1494; for this disease no name existed and a new one invariably had to be invented. No similar record exists of the sudden establishment of any other great disease among the larger part of the earth's inhabitants.

Syphilis was at once recognized as a new disease. It was a disease, usually of venereal origin, which, unlike other genital diseases, regularly had generalized cutaneous and systemic manifestations. The ancients were familiar with local genital diseases. References to them are common in both Occidental and Oriental literature. It is, however, a very striking

---

[1] *Beiträge zur Geschichte der Syphilis, insbesondere über ihren Ursprung und ihre Pathologie in Ostasien*, 1923.

fact that in all medieval and ancient literature, there is no certain reference to a disease of the genitals which is commonly followed by general manifestations. This peculiarity of the disease was recognized

Title Page from Grunpeck's *Tractatus de pestilentiali Scorra sive mala de Franzos*, 1496? (Jeanselme)

at the time as evidence of a new disease. No description of the syphilitic syndrome has been found prior to 1493.

Another evidence of its newness was its severity.[2] The disease compelled attention by the severity of its

manifestations. 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 characteristic of the great epidemic of syphilis at the end of the fifteenth century. In contrast with the trivial character of the early manifestations of syphilis as ordinarily seen in peoples among whom it has long been present, all evidence points to its severe character 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 assumed the character with which the world has since been familiar.

---

[2] This aspect of the subject has been vividly described by Cumston in an article "Syphilis in the Fifteenth and Sixteenth Centuries, especially at Paris," *British Jour. of Dermatology*, **35**: 331. 1923.

The early circumstantial evidence of the spread of the first epidemic of syphilis in Europe has been subjected to very severe scrutiny in order to find evidence in enactments against syphilis in Europe before Columbus' first voyage. Indeed all pre-Columbian literature has been critically examined to discover descriptions of syphilis: European, Arabic, Japanese, Chinese, Sanskrit. In the last thirty years the subject has taken on the spirit of partisan discussion, and no end of zeal and industry have been used in trying to find pre-Columbian documentary evidence of syphilis. If syphilis existed in ancient times unquestionable evidence of it certainly should be found in the licentious literature of the Greeks, Romans, and Arabians, who would have had no lack of ability or inclination to describe it as accurately as any of us moderns—so accurately that we would have been compelled to accept it. What a topic syphilis would have been for Aristophanes or Juvenal or the authors of the Arabian Nights. And yet no evidence in literature of the pre-Columbian origin of syphilis that will pass close scrutiny has been produced. The burden of proof to produce such evidence rests upon those who maintain its pre-Columbian existence; they have not been able to produce it.

Cumston has recently considered this subject in an interesting article.[3] He made an extensive examination of ancient literature for descriptions of syphilis. Although he is noncommittal in his conclusions, he found no descriptions which offer presumptive evi-

[3] *Medical Journal and Record*, **125**: 269. 1927.

dence so strong that would compel one to say even that it was likely syphilis existed in the Eastern Hemisphere before the return of Columbus.

Professor Karl Sudhoff is the most influential authority who has opposed the American origin of syphilis. At the International Congress of Medicine in London in 1913 he reported the results of his examination of German records antedating Columbus' discovery of America, and concluded that in references and enactments regarding "gros mal" he had found evidence of the existence in Europe of syphilis a very few years before Columbus' return.

Hans Haustein, in the light of Sudhoff's findings, made an exhaustive, critical examination of the same documents and of other Swiss, French and German records of the period both just prior and subsequent to Columbus' return. He confirms Bloch's findings and by a very full and detailed reëxamination of governmental enactments for the control of syphilis established the evidence of the spread of syphilis through Europe after Columbus in the chronological sequence which I have already indicated. He shows that "gros mal" of the middle ages, on which Sudhoff lays so much stress as evidence of syphilis in the middle ages, was not used to denote syphilis, but epilepsy, the usage which we still have in "gros mal" and "petit mal." This is not only his opinion, but the opinion of many other authorities who have examined the subject, such as Dr. Eugene Mayer and Professors Th. Kalepsky, Leonardo Olschki of Heidelberg, Ernest Wichersheimer of Strassburg, E. Jeanselme of

Paris, Ferdinand Brunot of the Sarbonne, Max Kuttner of the University of Berlin, Kr. Nyrop of the University of Copenhagen, and Walter von Wartburg of the University of Leipzig. Haustein shows that the term "bäsen blättern" which was used in the Edict of Maximilian, and in the chronicles of the German states in 1495–96, was a new term to describe the new disease, and was used repeatedly with the phrase "the never before seen and heard of disease." In particular he examined the famous Mandate of Maximilian (the "Edict on the Sins against God"), which is the earliest known German state document on syphilis. He shows that this was first promulgated August 7, 1495, and calls attention to the fact that Fuchs suggested in 1843 that this Mandate showed that syphilis had spread to Germany by the summer of 1495. He further finds that the text of the Mandate as issued by the Council of Lindau, of which much has been made, was formulated in the winter of 1496-97. The passage on the "bäsen blättern" was discussed in the Council and added to the text January 12, 1497, and the mandate was released by the Council February 1, 1497, and printed in that month. Haustein concludes from his investigations that the first promulgation of the Edict of Maximilian did not precede the known spread of syphilis over Europe after the dispersion of Charles VIII's army, but on the contrary was a result of the appearance of the epidemic in Germany at that time. He further concludes that in the light of the dates of the Mandate, which he has established, the text of the Mandate as

issued at Lindau in 1497 followed the early enactments of the various cities against the new disease in the year 1496, rather than preceded them.[4]

A careful study of his paper forces the opinion, I believe, that John Lane expressed to me in a personal communication, that "Haustein has annihilated the position of Sudhoff."

If, on the one hand, there is no conclusive evidence of the existence of syphilis in Europe before 1493, there is, on the other, astonishing authentic historical evidence of the American origin of syphilis which has been brought to light through the labors of Montejo y Robledo, a Spanish army surgeon who reported his findings to the Fourth Congreso Internacional de Americanistas at Madrid in 1882. The importance of Montejo's work was overlooked for twenty years; Selar called attention to it in 1895, but it was first emphasized by Iwan Bloch in his great work on the origin of syphilis, published in 1901.[5] Bloch's work is fortunately available in an English summary which he made in his contribution to the *British System of Syphilis* (1908). I also summarized the subject, following Bloch, in *Syphilis as a Modern Problem* in 1915. Lately Herbert U. Williams, Professor of Pathology at the University of Buffalo, and Professor J. P. Rice, Professor of Romance

[4] Many excerpts from the edict of Maximilian and of many other enactments against syphilis from 1495 to 1500, as well as the entire edict against Le Gros Mal of Dijon of 1463, are reproduced in facsimile by Haustein. *Arch. für D. und S.* **131,** 251–338, 1930.

[5] *Ursprung der Syphilis,* Jena, 1901.

languages at Buffalo, and Dr. Joseph Renato Lacayo of Granada, Nicaragua, have again examined Montejo's work and furnished translations of many of the passages. I can only refer briefly here to the facts which these examinations of Montejo's work revealed. Much fuller details will be found in this recent article.[6]

Montejo carefully examined the early Spanish chronicles of America. It was an enormous labor that involved not only first-class scholarship and native knowledge of Spanish, but access to the great accumulation of documents in the Spanish archives. Montejo gives extracts from numerous Spanish historians and scientists who were either contemporary with Columbus, or took part in the first Spanish exploitation of the Americas. He even unearthed one reference of two lines to syphilis in the *Life of Columbus* by his son Ferdinand. He quotes numerous passages from Oviedo and Las Casas, who were antagonistic to each other, but who agreed upon one thing, that syphilis was of American origin.

Oviedo (1478–1557) was in Barcelona at the time of the return of Columbus in 1493, and knew him 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 recited that the disease was contracted from Indian women by the Spaniards with Columbus, that it was brought by them to

[6] The American Origin of Syphilis, *Archives of Dermatology*, **16**: 683. 1927.

Spain and thus transmitted to the army of Charles VIII by Spanish soldiers; and that syphilis should be called the Indies disease, rather than the French or Neapolitan disease. He also mentions, in corroboration of Dias de Isla, yet to be considered, that one of the brothers, Pincon, contracted syphilis, and that it "is common among the Indians, but in those regions is not so dangerous as with us."

Let us quote a few sentences from Oviedo:

I do not speak from hearsay in any of these four things but from experience; although I am writing them down from memory, or more exactly, by referring to my notes which were written at the time when the things described in them happened. . . .

These Christians, first settlers of this island, suffered moreover much difficulty . . . from the disease of buas (for the Indies are the place of their origin). . . .

Many times in Italy I did laugh, hearing the Italians say the French disease and the French calling it the disease of Naples; and in truth both would have hit on the right name if they had called it the disease from the Indies.

Previously I said that Columbus returned to Spain in the year 1496 . . . after which event I saw and spoke with some of those that came back with him to Castile.

As the disease was something new the physicians did not understand it and did not know how to cure it, nor were there others with experience to advise about such a disease.

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 at-

tempts 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 (1474–1566) 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 malady . . . " (To relieve curiosity the other was chiggers W. A. P.)

This, let it be known in truth, was taken from this island, either when the first Indians left at the time when the Admiral D. Christobal Colon returned with the news of the discovery of the Indies, which men I saw myself soon afterwards in Seville, and these were in a position to communicate it to Spain, by infecting the air or in other ways (what a pointed warning); or when some Spaniards having already contracted the disease went on the first return voyage to Castile, and this could have happened between the years 1494 to 96; and because at this time King Charles of France, whom they call the Bighead, passed with a great army into Italy, to take Naples, and that contagious malady was in that army—for this reason the Italians thought that they had caught it from them, and from then on they called it the French disease. I myself sometimes endeavored to inquire of the Indians of this island if this malady were very ancient in it, and

they answered yes, . . . It is a thing well verified that all the incontinent Spaniards that did not have the virtue of chastity on this island were contaminated by it (recall, gentlemen, the clear warning that I brought to your attention a few moments ago), and out of a hundred perhaps not one escaped except when the other party never had had it.

The Indians, men or women, that had it were little affected by it, almost as little as if they only had smallpox.

In addition to Oviedo and Las Casas, numerous other of the early chroniclers of Spanish America (Pane, Sahagun, Hernandez), testify as shown by the researches of Montejo, to the pre-Columbian existence of syphilis in America. Sahgun (1499–1590), who went to Mexico in 1529, in his *History of New Spain* describes syphilis among the Aztecs of Mexico, and Francisco Hernandez (1514–78) also describes syphilis in Mexico.

But the testimony of Oviedo and Las Casas and the others is commonplace compared to the startling evidence which Montejo unearthed in the works of Dias de Isla, a physician at Lisbon at the time of Columbus' return. Dias was a physician of note, a surgeon for ten years at the Hospital of All Saints in Lisbon. He had a large experience in syphilis which he incorporated in a work prepared between 1510 and 1520. Montejo found not only the first edition of 1539 of Diaz' work, and the second edition, 1542, but also the original manuscript which is preserved in the National Library of Madrid. The manuscript contains some significant paragraphs which have been

omitted from the printed work. The manuscript was dedicated to King Emanuel of Portugal, who died in 1521, and Williams calls attention to this as evidence


Con priuilegio imperial
y del rey de portugal.

Tractado cõtra el mal
serpentino: que vulgarmen
te en España es llamado
bubas q̃ fue ordenado
en el ospital de todos
los santos d Lisbo
na: fecho por ruy
diaz de ysla.

Title Page from Dias de Isla's *Treatise Against the Serpentine Disease.* (Jeanselme)

that it was written before that date. Dias de Isla is known to have been in practice in Barcelona in 1493, when Columbus returned from his first voyage, and he was thus in a position to be a witness to the very

landing of syphilis in Europe. The title of Dias' first edition, put in English, is "*Treatise on the serpentine malady, which in Spain is commonly called bubas, which was drawn up in the hospital of All Saints in Lisbon . . . printed in the very noble and very loyal city of Seville, in the house of Domenico de Robertis, printer of books. Finished the twenty-seventh of September MDXXXIX.*"

The contents of his work are briefly as follows: Syphilis was unknown before the year 1493. It was brought by the crew of Columbus on their return from the first voyage to Española (Haiti). Dias called it the Disease of the Isle 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, Pincon of Palos.

Dias says:

It has pleased divine justice to give and send down upon us unknown afflictions, never seen nor recognized nor found in medical books, such as this serpentine disease . . . at the time that the admiral don Xristoual Colon arrived in Spain the Catholic sovereigns were in the city of Barcelona. And when they went to give them an account of their voyage and of what they had discovered, immediately the city began to be infected and the aforesaid disease spread, as was seen later on through long experience. . . . In the following year of 1494 the most Christian King Charles of France who then was reigning having gathered a great army passed into Italy. And at the

time that he entered the country with his host many Spaniards infected with this disease were in it and at once the camp began to be infected with the aforesaid malady, and the French, as they did not know what it was, thought it came from the atmosphere of the region. The French called it the disease of Naples.

Williams called attention to the importance of one of the paragraphs in the original manuscript which is omitted from the published editions, probably for reasons of policy, as follows:

As has been found by very long and well proved experience and as this island was discovered and found by the Admiral Don Christoual Colon at present holding intercourse and communication with the Indies. As it is of its very nature contagious, they got it easily; and presently it was seen in the armada itself in a pilot of Palos who was called Pincon [Martin Alonso Pincon, Commander of the Pinta.—W.A.P.] and others whom the aforesaid malady kept attacking.

This discovery by Montejo of the work of Dias on syphilis is one of the greatest literary finds in medical literature. If it seems to be too dramatic to be credible, let me remind you that the material exists and has been examined by scholars who corroborate the work of Montejo and each other: that Montejo's account and the various chroniclers confirm each other's reports; and that they were sober writers of history, reciting the facts in their experience, and not geniuses, like DeFoe, or Bunyan who alone could invent facts they had not experienced with such accuracy as to give them the air of complete verisimilitude.

BONES

There is another sort of evidence through which we can trace the history of syphilis, and that is the evidence of bones. Syphilis is one of the diseases which leaves evidence in bones that is at times so characteristic that it must be accepted. And all the positive documentary evidence of the bringing of syphilis to Europe by Columbus and the negative evidence of its non-existence in the Eastern Hemisphere before his time could be wiped out by the production of any bone certainly from the Eastern Hemisphere, unmistakably syphilitic and of authentic pre-Columbian origin. The challenge has rested upon those who advocate the pre-Columbian existence of syphilis in Europe to produce such bones. This they have not been able to do. Collections of pre-Columbian European bones have been studied again and again with this object in view, and yet so great an authority as Virchow, one of the world's greatest anthropologists and perhaps its greatest pathologist, said in 1896 that no authentic syphilitic bones of pre-Columbian date have been found in Europe.

Elliot Smith, one of the ablest paleopathologists, has recently given very striking evidence upon this point as the result of the examination of Egyptian skeletons. He says:

As a matter of fact, after examining the remains of something like 30,000 bodies of ancient Egyptians and Nubians representing every period of the history of the last sixty centuries, and from every part of the country, it can be stated quite confidently that no

trace whatever even suggesting syphilitic injuries to bones or teeth was revealed in Egypt before modern times.[7]

This subject also has been exhaustively studied by Williams.[8] He has examined not only the subject as it

ANCIENT SYPHILITIC SKULL FROM PARACAS, PERU
(American Museum of Natural History—Williams)

deals with American bones showing evidence of syphilis, but of European bones offered in evidence of the early existence of syphilis in the Eastern Hemisphere.

[7] G. Elliot Smith, Introduction to Bryan's *Ebers Papyrus*, p. xxvii. 1930.

[8] Archives of Pathology, **13**: 779, 931. 1932.

His extensive consideration is easily available and should be read; it is instructive not only upon this subject, but upon that of the pathology of syphilis and of the methods of archeology and paleopathology. I cannot do better than to repeat some of Williams' conclusions:

The diagnosis of syphilis from bones can be made to a practical certainty from a perfectly typical syphilitic skull, such as those described in this paper. Undoubtedly, many skulls that are syphilitic are not perfectly typical and would thus be rejected. The diagnosis from long bones is less certain, but in favorable cases a high degree of probability may be attained.

Of a considerable number of alleged finds of ancient syphilitic bones [in the Eastern Hemisphere], the following instances are the only ones that I can learn of that are entitled to be so regarded. It will be observed that they do not concern skulls, but only long bones.

He then considers these finds, five in all, and concludes that neither their antiquity nor their syphilitic character is certain.

On the negative side, there is a large amount of evidence from the Eastern Hemisphere. Practically all recent workers in Egypt reported that they failed to find bones showing evidences of ancient syphilis; Elliot Smith's statement that among more than 25,000 skulls examined by him, not one was syphilitic is impressive. The evidence from France was recently reviewed by Jeanselme and by Pales, both of whom decided that it is inconclusive or negative. In 1896, Virchow stated that he did not know of a single

ancient syphilitic bone from any locality; Virchow was probably better informed with regard to osseous material collected in Europe than any other person. I cannot learn of any find in any part of Europe outside of France since the time of Virchow [died in 1902] that can be regarded as highly suggestive of syphilis. Bloch stated that he had searched the Hunterian and other collections in London and Cambridge, with negative results. The late Professor Boldt of Amsterdam, in a personal conversation, informed me that he had studied many thousands of skulls taken from burial places of various periods; he had never found a syphilitic skull of pre-Columbian date; he had in his immense collection several typical syphilitic skulls of later dates. The late Professor Manouvrier of Paris gave me a practically identical report, also in a personal conversation. In other museums I have had the same experience. It is evident that physical anthropologists who handle vast numbers of ancient bones are keenly interested in the problem of syphilis. It is most unlikely that any authentic specimen of pre-Columbian syphilitic skull has been found in Europe and overlooked. Of course there are enormous territories in Asia and Africa that have never been explored in an archeologic sense.

The entire absence of syphilitic bones of pre-Columbian origin in Europe is as conclusive evidence as possible of the absence of syphilis. If syphilis had existed, it should be discoverable in some of the abundant remains.

On the other side Williams enumerates the six most important finds showing syphilis of pre-Columbian date in the Americas. These finds are from as widely separated areas as New Mexico, Tennessee

and Ohio, Peru and the Argentine. Most of these specimens are in all reasonable probability of pre-Columbian date. One skull examined by Williams himself and Tello is undoubtedly syphilitic, and with almost equal certainty of very ancient burial. He adds:

> The aforementioned cases have been selected because they are as nearly free from suspicion as any that can be found. It is proper to repeat in this summary the fact that many long bones of Indians showing evidence of disease resembling syphilis have been found in numerous places both in North and in South America. In contrast with the small number of bones from the Eastern Hemisphere that are suspected of showing ancient syphilis, the amount of material in America is almost embarrassing. . . . It seems to me that the evidence from bones points clearly to the conclusion that the Indians were afflicted with syphilis in a number of parts of America before the arrival of white men.

Means, in a recent report, comes to the same conclusion as a result of extensive roentgenological studies of skeletons of prehistoric mound builder Indians of Ohio.[9]

The case of the origin of syphilis, then, may be summarized in this way:

Syphilis appeared in Europe in the years immediately following the return of Columbus from his first voyage to America. It spread from Italy with the dispersal of the Army of Charles VIII of France in the spring of 1495. Spanish mercenaries were in

[9] *Am. Jour. of Roent.*, **13**: 4. 1925.

Charles' army who were regarded at the time as the source of the epidemic that attacked it. This source of the disease has been definitely mentioned in contemporary Spanish documents. It was recognized as a new disease and no name existed for it.

Its spread and recognition as a new disease can be traced through contemporary documents that have to do with the control of the epidemic. These documents are all subsequent to the return of Columbus. Attempts to show that some of these documents are of earlier origin and that there were descriptions of diseases identical with syphilis in the Middle Ages and earlier in the fifteenth century have failed. On the contrary the number of documents concerned with syphilis immediately after the return of Charles' army is innumerable. This circumstantial historical evidence is emphasized by the direct evidence, which was first unearthed by Montejo, of many Spanish documents of the period, specifically reporting the occurrence of syphilis in the West Indies, and its transmission to Europe by men in Columbus' fleet. All ancient literature has been examined for syphilis, but no convincing description of it has been found. It is inconceivable that if syphilis existed there should not have been many plain descriptions of it in ancient literature, with its prurient tendencies.

Evidence from ancient bones points only to America. The number of even suspicious bones found in the Eastern Hemisphere is relatively few. No convincing specimens have been found. In contrast, in America the number of ancient bones that are probably syph-

ilitic is large. Such bones have been found in many collections. Bones have been found from widely distributed areas which meet the exacting criteria of syphilis.

In subjects in which positive evidence of mathematical exactness cannot be offered, judgments must be founded on the preponderance of evidence. This is particularly true of such subjects as medicine and history. The preponderance of evidence for the American origin of syphilis is overwhelming.

Lecture II

THE DEVELOPMENT OF OUR KNOWLEDGE OF SYPHILIS

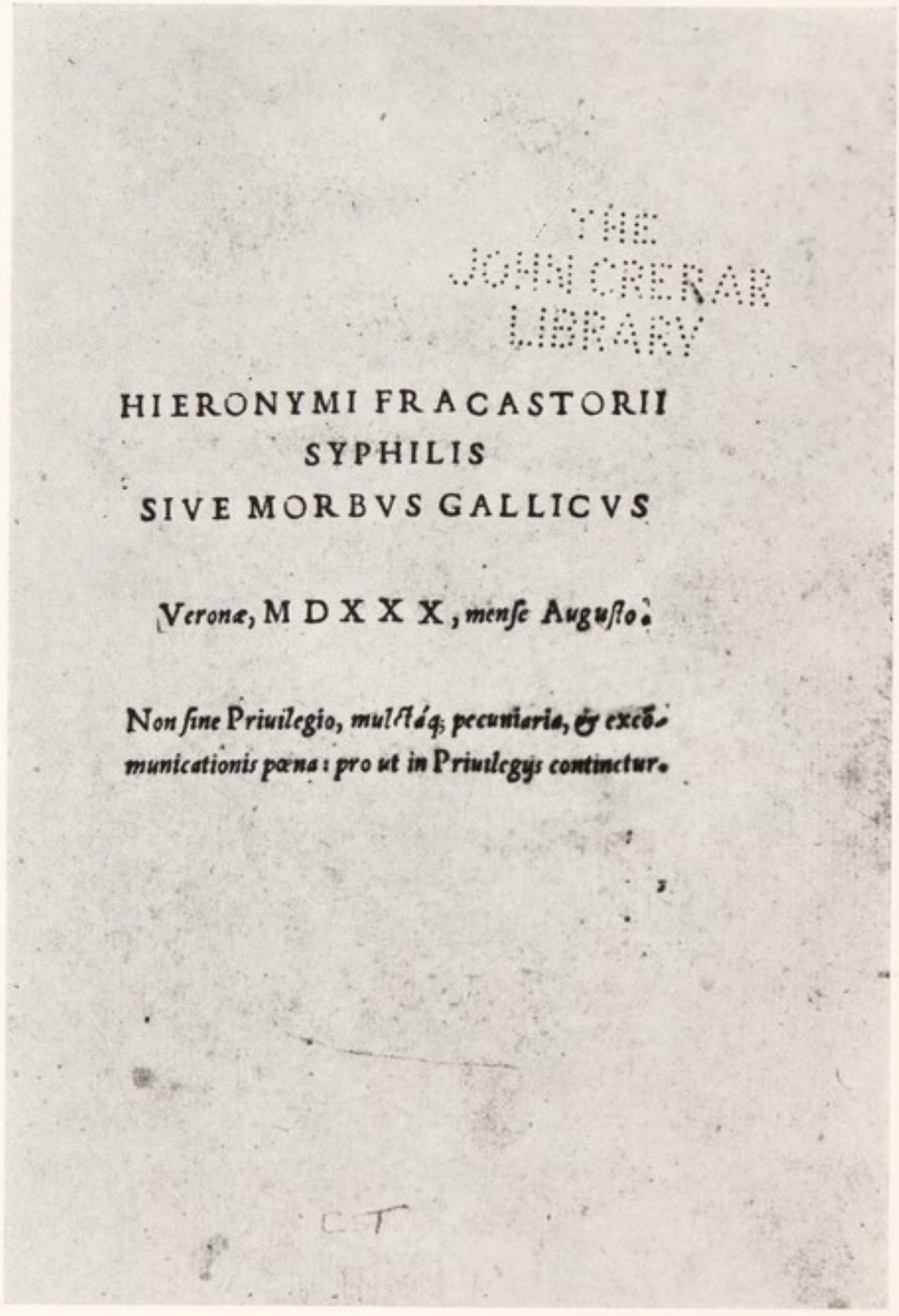
AFTER the appalling story of the beginning and the spread of syphilis over the world in the last years of the fifteenth and the first of the sixteenth centuries, we come to the history of the growth of the knowledge of syphilis through the eventful period of the last four hundred years. It is as interesting, if less dramatic than the story of its beginning, and even more significant. This story of the growth of our knowledge of syphilis is, as I have said, an epitome of the history of the growth of modern medicine.

The end of the fifteenth century was the beginning of modern science. A few pioneers like Roger Bacon and Petrarch, in the previous three hundred years, had given intimations, that we can now recognize, of the future of science, and the stirring of men's minds for learning is indicated by the foundation of many of the great universities in this period; but the actual achievements of modern science had hardly begun in 1500. Within only fifty years Constantinople had fallen, marking the end of the Roman Empire, and printing had been invented. Columbus had just discovered America, and Vasco de Gama had sounded the knell of medieval geography by finding the way to the East Indies around the Cape of Good Hope. Leonardo de Vinci, Paracelsus and Vesalius represent the very

beginning of modern medical knowledge, and their works, which mark a new level of medical knowledge, all appeared in the sixteenth century. It was one hundred years before William Harvey founded modern physiology by demonstrating the circulation of the blood.

But if the year 1500 marks the beginning of modern science, it was a splendid beginning. The invention of printing, the discovery of America, the discovery of a water route to the Far East, Copernicus' discovery of the heliocentric arrangement of the solar system, the Protestant Reformation, all of which occurred in this short period, are among the most significant events in history. And Leonardo, Copernicus, Columbus, Paracelsus, Luther, Vesalius, Magellan, are among the greatest names. Men's minds had burst the shackles of the Middle Ages.

It was at the beginning of this great period that syphilis spread over Europe, and it furnished a new stimulus to activity of medical thought. Here was a disease suddenly thrust upon the attention of man, concerning which classical authorities said nothing, and which must be studied in its own manifestations. One of the few things that can be reckoned to the credit of syphilis is that it was an ideal means of stimulating men's minds to objective study of disease at the opportune time when they had become prepared for it. Studies of syphilis began to be recorded immediately. Albert Dürer illustrated syphilis in a pamphlet published in 1496, and as early as 1497 or



Title Page from Fracastor's *Syphilis Sive Morbus Gallicus*.
Actual Size: 5¾×8¼
(Crerar Library)

1498 Bartholomew Steber's *Treatise on Syphilis* was published. Syphilis is indeed about the first illustration of the modern objective study of disease, by which method alone modern science in general has been enabled to make its great progress.

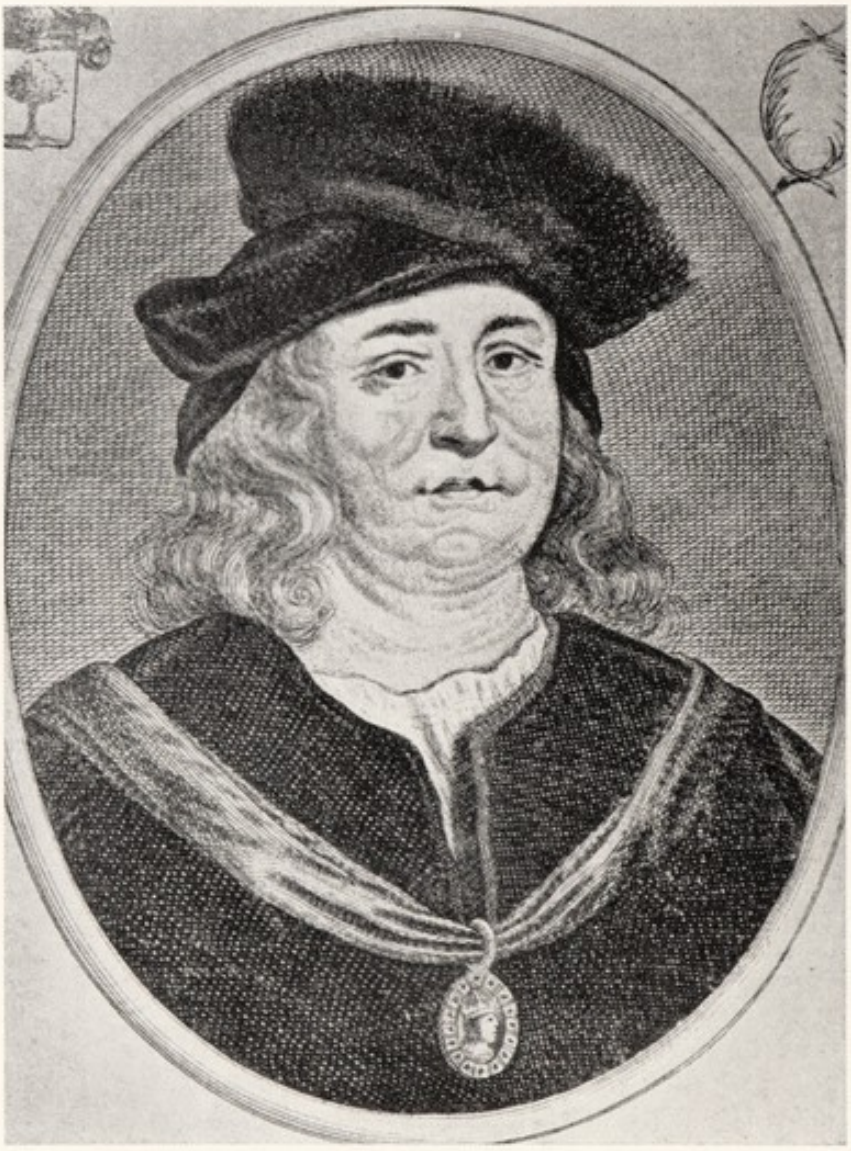
With the sixteenth century began what Garrison calls "the huge output of the syphilographers." This output is of course especially an index of the activity in the study of syphilis, but it is also an index of the activity of medicine as a whole during this period. The literature of syphilis in the sixteenth century and the knowledge of the disease which it shows is of surprising extent.

Proksch (*Geschichte der venereischen Krankheiten*), in his enumeration of the most important early writers on syphilis, gives a list of forty authors whose works have come down to us. Among these the most important, perhaps, were the following:

Paracelsus, who approached the disease with his characteristic independence and openness, not to say rebelliousness of mind, suggested its hereditary transmission (1530), and is credited with introducing mercury in its treatment (1568).

Fracastor, who has a better claim to permanent renown for his theory of the microbic origin of infectious diseases, in his poem "Syphilis sive Morbus Gallicus," published in Venice in 1530, immortalized himself by inventing the name syphilis. The name syphilis Fracastor gave to his hero, probably deriving it from σῦς (swine) and φίλος (lover). By this name the disease has since been known.

Others were: Leoniceno (1497), who described syphilitic hemiplegia; Lacumarcino, whose *De Morbo Gallico* (1524), was the chief work on syphilis of its



PARACELSUS
(Crerar Library)

time; Massa, who described neuralgic manifestations (1532); Botallo, who described cerebral blindness (1536); Ferro, who described joint lesions (1537).

According to Garrison, Gruner gives a list of 191 symptoms of syphilis described in this period.

It was during this time that Fracastor described typhus fever (1546), and Ingrassias described varicella (1543).

Knowledge of syphilis acquired in this early period.—Syphilis, with its constitutional symptoms, was dis-

FUMIGATION (sweating treatment of syphilis)
"For one pleasure a thousand pains." From the collection of engravings by Jacques Laniet of famous proverbs. Paris 1659–63. (Jeanselme)

tinguished from the long known venereal diseases at the beginning of this period. The chancre was recognized as a lesion of syphilis, and gonorrhea and soft chancre were separated from it by their lack of constitutional symptoms. Unfortunately Paracelsus began the confusion of all of them by calling syphilis French gonorrhea in 1530, and by the middle of the century it was current. This confusion was gradually

METHOD OF PREPARING THE BLESSED WOOD (Guiacum)
(Jeanselme)

cleared up by the end of the eighteenth century.

The syphilitic eruptions were described, although the different types were not clearly separated.

Mouth and throat lesions and loss of hair were recognized as symptoms of the disease, as were involvement of bones and joints, and of the nervous system and internal organs.

The infectious character of the chancre and of other genital lesions was recognized. Extragenital infections were known to be of common occurrence, such as infection of children from sleeping with syphilitic persons.

Remedies used.—Mercury in the treatment of syphilis comes into view almost as early as the disease itself. Paracelsus is given credit for having introduced it, but it had long been used by the Arabs in scabies, psoriasis, leprosy and other skin diseases, and was doubtless early tried in syphilis. The usual method of administration was by inunction, but it was also given by the mouth, by fumigation and by the application of mercurial plasters. Arsenic was probably used by Paracelsus as early as 1530. The use of guaiacum by the Indians is mentioned in the earliest Spanish chronicles, and it was highly prized. Various other vegetable infusions, sulphur baths and hydrotherapeutic measures were used.

Much opposition developed to the use of mercury. The first, and perhaps the most distinguished of its opponents was Fallopius (1523–62), who attributed gummata and bone and visceral syphilis to mercury. Fallopius in his *De morbo gallico* (1563), distinguished

THE POX

Treatment of the venereal disease by inunctions and inhalations. Title Page from Stephan Blankaart's *Venus belegert en Ontset*, Amsterdam, 1684. (Jeanselme)

between syphilitic and non-syphilitic condylomata. He also invented a sort of mechanical protection to prevent infection.

Jean Fernel (1506–88) made the important discovery that syphilitic virus would not pass through the normal skin; that a break was necessary for infection. He traced the course of the infection and showed that the chancre was the first lesion of the disease and that the general infection followed this.

Ambroise Paré (1510-1590), by means of the vaginal speculum, studied vaginal and uterine lesions. He first called attention to the characteristic indolence of the syphilitic bubo, and confirmed Paracelsus' observation of the heredity of syphilis.

The progress of knowledge of syphilis continued in the seventeenth and eighteenth centuries. The danger of indirect transmission of syphilis in medical practice was shown by Horst (1575–1636), who reported in 1628 almost 100 instances of infection by cupping. He, and later Palfey (1718) established the fact of the infection of midwives and physicians from syphilitic patients.

Colle (–1631) and Musitano, (1635–1714), reported infection from kissing and from drinking cups, and Musitano described chancre of the tonsil.

Bazin and Guenault, like Paré, again in 1628 called attention to the indolence of the syphilitic bubo, and emphasized the great diagnostic importance of the induration of the syphilitic chancre, 150 years before John Hunter made this observation.

Destructive syphilitic diseases of the nose and

mouth were described. Syphilitic lesions of the bones were fully studied. The recognition of many of the manifestations of syphilis of the nervous system,

GABRIELLE FALLOPPIO
(Crerar Library)

cerebral gumma, syphilitic meningitis, syphilitic neuralgias, and syphilitic spinal lesions date from this period. Schenck von Grafenberg (1531–98) and Severino (1580–1656) demonstrated in post mortem

examinations syphilitic lesions of the larynx, trachea and lungs. Valsalva (1666–1723), Baader and others established syphilis of the liver, spleen and kidneys. Of particular interest Lancisi, before 1720, called attention to the relation of syphilis to diseases of the heart and blood vessels and to aneurysm.

JEAN FERNEL

Jean Astruc.—The publication in 1736 of Astruc's *De Morbis Venereis* constitutes a landmark in the history of syphilis. With an intimate acquaintance with the literature of syphilis from its beginning, he summarized all the knowledge of the subject, and in

so doing performed a service which has made all subsequent students of the disease his debtors.

Van Swieten (1700–73), in particular, performed a great service by introducing treatment by means of the administration of mercury within the limits of its physiologic effect and by his success in checking

AMBROISE PARÉ
(Crerar Library)

the practice of treating syphilis by mercury carried to the point of producing severe salivation.

Boerhaave, in his *Aphorisms*, published in 1728, analyzed the course of syphilis, thus anticipating by a century the more complete work of Ricord.

Among the foremost contributions to the subject in the eighteenth century were those of the great

Morgagni (1682–1772) on syphilis of the internal organs. In his extensive study of morbid anatomy he established, in a way that ought to have been conclusive for all time, the occurrence of syphilis of the viscera. He described syphilis of the lungs and its complication by tuberculosis; syphilis of bones, and

VALSALVA

syphilis of the heart and great blood vessels; and he first described syphilis of the cerebral vessels. Morgagni also made valuable contributions to the distinction between syphilis and the local venereal diseases by his studies of the sequelae of gonorrhea; for he described cystitis, prostatitis, Cowperitis, and most of the other complications of gonorrhea in the genito-urinary tract.

In the latter half of the eighteenth century Stoll, Plenck, von Rosenstein, and Sanchez, emphasized the importance of hereditary syphilis, and even described the occurrence of late manifestations of hereditary

syphilis—the syphilis hereditaria tarda of later French writers.

During the same period the duality of syphilis and gonorrhea was reaffirmed by such students as Francis Balfour, Hales, Ellis, Tode, Andrew Duncan, Benjamin Bell, Swediaur and Ernst Horn. Bell and Balfour demonstrated experimentally the duality of syphilis and gonorrhea.

It will thus be seen that by the latter half of the eighteenth century there had been accumulated the great fund of knowledge of syphilis. To enumerate only some of the important items: The symptoms had been fully described, the distinction between gonorrhea and chancroid and syphilis had been made. The enormously important subject of syphilis of internal structures had been well worked out by many investigators. Hereditary syphilis was well known and its most important facts described. The dangers and importance were recognized of extragenital infections, and of mediate transmission of the disease; of infection by kissing and by innocent contact with infected individuals, as of children sleeping with syphilitic parents or of physicians and midwives from syphilitic patients; of infections from surgical instruments and from contaminated utensils. What a record of achievement in knowledge this is!

Since anesthesia and asepsis have made experimental methods possible in medicine, we are inclined to regard all our worth-while medical knowledge as of recent origin. I saw the statement recently by an intelligent writer than until fifty years ago 10

percent of medicine was knowledge and 90 percent mysticism. That illustrates the danger of not having historical perspective. Our knowledge of the gross

LANCISI

facts of clinical medicine is an accumulation of centuries. Many of the best descriptions of disease are old. Symptomatology and gross pathology have had long and intensive study and medicine has always

gone as far as it could with the knowledge which the times afforded. Contrary to the general impression, medicine has usually led among the sciences in the advancement of knowledge. And at the end of the eighteenth century, without modern knowledge of the

JEAN ASTRUC

basic sciences and without modern instruments of precision, medicine had advanced to the limit of possibility. Men were doing all that could be done in the state of general knowledge of the times in ascertaining the information which could be elicited by their unaided senses. Capacity for clinical observation and

DE MORBIS
VENEREIS
LIBRI NOVEM

IN QUIBUS DISSERITUR TUM DE ORIGINE, Propagatione & Contagione horumce affectuum in genere : tùm de ſingulorum Naturâ, Ætiologiâ & Therapeiâ, cum brevi Analyſi & Epicriſi Operum plerorumque, quæ de eodem argumento ſcripta ſunt.

Auctore JOHANNE ASTRUC, *Regi à Conſiliis Medicis; Archiatro Auguſti II. glorioſæ memoriæ, Poloniarum Regis, S. R. I. Electoris, & Ducis Saxoniæ; Medico Ordinario Seren. Principis, Ducis Aurelianenſis; & in Regio Franciæ Collegio Profeſſore Medico.*

EDITIO ALTERA,

Auctior & emendatior, in quâ additæ ſunt duæ Diſſertationes novæ.

TOMUS I.

LUTETIÆ PARISIORUM.

Apud GUILLELMUM CAVELIER, viâ Jacobeâ, ſub ſigno Lilii Aurei.

M. DCC. XL.

CUM APPROBATIONE ET PRIVILEGIO REGIS.

Title Page from Astruc's *De Morbis Venereis*

description has not since improved. Indeed it is probable that in capacity for clinical observation and description and the study of disease with their unaided faculties men have deteriorated in our times.

The history of syphilis perfectly illustrates all this. In the three hundred years between 1500 and 1800

BOERHAAVE

all the facts of syphilis that could be ascertained then had been worked out. I invite you to review the achievements in the study of syphilis that I have sketched in this lecture, and then see how short the list is of observations in syphilis that had not been made and recorded. Only tabes and paresis can readily be thought of, and even syphilis of the central nervous system had been recognized! The fullness of

knowledge of the clinical course and macroscopic pathology of syphilis that was achieved in the three hundred years before 1800 is convincing evidence of the marvelous capacity of the great clinicians of that period.

GIOVANNI MORGAGNI
(Crerar Library)

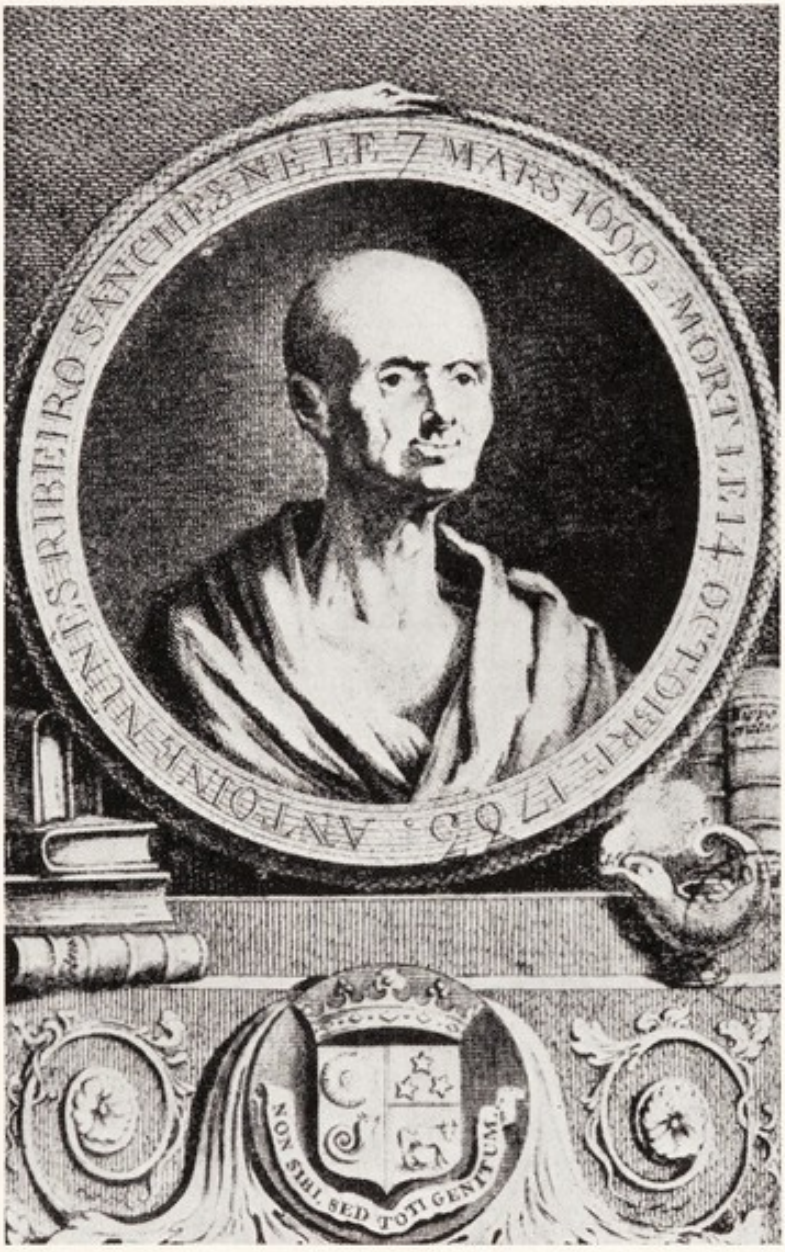
And what a list it is of the men who have studied syphilis: Paracelsus, Fracastoro, Fallopio, Jean Fernel, Ambroise Paré, Valsalva, Astruc, van Swieten, Morgagni Boerhaave, Francis Balfour, Benjamin Bell. They are among the giants of medicine. Syphilis

then, as now, was a part of every field of medicine and excited universal interest.

At this point John Hunter enters the picture, and his work on the venereal diseases marks an epoch—a startling and unfortunate reversal in the growth of knowledge of them—because of the confusion into which, through his great authority, the subject was thrown by his false views. The ages-old mistake of letting dogmas influence one's conceptions of disease has an almost unique example in John Hunter, Hunter of all men, who is enshrined in tradition as one of the ablest apostles of experimental medicine. Hunter's misconceptions of syphilis and his erroneous teaching were due to general doctrines of disease from which he deduced his conclusions. He fortified these conclusions by the famous experiment on himself in 1767 which he interpreted too narrowly. Hunter made no distinction between chancroid and chancre, and according to his theory the virus of gonorrhea and of chancre was the same. When this virus was inoculated on a "secreting" surface—a mucous surface—it produced gonorrhea; on a "non-secreting" surface, syphilis. To establish this theory, Hunter inoculated a non-secreting surface—his skin—with pus from a gonorrhea, and had the misfortune to infect himself with undoubted constitutional syphilis.

Of course the explanation, we know now, is that his experiment was made with pus from a mixed infection of gonorrhea and syphilis, but the possibility of such a mixed infection was contrary to Hunter's

doctrine of the occurrence of disease. Indeed, the possibility of such a mixed infection was not then recognized, and Hunter, taking no account of this



SANCHEZ

possibility, concluded that his experiment confirmed his view of the unity of syphilis and gonorrhea. Hunter's deductions carried him much further than

this. Although he knew fully the findings in syphilis of his predecessors he denied the occurrence of extragenital infections; the possibility of intermediate transference of syphilis through contaminated substances; the occurrence of hereditary syphilis, and of course, therefore, of the possibility of infection occuring from a child born syphilitic; and of syphilis of the internal organs. According to his interpretation of his observations he had not seen any of these manifestations of syphilis; their occurrence was contrary to his doctrines of disease; and, therefore, in spite of the great mass of accumulated observations he denied the existence of all of them. Hunter was the great figure in medicine of his time; the evidence of Morgagni and Lancisi and of all the other famous men who had worked in syphilis before him, and the contentions of his contemporaries, like Benjamin Bell, went for nothing. Hunter's views were accepted and after 1767 practically dominated the subject.

It is hard to find a stronger illustration—although there are many such—of the mischief wrought by erroneous opinions when backed by a great personality, than is offered by Hunter's unfortunate views. The study of the venereal diseases was hopelessly misdirected, and it was more than half a century before investigators were able to reconstruct a proper conception of them.

The history of syphilis for seventy years after Hunter's time, from 1767 to 1837, was one first of confusion and then of gradual groping into light. There were able investigators who were not carried

away by Hunter's dicta, and whose investigations all indicated the distinction between syphilis and gonorrhea, Benjamin Bell (1749–1846), F. X. Swediaur (1748–1824), Ernst Horn (1774–1848), and Richard

BENJAMIN BELL
(Crerar Library)

Carmichael (1779–1849). On the other hand there were, of course, many followers of Hunter, including Abernathy (1764–1831), F. A. Walsh (1780–1837), Radel (1749–1850) and A. G. Richter (1742–1812).

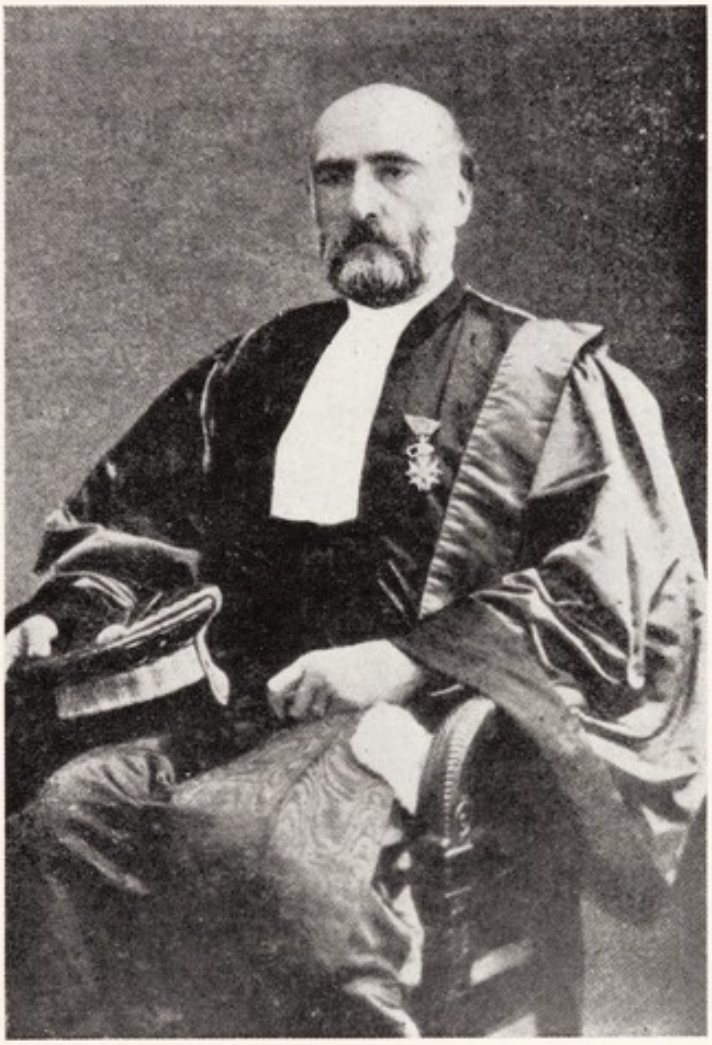
It was Philippe Ricord (1800–89) whose work in the Hôpital du Midi, Paris, between 1831 and 1860,

combined with that of his pupils and followers, reëstablished the fundamental part, and the larger part, of our present clinical knowledge of syphilis. Ricord's greatest contributions to syphilis were his conclusive re-demonstration of the specific character of syphilis

RICORD

and of its distinction from gonorrhea, and his analysis of the course of syphilis into the three stages—primary, secondary and tertiary. This division into three stages is of course conventional; it has, however, not only been found convenient for descriptive

purposes, but it has performed a great service in making it easier to comprehend the multiform symptoms which syphilis presents. The establishment of these two conceptions opened a way for the final

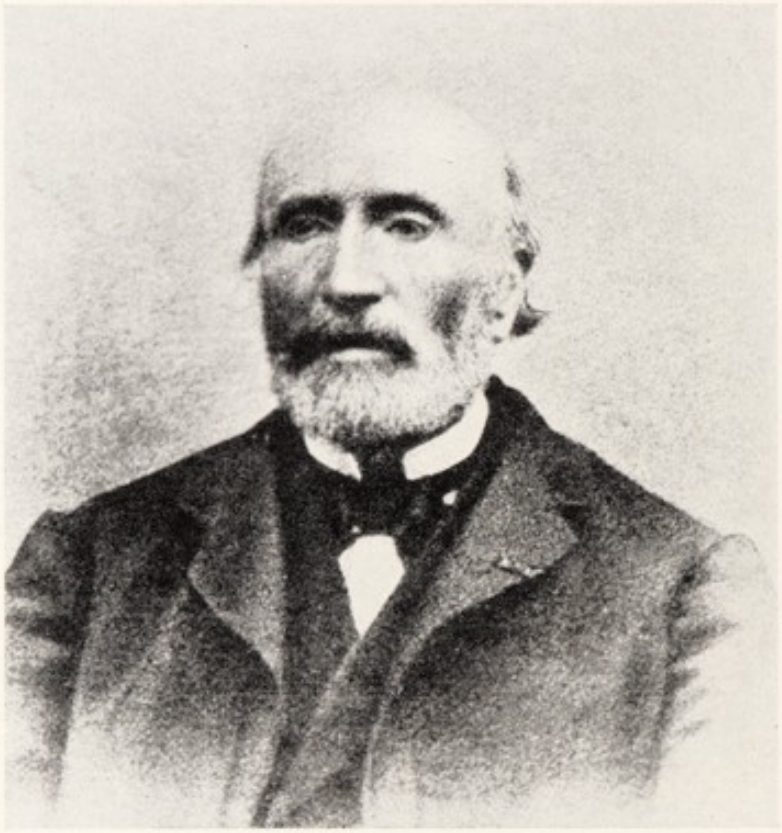


ROLLET

satisfactory study of the disease. Ricord determined the excessive rarity of reinfection with syphilis. He revived the use of the vaginal speculum first utilized by Paré, for the study of venereal diseases, and carefully described vaginal and uterine syphilitic lesions.

And, most important, he cleared away the confusion that had misled Hunter, by proving the occurrence of mixed infections with gonorrhea and syphilis, which explained the cases of syphilis arising supposedly from gonorrhea.

Ricord was mistaken in his view on three important subjects. He did not regard gonorrhea as a specific



CLERC

disease, and he held that the secondary and tertiary lesions of syphilis were not contagious. The specific nature of gonorrhea was proclaimed a few years later by Rollet, of Lyons, and the contagiousness of secondary lesions of syphilis was quickly established by the work of William Wallace and von Waller. But it is

only within very recent years that his views on the non-contagiousness of tertiary syphilis have definitely been proved to have been practically correct.

At the time that Ricord was doing his early work in Paris, the great Wallace was investigating syphilis

RUDOLPH VIRCHOW
(Crerar Library)

in Dublin. In 1835, while Ricord was denying the fact, Wallace established the contagiousness of secondary lesions of syphilis, and the year before this, in 1834, following the suggestion of Williams, he introduced the use of potassium iodid in the treatment of

syphilis. The introduction of the iodids in the treatment of syphilis, considering the time at which it was made and the need that existed for an adjuvant to mercury in the treatment, was perhaps the most im-

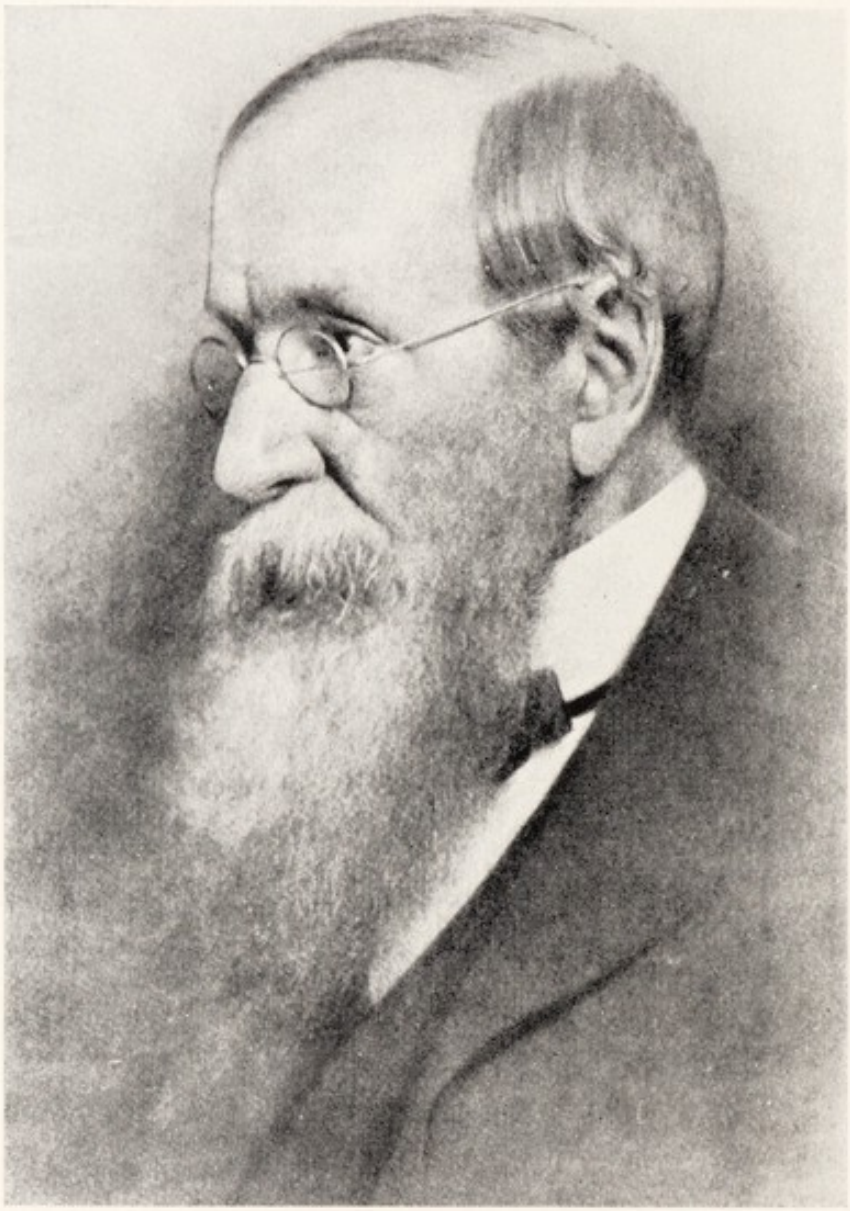
ALFRED FOURNIER

portant contribution to its treatment that was ever made. Certainly for another suggestion in the treatment of syphilis of equal importance we had to wait three-quarters of a century until 1909, when Ehrlich introduced arsphenamine.

With the impetus given to the study of syphilis by

Ricord, the confusion between the venereal diseases was rapidly cleared away, and the knowledge of syphilis was greatly advanced by the French school. Following Ricord's discovery in 1837 of the distinction between gonorrhea and syphilis, Bassereau determined in 1852, by comparative study, the distinction between the syphilitic chancre and chancroid. Rollet and Clerc, who introduced the name chancroid, a little later completely cleared away the confusion between the venereal diseases by establishing the existence of mixed infections of chancroid and chancre, and, indeed, of mixed infections of all of the venereal diseases. During the last quarter of the nineteenth century the clinical distinctions between the venereal diseases, determined by Ricord, Bassereau, Rollet and Clerc, were confirmed in the laboratory. In 1879 Neisser discovered the specific organism of gonorrhea. In 1889 Ducrey demonstrated in the pus of chancroid and in 1892 Unna demonstrated in the tissue the specific organism of chancroid. And, to anticipate, Schaudinn and Hoffmann, in 1905, discovered the organism of syphilis.

While the clinical problems of syphilis were being settled Virchow added his great work in the determination of its pathology. He confirmed and emphasized the importance of syphilis as a disease that affected all organs and tissues of the body. He showed the essential identity of all syphilitic infiltrations. He established the fact of the transfer of the virus through the blood to the various organs and he found the pathological evidence and explanation for the

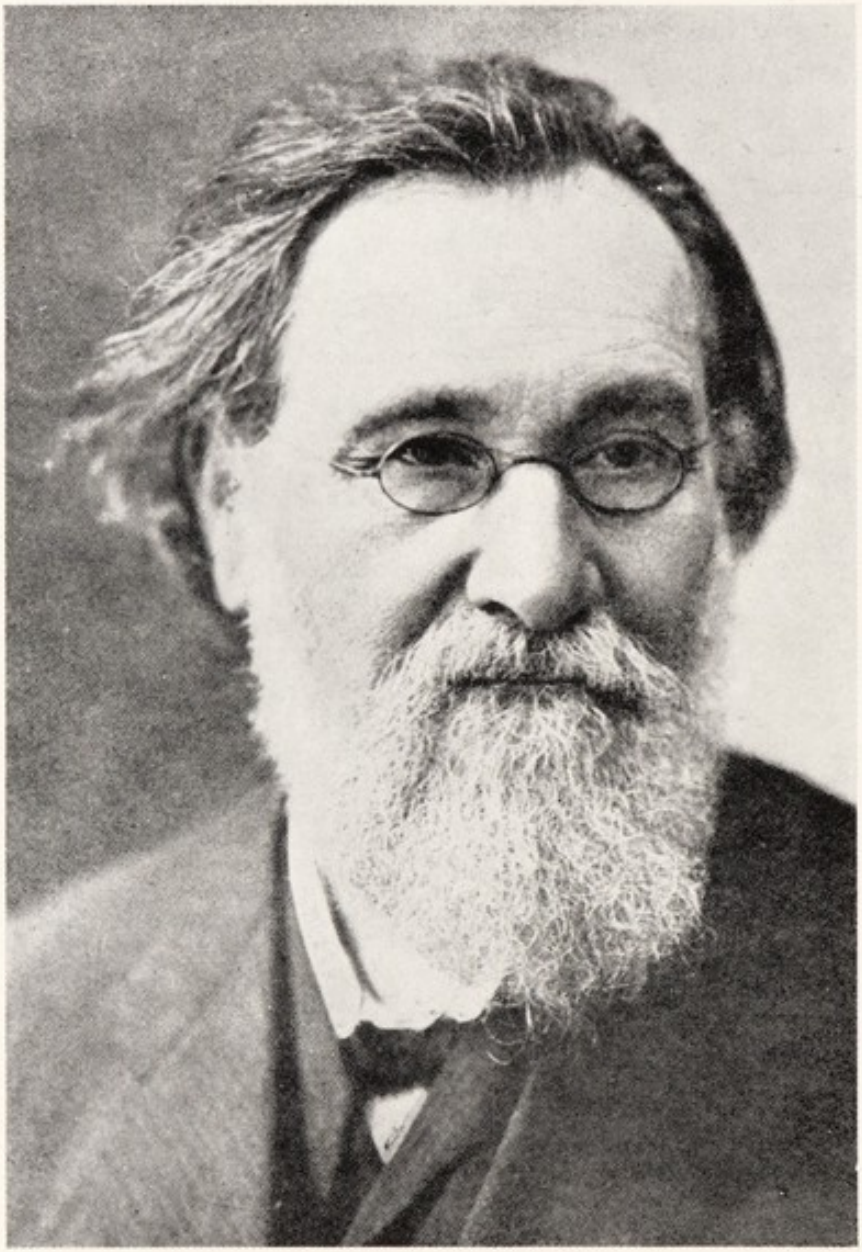


SIR JONATHAN HUTCHINSON

clinical variations in the latent and active periods of the disease.

The influence of Ricord gave rise to two great French schools of syphilology: that of Diday at Lyons and that of Fournier at the St. Louis Hospital, Paris. Largely through the work of these two great syphilographers and their disciples, clinical knowledge of syphilis has been brought to its present state. Diday and his pupils gave their attention chiefly to the problem of hereditary syphilis, and to them is due, in considerable part, the recognition of the importance of syphilis as a cause of hereditary dystrophies and deformities.

The work of Fournier and his disciples ranged over the whole field of syphilis. To Fournier, more than to anyone else, is due the recognition of the importance of syphilis as a cause of degenerative diseases. He was the founder and chief exponent of the modern study of the relationship of syphilis to the problems of society. He first compelled a realization of the difficulties of the problems of the treatment of syphilis. He established the necessity for the long-continued treatment of the disease, and he, more than anyone else, was instrumental in determining the conditions under which the marriage of syphilitics was safe. Fournier's greatest individual works, perhaps, were his demonstration, with Erb of the causal relationship of syphilis to paresis and tabes, his insistence on the essential identity of these two nervous syndromes, and his studies and propaganda on the subject of syphilis and marriage.



METCHNIKOFF

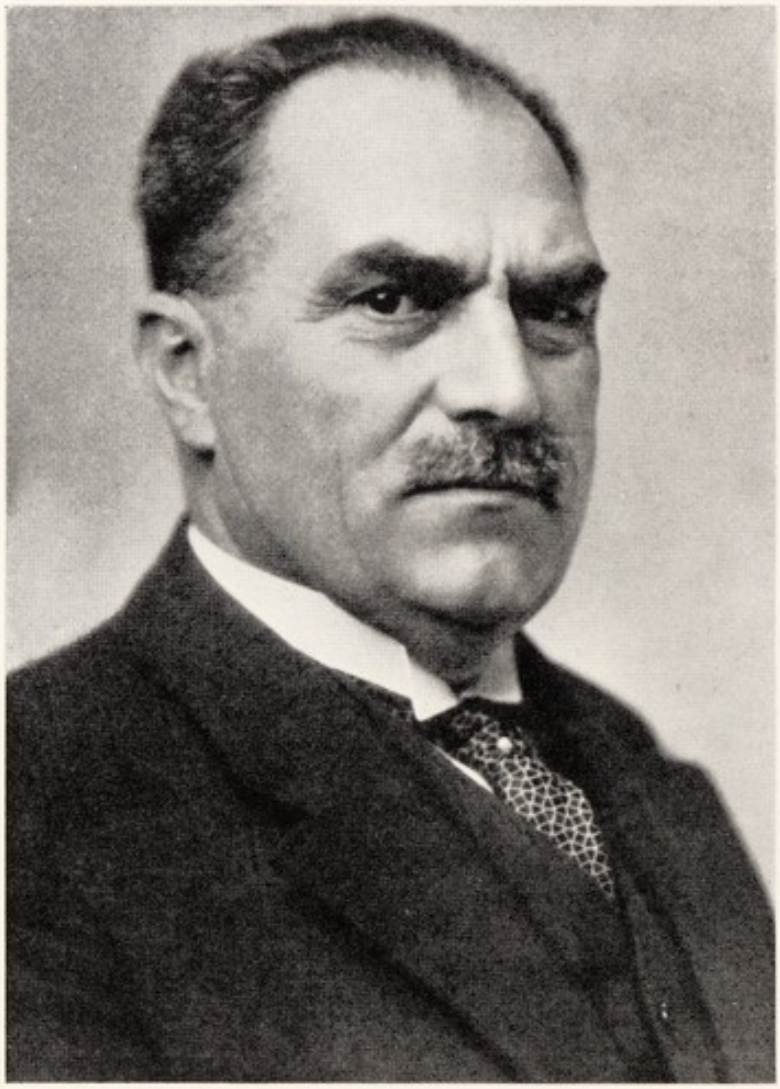
Following the French school, the clinical study of syphilis may be said to have been completed during the last fifty years of the nineteenth century. The clinical course of the disease, its pathological ramifications, and its hereditary manifestations were worked out to a point of practical completeness. To

TABLET TO FRITZ SCHAUDINN

this work syphilographers in all parts of the civilized world have contributed their part. Notable among these have been Jonathan Hutchinson in England; Profeta and Pellizzari in Italy; Virchow, Heubner, Oppolzer, Auspitz and Erb in Germany and Austria; Taylor, Keyes and Morrow in the United States. The work of these men brought the knowledge of syphilis to as high a point as seems possible of attainment by clinical study. Syphilology, in short, had achieved all that could be achieved by clinical methods through the most painstaking study, the highest order of intelligence, and self-sacrifice and courage—for the study of syphilis has meant self-sacrifice and courage —and it could court comparison in the fullness of its

knowledge with what has been done in any other disease.

Clinical syphilology had done its task. Nevertheless momentous questions in relation to syphilis re-



HOFFMANN

mained to be settled. The organism had not been discovered. While the treatment of syphilis presented the most brilliant example that specific treatment had to offer, excepting only those of diphtheria and of

malaria, important problems remained to be solved. Most important of all, it was not known how to inoculate syphilis into the lower animals, so that animal experimentation with syphilis was impossible.

BORDET

And until the study of syphilis could be carried out on animals many of the questions must remain unsettled. It was in these fields that syphilis found its problems confronting it at the beginning of the twentieth century.

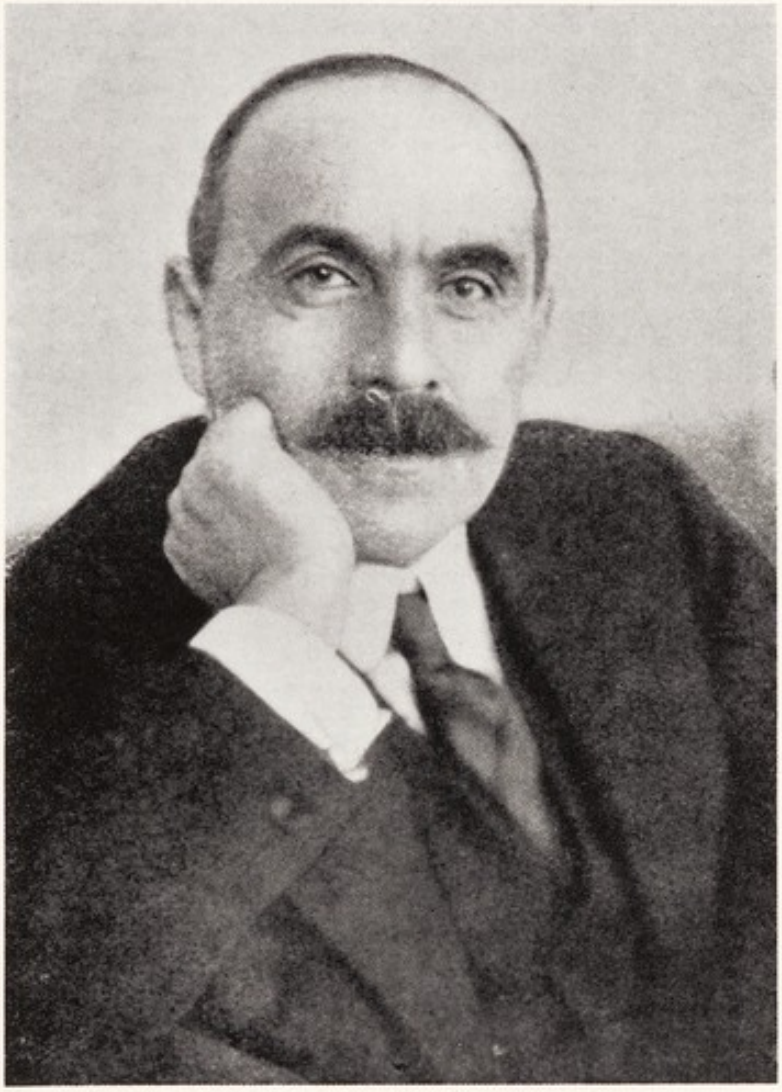
The situation at the beginning of the twentieth

century proved ripe for a great advance in our knowledge of syphilis. Beginning with 1903 one important discovery in syphilology followed another with a rapidity that is without parallel in any other disease. In 1903 Metchnikoff and Roux demonstrated that syphilis was inoculable in apes. In 1905 Schaudinn and Hoffmann ended the long search for the organism of syphilis by the discovery of the Spirochaeta pallida. In 1906–1907 Wassermann, Neisser and Bruck applied the serum-complement reaction of Bordet and Gengou to the diagnosis of syphilis, and developed as a practical test for syphilis what is now known as the Wassermann reaction. In 1911 Noguchi succeeded in cultivating in vitro the Spirochaeta pallida and completed the proof of the specificity of the organism by reproducing the disease in animals from his cultures. In the meantime there had been the development of arsenical chemotherapy of syphilis, begun by Uhlenhuth and carried forward so amazingly by Ehrlich in the introduction in 1909–10 of arsphenamine.

Some of these discoveries reveal the fundamental facts of syphilis, and they have opened up the whole subject to exact scientific study. The result is that within thirty years the entire field of clinical syphilis has been critically reëxamined. Our clinical knowledge obtained by four centuries of painstaking observation of the disease in man has in a few years been reviewed and controlled by animal experiments. Facts established by clinical study have been confirmed; many problems have been solved which

before were impossible of solution; and there has been added an immense accumulation of new exact facts.

The most important of these discoveries was that



WASSERMANN

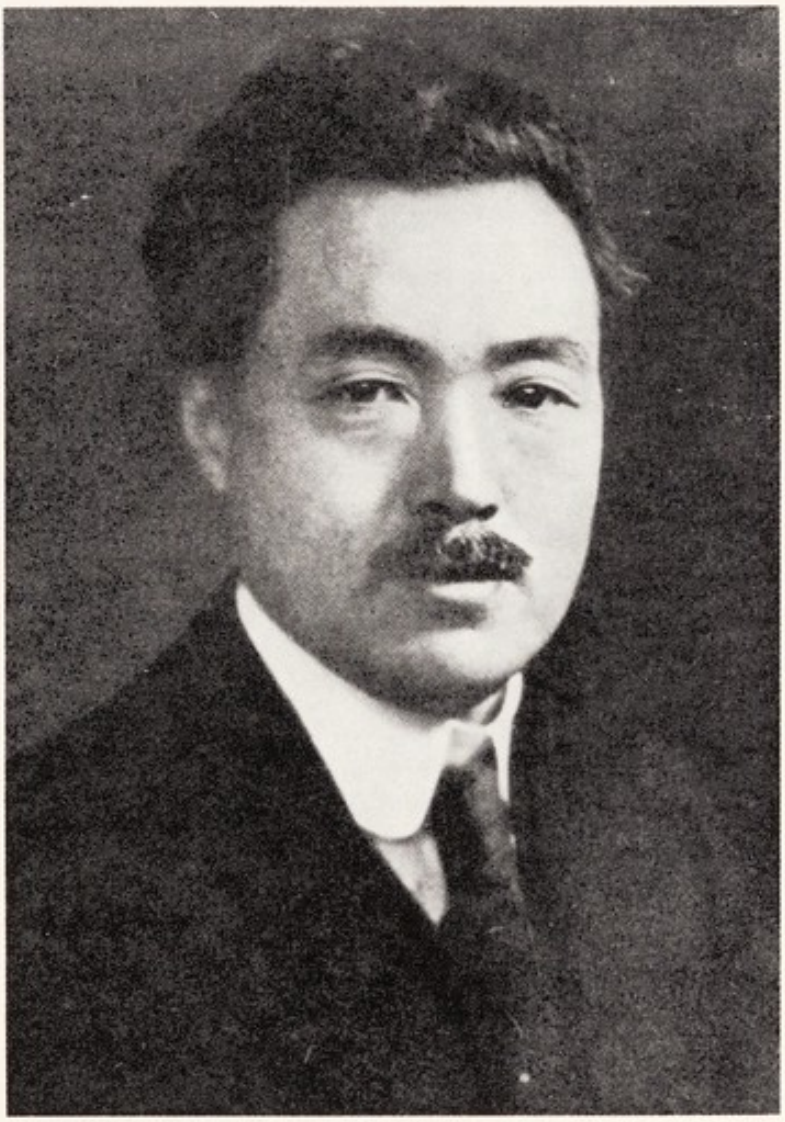
of Metchnikoff and Roux, that syphilis could be inoculated in apes. It was an essential fact; for without the ability to produce a disease at will in lower animals, it is impossible to make an exact critical study

of it. This discovery made it possible to utilize immediately the knowledge of the specific organism of syphilis and the Wassermann test for a complete investigation and has been chiefly responsible for the amazing increase in our knowledge of it. Metchnikoff and Roux' successful inoculation of the chimpanzee was the end of a long line of attempts to produce syphilis in animals. John Hunter tried and failed, and unsuccessful efforts have repeatedly been made by other investigators. Of course the ape would suggest itself as the most likely animal for this experiment, and from Auzias-Turenne in 1866, to Nicolles, and Maurice in 1892, and Charles in 1903, many unsuccessful attempts at the production of syphilis in apes had been made. It is an interesting fact that in 1879 Klebs[1] inoculated syphilis in apes, and that in 1881 Hensell announced that it could be produced in the eye of the rabbit.

The discovery of the Spirochaeta pallida, the specific organism of syphilis, reveals, of course, the fundamental fact of the disease. This discovery was the successful end of one of the most zealous searches in the history of medicine. From the earliest days of syphilis it has been recognized that the disease is due

[1] As a matter of fact Edwin Klebs, as early as 1875–77, inoculated apes with syphilis, and probably recognized the syphilitic spirochaete. Klebs was a versatile genius and his footprints are found in many fields of scientific medicine of that time. He recognized fully the significance of the discovery of the inoculability of syphilis in animals, but he could not make the world accept it, and it was lost until Metchnikoff and Roux' demonstration in 1903. (Arnold Klebs, *Science* **75**: 131. Feb. 12, 1932.)

to a specific virus; even in the middle of the sixteenth century following Fracastor's conception an animal virus was suggested. In 1837, before the days of mod-



HIDEYO NOGUCHI
(Crerar Library)

ern bacteriology, Donné found vibrios in syphilitic lesions which he described as the probable cause. Since the beginning of bacteriology as a science, the search for the syphilitic organism has been incessant,

and many premature announcements have been made.

Schaudinn and Hoffmann announced their discovery of the Spirochaeta pallida as the specific organism of syphilis in May, 1905, in a communication dated April 10, 1905. Previous to that time, Klingmüller and Baermann had determined through animal experiments that the virus of syphilis did not pass through a porcelain filter. This discovery, which was confirmed by Metchnikoff, showing that the organism of syphilis was not ultramicroscopic in size, stimulated anew the search for it.

The discovery of the Spirochaeta pallida was the result of the appointment by the German Academy of Science of a committee consisting of Fritz Schaudinn, a protozoologist, and Eric Hoffmann, a dermatologist, both young men of established ability in their fields. The story of the search for the organism of syphilis, and its final discovery by Schaudinn and Hoffmann, is one of the most interesting stories in microbiology, and is beautifully told by Metchnikoff in his "Microbiology of Syphilis" in the *British System of Syphilis*. I recommend to you to read it. One of the most interesting episodes in this search is Metchnikoff's account of his and Roux' failure to find the organism. With delightful frankness Metchnikoff relates how he and Roux, assisted by Levaditi who, as Metchnikoff said, "had a perfect knowledge of all the technical details of bacteriology," undertook a search specifically for spirilla as the cause of syphilis in syphilitic products obtained from his own infected monkeys. Their investigations were negative

and he says "in our third 'Contribution on Syphilis'[2] (we) expressed the opinion that the disease could not be attributed to any form of spirillum, but that it was probably caused by some non-motile organism."

EDWIN KLEBS.
From a portrait by H. Treuenfels. (Arnold Klebs)

They had hardly made their announcement, at least only several months had passed, when, as Metchnikoff says, "I received a letter from Schau-

[2] *Annales de l'Institut Pasteur*, 1904, pp. 661.

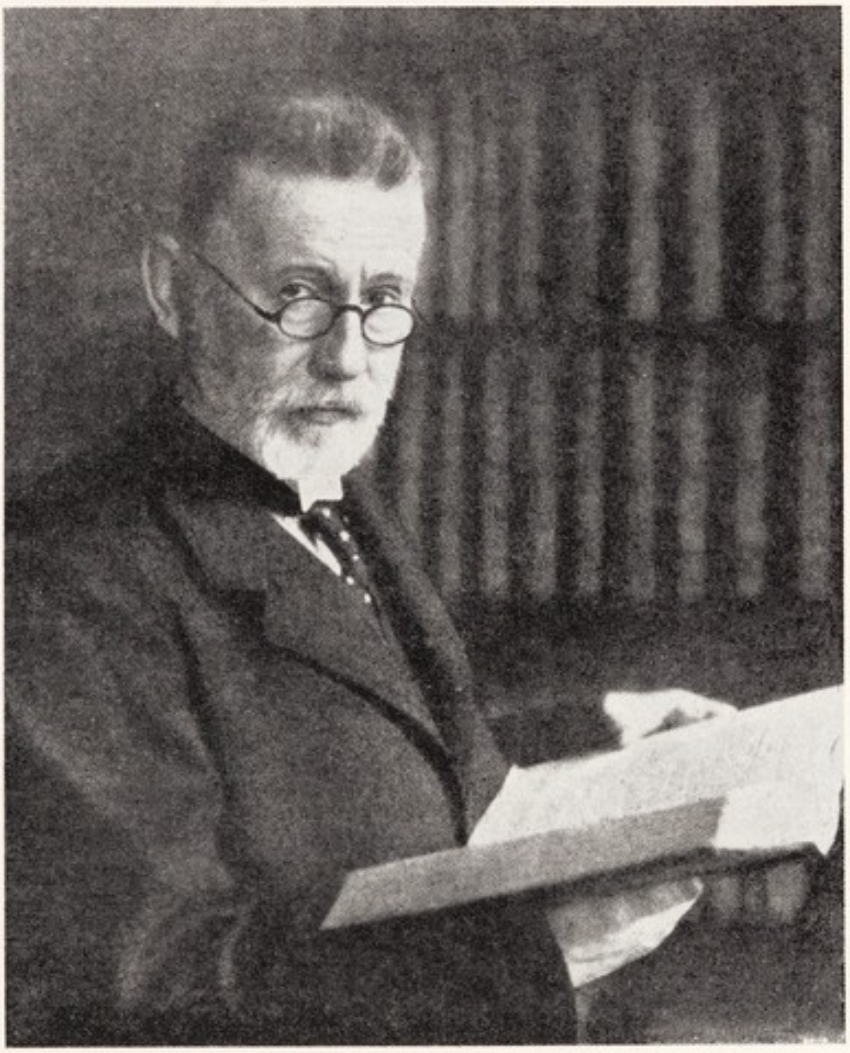
dinn, dated May 2, [1905], in which he told me of his discovery, . . . At the end of this letter Schaudinn expressed his opinion in the following words as to the two different varieties of spirochaetes: 'I have at the present time no doubt at all that the Spirochaeta pallida is distinct from the other varieties which are

P. UHLENHUTH
(Crerar Library)

to be found in the genital tract, although up to the present I can adduce no definite proof of my opinion.'" (Page 56).

(Note in this connection, when systematists are trying to establish the name *Treponema pallidum*, that Schaudinn gave it the name Spirochaeta pallida.

Metchnikoff emphasized the importance for Schaudinn's work of his separating, as a first step, the varieties of spirochaetes found in the genital tract, and adds "Owing to his differentiation of these two



EHRLICH

varieties of spirillar micro-organisms in the genital organs, Schaudinn was able to overcome the first difficulty which obstructed his work; and by so doing he may be said to have taken the position by an actual *coup de maître*."

The Wassermann reaction and the other specific reactions that apply to syphilis, and the development of arsphenamine and its derivatives for the treatment of syphilis, are outstanding illustrations of the application of our most modern scientific knowledge to the problems of disease; the one of the knowledge of biological reactions, the other of chemotherapy. Their story is a matter of current knowledge.

These late achievements in syphilology can only be described in superlative terms. The discoveries of Metchnikoff and Roux, and of Schaudinn and Hoffmann, are basic. The researches of Bordet and Gengou, of Wassermann, Neisser and Bruck, and of Uhlenhuth and Ehrlich, are as brilliant exercises of the mind as can be readily cited.

This brings the history of syphilis down to the present. It is a brilliant illustration of what medicine has been able to do in the short period, as history goes, of the last four hundred years, since men have put their minds intensively on the objective study of diseases and their rational explanation. It is a dull man who can contemplate it without a thrill of enthusiasm.

Lecture III

THE EPIDEMIOLOGY OF SYPHILIS

IN the epidemiology of syphilis we have, as usual, four factors to consider: (1) The reservoir of infection; (2) The infecting organism; (3) The susceptible host; and (4) The means of transmission. Let us take them up in this order.

The reservoir

The reservoir of syphilis is man alone. Modern research has shown that syphilis can be transmitted to certain animals, but the disease dies out spontaneously in them and is transmitted to other animals only by experimental methods.

The geographical distribution of syphilis includes all known inhabited parts of the earth. As men of European civilization have gone to the peoples of the rest of the earth in the last four hundred years, syphilis has gone with them. All races of men are susceptible to it, in apparently about the same degree. The Icelanders are said to be relatively immune, and so are the South Sea Islanders, among whom yaws is common, presumably because yaws causes increased resistence to it. But observations of this sort have to be taken with caution. They are like reports of individuals who are said to have reached excessive old age; fuller knowledge usually proves simply that accurate information is lacking.

Prevalence.—As far as we know the incidence of syphilis, allowing for factors which cause temporary local variations, is about the same at all times. Unlike acute infections such as diphtheria and the exanthams, there is no evidence to indicate waves of increase or decrease for which no explanation can be found. For example, the statistics of the Public Health Service of the United States for the last forty-five years show irregular variations from year to year, but no definite trend either up or down.

The prevalence[1] of syphilis among peoples and among classes is a matter of sexual habits. Sexual promiscuity is the source of syphilis, and the relative incidence of syphilis in any class is an index of its sexual habits. The occurrance of syphilis in an individual is not necessarily a stigma, for much of it, particularly in women, is contracted innocently, but a high incidence of syphilis in any class is a mark of low sexual morality. Because of factors which are obvious, the prevalence of syphilis varies widely in different statistics; from less than 1 percent to 20 percent or more of the population examined for syphilis. A large number of the more conservative statistics of Great Britain and the United States indi-

[1] Hazen's *Syphilis* (gives a full summary of statistics) 1928.

Parran, Syphilis as a Public Health Problem, *Proceedings of the Institute of Medicine, Chicago,* **9:** no. 8. Nov. 15, 1932.

Pusey, *Syphilis as a Modern Problem.*

Kiser and Bohner, *J.A.M.A.* May 7, 1932, p. 1631.

Usilton, Lida J., Prevalence of Venereal Diseases in the United States. U.S.P.H. Service Report 27, from **11:** no. 12. Dec. 20, 1930.

cate that the incidence of syphilis is from 6 to 10 percent. But these statistics chiefly concern men, and, as it is probably at least two or three times as frequent in men as in women, they indicate an incidence of syphilis for the entire population of about 5 percent. I believe that is a fair estimate. Recent statistics on this subject have been based on the presence of a positive Wassermann reaction. And it is a rather curious fact that the old statistics, such as Fournier's and Erb's which were based upon the history and the clinical findings alone, give about the same figures. These statistics concern average patients of all classes. When you analyze syphilis according to classes, most of them social, you get striking evidence of the relation between syphilis and sexual morality. In our civilization it is commonest, class for class, among those who lead the "loosest" lives. One certain indictment that can be made to hold against the use of alcohol is that, by temporarily breaking down the moral resistence of those under its influence, it is a factor for the spread of all venereal diseases.

European statistics indicate that it is more frequent in European cities than American. Many statistics indicate that it is much more frequent in urban than in strictly rural districts. The army statistics of drafted men do not bear out this point (Hazen), but on the other hand, Parran, on the basis of a very wide survey of syphilis finds that "five cases exist in cities for every one in rural districts."

In these same statistics Parran finds it twice as frequent in men as in women. That is a much higher

proportion in women than many other statistics show. Fournier put the proportion for women as low as one in ten.

The statistics for the prevalence of syphilis according to occupations are few, and cannot be regarded as being anything more than wide approximations. Stokes and Brehmer found 11.7 percent in railroad employees, 6.1 percent in laborers, 3.8 percent in business men and 1.5 percent in farmers.[2]

When we come to examine special classes, some of them pathological, we find the widest variations. "In certain Middle West rural areas and among certain university groups syphilis is a comparatively rare disease." (0.5 to 1 percent, Parran). Among private patients of the average class Vedder of Washington, Keidel and Moore of Johns Hopkins Hospital, and the Mayo Clinic each find an incidence of 5 percent. Taking many hospitals, the incidence of syphilis among admissions varies from 5 to 25 percent or more, varying with the class of patients which these hospitals serve. The Rosenwald Foundation, in a survey of negroes, found an incidence of 20 percent. In the pathological classes the proportion may run much higher. Varying statistics for criminals show an incidence of 15 to 35 percent. Among prostitutes the prevalence ranges from 38 percent to almost universal existence among old prostitutes. Among the insane various statistics show an incidence of 14 to 24 percent. Considering the rôle that paresis plays in insanity, it is surprising, I believe, that these sta-

[2] *Jour. of Industrial Hygiene*, 1: 419. 1920. Hazen 25.

tistics do not show a higher incidence among insane.

These statistics of the general prevalence of syphilis do not give us the information we desire concerning the dangerous reservoir of syphilis that exists; it is much smaller than the entire amount of syphilis, for syphilis, unlike many other infectious diseases, is for all practical purposes infectious only during the earlier part of its course. It may last through life, but the syphilitic patient is not always a reservoir of infection.

We have some findings from which we can approximate the prevalence of active infectious syphilis. The most extensive survey which has been made of the incidence of syphilis is one by the United States Public Health Service in coöperation with the American Social Hygiene Association. This survey has been made in such a way as to approximate accurately the incidence of syphilis among 26,000,000 people in the United States. It was a survey of the number of cases of syphilis under treatment by physicians on a given date—not of all syphilis. It shows that in this enormous population, 4.26 persons per thousand of population were under treatment for syphilis at a given date. This of course does not show the prevalence of syphilis at the time. It only takes account of patients who sought treatment—I should guess not more than one-tenth of the asymptomatic and other syphilis in existence at the time. According to these statistics, assuming a population of 130,000,000, there are under treatment in the United States at any given time over 500,000 cases of syphilis. Parran con-

cludes that there is actually "an annual crop of new cases in the United States of 871,000." That may be regarded as representing approximately the reservoir of dangerous syphilis infection. Turner[3] finds that of 10,000 consecutive cases of syphilis admitted to the syphilitic clinic of Johns Hopkins, 3100—31 percent—were in the contagious stage.

However we undertake to approximate the extent of the reservoir of active syphilis in this country or anywhere, we find it enormous, running into the hundreds of thousands of cases. And what makes the problem more difficult is that the reservoir is not localized to an extent that simplifies the handling of the problem. It is concentrated to a considerable degree in the urban districts, but the entire population of the country is exposed to it. It is not influenced by climate or other natural conditions, but only by man himself.

Age of acquiring syphilis.—The age at which syphilis is most frequently contracted is in early adult life. Fournier's statistics find it is contracted most frequently between the ages of twenty and twenty-six in men, the maximum frequency being twenty-three; in women between the ages of eighteen and twenty-one, the maximum frequency in the twentieth year. Of the men 8 percent and the women 20 percent contracted syphilis before the twentieth year. Haustein[4]

[3] *Johns Hopkins Hospital Bulletin*, Feb. 1930, p. 159.

[4] H. Haustein, Statistik der Geschlechts Krankheiten, *Handbuch der haut- und geschlechts Krankheiten*, **22**: 1927. (Quoted by Parran, p. 15.)

from recent extensive studies of syphilis in Europe arrives at the same facts. Syphilis is most frequently acquired between nineteen and twenty-four years; in women somewhat earlier than in men. My impression is that in this country the age of onset is a little older.

Is syphilis declining?—The most significant statistics upon this subject with which I am familiar are those of the United States Public Health Service, showing the percentage of syphilis found in the entire number of patients taken care of during each year by that service. These statistics cover thousands of men annually and are available for fifty years. They cover only one class of men, those engaged in marine occupations, but the variance in the amount of syphilis in this class will probably furnish a close index of the variations in syphilis in the population in general. These statistics of the United States Public Health Service, indicate no definite variation. Parran from the study of late surveys finds that syphilis is not declining. Contrary to these statistical facts there is a common impression among those who have much to do with syphilis that there is an appreciable decline in the last few years. The more widely diffused knowledge of measures to prevent infection and of the dangers of the disease among the intelligent, the smaller number of new cases of syphilis which practitioners are seeing—things like these have given rise to the belief that syphilis, at least among the upper third of the population, is decreasing. Statistics of the British Social Hygiene Council show a surprising reduction—one of 50 percent in the incidence of new syphilis in

the British population and a much greater reduction in the army.[5] Nowhere else except in Sweden has such a reduction been recorded. There is no reason to believe that the decrease, if it exists, is more than slight in the United States. Except in certain parts of the world, and the United States is not included among these, the reservoir of syphilitic infection is practically ignored. It thus becomes largely a matter of the sexual habits of the people and these habits average about the same at all times, so that we have the exposures to syphilis averaging about the same from year to year and its prevalence remains unchanged.

An important influence upon the reservoirs of syphilis should be treatment. If syphilis is gotten hold of in the first months of its existence, it can usually be quickly made non-contagious. The measures of treatment which we have now are more and more effective in controlling contagiousness the earlier they are applied, and also the more thoroughly and for the longer period they are carried out. Unfortunately evidence indicates that treatment is having little influence upon the reservoirs of infection. Parran finds that the average syphilitic patient remains under treatment only six and one-half months. Only 11 percent come in for treatment during the primary stage before the Wassermann becomes positive. Two-thirds of the total seek treatment only after secondary syphilis has developed—it may be long after—and one-half of those finally diagnosed as syphilis take no treatment

[5] *J.A.M.A.* February 27, 1932, 747.

during the first year. Under our present conditions, therefore, most of our reservoir of syphilis is undisturbed by treatment which could reduce it.

THE INFECTING ORGANISM

The Spirochaeta pallida is the cause of syphilis. There may be uncertainty concerning the authenticity of the cultivation of the organism in artificial media and of the experimental production of the disease from such cultures, but there is overwhelming evidence in favor of the pathogenicity of the Spirochaeta pallida. Experimental studies have completely confirmed the important fact of the low resistance and the very short viability of the Spirochaeta pallida outside the human body. Under artificial conditions it can be kept alive for several days. Noguchi succeeded in cultivating it in vitro and in growing it for an indefinite period. But, except under these entirely artificial conditions, its life outside of the living body is fortunately limited to a few hours. Kept under ordinary conditions, it loses its motility in five or six hours. Even under anaerobic conditions—and in the absence of air its viability is highest—it loses its motility in two days. By inoculation of apes it has been proved to be active only up to six hours after removal from the body. Material from chancres and condylomas, even when kept moist, remains virulent only from six to ten hours. Twenty-six hours after the death of a syphilitic patient Jacquet and Sezary found the spirochaetes all motionless, and Levaditi found them all motionless thirteen hours after death in

a syphilitic child. They are not affected by normal salt solution, but plain water or water containing a greater quantity of salt than is found in the blood, or soap and water destroy them almost immediately. They are almost instantly destroyed by the common antiseptics. Exposure to a temperature of 51°C. (123.8°F.) destroys them in one hour. At 10°C. (50°F.) they are destroyed in three hours. They can be kept alive for twenty-four hours on ice.

It follows from the low resistance of the spirochaetes outside the body that the danger from these organisms is in the active lesions of syphilis in man himself, or so shortly after removal from his lesions as to amount to the same thing. Consideration, therefore, of the spread and distribution of the spirochaetes throughout the body is of practical importance in the epidemiology of syphilis. For this purpose let us trace the growth and distribution of these organisms in the body.

The animal experiments of Neisser and others have confirmed the observation of Jean Fernel four hundred years ago that for infection to occur there must be a break in the horny epidermis. The spirochaetes do not penetrate an unbroken epidermis. Even when deposited in the mucous layer of the epidermis it takes some time for them to adapt themselves to their environment and their early growth is not vigorous.

It was formerly believed that the organism of syphilis did not begin to grow immediately after inoculation, and it is true that the early growth of spiro-

chaetes at the site of infection is relatively slow compared with their luxuriant growth after they have become fully established. Nevertheless, Neisser's experiments have shown that the growth and spread of the spirochaetes is so rapid that excision of the site of inoculation twelve hours after infection does not prevent the development of systemic syphilis. The first growth of the spirochaetes is in the mucous layer of the epidermis and in the lymphatic spaces and capillary walls of the corium. Here they multiply until they cause sufficient irritation to produce the chancre. In the meantime they spread along adjacent lymphatics, and in the perilymphatic tissues. During the earlier days of the chancre the spread of the disease is chiefly along the lymphatics, and for the primary distribution of syphilis the lymphatic system is chiefly responsible.

But there can be little doubt that in the end the general diffusion of the spirochaetes through the body is largely by means of the blood stream. Spirochaetes have been found in the blood before the Wassermann becomes positive—that is, within ten days of the appearance of the chancre—and the rapid diffusion of them at the beginning of the secondary stage—at the time of the appearance of the eruption—represents a sudden shower of spirochaetes which could only occur through the blood stream. Nevertheless, the blood is not a favorable medium for the growth of the spirochaetes, and the demonstration of them in the blood, even in the most florid stage of secondary syphilis, is difficult. Even during the early

active stage of secondary syphilis the disease is hardly to be regarded as a spirochaetal septicemia but rather as a condition in which the blood acts as a passive carrier for the organisms, the objective manifestations of the disease being due to the local reactions excited by the spirochaetes at the various sites on which they find lodgment and succeed in growing.

As Uhlenhuth and Mulzer have shown, the period of general diffusion of spirochaetes through the blood is of only a few weeks' duration, and, corresponding to the disappearance of the spirochaetes in the blood is the diminution in extent and intensity of the secondary lesions of syphilis. After the general diffusion of the disease, and the development of syphilitic lesions throughout the body, there is a building up of resistance to the disease that checks the luxuriant growth of the spirochaetes and in time gets the upper hand of them to the point that their number instead of increasing is rapidly reduced. Most of the foci of spirochaetes are destroyed, and the further growth of them limited to isolated colonies. We see the evidence of this in the subsidence of symptoms and in the rapid diminution or disappearance of spirochaetes from lesions previously showing them in abundance. Long before the end of the secondary period their presence is restricted to tissues in which they are best able to maintain themselves, or to foci of infection which are inaccessible to the attack of the body defenses or of remedies. It is to the persistence of some of these foci of infection that tertiary manifestations of syphilis are due.

This invasion corresponds with the evolution of the symptoms of syphilis. For about four weeks there are no symptoms; then the initial lesion appears. Eight to twelve days later spirochaetes have invaded the body far enough to produce swelling of the adjacent glands. At this time the invasion of spirochaetes has produced a sufficient reaction upon the tissues of the body to be indicated by a positive Wassermann. Three or four weeks after the appearance of the chancre the invasion shows in distant lymph glands such as the epitrochlear and cervical. In five or six weeks—at the time the initial lesion heals—the general infection of the body is indicated by the appearance of a generalized eruption. The disease has then become an acute systemic one.

The early period of the secondary eruption represents the peak of activity of the spirochaetal infection. Quickly after this the spirochaetes become still more difficult to find in the blood, and finally disappear except in certain foci. The manifestations of the disease then consist of local reactions which are conventionally called tertiary lesions, in which the number of spirochaetes is relatively few. This gradual subsidence of the disease is its usual course. A serious complication in the sanitary handling of the disease is the fact that flare-ups occur occasionally, in which there is a recurrence of active growth of the spirochaetes in some of the foci of infection in the skin or the mucous membrane, with recurrent lesions of the character of the secondary period. In these relapsing lesions there may be an abundance of spirochaetes.

The abundance or the sparsity of spirochaetes in the various lesions and tissues in syphilis is a matter of practical importance, for the experiments of Neisser and others have shown that the likelihood of infection from inoculation of spirochaetes is influenced by the number of spirochaetes which are introduced; the degree of contagiousness of syphilitic lesions therefore varies with the number of spirochaetes in them. The moist lesions of secondary syphilis are the dangerous ones; the initial lesions, and especially the moist lesions that occur on the skin and mucous membranes of the mucous orifices of the body. These are the most dangerous first because they contain the greatest number of spirochaetes, and second because, being moist, they are not covered by horny epidermis and have great numbers of spirochaetes upon the surface. Dry lesions are not in themselves dangerous because they are covered by horny epidermis, through which the spirochaetes cannot pass, and they do not have the spirochaetes upon the surface. The late lesions of syphilis upon the skin, the gummata, even the ulcerating syphilides, contain so few spirochaetes that they are, for all practical purposes, not contagious. In considering the dangerousness of syphilis to others, we do not need to take into consideration lesions which are not connected with the surface of the body because their spirochaetes are not where others can come in contact with them. Even superficial lesions that are covered by unbroken horny epidermis are not dangerous. The moist surface lesions are the ones that spread syphilis.

When it comes to the fluids of the body, and the secretions and excretions, they are not dangerous for the spread of syphilis. Even in the active stage of syphilis the secretions and excretions and the blood, unless they are contaminated by passing over active and open lesions of syphilis, contain so few spirochaetes that they are not contagious. To produce successful experimental inoculation in animals with blood requires a larger quantity of blood than would ever be duplicated in practical experience except in a transfusion. Infections from transfusions of blood from patients in the active stage of early syphilis have been recorded in a sufficient number of cases to make it a danger to be guarded against. The late syphilitics' blood has not caused the accidents. In the handling of syphilis the epidemiological problem, excepting inherited syphilis, is concerned with syphilis in the primary and secondary stages—almost entirely in the first and second years.

Exceptions to this are relapses of active syphilis to which I have briefly referred above. These relapses of active syphilis were formerly not regarded as a very important problem after the third year. This fact is shown by many old statistics such as the valuable statistics of Keyes of patients who married while actively syphilitic and took no particular precaution to prevent infection. Keyes' statistics showed that during the first year the chances that a syphilitic husband would infect his wife are 12 to 1, during the second year 5 to 2, during the third year 1 to 4, and all but nothing after the third year. These findings

belong to the pre-arsphenamine and the pre-Wassermann days. Modern statistics show a high number of relapses. The best record is that of Gennerich who in a large experience by thorough treatment with mercury and arsphenamine reduced the number of relapses in cases treated early in their course to 5 percent. Even favorable modern statistics still leave the fact that the most dangerous syphilitic is the one in the first year of his disease; that after that his danger to others rapidly subsides until after the fourth year it is practically nil.

TRANSMISSION

The transmission of syphilis may be either direct or indirect (mediate or immediate). As a matter of fact mediate transmission of syphilis is hardly an accurate conception because syphilis is never transferred through a vector or any sort of an intermediate host, but can only occur when spirochaetes are transferred by some neutral object (carrier) in the few hours before they can dry out and lose their vitality outside of the body. Nevertheless, indirect transmission of syphilis does occur not rarely. It may occur with any object which is recently contaminated with spirochaetes. It is most likely to occur through personal objects which have common use. It occurs most frequently with articles which remain cool and moist, and much less frequently with articles which are dry. The most frequent source perhaps of mediate transference is drinking cups in public places. It is

[6] L. C. D. Post, *J.A.M.A.* **100**: 4. Jan. 28, 1933.

rather surprising how infrequently it can be traced to barber's tools, toilet articles, toilet seats, restaurant utensils and things of that sort which would be suspected. This is of course due to the extremely low resistence of the spirochaeta pallida outside the body, particularly, in all probability, from its quick destruction by drying. The organism of tuberculosis remains virulent under favorable conditions outside the body for a couple of months or more. If this were true of the spirochaeta pallida it staggers one to imagine what might be the extent of syphilis.

The amount of syphilis resulting from mediate transmission is a relatively small part. It usually occurs as an extragenital initial lesion, but only a small proportion of extragenital chancres represent mediate transmission.

Extragenital chancres.—Most extragenital chancres are a result of direct infection. Many of them are of venereal origin. Many more, unfortunately, are due to innocent direct contact with syphilitic lesions. These innocent extragenital lesions are seen most frequently in physicians, dentists and nurses. It has always been a surprise to me that they are not more frequent in dentists. Kissing is one of the pathetic sources of extragenital chancres. Schamberg has recorded the dreadful accident of the infection of seven young girls by one young man at a party where kissing games were played.

All of these forms of extragenital beginnings of syphilis represent but a small proportion of the infections. Estimates of the proportion of extragenital

infection run as high as 5 to 7.5 percent. I believe the proportion in the whole population is much lower—hardly 1 percent. But, making all possible allowance for this sort of indirect transmission of syphilis, the fact remains that syphilis is essentially a disease due to sexual contacts; well above 90 percent is so contracted. This does not mean, however, that 95 percent of all syphilis is of extramarital origin, for among married women a considerable proportion is contracted in marriage. Fournier found in private practice that 20 percent of syphilis in women was acquired in marriage.

The source of syphilis that keeps it alive is prostitution. The men and women who confine their sexual relations strictly to one mate do not infect more persons than themselves, and are unimportant factors in the persistence of syphilis, because their syphilis dies with them. It is the sexually promiscuous, whether men or women, who perpetuate syphilis; among these the great source of the spread is prostitutes, whether clandestine or public.

THE PROPHYLAXIS OF SYPHILIS

As the foregoing summary shows, we know all the terms of the problem necessary to a successful sanitary attack upon syphilis. We know its reservoir, its organism and its epidemiological characteristics, the means of its transmission, the methods by which it can be controlled. It is a disease confined to man, infectious only by direct contact of its organisms with skin or mucous membrane where there is a break in

the surface. Medicine has fully established that these are necessary conditions for the transmission of acquired syphilis. If the problem of its control involved no more than the material factors, syphilis would be a relatively simple problem in sanitation. But these are only part of the factors. The control of syphilis involves the problem of the sexual relations. It involves the mores, the traditions and customs of society, sentiments and emotions, moral convictions that are the result of centuries, prejudices if you please. These are intangible because they are mental, but they are none the less powerful for that reason. It is these factors that make the problem so difficult.

THE SANITARY ATTACK ON SYPHILIS

This can be made from two directions: First, that of preventing contact of the infected with the healthy; and second, that of protecting the healthy from the danger of contact with the infected. In the first category comes protection from contaminated personal articles, segregation and quarantine, examination and regulation of prostitutes, notification of the disease, tracing down and control of individual foci of infection, the treatment of infected individuals to rid them of contagiousness.

Means of indirect infection.—Let us consider here first the least important and the most easily handled dangers; those of the common use of personal articles which may become contaminated with spirochaetes. Much can be done, and a large amount has been done in the last few years, by educating

the public to the dangers of the common use of personal articles. Public drinking cups and public towels are sufficiently dangerous to warrant their prohibition. The public should be educated to the general fact that personal articles in public places are not safe for common use. The necessity for care to avoid infection should be recognized with regard to all occupations that have to do with manipulating the body, or taking care of its physical needs. The cook or waiter, the barber, the manicure, the chiropodist, the masseur and Turkish bath rubber, and even the doctor, the dentist and the nurse may be the means of conveying syphilis; the careless and dirty individual in any of these occupations is a menace for syphilis.

MEASURES TO REDUCE THE DANGER OF THE CONTAGIOUS SYPHILITIC

The control of syphilitic patients dangerous to others is a practical problem which cannot at present be satisfactorily handled.

Isolation and quarantine.—Isolation or quarantine as a general measure for control of syphilis is impracticable with an endemic disease so extensive and so prolonged. Even if there were not social difficulties which made isolation and quarantine impracticable in syphilis, the number of syphilitics precludes the possibility of using these measures. It is no more practicable to quarantine a half-million of the vigorous adult population than it is, as Burke said, to "draw up an indictment against an whole people." It is, however, possible to control, even to quarantine

and isolate if necessary, flagrant spreaders of syphilis. Parran, Director of Health of New York State, has shown that this can be done with practical success. Individual cases of syphilis or groups of cases that are foci for the spread of the disease can, according to Parran's experience, be traced in the same way that smallpox or diphtheria can be traced. And flagrant offenders can be taken under control in protection of the public. This sort of control of conscienceless syphilitics, men or women, who are wantonly spreading the disease should be exerted, on every consideration of justice to others.

Notification.—The most that can be done in the direction of controlling the syphilitic person is notification and supervision. There are many reasons for notification of infectious diseases, and considering only its physical factors, it would be desirable from the standpoint of epidemiology to have notification of all syphilitics by name and address. That is impossible. Under ordinary conditions syphilis cannot be handled like tuberculosis or smallpox. Notification with identification of individuals cannot be carried out and experience has shown that complete notification against public sentiment is impossible. But approximately the same ends can be attained by notification of the sort which was tried first in what is called the West Australian Act. This provides that all cases of syphilis shall be reported to the health authorities, but without names or addresses. The obligation is then put upon the patients to take treatment and upon physicians to see that the patients

remain under treatment through the contagious period. If they fail to do this, they must be reported by name and address to the health authorities, and then they become their wards, under legal control and subject to compulsion in carrying out treatment. This is a practical measure which for success requires only reasonable coöperation on the part of physicians. It is a measure upon which most recent acts for the control of syphilis are patterned, and it offers the best measure for attack in this direction that has been devised.[7] This measure can be made effective for the control of dangerous carriers of syphilis. Chicago has the distinction of first adopting this measure in the United States. Neither here nor elsewhere in the country has the measure been successfully administered, although it is invoked in flagrant instances. Its failure thus far is due to lack of vigor in its administration and of coöperation of physicians. But these things are matters of education and take time. The principle of this act and its practicability are generally accepted, and the policy which it represents is sound and should be supported. Under this act vicious and careless carriers of syphilis can be combatted and the small epidemics whose importance Parran has emphasized can be checked and many cases of syphilis prevented.

State and municipal diagnostic examinations in locating syphilis.—The Wassermann examinations and

[7] I have discussed this subject in a series of editorials in the *J.A.M.A.* 1917. **68:** no. 5, p. 375; no. 6, p. 463, no. 7, p. 550, no. 8, p. 639, no. 9, p. 715.

examinations for Spirochaeta pallida which are done for diagnostic purposes by the state and municipal departments of health should furnish one of the valuable measures for the control of syphilis. In making these diagnoses, information is gotten through which, with the aid of physicians in most cases and by the invocation of its police power in recalcitrant cases, the public health services could exercise the necessary supervision over much of the active syphilis. To this end encouragement should be offered for diagnosis by means of the Spirochaeta pallida.This is particularly valuable because when Spirochaetae pallidae can be demonstrated dangerous syphilis is present. The diagnosis of early syphilis by the Spirochaeta pallida is a practical measure now since easy means have been developed for keeping them alive in capillary pipettes for forty-eight hours, which means that these examinations can be done by central laboratories. Wassermann examinations furnish a similar but less valuable indicator of the presence of dangerous syphilis, because they locate dangerous syphilis only in connection with the history. For public health purposes the Wassermann is only useful in early cases. Late syphilis, regardless of the Wassermann, is not for public health purposes a matter of concern, because it is not contagious. The syphilis that is dangerous to others is that syphilis which is demonstrable by examination for the pale spirochaetes and that early syphilis which is demonstrable by the Wassermann. And the knowledge of the existence of these cases which is gotten through diag-

nostic examinations is of great sanitary importance. Its value should not be minimized by confusing with it the knowledge of the existence of late Wassermann-positive syphilis, which for public health purposes is useless.

Examination and certification.—The statistics of syphilis in countries where certification and examination of prostitutes can be successfully carried out do not indicate that these measures have an appreciable effect upon its incidence. In the United States discussion of them as sanitary measures would be purely academic. Public sentiment in a predominantly Anglo-Saxon country such as ours renders impossible their effective use, and not enough argument for them can be produced to furnish convincing criticism of this attitude.

Treatment to control contagion.—The treatment of active syphilis to render it non-contagious is potentially perhaps our most effective means of sanitary attack. By this means the contagious period of syphilis may be reduced as a rule from several months to a few weeks, and thus the reservoir of syphilis proportionately diminished.

It cannot be claimed, however, that up to the present the use of treatment as a sanitary means for the control of syphilis has produced impressive evidence of any decrease in the general prevalence of the disease. The reason of course lies in the lack of widespread, thorough utilization of the method. In Parran's words, "syphilis never can be controlled while more than one-half of the cases are not recog-

nized for a year or longer after onset and while only one case in six comes for treatment during the first month." In this situation lies an indictment against public intelligence, and, it must be added, against medicine and public health administration. Effective policies for the control of syphilis mean that it must be seen to that, for the protection of the public, syphilitics are treated in the contagious stage of the disease, either at the public expense or at their own. Where they can afford it, they ought to be compelled to be treated at their own expense. Sanitary considerations indicate that we must promote as far as possible measures to improve this situation. The importance of the treatment of syphilis must be insistently impressed upon the medical profession and upon the public, and all practical measures must be fostered which will support and render more effective this method of attack.

The second direction of the sanitary attack upon syphilis consists in protection of the uninfected against the dangers of contact with the infected. The real problem here is that of offering means of protection from the dangers of sexual contact with active syphilitics. In this direction modern medicine has to offer singularly effective means of controlling syphilis by preventing infection after exposure.

In 1906 Metchnikoff and Roux announced, as a result of many animal experiments, that syphilis could be prevented with reasonable certainty by the prompt inunction of a 33 percent calomel ointment at the point of infection. Metchnikoff and Roux' ex-

periments on the subject finally culminated in the experimental inoculation of a man—as usual, a physician—who deserves to be recorded among the many examples of bravery and self-sacrifice in the study of the problems of disease. Objection having been made to the fact that a successful method of prophylaxis in monkeys indicated little as to its value in man, a young medical student in Paris, Paul Maisonneuve, offered himself for experimental inoculation. After Metchnikoff and Roux had become thoroughly convinced of the efficacy of the method, they accepted this offer. Maisonneuve after expert examination was found free from syphilis. He was thoroughly inoculated with syphilis from two patients in the active stage of the disease. An hour after the inoculations the sites were rubbed for five minutes with calomel ointment. At the same time four monkeys were inoculated from the same patients and under exactly the same conditions. One of the monkeys was treated with calomel ointment one hour after inoculation, exactly as was Maisonneuve; one was treated with the ointment twenty hours after the inoculation; two as controls were not treated. Maisonneuve did not develop syphilis, nor did the monkey that was treated with calomel ointment an hour after inoculation. The monkey treated twenty hours after inoculation and the two untreated monkeys all developed syphilis.

Extensive experience in the use of individual prophylaxis has abundantly proved it effective, when used within eight hours after exposure to infection.

In 1909, before the institution of personal prophylaxis, the constant non-effective rate for syphilis in the United States army was 2.68 per thousand men. In 1919, where measures of individual prophylaxis were instituted and carried out, the rate under similar conditions was 1.17 per thousand—a reduction of more than 50 percent. When the World War came the method had a searching test. Its value was completely established in the American army. Among the troops in this country during the war, where the method was systematically and intelligently carried out syphilis was practically stamped out. It is of course a method which for its best results requires conditions that are only present under the rigorous discipline of military service, but this is only because it is necessary to make men protect themselves. The method itself presents no difficulties. It is a method that needs only general utilization to be of great effect.

Parran has not seen results from personal prophylaxis to make him optimistic about it. But there can be no question of its effectiveness. The only question is its practicability. My impression is that it is producing already an appreciable effect upon the incidence of syphilis among the intelligent classes, and that at the present time it is the most useful measure for the reduction of syphilis that we have.

SYSTEMIC PROPHYLACTIC TREATMENT[8]

If systemic treatment can abort syphilis, when undertaken within the first ten days after the appear-

ance of the disease, the use of systemic treatment to abort infections after inoculation before the appearance of symptoms is an obviously logical procedure, and although such use has doubtless occurred to many, Neisser is given credit for the suggestion in 1914. The early reports upon it were not encouraging, but in the last few years experimental evidence and clinical experience have indicated strongly its effectiveness. We have another illustration of the courage of medical men in the experiment of Magian in 1919, in establishing the effectiveness of this method. So strongly was he convinced of it that he inoculated himself with material from a chancre known to contain many spirochaetes, and succeeded in aborting it. In known exposures to syphilis, where it is too late for local prophylaxis, this method should be carried out. It offers, through treatment, a good prospect of preventing the development of the disease and is a potential factor in its control.

Metchnikoff and Roux' method of personal prophylaxis is the first effective, satisfactory method discovered, but it is only the last of innumerable attempts at prophylaxis that go back to the very time of the beginning of syphilis. None of these have been successful; all of them have been repudiated and most of their authors heaped with obloquy, because any method of the sort has been regarded by a part of the community as immoral and an encouragement to sexual license. If syphilis is to be regarded as

[8] This subject is discussed in detail in Schamberg and Wright's *Treatment of Syphilis*, p. 329.

a proper punishment for sexual irregularity, then all attempts to prevent its spread are unjustifiable, and the whole effort against it falls to the ground. But it is hard to believe that intelligent men and women that pretend to be humane will, as a class, accept this attitude; and if they will not, they must desire to see the diffusion of knowledge of any means that will check the spread of the disease.

Neither personal prophylaxis of syphilis nor the reduction of the contagiousness of syphilis by treatment is open to the objections that lie in any sort of legal recognition of prostitution, which is so obnoxious to a large school of moralists. There are, in fact, none of the usual insuperable moral obstacles to the wide adoption of these two methods of prophylaxis. From the sanitary standpoint their systematic application for the control of syphilis is as rational and as practical, as the systematic attack on the mosquito is for the control of yellow fever. When their adoption becomes general, medicine can claim, I believe, to have furnished means for the control in great part of the ravages of this hideous scourge of modern man.

This consideration of prophylaxis of syphilis has been confined to the measures which medicine has to offer in the sanitary prophylaxis of the disease. The medical profession is, I venture to believe, more keenly interested in the social aspects of the problem than any other group in the community, for the reason that it has a more intimate knowledge of the difficulties and perils and miseries of syphilis. But the social and moral problems involved in the control of

syphilis are not problems on which medicine can presume to speak with the greatest authority. These problems belong to sociology. I dare to urge, however, that if syphilis is ever to be controlled the sanitary attack upon it must be effectively utilized.

I am far from any desire to minimize the importance of the efforts to control syphilis and the other venereal diseases by methods of social and moral prophylaxis. It would seem to be the bounden duty of right-minded parents to have their children properly informed about the obvious facts of sexual life and about the dangers of the venereal diseases. How important it is that the knowledge of the dangers of venereal diseases should be gained in youth, is shown by the fact that frequent infection with syphilis begins by the eighteenth year and occurs most often between the twentieth and twenty-fourth year. It surely makes for the reduction of venereal diseases to inculcate the importance of high standards of morality and the hygienic value, to say nothing of other things, of clean living. It is the duty of society to protect its youth and its young manhood and womanhood, as far as possible, from the temptations that arise from improper suggestions and surroundings and associates. It must be said that society as a whole makes no apparent effort in this direction. Rather its literature, drama, fashion of dress and social forms stimulate sex in every way that prurient ingenuity can devise. Society is derelict in that, but nevertheless the traditions of high living that prevail in the sober intelligent part of society and that result

in high moral standards are now the only factors that have great effect upon the prevalence of syphilis. Continence is the only insurance against syphilis. Intelligence and high moral character are the best prophylactic measures that we have. But for them, Heaven protect us from the vision of what might be.

But do all we can by such measures, we still have the biological fact that moral restraints, in the worst part of the population, have no effect, and, in the best part, break down. The sexual appetite, after hunger, is the dominant influence of man in the whole conduct of life. In the face of the inadequacy of moral prophylaxis to meet the situation completely, medicine can offer sanitary methods which are a valuable support in the fight, and which can minimize the ravages of syphilis, if not completely control it. It can control syphilis as far as it can handle it practically as a sanitary problem. We should strive to make it as far as possible such a problem.

INDEX

THIS BOOK

THE

HISTORY AND EPIDEMIOLOGY

OF

SYPHILIS

was set, printed and bound by The Collegiate Press of Menasha, Wisconsin. The cover design is by the Fox Studio of Springfield, Illinois. The type face is 12 on 14 point Monotype 31 E. The type page is 21 x 38 picas. The text is 100 pound White Polychrome Enamel. The end sheets are 50 pound White Antique Buckeye. The jacket is No. 0360 Silver Artcote Graphic. The binding is Du Pont Fabrikoid Linen Embossed Silver