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Lambkin, F. J.
Treves, Frederick, 1853-1923.
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Publication/Creation

New York : William Wood, 1911.

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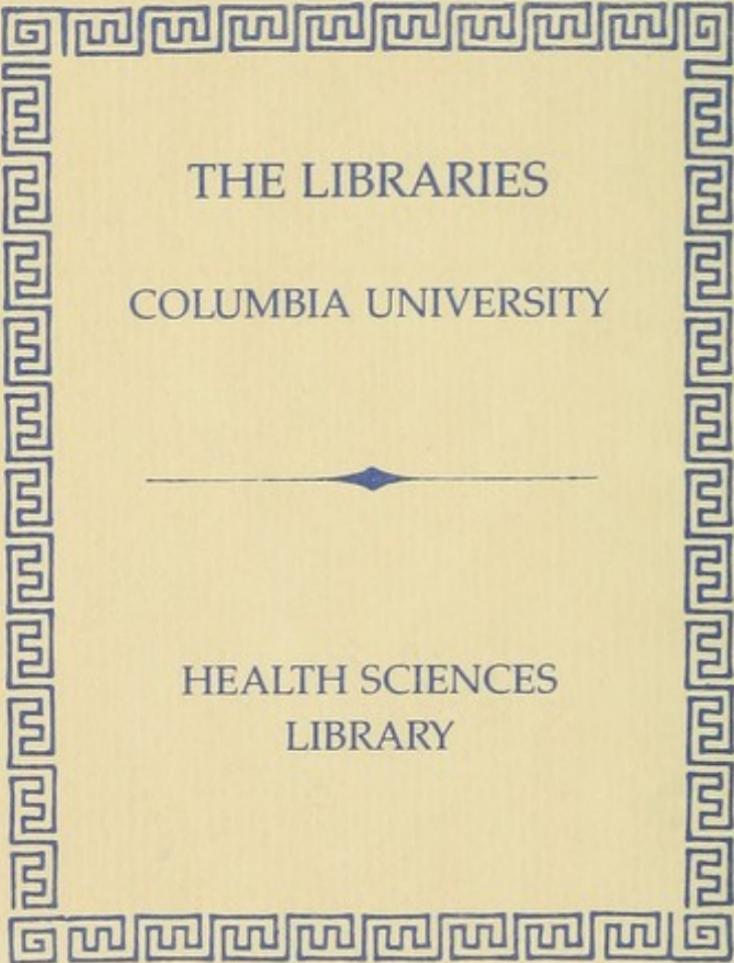


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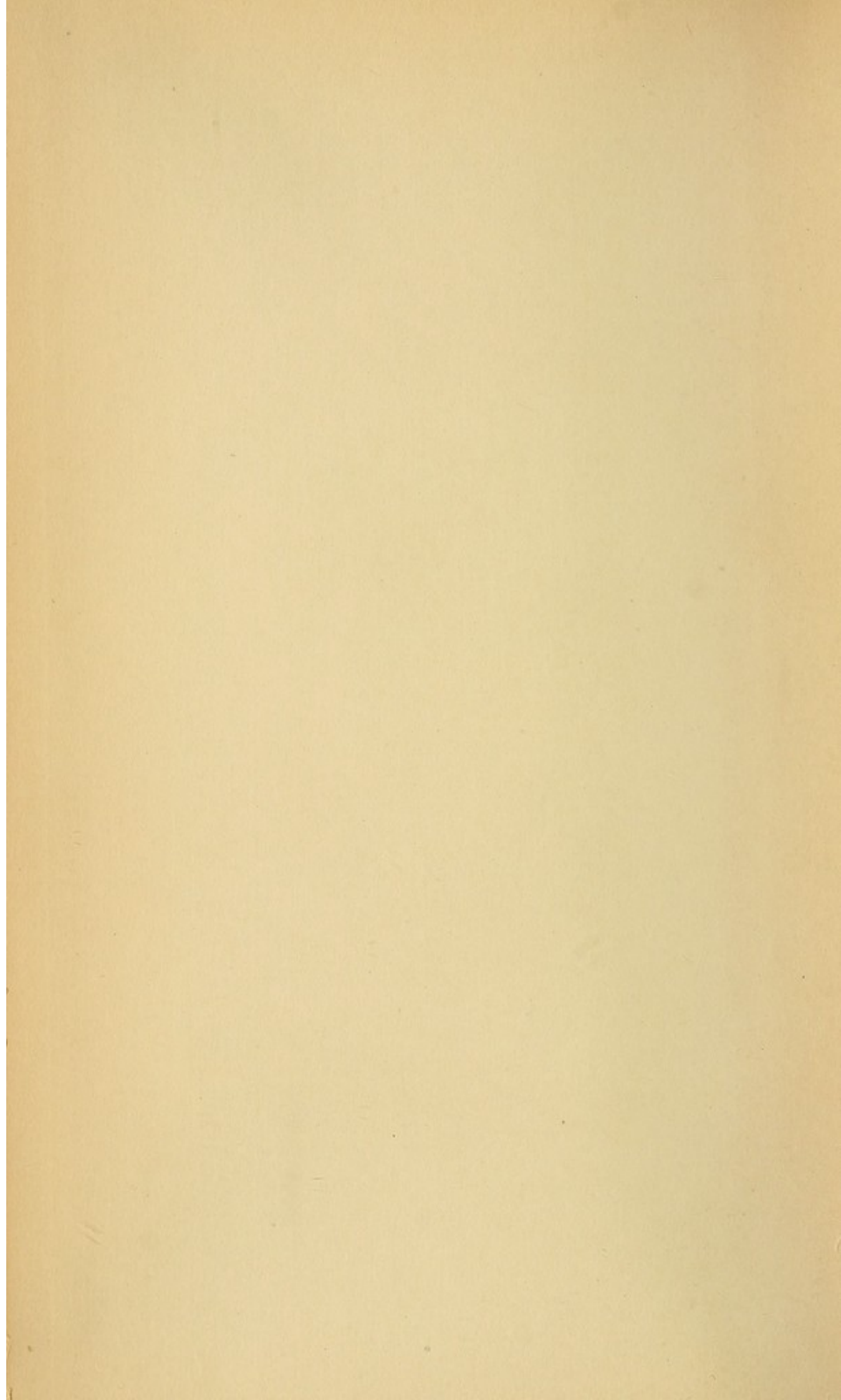




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SYPHILIS

ITS DIAGNOSIS AND TREATMENT



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SYPHILIS

ITS DIAGNOSIS AND TREATMENT

BY

F. J. LAMBKIN, COL. R.A.M.C.

LECTURER ON SYPHILOLOGY, ROYAL ARMY MEDICAL COLLEGE, LONDON
LATE SPECIALIST AT THE ARMY HEADQUARTERS, INDIA, ETC.

WITH PREFACE BY

SIR FREDERICK TREVES, BART., G.C.V.O., C.B., LL.D.

NEW YORK
WILLIAM WOOD & COMPANY
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PREFACE

PROBABLY no isolated disease has been the subject of so extensive and contradictory a literature as syphilis.

The prevalence of the malady, the distressing symptoms with which it is associated, and the lamentable results to which it may lead in its later stages, serve to explain the attention it has received from surgical writers.

A review of the literature of the subject reveals the circumstance that it is upon the question of the treatment of the disease that the most copious dissertations have been bestowed. There is hardly a drug known to medicine that has not, at some time or another, been advocated as effective in the management of this complaint.

At an early period one fact arose into prominence out of the chaotic mass of dicta with which the treatment of syphilis was confounded—the fact that mercury had a beneficial effect upon the disease. This conviction, carried into practice, led to some extravagance of action. There soon came to be recorded two periods of extremes in the use of the drug. At one period mercury was administered in amounts so large as to deliberately produce the phenomena of mercurial poisoning; at the other period the employment of the drug was condemned, not only on the ground that it was useless, but on the belief that it caused some of the grosser lesions with which the late stages of the complaint were associated.

There are reasons to believe that a sound mean has now been reached between these two diametrically opposed positions. While no one would claim that an infallible or perfect method of treating syphilis has been arrived at, it must at least be owned that a course of treatment has been evolved which gives better results than have hitherto been attained, and which is attended with but few drawbacks or objections.

In the treatment of syphilis by the intramuscular method Colonel Lambkin's name has for long been conspicuously associated. His opportunities for studying and treating the disease have been probably unique, for he has been engaged for a considerable period in the treatment of syphilis in the army, both in England and in India, and has, for some years past, been in charge of the chief military hospital devoted exclusively to venereal affections. He has worked patiently, cautiously, and with circumspection.

The army affords an unequalled opportunity for estimating the value of any measure of treatment directed against the disease. Syphilis is unfortunately common among soldiers, while the treatment advised can be carried out systematically and continuously, and the patient can be watched from the time the disease is recognised until he ultimately leaves the service.

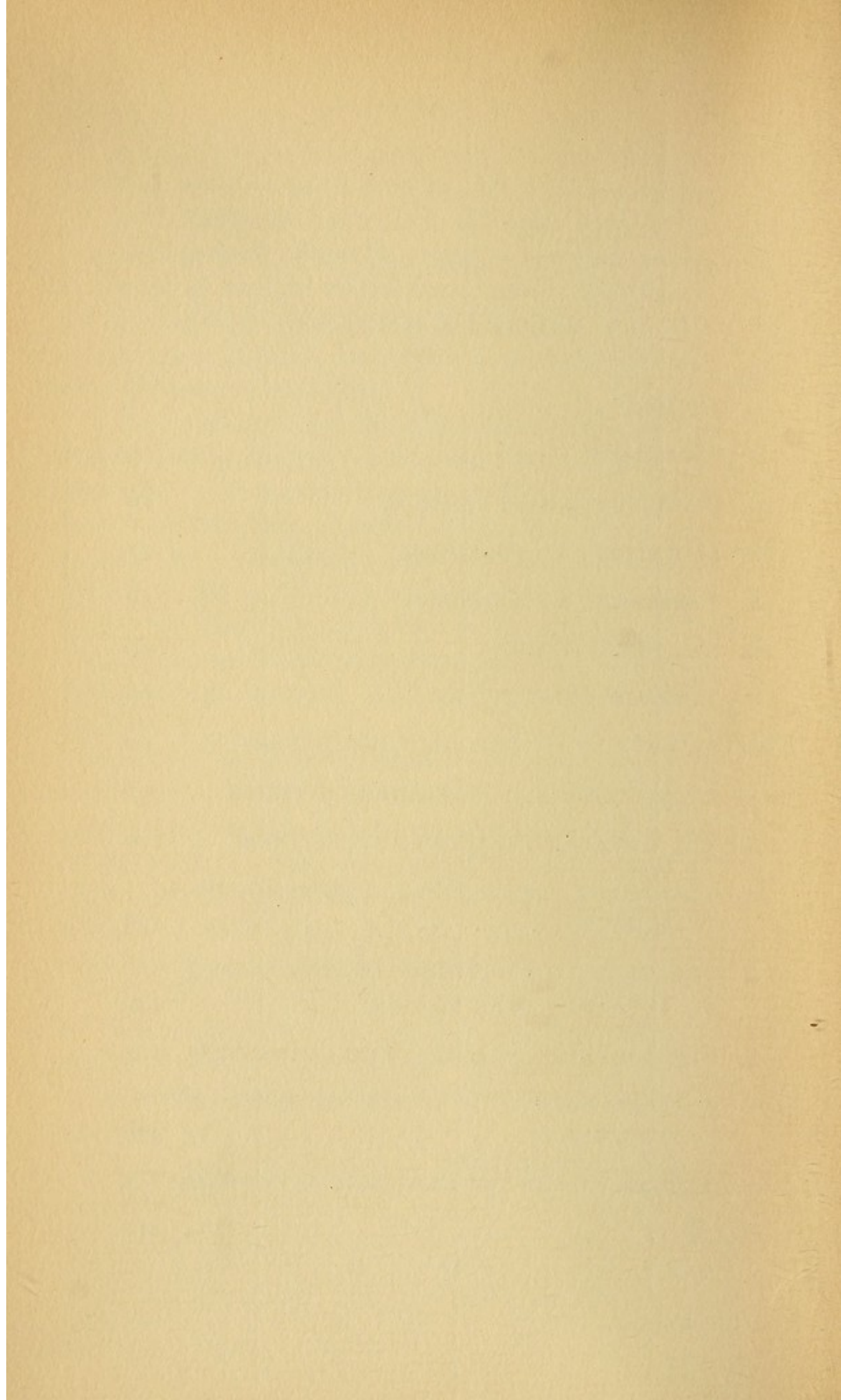
Colonel Lambkin's experience has been so exceptional that it may be claimed for him that in a department of practice to which he has devoted the best years of his life he speaks with an authority which cannot be lightly put aside.

FREDERICK TREVES.

JULY, 1910.

CONTENTS

CHAP.	PAGE
I. HISTORY	I
II. PATHOLOGY	9
III. CLINICAL COURSE: CHANCER	16
IV. DIAGNOSIS AND PROGNOSIS	27
V. TREATMENT OF CHANCER	40
VI. SECONDARY PERIOD	45
VII. TERTIARY SYPHILIS	69
VIII. AFFECTIONS OF THE NERVOUS SYSTEM	90
IX. PARASYPHILIS OR QUATERNARY SYPHILIS	96
X. THE GENERAL TREATMENT OF SYPHILIS	110
XI. TREATMENT OF SYPHILIS (<i>continued</i>)—IN- UNCTION	128
XII. TREATMENT OF SYPHILIS (<i>continued</i>)—THE INTRAMUSCULAR METHOD	142
XIII. TECHNIQUE OF THE INTRAMUSCULAR METHOD	164
XIV. ARYLARSONATE AND OTHER METHODS OF TREATMENT	170
XV. MODERN AIDS IN THE DIAGNOSIS OF SYPHILIS	179
INDEX	187



SYPHILIS

ITS DIAGNOSIS AND TREATMENT

CHAPTER I

HISTORY

THE history of Syphilis has for the purpose of consideration been divided into: (1) its origin generally; (2) whether its existence is of prehistoric antiquity; (3) its first appearance and introduction into Europe; (4) its first appearance and introduction into England. As to its origin, although this is probably the most interesting part of the whole question, and has formed the subject for much controversy during the last century, more especially the last decade, it cannot be said that any definite conclusion has resulted therefrom, other than that it is now fairly settled that it has been known to have been present in the West Indian Islands and Central America from time immemorial; but as to the direct origin of the disease nothing is known.

With regard to its existence being of prehistoric antiquity, this question has also been the theme for much discussion, some holding that evidence points to an affirmative answer being given, whereas others deny it

and claim that it was quite unknown anywhere until the close of the fifteenth century; and even now it cannot be said that the conclusion which has been arrived at, *i.e.* that the disease has a prehistoric existence, has been absolutely proved. The evidence in favour of the former is, to say the least, doubtful, resting, as it does, on writings which speak of the existence in prehistoric times of certain ailments which are supposed to be descriptions of syphilis, and also on the discovery of human bones bearing the signs of syphilitic lesions. As regards the writings, Hippocrates describes ulcers of the mouth and genital organs, and Thucydides mentions diseases of the sexual organs, hands, and feet occurring in the plague of Athens, which is supposed to have been an epidemic of syphilis. Lancereaux believes the "ficus" of the Romans and "sykos" of the Greeks to have been syphilis.

From a collection of medical writings made in 1230 B.C. by the Emperor Hoang-ti, it would appear that in those far-off times the Chinese were fully acquainted with syphilis, which they treated with mercury, and that they recognised the hereditary transmission of the disease. The veracity of this statement has recently been questioned by Okamura, a Japanese writer, who maintains that, according to the old Japanese and Chinese authors, syphilis was unheard of in either country until the middle of the sixteenth century of our era.

It is asserted that syphilis was known in India 1000 B.C., this assertion depending mainly on the descriptions of certain diseases taken from the "Ayurvedas" of Susruta, which are supposed to appertain to syphilis.

Syphilis has also been supposed to have been known to the Hebrews ; this is founded on scanty and uncertain Biblical quotations, *e.g.* Lev. xiii., which gives an account of leprosy, but which it is surmised was really syphilis.

The other evidence on which the prehistoric existence of syphilis is founded, *i.e.* the discovery of human bones showing signs of syphilitic lesions, is, to say the least, a broken reed to depend upon, owing to the paucity of bones which have been discovered in such a condition. It would have been expected that, if the disease had existed to any extent, innumerable skeletons showing syphilitic signs would have been discovered in the Old World. For instance, it might be thought that royal Rome, with all the excesses of the Middle Ages, would have furnished plenty of evidence in this direction ; but this has not been the case.

The fact is that, in spite of the most painstaking research among thousands of human skeletons of prehistoric and ancient origin, there does not exist one bone showing unequivocal signs of syphilis. The existence of one bone in this condition, which at the same time could be taken for certain to be of prehistoric origin, or could be at least referred to a period prior to 1493, would at once put an end to discussion as to the age and origin of the complaint ; but unfortunately such is not the case, for it is certain that no bone in this condition is found either in German, English, or French collections or museums.

As to the question of the antiquity of syphilis, and whether it existed in prehistoric times, the evidence in

favour is of too doubtful a character to enable a definite conclusion to be come to regarding it; at the same time it is of a sufficiently stable kind to admit of the probability of such being the case.

The first authentic appearance of syphilis in European countries dates between 1493 and 1500, which years are more or less accurately mapped out as those which saw the introduction of the disease. It has been proved beyond doubt that it was brought into Spain by sailors of Columbus returning from Haiti and Central America in 1492, and that it spread to Italy from Spain.

The campaign of Charles VIII. of France during 1494-5, as a result of which many mercenary bands, accompanied by a great following of women, collected in Italy, and there got in touch with each other, formed the most favourable opportunity for the spread of the disease; and there can no longer be any doubt that the latter first attracted attention in Europe when the French under Charles sojourned in Italy, especially in Naples—hence the dates between February and May 1495. Critics are unanimous as to this, and also consider an invasion from without as having occurred, for which they blame the Spaniards. It is known that after the arrival of Columbus in Barcelona, on his return from America and the island of Haiti in 1494, syphilis spread there amongst the inhabitants. The following year Charles VIII. of France began preparations for his campaign, and attracted mercenaries from neighbouring countries, amongst whom were many Spaniards infected with syphilis. Thus it

came about that the disease spread during the stay of the French army in Italy.

Evidence goes to show that the followers of Columbus first contracted the disease in the island of Haiti, and in Central America. According to Diaz de Isla, a learned physician of Barcelona, who himself witnessed the invasion of syphilis in Spain, the disease had been known in Haiti (Españole) from time immemorial, and Oviedo completely concurs in this American origin of syphilis, and declares it to be a specific disease of the Antilles and Central America. According to Oviedo, syphilis was communicated by the Indian women to the first Spaniards who came there with Columbus, and brought by them to Spain, whence it spread to the army of Charles VIII. Amongst his informants, Oviedo includes both those who accompanied Columbus upon his first voyage and those who were with him on his second. Las Casas, a contemporary physician of the time, whose father was with Columbus during the second voyage, and who himself had lived in Haiti, testifies to the existence of syphilis in the latter place before the advent of the Spaniards. He says: "I took the trouble upon several occasions to interrogate the Indians as to whether the disease was of great antiquity, and they answered Yes, that it dated from a period long before the arrival of the Christians, its origin being beyond the memory of man; and it is an undoubted fact that all Spaniards addicted to sexual excesses, and who did not observe the virtue of continence, were attacked by the disease, not one in a hundred escaping." Again, Oviedo, in his

report to the Emperor Charles V., says: "Your Majesty may take it for certain that this disease has originated in the West Indies, where it is common amongst the Indians, and in those regions it is not so dangerous as with us."

Thus the reports of all these contemporaries are unanimous as to syphilis being of American origin, and that it was the syphilis of Haiti which eventually spread through Europe and the Old World. Confirmation of these narratives of Diaz de Isla, Oviedo and Las Casas concerning the origin of syphilis in Europe, can easily be obtained from documents and chronicles of contemporary Spanish and Italian writers, amongst whom was Senarega, who states categorically, in his history of Genoa, that syphilis had appeared in Spain two years before the campaign of Charles VIII., *i.e.* in 1493, where it had been introduced from the Far West; and the contemporary Italian physicians of the time declare that syphilis came to Italy from Spain.

The conclusions arrived at are: (1) That syphilis was unknown in Europe prior to the year 1493; (2) That its home is America, or, as far as Europe is concerned, the island of Haiti, whence the crew of Columbus brought it after the latter's first voyage.

Introduction into England

Everything points to syphilis as having been brought to England by English soldiers, who were fighting in Italy as mercenaries, and returning home took the disease with them. All contemporary writers of the day are very

explicit on this subject: the date of this would be the end of the fifteenth century.

In Scotland it is first heard of in 1497, a decree being published then by James IV. ordering all persons suffering from syphilis to leave Edinburgh: they were to be taken to an island opposite Leith and there treated.

The history of syphilis from the above date to 1767 was one of varying fortune, doubts being cast upon the identity of the different venereal disorders, until the celebrated John Hunter made the mistake of his illustrious career, an error which was destined to produce a period of decay in syphilology that was to last for years.

Hunter's Mistake

In 1767 Hunter inoculated himself on the prepuce with pus from a purulent gonorrhea, which produced a chancre, followed by constitutional syphilis, from which he concluded that the secretion of gonorrhea was capable of producing gonorrhea, chancre, and syphilis, and that all three were identically the same disease. He made the further mistake of stating that the blood and secretions of syphilitics were incapable of transmitting such contagion. It may be imagined how these doctrines put back the clock in the advancement of the knowledge of syphilis; there was no progress until the time of Ricord (1800-89), who proved conclusively, by repeated inoculations, that gonorrheal secretions pure and simple never produced chancre or constitutional syphilis. He further came to the following conclusions as regards syphilis:

firstly, that during the primary stage, which consists of the chancre, it was auto-inoculable, its induration being the expression of the passage of the poison into the organism; secondly, he maintained that in its secondary stage syphilis is not contagious, but is capable of transmission to the offspring; and thirdly he described the encroachment of the poison upon the bones and viscera; during this, the third stage, he said that syphilis is neither contagious nor is it transmissible to the offspring. Ricord also differentiated between the hard and the soft chancre; the micro-organism of the latter was afterwards discovered by Ducrey in 1889.

Undoubtedly to Ricord's teaching we owe the scientific basis on which the future study of the disease was to be grounded, and which eventually led to the formation of the most important conclusions upon the nature and cause of syphilis. In 1903 Metchnikoff and Roux made the all-important discovery, that syphilis is transmissible to monkeys, and in 1895 Schaudinn discovered that the origin of the disease is due to a protozoon which he named the "*Spirochaeta pallida*."

CHAPTER II

PATHOLOGY

ALL the lesions of syphilis consist of an interstitial infiltration of embryonic cells, constituting an inflammatory neoplasm, which undergoes resolution in the case of the chancre and secondary lesions, but tends to the formation of fibrous tissue in the tertiary. A syphilitic neoplasm consists of both round and giant cells; an accumulation of these (which can often be seen by the naked eye) is called a miliary gumma, and a collection of the latter give rise to gummata, which may attain to almost any size. In the tertiary lesions a meshwork of fibrous bands can be seen intersecting the whole or part of an organ, and in these meshes gummata are found of various sizes, appearing as yellow masses; each gumma is surrounded by a fibrous capsule, and in some of them the centre is seen to be undergoing caseous degeneration, which is probably due to either obliteration of vessels, overcrowding of cells, or to the direct action of the syphilitic poison itself on the cells. This latter supposition is now generally accepted as correct, and is supported by Levaditi's discovery of the *Spirochæta pallida* within the parenchymatous cells. The changes caused by syphilis consist

of peri-arteritis, which leads to obliteration of vessels; inflammatory infiltrations, tending to interstitial fibrosis; and certain results due to the direct action of the poison on the parenchymatous cells. Besides its direct action on the blood and cells, which produces the ordinary syphilitic symptoms, the virus of syphilis has a toxic effect on the cells, which leads to degenerations resulting in certain effects and sequelæ, to which Fournier has given the name of Parasyphilis, among these being: leucoderma, tabes, general paralysis, epilepsy, leucoplakia, various muscular atrophies, diabetes, Bright's disease, arterio-sclerosis, various osseous lesions, tuberculosis and epithelioma; add to these an hereditary parasyphilitic affection caused by the arrest of development—both physical and mental malformations, rickets, hydrocephalus, meningitis, infantile general paralysis, tabes, etc.

Induration

The first lesion of syphilis is the indurated chancre which constitutes primary syphilis, and the induration is peculiar to it. As a rule the chancre appears as a superficial erosion with no definite borders; it is usually circular in form, dark red in colour, becoming greyish later on, and exuding a thin sanious fluid. Between the fifth and tenth day after the first appearance its edges begin to harden; this hardening or indurating process goes on around the original erosion up to about the twenty-fifth day, when it ceases, and may then begin to be absorbed; it usually has disappeared at the end of two months. The induration is not the result of inflammatory action,

as can be seen by the absence of pain or itching, but it is formed by a process of small-celled infiltration and hyperplasia of connective tissue cells. Epithelial and giant cells are also present, whilst the small arterioles and veins are obliterated by peri-arteritis and endo-phlebitis.

The amount of induration varies in different chancres, from slight hardening of the borders of the lesion, to the extent of forming a hard lump the size of a hazel-nut.

Amount of Induration: what relation has it to the progress of the disease?

There is a general idea that the future of the syphilitic attack depends much on the amount of induration which develops at the site of the original point of infection—that is, that the greater the induration the more severe will be the after-symptoms and lesions, and *vice versa*. My personal experience shows that it is not the *amount* but the *persistence*, in spite of thorough treatment, of the induration, which indicates a severe attack.

BACTERIOLOGY

The microbiology of syphilis dates back to a period before that of microbiology itself. Before there existed any idea of the part played by microbes in fermentation, it was supposed that syphilis was caused by certain minute organisms and, twenty years before the discovery of lactic acid fermentation by Pasteur, discussions were frequent as to the microbiology of syphilis.

When once micro-organisms had been discovered in a whole heap of different infectious diseases, numbers

of bacteriologists set to work to search for the supposed organism of syphilis, amongst them being Weigert and his pupil Lustgarten. The latter discovered a bacillus in various syphilitic lesions, which eventually was to be known as "Lustgarten's bacillus," and which for a time was considered to be intimately connected with the cause of syphilis, but was subsequently discarded. Then De Lisle thought that he had discovered that syphilis was caused by a certain large bacillus, but his theory could not be confirmed.

Search for syphilitic bacteria having completely failed, scientists began to believe that the microbe of syphilis might be a protozoon, and soon Seigel published an essay in which he described his discovery of a small protozoon in syphilitic secretions; this he believed to be the real organism of the disease, and he named it "*Cytoryctes luis*."

Spirochaeta pallida was first seen by Schaudinn in some papules round the vulva of a woman, who was suffering from a hard chancre in the same region.

From further research Schaudinn was able to show that in the genital organs two varieties of spirilla are to be found. One of these may be found under both conditions, whereas the other is only present in syphilitic lesions. The former he called *S. refringens*. It is larger than *S. pallida*, and its spiral turns are fewer and much better marked; it is easily stained by any method, especially by Giemsa's, and is much more intensely stained than *S. pallida*. The latter is smaller, more delicate in appearance, and its spiral turns are more numerous, and

not so well marked; it stains with much difficulty by any method. Schaudinn and Hoffmann were able to prove definitely that *S. pallida* is to be found only in syphilitic affections; further, that it is to be found not only on the surface of syphilitic human papules and chancres, but also in the deep tissues of the enlarged syphilitic glands. At first these spirilla were only found in primary and secondary lesions of the genital organs, but with improved technique they were soon demonstrated in secondary lesions far removed from this region—*i.e.* in the blood, lymph, lymphatic vessels and glands, also in the saliva and urine of syphilitic patients; and, finally, they were found by Spitz, in 1905, in gummata, also by Schaudinn, who showed them in the peripheral layer of a gumma of the liver of a syphilitic child.

In the vascular system Reuter found these organisms in sections of the aorta of an old syphilitic who had dropped dead—a fact which was confirmed by Schaudinn. Soon it became an established fact that the specific spirilla were to be found in the primary, secondary, and tertiary lesions of syphilis, but up to the present they have not been demonstrated in those affections known as parasyphilitic.

As regards hereditary syphilis, the organisms were soon found in almost all the tissues of new-born children affected with the disease, especially in the liver and in certain parts of the skeleton—*i.e.* the periosteum, bones, etc.

Important as was the discovery of the *S. pallida*, an equally important one was the announcement by Metchnikoff

and Roux in 1903 that syphilis is communicable to animals; they succeeded in conveying the disease from a human syphilitic to a chimpanzee by inoculation, producing in the latter a primary syphilitic chancre, which was afterwards followed by a secondary train of symptoms. This experiment they repeated over and over again in the chimpanzee with similar results; but monkeys of the lower kind, such as macaques and papion, did not respond to it so readily, syphilis being limited to a modified chancre, which was not followed by secondaries. The chancre produced was an œdematous nodule, which was followed by desquamation, no ulceration taking place, nor was induration or adenitis well marked, which points to the resistance of these lower animals to syphilis. It has been established that monkeys are more refractory to syphilis the farther they are removed from the anthropoid, and that the chancre of the macacus was really syphilis. Metchnikoff and Roux, by producing the disease in a chimpanzee they inoculated from it, proved it.

These researches led to various attempts being made to prepare an antisymphilitic serum, but up to the present all have failed.

With regard to the situation where the organism is best found, my own experience is that it is easier to demonstrate it in hereditary lesions than in those of acquired syphilis, and in early secondary rashes and mucous lesions than in the chancre; it is more abundant in the deeper parts than superficially. Levaditi states that, although present in the blood-vessels, the *Spirochæta pallida* is rarely found in the blood itself, from which

fact it is now generally believed that the latter simply acts as a conveying medium, but not as one in which the organism is developed.

EXAMINATION for *Spirochæta pallida*

Search for the *Spirochæta pallida* has been rendered much easier by the introduction of the dark background. The material should, when possible, be taken from the deeper parts of a lesion, and having done so, it should be placed on a cover-glass, spread out, a little normal saline solution added to it, and there and then examined under a $\frac{1}{12}$ in. immersion lens on a dark background. The *S. pallida* is a very delicate, mobile, spiral organism, varying in length from 4 to $14\ \mu$ (about the size of a red corpuscle), and about $\frac{1}{4}\ \mu$ in thickness. It differs from the spirochæte with which it is most likely to be confounded in that the latter is generally found on the surface of lesions, whereas the *S. pallida* inhabits the deeper parts; also the *S. pallida* is smaller, is less refractive, is harder to stain, has more numerous spiral turns, and retains its spiral form both in motion and at rest. It stains pink with Giemsa's stain, whilst other spirochætes stain blue.

CHAPTER III

CLINICAL COURSE : CHANCER

Clinical Course of Syphilis

THE clinical course of syphilis is divided into six stages :

1. The stage of primary incubation, that between exposure to infection and the appearance of the chancre.
2. The primary stage, during which the chancre develops and glands enlarge.
3. The secondary incubation stage, that between the appearance of the chancre and the stage of secondary symptoms.
4. The secondary stage—the period during which fever, neuralgic pains, and syphilis of the skin appear.
5. The intermediate stage, during which the patient may be practically free from any signs.
6. The tertiary stage, which is characterised by the formation of gummata, periostitis, osteitis, etc.

The Initial Lesion

The first lesion of syphilis is the chancre, which makes

its appearance at the site of inoculation in from twenty-five to thirty days after exposure; this latter is a fair average time, and as a rule it may generally be surmised that a sore appearing after ten days from the date of exposure is syphilitic.

The chancre is generally single, but is very often multiple, and there may be as many as six, seven, or even more initial lesions.

The chancre begins as a small, sharply-rounded, excoriated spot, the surface of which is on a level with the surrounding parts. It looks exactly like an erosion. The colour is dull red, and later on may assume a coppery hue. At first the primary lesion may cause little or no disturbance, the patient's attention being generally called to it by some itching. For the first five or six days there is nothing very characteristic about it, but at the end of that time induration may become perceptible round its edges, and this increases and may become more evident and pronounced up to the end of two or three weeks after being first noticed. This induration is typical of the syphilitic chancre. As regards the induration, stress must be laid on the fact that at first it is not present, and may not become sharply defined until the tenth day, which fact has led to innumerable mistakes.

Induration is a peculiar hardness of the tissues around and beneath the sore, and is formed without any inflammation having taken place; no pain, heat, or redness occurs during its formation. It is peculiarly circumscribed, and it remains after the chancre has healed, and may continue to do so for weeks or months.

Nature of the Chancre

A chancre is formed of small-celled infiltration and hyperplasia of the connective tissue cells, which is supported in a meshwork of thickened blood-vessels, some of the latter being entirely obliterated by sclerosis. This condition constitutes induration.

Chancrous Erosion

The chancrous erosion is by far the most common form in which the primary lesion is found. It is most marked on the inner side of the prepuce. In shape it is commonly circular or ovoid, but sometimes of an irregular shape. Its floor is but slightly, if at all excavated; its surface, from which a serous secretion oozes, is smooth and polished: usually there is but one such lesion, but, as already stated, there may be as many as five, six, or seven. Owing to the absence of induration in the first stage of these chancres, diagnosis may be difficult, but the absence of itching and burning, their dark colour and chronicity, their late appearance after exposure, may help in distinguishing them from herpes, with which they are likely to be confused.

Induration of Chancre

When the chancre remains superficial the induration is spread out into a disc-like mass; it is then called the "parchment-like sore," and is mostly found on the integument of the penis and in the vulva. Indurated chancres are generally found in the sulcus coronarius, near the frænum.

Varieties of Chancre

The chancre may assume various shapes, when it is called by different names: the dry papule, ecthymatous chancre, silvery spot, annular chancre, and mixed chancre.

Dry Papule

The dry papule is found mostly on the integument of the penis at the base or pubic part. As a rule it is solitary, and appears, as its name implies, as a dry, hard papule. It is a very characteristic form of the true chancre.

The Ecthymatous Chancre

This is simply a chancre which becomes covered with pusc crusts, and may be developed from either a dry papule or a chancrous erosion. It is simply a chancre whose surface has become irritated, and ulceration has taken place, with the consequent formation of pus.

The Annular Chancre

The name of "annular chancre" is given to those sores in which the induration assumes a ring-like shape, and in which the centre is less thickened and infiltrated. This form of chancre is found generally on the internal surface of the prepuce, sometimes on the glans, and very often on the cutaneous surface of the penis.

The Silvery Spot

This was first described by Taylor, and is a rare condition. Its site is generally the glans and about the meatus. At first it looks like a pin-head spot which had been touched

with carbolic acid: this lesion increases slowly, and is subsequently raised up well above the surface by the induration. It preserves the integrity of its surface until it reaches an area of 2 mms., when it disappears, and is replaced by a smooth, shiny surface on an indurated base.

Various other Chancres

Besides the above there are many other chancres which go by various names: the inflamed, phagedenic, relapsing (which may be true or false), and the mixed chancre.

The two former are what their names imply.

The Mixed Chancre.

It is possible for both simple chancre and syphilitic chancre to co-exist at the same time, and either may be inoculated on the other. If the virus of syphilis be inoculated at the same time and at the same spot as the simple chancre, a hard sore will develop in time at the point formerly occupied by the soft sore. On the other hand, a soft sore may be inoculated on the top of a syphilitic chancre, resulting in an ulcerating sore situated on an indurated base, thus constituting the mixed chancre. (*See p. 26.*)

Pain and Inflammation

Absence of pain and inflammation is common to all uncomplicated chancres, the patient's attention being generally first drawn to its presence by some degree of itching; but even this may be absent, and the chancre fully developed before it is noticed.

Recurring Chancre

Recurring chancres are of two kinds—false and true.

False Relapsing Chancre.—The former has generally been described as a fresh induration appearing at, or perhaps near, the site of an old sore. This induration may appear without any apparent cause as to treatment or otherwise; and at almost any time, from a few weeks to ten or twelve years after the healing of the original chancre. Usually its surface remains intact, but may become ulcerated, and then simulate a disintegrating gumma.

True Relapsing Chancre.—Having entirely disappeared under treatment, the induration reappears at the site of the old sore, and assumes exactly its previous condition; its surface may become broken, and to all intents and purposes the old chancre may reappear, to be got rid of again by specific treatment. This chancre, to the writer's mind, is almost solely dependent on the line of treatment which is adopted: should this be dropped too early, then the induration is likely to reappear, and is then, no doubt, a fresh nucleus for the *Spirochæta pallida*.

SEATS OF CHANCER

The primary lesion may be seated on any part of the body which may have been exposed to infection; hence they occur more frequently on the genital region, which is the generally exposed part. Chancres are divided into genital and extragenital.

Genital Chancre

Two-thirds of all chancres are found on the mucous membrane of the prepuce just behind the corona, or on the surface of the glans penis, but they are found also at the urinary meatus, within the urethra, at the base of the penis, scrotum, groin, and anus, and these assume certain definite characters according to the sites occupied: thus chancres of the surface of the glans penis are generally flat at first, becoming depressed later on, and surrounded by a laminated layer of induration: chancres of the coronal glans show a tendency to be raised above the surface, induration is well marked, extensive, and nodular.

Chancres of the Urinary Meatus

In these chancres either one or both lips of the meatus may be involved, but both are generally affected. The mucous membrane is found thickened, and the lips are glued together by a scanty viscid discharge. Induration in these chancres, although limited, is well marked. Needless to say that chancres of the meatus may be mistaken for gonorrheal ulceration and *vice versa*, and further that a correct diagnosis is rendered all the more difficult when gonorrhea coexists.

Chancres of the Urethra

I believe these to be more common than is generally supposed, and the reasons for this are obvious—they are concealed from view, cause little disturbance, and are so likely to be mistaken for gonorrhea that, in nine out of ten cases, this latter happens, at least until things are

well developed. Chancres attacking the urethra are met with usually just within the meatus or in the fossa navicularis, but may occur lower down the urethra. There is pain on micturition ; slight thin yellow discharge and hardness can be detected along the urethra in a circumscribed degree ; sometimes when the finger is passed along the course of the canal it gives the sensation as if there was "a piece of the stem of a clay pipe" in it. These lesions can best be detected by means of internal manipulation or seen through a meatus canula of a urethroscope.

Chancre of Base of Penis

Occurs on the skin on or about the root of the penis. When first seen it looks like a scratch or abrasion about the size of a pea ; this enlarges slowly, becomes eroded, flat or depressed, until it reaches the size of a sixpence, or in some cases a shilling ; it is nearly always circular in shape, edges markedly hard, and when taken between the fingers laminated induration is well marked—in fact, it is in these chancres that this form of induration is best marked.

The surface of the chancre erodes and sometimes ulcerates, but the latter is rare ; it is covered with a whitish yellow false membrane, on the removal of which a weeping surface is left. Sometimes the surface looks like the top of a pepper caster.

Chancre of the Scrotum

Commences as a patch of circumscribed erythema. The skin soon desquamates and leaves little cracks or

fissures exuding a clear serum; these cracks unite by erosion, and a shallow ulcer, circular in shape, situated on a hard base and with well-marked indurated edges, remains. In other cases the surface of this form of chancre is covered with brownish crusts of dried epithelium, which keeps on re-forming as often as removed, or again the syphilitic lesion in this locality may be in the form of a tubercle.

Preputial Chancres

When placed at the end or termination of the prepuce, these chancres are ragged, and give the end of the prepuce the appearance of having been split in one or two directions; these splits look at first like scratches, the edges of which are indurated or generally inflamed. The prepuce in this situation is usually thickened.

Sub-preputial or Concealed Chancres

A chancre of the prepuce may be rendered invisible owing to phimosis, either congenital or acquired, the latter being the result of the inflammation caused by this very chancre.

In this case, besides the phimosis, there will be a thin yellowish discharge, which can be gently squeezed out; little or no pain on urinating, or other sign of gonorrhea. Should an indurated sore be present beneath the foreskin, this hardening can generally be felt by manipulating the member with the fingers. But in any case the surgeon ought seldom to be long in doubt, as means ought to be taken to expose the sore at once.

Chancres of the Anus

These may be situated at the margin of or entirely within the anus. The former generally present a thickened, fissured and ulcerated surface devoid of deep redness. They are of a rose-red tint, and present a medium degree of induration at their bases. Sometimes these chancres assume the characters of fissures with pale, smooth margins and pale-red surface. Their bases are resistant to the touch, and they are far less tender than ordinary "fissure" of the anus—an important point in diagnosis.

When situated within the anus the chancre will, of course, be concealed.

Chancre of Groin

This chancre comes within the scope of perigenital chancres. It may occur, *a priori*, from direct inoculation, or as a secondary contagion to an open bubo. In the first case it will appear like an indurated chancre of the general integument, to be afterwards described. Should an open bubo become infected with syphilitic virus, the chancre will generally attack one or both lips of the wound. The latter remains gaping, and a sore or nodule appears on one of the lips. This slowly enlarges until an ulcer is formed, which soon becomes planted on a well-marked indurated base. The open bubo may continue to heal, all except the part at and about the chancre, which remains open and indolent-looking.

Chancroid Inflammation

The chancroid virus may be implanted simultaneously with or later than the syphilitic. In either case the character of the syphilitic chancre will be modified in appearance. Of course it would be quite possible for the chancroid to heal up before the syphilitic virus took effect, but this would be the exception. More commonly the chancroid persists, the spreading, inflamed, punched-out-looking ulcer becoming gradually enveloped in induration as the full local development of the syphilitic lesion is reached. In the other case, when the chancroid virus is inoculated on the chancre, the result is chancroidal ulceration, on the disappearance of which the induration remains. Ulceration of a chancroid may cause sloughing of an indurated mass—a result which leaves no local indication of syphilis.

A sore of the above description is called a “mixed chancre.”

CHAPTER IV

DIAGNOSIS AND PROGNOSIS

IT is wise never to give a positive opinion as to the nature of a chancre simply on the local examination of the lesion itself, as although in most cases it may be an easy matter to form a definite opinion from this alone, still it must be remembered that it has no certain sign.

Signs of a Syphilitic Sore

1. Its incubation—a sore beginning in from ten days to four weeks after exposure.
2. A sore beginning as a painless macule or slight erosion, spreading slowly and becoming indurated, exuding a thin scanty discharge from its surface, which latter may be covered with crusts or false membrane.
3. Should it be followed by the neighbouring glands becoming increased in size, without pain or inflammation, forming a chain of little tumours, the evidence of the syphilitic nature of the lesion is much strengthened.
4. Should the *Spirochæta pallida* be found in the secretion from the sore, then a definite opinion may be given as to its nature.
5. A positive reaction with Wasserman's test will of course strengthen the evidence.

Difficulties of Diagnosis

The difficulties of diagnosis met with are: the history of incubation may be vague and uncertain; induration absent, or marked, or so slight as to be indefinable; enlargement of neighbouring glands may be absent; the non-discovery of the *Spirochæta pallida* in the sore—always a difficult matter to find it in primary sores.*

Differential Diagnosis of Chancres

The character of a mixed chancre having already been discussed, it suffices here to say that when a sore appears later than ten days after exposure, followed by induration which becomes inflamed and ulcerated, with consequent destruction of the induration, which makes the lesion look like a simple one, the probability is that it is a mixed chancre; being in other words a syphilitic chancre, which, becoming infected by some septic matter, has taken on the features of a soft sore from inflammation and ulceration.

It would thus lose the distinction of the induration, and presenting only the features of the simple sore, the probability is that it is a mixed chancre, which surmise will be further strengthened should the lymphatic glands in the neighbourhood become indolently enlarged.

DIAGNOSTIC POINTS BETWEEN A CHANCRE AND CHANCROID

Chancre	Chancroid (Soft Chancre)
<i>Origin</i>	<i>Origin</i>
Due to inoculation from syphilitic lesion, blood, or other syphilitic discharge.	Due to inoculation from chancroidal discharge.

Incubation

Over ten days ; average time, three to four weeks.

Commencement

Erosion, papule or ulcer.

Number

Single, at times multiple (exceptional).

Shape

Symmetrically irregular.

Depth

Superficial erosion, scooped out, flat or elevated.

Edges

Sloping.

Floor

Red, livid, copper-coloured ; often iridescent. Sometimes covered with false membrane.

Secretion

Scanty sanious serum. Not readily auto-inoculable, and only so during first ten days of existence.

Incubation

No definite period ; generally under five days.

Commencement

Pustule or open ulcer.

Number

As a rule multiple ; often on opposing surfaces, from auto-inoculation.

Shape

Round, oval.

Depth

Deep, perforating whole thickness of skin and mucous membrane.

Edges

Abrupt and sharply cut.

Floor

Whitish grey or yellow.

Secretion

Abundant and purulent. Readily auto-inoculable.

Induration

Exists as a rule: firm, cartilaginous, circumscribed.

Induration

No induration, as a rule; if present, not circumscribed, but shades off into adjacent tissues.

Frequency in one Subject

One chancre affords protection in ninety-nine per cent. of cases.

Frequency in one Subject

No protection.

Glandular enlargement

Neighbouring glands indolently enlarged, firm, movable, no inflammation. When the sore is situated on penis, glands of both groins uniformly enlarged. No pain.

Glandular enlargement

Inflamed, painful irregular suppuration. Glands on both sides not uniformly enlarged.

Micro-organism

Present: *Spirochæta pallida* generally found.

Micro-organism

Spirochæta pallida never present. Ducrey's bacillus present.

Effects of Treatment

Local treatment ineffectual.

Effects of Treatment.

Local treatment curative.

Auto-Inoculation

It was formerly believed that the chancre was never auto-inoculable; it is now an established fact that during at least the first fortnight of its existence it is auto-

inoculable—that is, is capable of reproducing a like lesion if inoculated in some other part of the body. Mercurialisation of the patient renders this impossible.

Syphilis and Yaws

The one other disease in which the *Spirochæta pallida* was thought to have been found, is the one which mostly resembles syphilis—namely, Yaws (parenga or pian). The points of difference between them are :

Syphilis

1. Primary lesion.
2. Induration generally marked.
3. Neighbouring glands enlarged and nodular.
4. Auto-inoculable up to a certain time only.
5. Apes which have been infected with syphilis unable to transmit same to those already suffering from syphilis.

Yaws

1. No primary lesion.
2. No induration.
3. No glandular enlargements.
4. Always auto-inoculable.
5. Apes capable of being infected by inoculation and re-transmitting yaws to other apes, and to those suffering from syphilis.

Castellani now differentiates between the *Spirochæta pallida* and the organism which he believes to be the cause of yaws, and which he calls *Treponema pertenue*.

Extragenital Chancres

Chancres may be situated on any part of the body, but are found generally on those parts which are most exposed to infection, such as the mouth, tongue, and tips of fingers.

Modes of Conveyance

These may be either direct or mediate : by direct contact with a syphilitic lesion, as by kissing ; or by mediate contagion through contaminated spoons, forks, drinking utensils, pipes, etc., etc., and again through the agency of infected surgical or dentists' instruments.

Principal Extragenital Chancres

It will be necessary here to consider a few of the most important extragenital chancres, as their diagnosis is often rendered difficult owing to the position or locality in which they are situated.

Chancre of the Lip

Begins as a chap or fissure. At first there is nothing characteristic about it, but in time it becomes an indolent ulcer with early marked "cartilaginous" induration ; later on the submental glands become indolently and painlessly enlarged. In appearance it is an indolent elevated sore, papule or pustule ; its surface is smooth, and exudes a scanty, glistening discharge. When taken between the thumb and finger it feels like a lump of gristle.

The chief lesion that labial chancres may be mistaken for is epithelioma, but the following points may serve to differentiate between them :

Labial Chancre	Labial Epithelioma
<i>Age</i>	<i>Age</i>
Any.	Generally about middle life.

<i>Site</i>	<i>Site</i>
Usually upper lip.	Involves lower lip generally.
<i>Sex</i>	<i>Sex</i>
Both.	Nearly always the male.
<i>Local Symptoms</i>	<i>Local Symptoms</i>
A painless papule, erosion or ulcer. Regular outline, surface smooth and has indurated edges ; discharge is scanty and thin.	A painful, irregular, rugged sore, bleeds easily ; if induration be present it is irregular ; discharge thick and offensive.
<i>Course</i>	<i>Course</i>
Develops in a few weeks, followed in about two weeks by submaxillary glandular enlargements.	Develops very slowly, taking as many months as the chancre does weeks. Glands not affected for months after sore appears.
<i>Spirochæta pallida</i>	<i>Spirochæta pallida</i>
Present.	Not found.
<i>Mercury</i>	<i>Mercury</i>
Causes disappearance.	No effect.

Chancre of Tongue

Chancres of the tongue involve the anterior half, dorsum, sides, or tip ; and may appear :

1. As a superficial erosion seated on an indurated base.
2. As a deep ulcer with sloping edges on a hard base.
3. As a dense sclerotic mass with unbroken surface.

Chancre of the tongue very often simulates an ulceration caused by a carious tooth.

Chancre of Tonsil

This is rare, but may be mistaken for some ordinary throat affection, from which it may be differentiated by its being unilateral, indurated, persistent, and accompanied by indolent glandular swellings under the sterno-cleido mastoid.

Chancre of the Eye

This may be palpebral or conjunctival. Contagion may be carried by the fingers, by spitting, or by a contaminated towel. The surgeon may become infected during examination of the throat or mouth of a syphilitic patient; one of the worst cases of syphilis I have seen occurred in a surgeon who during an operation was infected by some matter finding its way into the eye.

Appearance.—An ocular chancre usually begins as a papule, which generally becomes indurated, then eroded, and sometimes ulcerated, and is followed by indolent enlargement of the glands in the vicinity of the ear and angle of jaw.

Chancre of the palpebral margin may be mistaken for a sty, an error which may be avoided by watching the development of induration and the glandular swellings which always accompany the former.

Conjunctival chancres may be found on the palpebral or ocular conjunctiva, but more often on the former, in which case the eyelid is everted, and there is conjunctivitis

and chemosis. The chancre may be nodular, round, or oval, or a simple hard erosion.

Facial Chancre

Facial Chancre may occur from kissing, spitting, or razor-cuts, the latter being not uncommon. The cut, having healed, reopens, and becomes covered with crusts and surrounded by induration, and erosion and ulceration follow, with indolent swellings of the submaxillary and parotid glands. I have recently seen a chancre on the cheek of a medical man, the result of a razor-cut becoming infected whilst he was attending a midwifery case. These lesions are generally well marked, and easy to diagnose, but have been mistaken for sycosis and eczema.

Chancre of Finger

Of all extragenital chancres those of the fingers are most common, occurring generally among medical men, dentists, and midwives; but they may arise in any one, and have often occurred as the result of bites. They usually are found at the edges or base of the nail; they are most commonly eroded, and often ulcerated, induration being well marked and extensive. Oftentimes this class of sore develops so insidiously and looks so innocent that it goes unnoticed by the patient, and is apt to be overlooked until later symptoms appear. On the other hand, this chancre may develop into a large, hard, fleshy mass, purplish in colour, of soft surface, with exuberant vegetations on it. One type of sore resembles a whitlow; the terminal phalanx of the finger is red, swollen, painful

and sensitive, whilst the surrounding tissue is indurated. These chancres are remarkable for their long duration and painful character; the nail nearly always separates from the finger, and very often the bone necroses. In such sores the axillary and epitrochlear glands always become indolently enlarged.

Vaccination Chancre

This is much rarer now compared with the days of arm-to-arm vaccination. If the vaccination "takes," the pustules run a normal course and heal up; or healing may be delayed, leaving an ulcer with smooth surface exuding a scanty discharge. It is painless, and soon becomes indurated; and later the anatomically related glands become enlarged and nodular. Should the revaccination not "take," a characteristic chancre forms.

Chancre of the Breast

This is usually caused by a syphilitic infant nursed by a healthy woman. The lesion appears either on or about the nipple or on the mammary integument. It may begin as a fissure, crack, or erosion without pain, exude a scanty sanious discharge, and finally become indurated and accompanied by indolently enlarged axillary glands.

Chancres of the General Integument

Chancres occur at any point of the body which may have been exposed to infection—*e.g.* in the process of tattooing.

PROGNOSIS OF CHANCER

From a local point of view this is always favourable ; generally at the end of three or four weeks the chancre becomes cicatrised and the induration disappears, leaving a scar which is at first pigmented but eventually becomes white. The healing of the sore will depend very much on the constitutional treatment, but even without this it will often ensue spontaneously. Ulceration from a syphilitic chancre seldom leaves any deformity, owing to the fact that any destruction of tissue is at the expense of the infiltration ; deformity will, of course, result from phagedæna. Chancres situated in certain parts will often give rise to grave symptoms : for instance, on the tongue or tonsil, causing difficulty of mastication and swallowing ; or in the eye, leading to severe ophthalmia, and in the urethra producing stricture.

Relation of Character of Chancre to Subsequent Progress of the Disease

What relation, if any, exists between the source of contagion and character of the chancre, and the subsequent progress of the disease ? This question has led to much discussion, but the following deductions appear to be justified :

1. It is impossible to predict the form of chancre which will follow from a certain source of infection.
2. Many authorities think, and to a certain extent I agree with them, that the severity of the constitutional disease bears a relation to the character of the primary

sore; *i.e.* an ulcerating sore is more often the prelude to one of the severer forms of eruption than an ordinary dry papule, and, generally speaking, the more marked the induration the more likely are sclerotic lesions to follow.

3. A short primary or secondary incubation denotes the probability of a severe case. Hallepeau maintains that chancres situated on the prepuce or vulva and at the anus are more often followed by severe symptoms than those found elsewhere: the writer's experience is that the worst forms of syphilis he has seen have followed one of the extra-genital chancres.

Primary Lymphatic Enlargements

At the end of the first or second week after the appearance of the chancre the lymphatic vessels leading from it may be felt enlarged, like whipcord, though there is no pain or inflammation; at the same time the glands associated with these vessels become painlessly enlarged and hard. The glands thus affected are those in the immediate vicinity of the chancre: the inguinal in the case of genital chancres, the submaxillary and submental in chancres of the tongue or lips, the preauricular glands in chancres of the eyelid, and the axillary in those of the fingers. These enlargements are never great, hardly ever exceeding the size of a marble, are hard, indolent, painless, and easily movable, and scarcely ever suppurate. Rarely is it that a syphilitic chancre is unaccompanied by these enlargements; at the same time it must be remembered that these vessels and glands are also liable to become enlarged as the result

of the presence of a chancroid, herpes, or any other local irritation. The following points may help to differentiate between the two conditions :

Specific Lymphangitis

Hard and painless ; no inflammation ; terminates in resolution under specific treatment.

Inflammatory Lymphangitis

Hard, painful, tender, and red ; overlying skin œdematous ; often ends in suppuration, not affected by specific treatment.

The same points will also apply to the glands themselves.

CHAPTER V

TREATMENT OF CHANCER

PERSISTENT efforts have been made from time to time to set aside the possibility of syphilis by the destruction of the primary lesion, either by excision, chemical means, or by the actual cautery. Results have been disappointing, as not only have the measures of destruction failed to relieve the local symptoms, but also to prevent secondary signs. In the face of these results the question arises, ought excision of the primary lesion to be carried out? If this lesion is looked on as but the local expression of an intoxication generalised at the outset, common sense would point to the uselessness of such a procedure. On the other hand, if the view of probably the majority of syphologists of to-day be adopted—that the initial sore or lesion is the local point from which, after multiplication, the microbe of the disease or its toxin is swept through the system—then I should say that, given certain conditions, the destruction, either by excision or otherwise, of the sore should be done. But there is only one class of case in which this abortive method is applicable with any reasonable hope of success—in the case of a very young chancre of a few hours' date,

without induration and without satellite glands. Unfortunately such conditions greatly restrict the applicability of the proceeding, as ninety-nine out of a hundred chancres seen have been in existence for days, and, in fact, the chancre met with fulfilling the conditions indicated must be a rare event.

Destruction of the Syphilitic Virus in Situ

The experimental work of Metchnikoff shows that the syphilitic poison can easily be destroyed in the laboratory by drying, cooling to a point below 50° F., or by heating it to a temperature of 122° F. for half an hour. From this fact he has endeavoured to destroy the *Spirochæta pallida in situ* by thoroughly rubbing into the point of inoculation an ointment consisting of calomel 10 gms., lanolin and vaseline 30 gms., and is satisfied this will prevent infection if done within eighteen hours of inoculation. He had the advantage of proving this on the person of a student who offered himself for such experiment, and in this case it was a complete success. The same results have followed in the case of innumerable monkeys, which were inoculated with the virus and controlled. Without doubt it is a procedure which should be preached broadcast.

As regards the local treatment of chancre, it is of the utmost importance that no stimulating nor caustic applications should be made; for, in the first place, should the lesion be simple in nature, burning it with acids, etc., will not destroy it, but will transform it into an inflammatory nodule, and cause it to markedly resemble a hard chancre, and thus doubt and uncertainty in diagnosis is the result.

On the other hand, if the lesion is an incipient chancre, cauterisation, however complete, cannot destroy it, but may cause an œdema which may be troublesome to cure. Any breach of surface, therefore, should be kept scrupulously clean, and be covered with lint or absorbent cotton moistened with boiled or distilled water, or a mild sublimate solution (1 in 2,000), or very dilute carbolic lotion applied; peroxide of hydrogen, 1 in 6 of water, makes a good application. As the chancre increases in size it may be dressed with black or yellow wash.

Powders, such as boric acid, aristol, europen, dermatol, and last, but not least, iodoform, dusted on may be of great benefit. The best of these is iodoform; its odour is certainly against it, but with care much of this inconvenience may be obviated. It should be used sparingly, and not allowed to fall on sound parts or upon clothes. Should the sore be under the prepuce it may be kept at a minimum by packing cotton in the preputial orifice. It must be remembered that iodoform is applicable only to unhealthy and necrotic surfaces, and should be discontinued when these cease.

In the case of chancres covered with a false membrane, or those which have a tendency to ulcerate and become destructive, it is important that a caustic effect should be produced, and this is best done by washing the lesion well with soap and water, and then irrigating it with a 5 per cent. carbolic solution. It should be dried, and a solution of cocaine applied to it, and then it should be dried again. Better still, as a preparatory method, is to mop the surface freely with peroxide of hydrogen,

equal parts with water, or with Merck's perhydrol ; apply the cocaine, dry the parts, and then apply the caustic ; for the latter nothing is better than fluid carbolic acid or pure nitric acid.

Calomel very often acts promptly and efficiently on chancres showing a disposition to destruction, and is always a useful dry dressing in clean but indolent sores.

Bearing in mind that the indurated chancre is probably the seat where the spirochætæ multiply and the focus from whence they spread throughout the system, it is all-important that a specific action be brought to bear on all chancres which show a tendency to become indurated. Having by proper means produced a healthy surface, the chancre should be treated with mercurial ointment. The surface having been washed and rendered as nearly as possible aseptic, a layer of absorbent lint well smeared with Ung. hydrarg. Metchnikoff's 30 per cent. of calomel ointment, or oleate of mercury, 5 per cent., should be placed upon it and kept in constant apposition, and this dressing should be changed two or three times a day.

As a rule, salves and ointments (other than mercurial) should be avoided, exception being made when the discharge is thick and sticky.

The Treatment of Phagedænic Chancres

The treatment of chancres complicated with phagedæna is exceptional ; most to be depended on is continual immersion in hot antiseptic solutions. In the case of such a sore on the penis this can best be carried out

by immersing the latter in hot water contained in such a vessel as a bed-urinal, allowing it to remain there for long periods: the water, of course, requires frequent changing; an ordinary-size bath may be used for the same purpose. Should the phagedænic action go on, cauterisation, either by chemical means or the actual cautery, must be undertaken. The best of the former is crude chromic acid. The patient should be placed under a general anæsthetic, or the parts rendered insensible by a local one (I prefer the former); then the sore having been thoroughly dried, the chromic acid is applied to it; a black slough remains, and this is detached by charcoal poultices, leaving a healthy surface as a rule; however, a second application may be required. Instead of chromic acid, strong nitric acid may be used. Some cases of phagedæna may require the actual cautery, and all require watching, as they are rapid in their progress, and require prompt recognition and treatment.

CHAPTER VI

SECONDARY PERIOD

The Period of Secondary Incubation

THE period of secondary incubation is the time between the appearance of the chancre and the development of secondary lesions, and this averages from forty to fifty days, during which the chancres may have healed and disappeared completely, and the disease, as far as any constitutional symptoms are concerned, appear to be quiescent. Undoubtedly during this time the virus is becoming disseminated throughout the system.

The conditions influencing the length of this period are the presence of malignant syphilis, or when the disease attacks constitutions which are already undermined from various causes. Then the period of secondary incubation is shortened, whereas the contrary takes place when the disease attacks those of robust constitution, or when it is of a non-virulent kind.

The Evolution of Syphilis

After this comes the stage of secondary symptoms, during which, to begin with, the virus manifests itself

on the accessible lymphatic glands not anatomically connected with the primary lesion.

Already it has been seen that within a week or so after the appearance of the lesion, those lymphatic vessels and glands in its vicinity become enlarged and indurated ; but care must be taken to differentiate between this and the enlargement of the glands under consideration. The glands which are most affected are those situated in the neck, axilla, and groin, all of which become swollen as a result of the essential hyperplastic process produced by the virus. It is now generally recognised that the changes in the deep glands are among the most frequent and most constant of the effects of syphilis, either in its secondary or tertiary stages ; in other words, they are its constant accompaniment. The other glands most frequently affected are the prevertebral, lumbar, iliac, and femoral. Specific enlargement of the lymphatic vessels and glands is characterised by three symptoms—induration, absence of inflammation, and persistency. During the course of the disease this condition of the vessels and glands may disappear, but more frequently they remain enlarged for months, and even years, after all other symptoms of the existence of the disease have disappeared. Resolution without suppuration is almost the constant termination, but suppuration may occur should the chancre become infected with pyogenic microbes.

Treatment

Mercurial ointment should be well rubbed into the skin over the enlarged glands daily.

Course of the Disease

The general or constitutional symptoms which usher in syphilis vary in different cases. In some there is well-marked fever, especially towards evening, when it may reach as high as 103° F. : in others this fever presents a distinctly remittent type. Various neuralgic pains are complained of, especially headache, which is nearly always nocturnal, and which varies in degree from being quite mild to one in which the patient's suffering is very great. This headache generally affects the back of the head. Other pains of a neuralgic kind may be present, attacking mostly the fifth nerve, and may be seated in the intercostal, sciatic, or anterior crural nerves. Insomnia is a symptom sometimes complained of.

Cachexia

Early in the secondary stage a condition known as "syphilitic cachexia" takes place—loss of appetite and strength, emaciation, and a pale sallow complexion, pulse rapid, weak, and small—and the temperature runs up: the patient is dejected, nervous, and apprehensive. This condition may be postponed in some cases (especially in those which undergo early mercurial treatment) to quite late in the course of the disease.

The Osteotic Pains

Osteotic pains of different kinds are a frequent accompaniment in the early period, the bones affected mostly being the cranium, ribs, sternum, and clavicle, and there may be great tenderness; these pains and this tenderness are much worse at night.

Rheumatic Pains

Some of the most constant symptoms in the early period of syphilis are pains in the muscles, fascia, and joints, the muscles affected being those of the extremities, the fascia in the same part, and the joints engaged are usually the larger ones—the hip, knee, and especially the elbow—but often the wrist and phalanges are attacked.

Hyperæmia of Pharynx and Tonsils

One of the points in which syphilis resembles the acute exanthemata is its strong tendency to attack the fauces. As a rule the throat suffers subsequent to the appearance of cutaneous lesion, but frequently the reverse occurs; very often it is affected without giving any trouble, and is only discovered on inspection.

In many cases there is no superficial lesion other than slight excoriation; in others mucous patches may be present. There is often a good deal of tonsillar swelling. The follicles become enlarged and prominent; or they may rupture, giving rise to excoriations. In the more chronic cases patches are present on the tonsils and palatine arch; or there may be yellow ulcers sharply defined. One affection constantly seen on the fauces, hard palate, inside of cheeks and lips, is scattered milk-white spots called "plaques"; they may be of any shape and size, or they may run into each other so as to cover a large space; parts of their surface may be reddened, showing only a little white opacity here and there. These spots run a slow course, and may recur over and over again during the first and second year of the disease.

Albuminuria and Nephritis

About this time albuminuria may appear, and there is no doubt that early, and sometimes rather late, in the secondary stage, a mild or severe form of nephritis may occur.

Some authors believe, and the writer is with them, that syphilis causes the same condition in the kidneys as do other infectious diseases.

The symptoms of this nephritis may be wanting, and the condition only discovered by examination of the urine; on the other hand, it may give rise to œdema of the lower extremities and face with lumbar pain.

The majority of these nephritic cases are benefited much by antisyphilitic treatment, with, of course, strict attention to diet.

Angina Pectoris

This condition, with all its classical symptoms, is seen on rare occasions, both in the secondary and tertiary periods.

SECONDARY ERUPTIONS

The next in sequence of events, as the case proceeds, is the appearance of skin eruptions. Unlike all other specific poisons, that of syphilis produces not one or two definite cutaneous affections, but an immense variety of them. They are known as syphilides or syphilodermata. The early eruptions of the secondary stage of syphilis are distributed symmetrically and generally over the body, involving the superficial layers of the skin; the later ones, although symmetrical, are less copious,

and have a tendency to invade the deeper layers of the skin.

As to the causes which influence the production of the different forms of eruption, we are in ignorance. All that can be said definitely on the subject is that a patient who is in a bad state of health is more likely to develop eruptions which suppurate and ulcerate than he would otherwise have been if infected when in robust health ; and that patients predisposed to certain non-syphilitic skin diseases, such as ordinary psoriasis or lichen, are apt to be affected with a squamous syphilide or with a papular one. A phagedænic chancre is much more likely to be followed by pustular eruptions than is the ordinary indurated sore. The fact is that pustular and rupial eruptions and serpiginous syphilides are really the results of mixed infections.

Features of Syphilides

To almost all syphilides certain features belong :

1. *Colour and Pigmentation.*—At first pinkish red, this soon fades to a brownish colour, said to be coppery or to resemble raw ham in appearance, the cause being probably some chemical change in disintegrating blood-discs which have been extravasated into the tissues. At first pressure dissipates the colour, but not so later on.
2. *Absence of Pain and Itching.*—They do not cause any irritation to the skin.
3. *Tendency to assume a Circular Form.*—This is most noticeable in the case of small papular rashes.
4. *Polymorphism.*—The circumstance of several varieties

of lesions occurring in the same eruption is important. Sometimes macular, papular, pustular, and scaly patches are present together.

5. *Peculiar Localisation*.—Syphilitic eruptions are often found in regions rarely the site of simple lesions. Syphilides are irregular in their distribution, their favourite localities being the forehead, the sides of the feet, and palms of the hands.

Diagnosis of Syphilitic Eruptions

In most cases a correct diagnosis must be based not so much upon the recognition of characters common to all syphilides as upon an accurate acquaintance with each of them individually. It is therefore essential that they should be classified. Syphilides may be divided into those which appear early and those that show themselves late. The former seldom appear beyond the first twelve months; the latter rarely occur within the first year, and their appearance may be postponed for several years.

Classification of Early Syphilides

- I. Erythematous.
- II. Follicular { Lichen.
Acne.
- III. Papular (Lenticular) { (a) Psoriasis.
(b) Mucous Patches.
- IV. Squamous.
- V. Vesicular.
- VI. Tertiary Syphilides.

The Erythematous or Roseolar Syphilide

This is the earliest and most common of all syphilitic skin eruptions, coming out about the same time that the general lymphatic enlargements become apparent. It consists of oval or round spots, with distinct or irregular outlines; their colour varies from a delicate rosy pink to a decided red. It is probably present in all cases of syphilis, but may escape notice on account of its extreme faintness. It is usually seen on the front of the abdomen, chest, sides and back of trunk; sometimes, although rarely, it invades the face and neck. It is also found on the limbs on their flexor aspects; it avoids the hands and feet. It takes about a week coming out, but may develop so rapidly as to be taken for measles. A pale, scanty eruption of roseola often fades in a week or fortnight, whereas a darker and more abundant one may be visible for weeks, and then may assume a squamous or papular character. This syphilide is apt to relapse, and may occur at any time during the first year, and even in the second.

The Follicular Syphilide

Of this there are two distinct varieties. One consists of small, pointed, dry elevations or papules, generally scaly at the summit, and their bases may be surrounded by a white desquamating cuticle; they may be irregularly scattered, or in clusters. This rash is slow in its course, developing itself by successive crops, and subsiding after several weeks or even months. Sometimes the little papules pass into pustules, and on disappearing

always leave minute white cicatrices. The other variety of this follicular eruption consists from the first of pustules which are small and pointed, with swollen red bases ; they may be present in immense numbers, not only on the face, but also on the chest, trunk, and back.

The Papular Syphilide

is known as the "Lenticular Syphilide," and consists of red, shiny elevations, which feel hard and shotty, and vary in size from a millet seed to the size of a split pea. They develop rapidly, coming out in a few days, and develop in crops ; they are generally scattered irregularly over the body, are sometimes numerous on the forehead and neck, and occasionally appear profusely on the face. These papules remain for a long time, sometimes for months, when they gradually decline ; at other times their surface or summit softens and becomes covered with a brown crust.

This eruption is of two kinds : the small flat papular syphilides, and the large flat papules. The former begin as minute red spots, which rapidly increase in size until they reach a diameter of perhaps one-fourth of an inch. They are round or oval. The papules are first seen about the shoulders, neck, and sides of chest, and later on they appear on the forehead at the margin of the scalp, and on the face, chiefly about the nose, mouth, and chin, and eventually they may invade the trunk generally.

The large flat papules are either round or oval, having a diameter of an inch in some cases. Their surface is

flat and covered with a few adherent scales; colour red, becoming coppery; they are very chronic, and cause neither pain nor itching.

On thick cuticle, like that of the palms and soles, the spots are not raised into papules, but form round, horny plates with copper-coloured margins. After a time these plates become detached, and their place is taken by thick crusts or scales, or an ulcer is formed, and this is the condition which constitutes "syphilitic palmar or plantar psoriasis." The early appearance of this syphilide is supposed to be the herald of a severe form of syphilis.

The Squamous Syphilide

Generally known as "Syphilitic Lepra," these lesions are flat and hardly raised above the surface; they are covered with silvery scales, underneath which is a coppery glistening base. The scales are easily detached, but accumulate over and over again. This eruption is rather a late one; the spots are always scattered, few, and confined to one particular region: for instance, they may be limited altogether to the thighs or palms of the hands or soles of the feet.

The Circinate Syphilide

A particular variety of this eruption is the "Circinate Syphilide," which is fairly common. It assumes the shape of rings, and resembles very much *Tinea Circinata*; but the exfoliation of the margin is generally profuse, and the silvery scales become easily detached; the rings are few and scattered, their favourite site being the front of

the thighs, but they may appear anywhere from the forehead and face downwards. This eruption is very prone to relapse, coming out as late as the fifth year.

The Vesicular Syphilide

This is a rare variety ; the vesicles are, as a rule, small. They may come out profusely all over the body, or in groups, the face and genitals being usually the selected spots ; these vesicles are filled with a clear fluid, which generally dries up, but sometimes they become pustular.

The Pustular Syphilide

These syphilides constitute an important group, which, though less common than the erythematous or papular form, may appear in the earlier stages of syphilis at any time, and late in its tertiary period. They consist of pustules of all sizes, each of which is seated on a firm base ; they may be present in immense numbers, especially in the face and trunk ; they come out rapidly and in successive crops, accompanied by much febrile disturbance ; they relapse even after a year. They dry up into brown or black scabs, and leave large stains, which ultimately pass into shallow, flat cicatrices. In other cases the inflamed bases continue to spread long after the summits have scabbed over ; thus, as the crusts increase in size the older parts are continually being pushed up by the collection of fresh material underneath, so that they assume a conical shape and look like shells, whilst others acquire enormous sizes. This variety of eruption is called "Rupia."

Some Special Varieties of Syphilide

Besides those described, other forms of syphilides are common—viz. pigmentary, acneform, and malignant precocious syphilides.

The Pigmentary Syphilide

This is seen in two distinct forms—viz. in spots or patches of various sizes, or as a diffuse pigmentation which, later on, becomes the seat of leucoderma ; this latter is the retiform pigmentary syphilide.

The evolution of this syphilide may occur as early as the third month, but it usually appears about the sixth, or towards the end of the first year, and often is postponed until the second or third year of infection. It occurs generally in women. The parts of predilection are the lateral surfaces of the neck, face, or forehead.

The first variety of the pigmentary syphilide consists of round or oval plaques, which may have sharply defined borders, and their colour is light brown.

The second form—the lace form—is much more common than the former ; slowly or rapidly the neck becomes discoloured, the tint being café-au-lait. Scattered irregularly over the pigmented surface are irregular or oval white spots, which gradually enlarge and increase in numbers until the neck is covered with them and the skin assumes a lace-like character—hence the name.

Other Early Secondary Symptoms

Anæmic alteration in the blood.—Anæmia is generally a marked symptom, for even before the enlargement of

the lymphatic glands the patient becomes pale, listless, and loses weight, and is evidently gravely debilitated; there is a general "impress" about him which is very apparent to the expert. Examination of the blood shows deficiency in hæmoglobin and red cells with some increase of the white. These changes become more marked as the case proceeds, and vary in intensity with the severity of the disease.

SYPHILITIC AFFECTIONS OF THE VARIOUS MUCOUS MEMBRANES

Erythema of the mucous membranes is usually confined to the neighbourhood of the fauces and to that of the outlets of mucous canals, especially around the genital organs and anus and the mucous membrane of the mouth. The most common syphilitic lesions of the mouth are mucous patches, which consist of greyish white areas termed "opaline patches." Their site is generally the angles of the mouth, inner surface of the cheeks and dorsum of the tongue. They occur most often in the mouths of inveterate smokers, and are due to proliferations of the epithelium; they are sometimes fissured or eroded, are very obstinate, and persist long after all signs of the infection have apparently passed away.

Superficial Affections of the Tongue

The mucous membrane of the tongue may also become hyperæmic either in whole or parts; when the latter is the case, white oval patches of erythema are scattered over the

dorsum. From these the epithelium may be removed, leaving an eroded or perfectly smooth surface forming the well-known "plaques."

Mucous patches of the tongue are very frequent, their usual position being the top and sides of the organ. Smokers are particularly liable to them. Sometimes the tongue becomes extensively fissured as the result of the erythema. Mucous patches have been called psoriasis of the tongue and leucoplakia. They are usually early visitors, but also occur in the secondary stage as well as in the tertiary, and when late in the latter belong rather to the parasymphilitic affections than to lesions which are the outcome of direct syphilitic infection. These lesions are very prone to lead to epithelioma.

Treatment of Mucous Patches

Patients must be warned as to the danger they are to others when suffering from these lesions. Smoking is to be prohibited altogether; the morbid spots are to be sprayed two or three times a day with a solution of perhydrol 1 in 4, or nitrate of silver 5 grains to 1 ounce. They should also be touched daily with a solution of chromic acid 5 grs. to the ounce, and if this does not improve them, one of 20 grs. to the ounce, or with pure carbolic acid. The mucous membrane of the mouth should be kept as healthy as possible by means of mouth washes of chlorate of potash, borax, perhydrol or carbolic 1 in 40. The application of the stronger solutions should only be made at intervals of two or three days.

Curettage may be necessary.

Syphilitic Affections of the NOSE

The nasal mucous membrane may be the seat of erythematous inflammation with consequent ulceration, leading very often to increase of adenoid tissue, which latter tends to blocking up the nasal passages and causes much suffering.

Treatment.—Strong stimulating applications should as a rule be avoided; spraying frequently with mild solutions of boric acid, peroxide of hydrogen or perhydrol; insufflation of equal parts of iodoform and boric acid.

Mucous Patches of Genital Organs

The favourite seat of these is the anus and perinæum, but similar patches occur near the angles of the mouth, and between the toes. The most frequent form they assume about the anus is that known as condylomata, which consist of broad raised patches, edges well defined, surface sometimes dry, but much oftener moist and coated with a dirty grey secretion which gives off a sickly smell. The lesions consist of cell-infiltration of the cutis, with the addition of overgrowth of the papillæ; they sometimes become confluent, and then a large portion of skin is involved; and occasionally large cauliflower-like excrescences are formed, which are called vegetating papules.

Treatment.—Absolute cleanliness of the parts, with dryness, which is best obtained by the interposition of some absorbent material; black or yellow wash is very efficacious.

In the case of condylomata these lesions should be destroyed with fuming nitric acid (nothing is better), acid nitrate of mercury, or pure carbolic acid. After cauterisation the surfaces should be well cleansed and dried, and dusted over with some powder such as starch, boric acid, resorcin, or calomel.

Affections of the LARYNX

Erythema of the larynx may be so slight as to cause no other symptoms than slight huskiness with moderate catarrh. It occurs in patches, which give the mucous membrane a mottled appearance, or it may cause diffuse redness. Chronic inflammation of the larynx is common in the later stages. Early laryngitis usually disappears rapidly with specific treatment; but locally sprayings of nitrate of silver 3 grs. to ʒij are good. Should ulceration be present, insufflation of iodoform and boric acid will be found excellent.

Affections of the HAIR

Alopecia is a common and early symptom of syphilis: there may be either total or partial loss of hair. The former consists of a general shedding of the hair, causing total baldness, but this is rare: more commonly the shedding is irregular, and hair comes out in patches, leaving circular bare spots; this alopecia may attack the moustache and beard. As a rule the hair grows again rapidly, unless there be destruction of the papillæ, when there will be permanent baldness.

Treatment.—Hair to be cut quite close or shaved; daily

the scalp should be well rubbed with an ointment of white precipitate (30 grs.), cold cream (1 oz.); parts to be thoroughly washed each morning with soap and bran-water; a lotion of bichloride of mercury (1 in 1000) to be applied twice or three times during the day.

Secondary Affections of NAILS

Onychia—Secondary affections of the nails are of two varieties—*Onychia* and *Paronychia*. In the case of the former the nail becomes dry, brittle, and breaks on little pressure; its surface is rough, and presents longitudinal fissures and minute depressions in which dirt collects, and gives the nail a speckled appearance. The epidermis under the free margin is usually thickened and scaly.

Paronychia—Of *Paronychia* there are three forms: ulcerative, indolent, and diffuse. The ulcerative form may begin as a papule; ulceration of this takes place, and extends along the sulcus at the attached border of the nail; the nail loses its lustre and becomes detached, and from beneath it offensive pus exudes; gradually the nail is undermined and destroyed. In the non-ulcerative variety the border of the nail is thickened and infiltrated, and there is a papular ring round it: the colour is dead red and the surface may be scaly. The nail usually loosens and drops off. The diffuse form begins as an inflammation or rather hyperæmia of the tissue surrounding the nail. At first there is no pain, and the colour is dull red, which as the case proceeds becomes coppery, and the parts become swollen and bulbous; eventually the nail itself becomes engaged, and is then destroyed.

Treatment.—In the case of Onychia, the affected finger should be soaked frequently in a solution of bichloride of mercury (1 in 1000), and the nails kept carefully trimmed. In ulcerative Paronychia the diseased surface should be exposed as soon as possible and cauterised with nitric or chromic acid, and water dressings applied, followed by the application of iodoform. Prolonged immersion of the hand in a warm solution of bichloride of mercury is very beneficial.

Secondary affections of the nails generally appear within the first ten years, but may occur very much later.

Secondary Affections of the EYE

Iritis.—Among the early secondary affections of the eye iritis takes first place, and it is of two kinds—*simple plastic iritis* and *parenchymatous iritis*. *Plastic iritis* often occurs about the second month, and is characterised by severe supra-orbital pain, worse at night, and by contracted and sluggish pupils; the iris is discoloured and adherent to the lens, and there is vascular injection of the cornea. *Parenchymatous iritis* presents yellowish brown nodules on the pupillary border of the inflamed iris. The nodules are very distinct, and together with the ordinary signs of iritis go to form true syphilitic iritis. This variety of iritis may appear like the plastic in the early months, but may be delayed to a much later period.

Treatment.—The local treatment of iritis consists mainly in the free use of atropine, a solution of which (gr. v to ʒ j) should be dropped into the eye every second hour until

good dilatation is brought about. Pain may be relieved by hot compresses over the eyes and the application of leeches to the temple. Subconjunctival injections of bichloride of mercury may be necessary in obstinate cases. Atropine is essential in the treatment of iritis. It should be ordered at the beginning and persevered with during the continuance of the attack, the object being to keep the pupil dilated, and by so doing to break through any adhesions which may have formed between it and the capsule of the lens. Also it always relieves irritation, and by paralysing accommodation places the eye in a state of rest. Should the pupil become closed by the effusion of lymph on to the pupillary margin of the lens, an iridectomy should be done when inflammation has subsided, for the purpose of making an artificial pupil and preventing a recurrence of iritis.

Other Secondary Affections of the Eye

Other affections to which the eye is exposed in syphilis are cyclitis, choroiditis, irido-choroiditis, and retinitis ; but these are not common, and occur generally in the later stages.

Secondary Affections of the Nervous System

The secondary nervous affections are : neuralgia, cephalalgia, paralysis (especially of the muscles of the eye and face), hemiplegia, paraplegia, and chorea.

One of the earliest symptoms of secondary syphilis is *neuralgia*, affecting the superficial nerves of the scalp, and producing the well-known phenomenon of "nocturnal

headache," which consists of a dull pain, beginning, especially towards sundown, in the back of the neck, running to the top of the head and perhaps lasting for hours.

Cephalalgia is more a feeling of tension than of actual pain. It is generally located in the occiput, and nocturnal exacerbations are marked.

Motor paralysis of the muscles of the eye and face are common even early in syphilis, and are usually the result of compression of the nerve-trunk by periostitis in the early stages and gumma in the later.

Although *hemiplegia* and *paraplegia* are generally classed as belonging almost exclusively to the tertiary period, that they occur quite early in the secondary stage oftener than is thought is the writer's belief. He has met with two cases where they took place in the third month, another in the fourth, and several occurred in the sixth to the eighth month after infection.

K. G——, aged fifty-two, a medical man, noticed a small papule on one of his fingers in or about the first week in February 1907; this persisted for about a month, when it passed away. The question as to its being syphilitic or not was considered, but it was pronounced to be not. Six weeks later the glands in the axilla and neck became enlarged, but no rash appeared. At the end of two months he began to take "grey powder" daily. He was apparently quite well until the morning of April 25, when, endeavouring to reach out of bed to get his watch, he found he could not move his arm (right), and the leg of the same side was in a similar

condition. This patient, under energetic specific treatment, made a good recovery, regaining the full use of both limbs.

E. T——, a soldier, contracted the disease in March 1908. Hard sore, with subsequent adenitis and a roseolar eruption. Had but a modified treatment, as he deserted, and was found in the street by the police unable to walk. He stated to me that he had not suffered from any premonitory symptoms, but that after a drinking bout he found himself in the street unable to walk. This occurred at the end of June, three months after infection. Under treatment this man regained complete use of his legs, and is still serving.

H. C——, a soldier, contracted the disease in October 1908. The primary lesion was considered to be a "soft sore," and he had no specific treatment. On waking one morning in February 1909, he found he could not move his right arm or either leg; he passed his urine and fæces involuntarily. Under calomel injections he made a wonderful recovery, and is still serving. Practically all the cases of hemiplegia and paraplegia which have come under the author's notice had received either no specific treatment or a very modified form of it.

Hemiplegia is due to endarteritis or thrombosis of the middle meningeal artery, whilst paraplegia results from meningitis of the membranes of the cord.

A variety of phenomena depending on the extent of the lesions may accompany syphilitic hemiplegia, such as paralysis of various nerves, aphasia, optic neuritis, and epilepsy; mental depression is constant.

Prognosis and Treatment

The prognosis is better in syphilitic hemiplegia or paraplegia than in the simple form, much depending on the amount of specific treatment already given, and on the energetic way it is carried out after the onset of the paralytic symptoms.

Secondary Visceral Affections

There may be albuminuria due to syphilitic nephritis, pleural effusion from pleuritis, and congestion of the liver causing jaundice.

The osseous system is often one of the earliest attacked by syphilis. It begins as a simple periostitis, running on sometimes to inflammation of the bone itself. The tibia, clavicle, sternum, bones of the cranium and the ribs are mostly attacked, and in the order named.

Periostitis

This is often a very early secondary, coming on sometimes before the appearance of any rash, etc., but it is more often seen between the sixth and ninth month. It is a subacute affection; it appears as a swelling over one of the bones already quoted, which is elastic, tender, and painful. The pain is sometimes intense, especially at night-time. Under treatment this lesion will generally subside, leaving no trace behind it; but often the bone itself becomes engaged, when the inflammation is sometimes followed by suppuration. In any case bony nodules called osteophytes remain at the seat of attack.

Secondary Affections of the Joints

The secondary lesions as far as joints go are of two kinds—acute and subacute. The acute generally attacks the elbow joints both at the same time. There is slight swelling accompanied by severe pain, which is always intensified at night-time, and there is usually a marked rise of bodily temperature, which may reach 104° F. The *subacute* variety, which is far more common than the former, very often attacks one knee only. There appears a swelling of the joint which is unaccompanied by pain, or if the latter does exist it is only slight; bodily disturbance and pyrexia are insignificant, and it generally ends in resolution; the amount of fluid secreted is usually small. A peculiar feature of this variety is the intermittent character of the effusion.

Rheumatoid Pains of Secondary Syphilis

Some of the most constant symptoms in the early months of syphilitic infection are pains in the muscles, bones, and joints. The muscles attacked are chiefly those of the extremities, whilst the joints affected are the ankle, elbow, wrist, and phalanges. These pains begin at sundown, and get gradually worse at night.

Secondary Affections of the Tendons

Teno-synovitis may come on at an early stage, and is characterised by effusion, tenderness, and swelling along the course of a tendon. Sometimes it is limited to one, such as the tendo Achillis, more rarely it attacks several

at the same time, and there may be severe pain and tenderness over them.

Treatment.—Little can be done locally for these affections; everything depends on constitutional treatment. Pain can, of course, be assuaged by the usual methods, and when very severe morphia hypodermically is indicated.

Secondary Affections of the Epididymis and Testicle

As secondary affections these are not common. When the epididymis is attacked the lesion appears as an acute inflammation, which readily subsides in resolution under treatment. Inflammation of the testicle itself is very rare in early syphilis, and when it does occur it follows the course of ordinary acute orchitis, resolution being generally the result.

Specific Treatment

In speaking of the treatment of all secondary affections it is presumed that specific treatment is strictly adhered to in all, as no local measures will avail in its absence.

CHAPTER VII

TERTIARY SYPHILIS

WHEN not exterminated in its secondary stage syphilis passes into a chronic condition, when it is called tertiary.

Tertiary syphilitic affections present many differences from those of the secondary stage: they are of deep development, of compact structure, and slow growth; they are less numerous and more isolated than secondary lesions, irregular in their course, and much more deeply seated and destructive in their tendency. Secondary affections have a tendency towards resolution, tertiary ones favour progression. The viscera are rarely attacked in secondary syphilis, whereas in the tertiary stage they suffer deeply from a chronic infiltration which produces nodules and tumours called gummata.

It is almost impossible to write a clear and defined description of tertiary syphilis, as each case differs so much in the mode of onset and progression. In some cases what we know as tertiary lesions make their appearance as early as the third or fourth month, while the roseolar rash is still present. The patient appears suddenly to change for the worse; any skin lesions present ulcerate and suppurate, these ulcers spread over the body,

and the patient becomes weak and cachectic. In other cases tertiary syphilis manifests itself in hemiplegia, paraplegia, and other nervous lesions, and generally these cases are rapid and severe. The majority of tertiary syphilis cases occur in the third or fourth year and onwards from the date of infection. The following tissues and organs are attacked in sequence: the skin, nervous system, osseous system, mucous membranes, and viscera.

Some authorities believe that tertiary syphilis is not true syphilis, but that it is a chronic condition left behind by the active disease; seeing that the tertiary lesions may co-exist with the secondary, this belief seems illogical. The discovery of *Spirochaeta pallida* in tertiary lesions points to these being due to the same condition as secondary syphilis, modified no doubt by the attenuation of the virus. It has been proved that syphilis can be reproduced by inoculation with matter taken from gummata and other tertiary lesions.

The chief causes of tertiary syphilis are inadequate treatment, overwork, enervating climates, excesses of all kinds, more especially alcoholism. Malaria is also a very special adjunct to tertiary syphilis.

Cutaneous and Subcutaneous Affections

Gummatous syphilides are typical of tertiary syphilis. The perivascular cell infiltration forms an inflammatory neoplasm in the skin, which has a tendency to soften and to ulcerate. Some of these syphilides become ulcerated almost from the commencement, whilst others ulcerate at one part and heal at another.

Simple Gummatous Syphilides

The gummatous syphilide is of two kinds: simple and ulcerative. The first is formed by dark red, copper-coloured nodules of slow evolution; the extending margin of this syphilide is *circinate* or *serpiginous*. After healing, a brown macule is left, followed by a depressed cicatrix, and there is destruction of tissue without ulceration.

Ulcerative Gummatous Syphilides

These syphilides may consist of a number of nodules, which eventually coalesce, or of a single large nodule with extensive serpiginous ulceration. Progress is slow and painless, and inflammatory reaction absent. The nodule may undergo resolution without any treatment; but, on the other hand, it may persist for years. Generally specific treatment has a marked effect. Under this it heals rapidly, leaving a cicatrix which, at first pigmented, ultimately becomes a white depression circular or annular in shape.

Subcutaneous Gummata

These appear as nodules in the hypodermic tissue. They are hard, painless, and freely movable at first. Later on they become caseated and adherent to the skin, which they perforate, and form an ulcer with the characteristics already described. When they have healed depressed pigmented cicatrices remain.

Treatment of Gummatous Syphilides

Specific treatment is, of course, absolutely necessary, but much can be done locally for ulceration. Dressings

of iodoform, mercurial ointments (red and yellow oxide or white precipitate) are very good; also perhydrol (Merck), in a concentrated solution, applied two or three times a day, or calomel applied in powder or fumigation. It is in these gummatous syphilides that iodide of potassium is so useful. Iodipin given by intramuscular or subcutaneous injection is of much benefit.

THE ALIMENTARY SYSTEM

Tertiary lesions of the *lips* are not common, but they are important owing to their liability to being mistaken for cancer, and *vice versa*. They may appear as a tubercular formation or as a gumma. The former is very apt to relapse. In shape it is usually circinate, and may extend so as to involve most of the lip. It may appear as diffuse infiltration, the mucous membrane of the lip becoming swollen and red. In other cases this lesion assumes the character of a hard circumscribed gumma in the substance of the lip. This may be taken for cancer, but in the gumma the lymphatic glands are not enlarged; the skin over this gumma may ulcerate, and then it may be mistaken for a chancre.

The Tongue

Gummatous inflammation attacks the tongue with great frequency, in numerous forms, and at any time.

Superficial Glossitis

This sometimes arises in habitual smokers. On examination the tongue is found to be swollen, bright red, and

indented at its edges with marks of the teeth. The dorsal surface is devoid of fur, and the papillæ may have disappeared over a large surface. The tongue itself is freely movable, and can be protruded to its normal extent. Its surface is moist, tender and painful. There is little induration.

In other cases the lesion consists of patches of round or oval shape and deep red colour; they are slightly raised and indurated, and when healed leave milk-white patches. They run a very chronic course, and are painless throughout; sometimes they soften and give rise to ulcers, fissures, or erosions.

Sclerosing Glossitis

This is characterised by swelling, most marked on the dorsal surface of the tongue, the central part being most frequently affected. Disappearance of the papillæ gives a smooth appearance to the mucous membrane covering the affected parts. Fissures and ulcers are produced, the former radiating outwards from the central raphé. The course of this lesion is also very chronic. The lymphatic glands seldom enlarge.

Gummatous Glossitis

This occurs about four to six years after infection, and the gummata may be either superficial or deep. The former are usually situated on the dorsum of the tongue. They are small nodules projecting into the mucous membrane, where they can be felt as hard bodies, not always very well defined. Unaffected at first, the mucous membrane

covering a nodule eventually softens, and an ulcer is formed, with a typical "washleather" slough as its floor. The deep gummata may lie at any depth in the tongue's substance. They occur at any age, and are often found in children, but generally appear in middle age. They form painless indolent swellings, with the mucous membrane covering them unaltered. They are not, as a rule, tender. Sooner or later they soften, the mucous membrane gives way, and ulceration takes place. Needless to say, this is a very chronic and obstinate affection.

Differential Diagnosis

Gummata of the tongue may be mistaken for either innocent or malignant tumours. The points of distinction between *innocent tumours* and *gummata* are these. The former are often polypoid, the latter never; innocent tumours are, as a rule, well defined, whilst gummata are not; the former are generally single, gummata more often multiple; innocent tumours are often, gummata never, lobulated.

The diagnosis between gummata of the tongue and cancer turns upon the following differences: Cancer is nearly always single, gumma often multiple. The former tends to attack the borders of the tongue, the latter as often the middle. Cancer often forms opposite a carious tooth, whereas gumma has no connection therewith. Cancer is usually a disease occurring in patients past middle life; gumma is found in those between twenty-five and thirty years of age. The tongue in gumma is freely movable, whilst its mobility is impaired in cancer.

The microscope and history will also furnish help in differentiating between the two affections.

Fissures and Ulcers of the Tongue

may occur both in early and in late syphilis. The latter are very often found in the dorsum, and are caused by softening of the gummata. Ulceration begins as a small hole, which quickly enlarges by the giving way of the infiltrated tissue surrounding the tumour. A cavity is formed with sharply cut, ragged undermined borders and sloughy floor. Symptoms are usually singularly slight, considering the condition; the patient suffers in many cases little inconvenience other than a feeling of thickness of the tongue, pain being practically absent at first, though sometimes troublesome while ulceration is proceeding.

Treatment of Tertiary Affections of the Tongue

One thing is very certain, *i.e.* that smokers suffer much more often from these affections than non-smokers; hence smoking should be forbidden altogether, or at least much curtailed, and in fact all irritation or anything likely to facilitate it should be avoided, hence spirits and hot condiments should be forbidden. The dentist should be visited, to have the teeth examined and put right when required, all tartar being scraped off. It goes without saying that specific treatment is all-important in these affections; the writer has found calomel by injection most useful, and the arylarsonates especially beneficial. Iodide of potash is also essential.

Cracks and fissures should be well dried, and then painted with a solution of either chromic acid (gr. x to ʒj) or of perhydrol or peroxide of hydrogen. When there is much inflammation of the parts the following application may be made to the ulcers :

R	Iod	grs. ij	=	grm. 0.41
	Potassi iodidi		grs. xx	=	grm. 1.37
	Tinct opii	ʒv	=	grm. 0.31
	Ol. menth. pip.	ʒv	=	grm. 0.31
	Glycerini	ad ʒi	=	c.c. .30
Solve et Misce							

The Palate

Gummatous infiltration affects both the hard and the soft palate as well in acquired as in inherited syphilis. It begins either as a local gummatous mass or as a diffuse infiltration. In the former case it projects from the soft palate as a flattened tumour, which is at first hard and elastic, but eventually softens and breaks down, leaving a gummatous ulcer behind. The diffuse variety is much oftener seen. The soft palate becomes thickened and congested ; this may be limited to a part, or it may involve the whole arch of the soft palate. Later on softening of this infiltration and ulceration takes place, and the ulceration may extend to the velum palati, the uvula, and pillars of the fauces, and through the entire thickness of the soft palate, so that perforation is the result. Perforation causes the voice to become nasal, and fluids regurgitate through the nose. When the perforation is small, it may close by granulation ; when it cicatrises, the palate is left scarred and deformed.

Differential Diagnoses

Differential Diagnoses will have to be made between gummatous infiltration of the palate and lupus, tubercle and cancer.

Lupus runs a much more chronic course, and creeps over the surface of the palate, whereas the syphilitic affection begins in the deeper tissues. *Lupus* does not affect the bone, whereas *gumma* does.

Tubercular ulceration is shallower than syphilitic; it is more limited in extent, and has sharply-cut edges, whilst its base is red and more granular. The lymphatic glands in its neighbourhood are often enlarged in tuberculous ulceration, but are seldom so in syphilis. Tubercle very rarely leads to perforation, the contrary being the case with syphilis. Tuberculous ulceration is unaffected by specific treatment or potassium iodide.

Treatment

Treatment consists in arresting the ulceration by specific treatment and iodide of potassium. Locally the palate should be frequently sprayed with dilute solutions of iodine or perhydrol, and kept as clean as possible. No surgical procedure should be undertaken until all ulceration has ceased.

Tertiary Affections of the Pharynx

The pharynx is liable to the same syphilitic manifestations as the mouth. In some cases the entire soft palate is destroyed by ulceration: necrosis of the hard palate occurs, the mouth, nose, and pharynx being converted into one cavity. In others the ulcerative process

is limited to the border of the velum and pharyngeal wall ; adhesions form, and divide the cavity of the pharynx into two distinct chambers, one communicating with the posterior nares, the other with the mouth.

Tertiary Affections of the Larynx

These consist of chronic inflammation leading to thickening or hypertrophy of the mucous membrane, and accompanied by superficial ulcers from which spring vegetations. These vegetations may be of such a size as to impede respiration. The cords may also become much thickened, causing in some cases complete aphonia. Later on deep ulceration may occur, the epiglottis and aryteno-epiglottic ligaments being destroyed. These ulcerations are liable to be mistaken for malignant disease, from which they differ by being of slower growth, non-painful ; and whereas in cancer the submaxillary glands are from an early date infiltrated, they are not so in syphilis. Gummatous tumours may also occur as a tertiary lesion in the larynx.

The Trachea

In tertiary syphilis the trachea is subject to gummatous infiltration and connective tissue proliferation. The former leads to ulceration and necrosis of cartilage. The healing of the ulcers may leave cicatricial contraction, which may lead to either complete or partial contraction of the trachea.

The Lungs

The morbid processes of syphilis in the lungs consist of indurations and gummata, which occur in either the

middle or lower lobes rather than at the apices. Fibrous bands enclosing islets of lung tissue are formed. The bronchi in relation with these are flattened and the alveoli are filled with exudation containing leucocytes and desquamated epithelial cells. The pleura is often thickened and adherent about these areas. The surface of the lung is puckered and furrowed.

Gumma of the lung is more common than the above condition. The gumma may be deposited in any part of the organ, but is mostly found in the lower lobes. Softening takes place in the centre of the mass. The parts around may be thickened by proliferation of cells, and around the whole mass there is always a zone of indurated tissue. The degeneration of the centres leads to liquefaction and evacuation of the fluid, which is the cause of much irritation to the bronchi. Cough, dyspnoea, hæmoptysis, and muco-purulent sputum may all be present, but the tubercle bacilli are absent from the latter. In all lung lesions beginning in the lower lobes, and slowly progressing without fever, syphilis should be suspected.

The Liver

Of all the abdominal viscera, the liver is the most frequently attacked by tertiary syphilis, the conditions produced being (1) amyloid degeneration, (2) perihepatitis, and (3) hepatitis, either diffuse or gummatous. The first is the result of cachexia. In perihepatitis there is thickening of the capsule with adhesions to surrounding parts. In hepatitis there is great increase in the connective tissue, accompanied by shrinking and the formation of fibrous

bands ; by the contraction of these bands the liver becomes lobulated and nodular on the surface, so that a "ploughed-up" appearance is caused. Gummata are frequently found in the liver, and consist of a central zone of yellow matter, a middle zone of fibrous tissue, and an outer of dense hepatic tissue. The yellow matter in the central zone is often absorbed, when it is replaced by a mass of fibrous tissue, which causes puckering of the surface of the organ.

Symptoms

The liver may be enlarged, irregular, and nodular. Pain in the hepatic region is common, and may be sharp or dull and persistent. In perihepatitis the pain may be very severe. As a result of pressure ascites may occur. Marasmus is often present, accompanied by albuminuria and persistent jaundice. On the whole the symptoms in tertiary syphilis of the liver are mild and not at all distinct, so that the disease may be entirely overlooked.

Tertiary Affections of the Spleen

These may consist of infiltrations, either interstitial or gummatous. The former begin around the blood-vessels, producing a diffuse connective tissue which presses on the splenic pulp and causes contraction of the organ. Gummata occurring in the spleen are small, and are sometimes found single, whilst at other times they may be numerous. When freshly formed the gummata have a reddish-grey colour ; when old they are dry and of a yellow colour. They cause contraction of the splenic capsule.

The Stomach and the Rectum

Tertiary affections of the stomach are very rare, and there are no regular symptoms which are pathognomonic of them. When they do occur they consist of gummatous infiltration of the walls.

The rectum may be attacked in tertiary syphilis in three ways: by ulceration, by gumma formation, or by the development and contraction of fibrous tissues. All these varieties may lead to stricture of the gut. Indurating œdema complicates all three; the process extends to and surrounds the anus; the walls of the rectum become thickened and ulcerated, a condition which ends in stricture. Ulceration of the mucous membrane on the surface of the indurating mass very often leads to abscess and fistula.

The Kidney

The kidney is liable to be attacked in three ways—by gummata, by interstitial nephritis, and by amyloid disease. Gummatous infiltration of the kidney is rare, and is usually associated with the same condition of other organs, such as the liver and spleen. Nephritis is of the chronic interstitial variety, and leads to the granular contracted kidney presenting the usual symptoms of that condition. Amyloid disease is the commonest renal result of tertiary syphilis, and is also nearly always associated with amyloid degeneration of the liver and spleen.

Treatment.—In these affections of the kidneys mercury must be given cautiously, but at the same time specific

treatment must be carried out by injection either of the soluble salts or of one of the amylarsonate preparations, the latter being very applicable in such cases.

The Muscles and Tendons

Myositis occurs as the result of tertiary syphilis in three forms: the hyperæmic, the chronic infiltrative, and the gummatous nodular. Myositis, when chronic, tends to more or less contraction; pain is usually of a dull, aching character. One or more muscles may be attacked at the same time; those most frequently involved are the flexors of the upper extremity, especially the biceps.

Globular, fusiform, or flat gummatous tumours may occur in the muscle. When superficial they become adherent to the aponeurosis, which becomes inflamed and hypertrophies. They are best detected when the muscle is relaxed. They excite little pain, their chief inconvenience being interference with motion. These tumours may undergo softening, break down and form deep ulcers.

Tertiary lesions of tendons take the shape of tenosynovitis, with hyperæmia of the sheath and serous effusion. They form elastic, often fluctuating tumours, and may be painful. Gummata sometimes form in tendons.

Tertiary Affections of the Bursæ

In tertiary syphilis the patellar bursæ are frequently attacked by painless gummatous infiltration, elastic to the feel. It very often becomes inflamed, softens and breaks down, and then is very tedious.

Tertiary Affections of the Bones

The tertiary affections of the bones consist of osteo-periostitis, exostoses, and gummatous infiltration. The bones most frequently attacked in osteo-periostitis are the tibia, ulna, clavicle and sternum, also the bones of the cranium. The signs of this lesion are ill-defined tumours of different sizes, adherent to the osseous tissue; they are very tender to pressure and very painful, especially towards evening. As a rule they end in absorption and undergo resolution; in other cases inflammation takes place; the skin becomes adherent to the tumour, is reddened and thinned; softening takes place, and an opening is formed; eventually the superficial portion of the bone becomes necrosed and comes away.

Exostoses are the result of eburnation of bony tissue; when this takes place resolution is not possible; the node or tumour remains stationary. As a rule these lesions give little trouble, but sometimes, when situated on the internal surface of the cranial bones, they may cause convulsions, epilepsy, and various forms of paralysis.

Gummatous Osteo-Periostitis

The bones most frequently attacked are those of the cranium, where one or more nodes are developed; the bones of the face are also very liable to be attacked, especially the malar, superior and inferior maxillary bones; the first symptoms are swelling and pain, and very often the whole bone is destroyed. The vertebra may be the seat of gummatous osteitis, when a condition called "syphilitic spondylitis" is formed. This gives rise to various

symptoms, according to its localisation : when the vertebra in the cervical region are attacked, paralysis of all four limbs may take place ; when in the dorso-lumbar, paralysis is limited to the lower limbs. Syphilitic disease of the vertebræ differs from tuberculosis in not causing destruction of the whole body of the vertebra, hence in the former there is generally an absence of angular curvature.

Joint Affections

(*a*) Synovitis, subacute and chronic ; (*b*) Gummatous deposits in the synovial membranes ; (*c*) Gummatous changes primarily in the bones ; (*d*) Spreading to the joint from the surrounding parts ; (*e*) Ankyloses.

Synovitis of the tertiary period is markedly subacute ; there is but slight pain or impairment of movement ; the effusion into the cavity takes place slowly and is never very great. A marked feature is the tendency of this affection to become stationary. There is seldom any suppuration or any other degeneration, in marked contrast to tubercular affections of the same parts.

Gummatous arthritis generally attacks the knee-joint. It begins in an insidious manner, there being but slight pain and but little effusion. It may set up acute arthritis, ending in complete destruction of the joint and leading to ankylosis.

When the gummatous disease begins in the bones, osteitis affects both the epiphysis and the diaphysis, causing enlargement of the bone near the joint. It is frequently preceded by nocturnal pains, though later on pain is but slight.

The Fingers and Toes

Dactylitis syphilitica is a condition due to gummatous deposit, which may begin in the bones and periosteum, eventually implicating the joints; or it may commence in the subcutaneous tissue of the fingers and toes, and also may extend to the joints.

In the former case the disease develops slowly as an enlargement of one of the fingers or toes. The skin over it becomes stretched and swollen; pain is slight, and may be completely absent. Only one phalanx may be attacked at a time, but usually two or more, and eventually the whole finger or toe becomes implicated. The fingers are attacked more often than the toes. The swellings may remain in the same indolent condition for a long time, and then the gummatous deposit is either absorbed or softened and discharged through a sinus. The bone is generally left permanently deformed, and may be partly absorbed and shortened or thickened.

The Testes

Affections of these organs consist of chronic hyperplastic processes of the body of the testis alone or of its coverings as well. This lesion begins without inflammation or pain. The organ is uniformly enlarged, hard, firm, and less sensitive than in its normal state. There may be an accompanying hydrocele. The testicle may sometimes be found to contain masses of induration, which form projections on its surface; the latter may coalesce and form a

hard resistant mass which may remain for years, or softening and breaking down may take place and an abscess cavity be left.

Treatment.—Specific treatment of course is necessary, and without it little can be attained locally. Strapping the testicle with mercurial plaster and tapping a hydrocele when present, may be used as adjuvants.

THE CIRCULATORY SYSTEM

Lesions in the arterial system, inside or outside the cranium, are invariably present, and constitute the most important pathological element in all cases of syphilis, endarteritis, panarteritis, peri-arteritis and endoperi-arteritis, all being constantly found, sometimes in the same subject. The arterial changes may, in rare cases, manifest themselves before the end of the first year, especially in the neighbourhood of the base of the brain, but usually they are delayed till after the third year, and often they do not give rise to symptoms till a much later period, when they may end in atheroma of the aorta, aneurysms, or aortic regurgitation.

Several types of syphilitic arteritis are recognised, the best marked being the obliterative, in which the most advanced changes are seen in the inner coat of the vessel, constituting the condition known as "Endarteritis obliterans." The intima is thickened sometimes more on one side than the other ; the internal elastic lamina usually remains intact, but it may be absorbed. The tunica adventitia is generally found infiltrated with round cells

and the vasa vasorum thickened. The tunica media is sometimes also affected, and when this takes place the muscle cells are atrophied. The wall of the artery, being deprived of its elastic and muscular elements, offers less resistance to the blood pressure, bulging takes place, and an aneurysm is formed. Thickening of the intima causes anæmia of the parts supplied by the affected vessel. The result will depend on the localisation of the latter, and much will depend on whether it is a terminal artery, or if there is collateral circulation. In the latter case there will be loss of or diminished function. If the vessel is situated in a lower limb the latter will be weakened. Should it be the coronary arteries which are engaged, angina pectoris may result; should the affected vessel be in the brain, dizziness, etc. will follow. Obliteration of a terminal artery will cause arrest of function, and in the case of the cerebral arteries, softening of the brain.

Endarteritis obliterans is characterised by a proliferation of the endothelial tissue, and the media and adventitia are infiltrated with small cells. In gummatous periarteritis nodular gummata may develop in the adventitia, producing globular swellings which may attain considerable size. These swellings are not infrequently found in the cerebral arteries. Endarteritis obliterans, when it attacks the vessels of the limbs, may cause gangrene, the signs of which consist of pain lasting over a long period with perhaps no other symptom but œdema. Charcot describes a peculiar gait, which he says is a sure sign of arterial constriction,—when walking there is a sudden attack of numbness and weakness accompanied by pain

and cramp in the limb. In two cases which occurred in the author's practice, the first symptoms took place in the cricket field: the patient was about to deliver a ball in bowling when he experienced a numbness in the calf of one of his legs, and this was followed by sharp pain; these passed away, but it was the beginning of endarteritis obliterans, which eventually resulted in loss of the limb. The second case happened to a tennis player, who, whilst serving, suddenly experienced pain and numbness in the right arm, which recurred fairly frequently after this, and was put down as a "tennis elbow"; this case also ended in amputation of the limb about two years later. In endarteritis obliterans the calibre of the artery is slowly but progressively occluded, until it is completely so, when gangrene sets in, resulting in the loss of the affected limb or part of it. The process may attack one limb after another, and the writer remembers one case in which both arms and both legs had been amputated for endarteritis obliterans.

Atheroma

Atheroma is a secondary degeneration of the coats of an artery brought about by endarteritis of its vasa vasorum, causing defective nutrition of the walls of the vessel, and by the toxic effects of the syphilitic virus itself on the vessel. This leads to what is known as atheroma and to endarteritis deformans. Of the many causes of atheroma syphilis is the most important. There is a local syphilitic arteritis most commonly seen in the aorta—aortitis which is a prime factor in the production of aneurysm; and

there is a late diffuse change, comparable to the para-syphilitic lesions of the nervous system.

Aneurysm

As a cause of aneurysm syphilis stands pre-eminent; the arguments in favour of this being the case are:—the frequent coexistence of aneurysm with other syphilitic lesions such as cerebral arteritis, the number of cases of aneurysm with histories of syphilis, and the frequency of aneurysm in locomotor ataxy, which is now known to be almost solely of syphilitic origin.

CHAPTER VIII

AFFECTIONS OF THE NERVOUS SYSTEM

THE nervous system in tertiary syphilis is nearly as frequently attacked as the skin and mucous membranes taken together. Nearly three-fourths of all spinal-cord diseases are due to it, as are those of brain disease. Syphilitic nerve affections may be developed as early as the fourth month, and as late as the twentieth year after infection. Fournier's figures show that in about one-ninth of all cases of ordinary cerebral syphilis the symptoms of hemiplegia occur during the first year of the disease, and a much larger percentage of spinal cases occurs before the expiration of this early period. In rare cases described as "malignant," cerebral and spinal affections have been recognised before the disappearance of the primary induration at the site of infection. Nervous symptoms are especially likely to appear in individuals of the neurotic type, and chorea, migraine, neuralgia, etc., are common in the history of such persons. Mental anxiety and strain, sexual and alcoholic excesses are certainly predisposing causes, and last, although not least,

comes "insufficient treatment," which is indeed one of the main factors in tertiarism.

The following figures speak for themselves :

Fournier's statistics of 100 cases of cerebral syphilis of which the previous history of treatment was known

After thorough treatment	5
After modified but insufficient treatment	6
After seven to eighteen months' treatment	10
After one to six months' treatment	70
After no treatment	4
After treatment by iodides exclusively	5
	<hr/> 100

The above shows that 5 per cent. only occurred after thorough treatment, as against 95 per cent. after insufficient treatment.

In tertiary syphilis of the nervous system, the latter may be affected by the syphilitic virus, by its causing inflammation of the membranes or blood-vessels with subsequent occlusion of the latter; by gumma of various parts of the brain; by its lowering the vitality of the cells, laying them open to parasyphilitic affections—general paralysis, tabes and epilepsy. Inflammation of the membranes (meningitis), generally affects the base of the brain and may extend down the membranes of the cord; gummatous deposits nearly always originate in the membranes—they are generally small, and are scattered round the vessels, and are of a greyish red colour; when occurring in the substance of the brain they are usually an extension from the meninges. At other times the gummata may be single and large, in which case they are

mostly found at the base of the brain ; they are greyish yellow in colour. Adhesions form between them and the dura mater, which may be much thickened. The chief lesion in cerebral syphilis is endarteritis, which causes narrowing of the lumen of the affected vessels, and consequently deficient blood supply to the parts of the brain dependent on them ; should they become completely occluded, softening of the brain surface takes place. The symptoms of cerebral syphilis will vary according to the part of the brain which is engaged, thus, when the lesion is situated in the convexity of the brain it may lead to epilepsy, disorders of the mind, and paralysis ; whereas, when on the base, paralysis will follow from implication of the nerves at the base of the brain. There are no symptoms which can be described as pathognomonic of syphilis of the brain, but the following are suggestive of it :—

Epilepsy occurring at middle or adult life without loss of consciousness ; aphasia ; paralysis of certain muscles (ocular), paralysis, mental disorders, more especially loss of memory, hemiplegia, and general loss of health. Of these hemiplegia is perhaps the most common, and is due to endarteritis of the middle cerebral artery, but sometimes to the pressure of gummata. Syphilitic hemiplegia as a rule sets in suddenly, although it may have been preceded by headaches, numbness, and transient paresis of the ocular muscles ; sensation is generally unimpaired, and it may or may not be associated with mental disorder.

Tertiary Syphilitic Affections of the Spinal Cord

The spinal cord is one of the most favourite sites of tertiary syphilis; the lesions produced being the result of inflammation and some degeneration, probably caused by endarteritis. Tertiary syphilis attacks the cord in a very irregular manner, and is not limited, as in locomotor ataxy, to the posterior columns, but may attack any other part, or all the systems at the same time, and is very often associated with syphilis of the brain.

As in the brain, so in the cord, tertiary syphilis may affect the membranes alone, the cord itself, or both together, the latter being most often the case; all three membranes are usually affected together, and when the cord is engaged its posterior columns are the favourite sites.

The symptoms of spinal syphilis vary much owing to the irregular distribution of the lesions, and consist chiefly of pain along the spine—girdle pain—accompanied by motor, sensory, and trophic symptoms. Later on paraplegia sets in, with affections of the bladder and rectum.

The principal lesions of tertiary syphilis of the spinal system are meningitis, myelitis, and meningo-myelitis. *Meningitis* is very often an early affection. *Myelitis* may be acute or chronic; the former sets in suddenly, with acute and severe pain somewhere about the dorso-lumbar region, followed in a few days by paraplegia; both lower limbs become totally paralysed, and a fatal termination very often is the result. Chronic myelitis is the commonest syphilitic affection of the cord, and

commences with sensations of numbness and tingling of the feet, followed after a long period by affections of the bladder and rectum. Sometimes incontinence takes place, at others retention is the rule. The disease is slow in its progress, but eventually the lower limbs become partially paralysed. Knee-jerks are irregular, being more marked on one side than the other, and there may be anæsthesia or hyperæsthesia in irregular patches. Cramps in the legs are also, as a rule, a great trouble. The disease may be arrested in its progress, but such cases are rare; the majority, in the absence of early treatment, becoming hopeless paralytics.

Leucocytosis of the Cerebro-spinal Fluid

Widal and Ravant discovered that lymphocytosis of the cerebro-spinal fluid always accompanies organic disease of the nervous system, more especially tuberculous and syphilitic meningitis, as well as tabes and general paralysis, but that it is absent in functional diseases. Hence they advocate lumbar puncture in all cases of syphilis with nervous symptoms; the presence of lymphocytosis being an indication for energetic treatment. Undoubtedly this is a valuable means of diagnosis.

Treatment of Cerebro-spinal Syphilis

The treatment of cerebro-spinal syphilis must be commenced as soon as the diagnosis has been made. To be of use treatment must be of an intensive character, mercury being, as usual, our sheet-anchor; by far the best form to administer it in these cases is by calomel

injections. Oral administration under such conditions is practically useless. Failing calomel injections, inunction à l'Aachen (Aix-la-Chapelle) is the best. I have seen many cases of cerebro-spinal syphilis make wonderful recoveries under these injections. My plan is to give gr. $\frac{3}{4}$ of calomel by intramuscular injection twice a week for four weeks, then to suspend the treatment for a period of two weeks, and then repeat the course, at the same time being guided by the symptoms, etc., as to continuing it further. During the intervals iodide of potassium ought to be given in not smaller doses than gr. xv three times a day, and for not longer than ten days at a time; the dose being gradually increased to gr. xxx. three times a day.

CHAPTER IX

PARASYPHILIS OR QUATERNARY SYPHILIS

MANY years, it may be, from the primary sore and from any active manifestations, certain diseases may follow, not directly syphilitic, but dependent in some way upon its poison, and hence termed parasyphilitic affections, the chief of which are locomotor ataxia, general paralysis, and epilepsy. Of these, Fournier and Mott maintain that tabes and general paralysis are pathogenically identical, and only different aspects of the same disease. Both are caused by syphilis, and appear about the same time after infection ;—Argyll "Robertson pupil" and lymphocytosis of the cerebro-spinal fluid are common to both. These authorities also say that the primary lesion in both tabes and general paralysis is the same, being a dystrophy of the neurones, the sclerosis and thickening of the membranes being a secondary result of degeneration.

Tabes or Locomotor Ataxia

Tabes, tabes dorsalis, or locomotor ataxia, is an affection characterised clinically by sensory disturbances, incoördination, trophic changes and involvement of special

organs, particularly the eye. Anatomically there are found degenerations of the root fibres of the dorsal columns of the cord, of the dorsal roots, and at times of the spinal ganglia and peripheral nerves. At the present time tabes is looked on as essentially a syphilitic disease. Moebius says, "The longer I reflect upon it, the more firmly I believe that tabes never originates without syphilis." Erb, Fournier, and Gowers show that in from 50 to 90 per cent. of all cases of tabes there is a syphilitic history, and Erb's latest figures show that of three hundred cases of tabes 89 per cent. had a history of this disease.

The importance of the rôle played by syphilis in the production of tabes and general paralysis becomes more and more evident as time goes on. Collins in a series of 140 cases of tabes obtained a definite history of syphilis in 70 per cent. of them, whereas out of 140 cases of nervous diseases other than tabes or general paralysis only 8.5 had had syphilis. Additional proof of the syphilitic origin of tabes and general paralysis is afforded by the results of cyto-diagnoses of the cerebro-spinal fluid by lumbar puncture. Widal, Sicard, and Ravant found distinct lymphocytosis in 36 out of 37 cases. Lymphocytosis is often distinct in the very earliest stage, even preceding "Argyll-Robertson pupil" or loss of knee-jerks.

Exciting Causes.—Excessive fatigue, over-exertion, injury, exposure to cold and wet, all no doubt contribute to the development of tabes.

A good many cases are on record of the existence of the disease in both husband and wife, and a few where children were also affected.

Theories as regards Actual Lesion.—Maries and Guillain believe in a "lympho-angiotic" theory—that tabes is due to a syphilitic affection of the posterior lymphatic system of the cord.

Magrath maintains that it is due to the spread of a chronic syphilitic meningitis to the posterior roots.

Ferrier comes to the conclusion concerning tabes that the most feasible hypothesis is that its essential lesion is a dystrophy, probably toxic in origin, affecting the sensory protoneurones as a whole, manifesting in degeneration of its intraspinal prolongations, and that the toxin in tabes is generated by the syphilitic virus. The toxin of syphilis differs from others inasmuch as the disease is a progressive one, and does not tend to come to a standstill, as in other toxin-produced degenerations.

Purves Stewart shows that lymphocytosis of the cerebro-spinal fluid is constantly present both in tabes and general paralysis from the very start, and is uninfluenced by the most energetic anti-syphilitic treatment, unlike other lesions of the central nervous system.

Ford Robertson's Theory.—Another theory concerning tabes is that of Ford Robertson, who says: "We have found that bacilli of the diphtheroid group can be found to be invading the tissues in all cases of advancing tabes and general paralysis; the chief seats of invasion are the naso-pharyngeal and oral mucosæ in cases of general paralysis and the genito-urinary tract in tabes." He has named the bacillus—*bacillus paralyticans*. He further states that he has seen cases of general paralysis and tabes

much benefited by anti-bacterial serum prepared in the sheep by immunisation with these special diphtheroidal cells.

Symptoms.—In typical cases there are three stages of the disease—the pre-ataxic, the ataxic, and the paralytic stages. In the **pre-ataxic stage** the chief symptoms are pains, ocular symptoms, bladder symptoms, trophic disturbances, and loss of deep reflexes.

Pains, usually of a sharp, stabbing character—hence the term “lightning pains.” They last only a second or two, and are most common in the legs or about the trunk; they dart from place to place. At times they are of a burning character, and when they disappear leave the areas they occupied tender to pressure. They occur at irregular intervals, and are prone to follow excesses of all kinds, exposure to cold and damp, and to come on when the health is impaired. In rare cases, as pointed out by Gowers, these pains may constitute the only symptom of the disease.

Recently the writer has had experience of three cases of tabes where lightning pains and “Argyll-Robertson pupil” had been the only symptoms in periods varying from ten to seventeen years.

Ocular Symptoms consist of—(a) optic atrophy; (b) ptosis; (c) paralysis of the external muscles of the eye; (d) “Argyll-Robertson pupil,” in which there is loss of the iris reflex to light; but the power of contraction is demonstrated when a patient looks at a near object—accommodation. The pupils are generally contracted, sometimes to a pin-point.

Bladder Symptoms.—The first warning of the onset of the disease may be a certain difficulty in emptying the bladder. In many cases of tabes the sexual desire is very often increased early in the disease, but rapidly becomes diminished, and later on is totally abolished.

Trophic symptoms, although belonging mostly to the later stages, very often occur in this, the incipient stage, when it is not uncommon to find a perforating ulcer of the foot.

Loss of Deep Reflexes.—One of the most reliable signs of tabes is diminution or absence of the knee-jerks (Westphal's sign), and this early and most important symptom may occur years before ataxia appears; also loss of ankle jerks. The combination of loss of either of these with one or more of the symptoms mentioned above, especially with lightning pains or "Argyll-Robertson pupil," is practically diagnostic.

Tabes may never progress beyond this stage. A peculiarity is that when optic atrophy comes on early, ataxia rarely supervenes.

Ataxic Stage.—Ataxia develops gradually; one of the first indications of it is the patient's inability to get about in the dark, or to maintain his equilibrium when washing his face with his eyes shut.

When the patient stands with the feet together and the eyes closed, he sways and loses his balance (Romberg's sign). He cannot stand on one leg, and is unable to start off promptly at the word of command. On turning quickly he is apt to fall. Gradually the characteristic gait of ataxia comes on: the patient starts unsteadily,

with his legs somewhat apart, lifting his foot too high and jerking out the limb, which comes down with a sudden stamp caused by the entire sole striking the ground at once. The incoördination is not limited to walking, but extends to the performance of other movements: if the patient, whilst in the recumbent position, is asked to touch one knee with the other foot, the irregularity of the movement is very marked. Incoördination, although less observable in the upper limbs, is very often evident, as instanced by the difficulty which the patient experiences in buttoning his coat or collar. There is no paralysis, and the muscle-reactions are normal; but the subject of ataxia is unable to co-ordinate his muscles harmoniously.

Sensory symptoms increase as the case goes on; the lightning pains come on oftener and persist longer. Other symptoms are tingling and "pins and needles" in the feet, with areas of anæsthesia and hyperæsthesia; a feeling as if a layer of cotton wool were interposed between the soles of the feet and the ground; "pins and needles" in the arms and hands. A frequent and constant symptom is a feeling of "bands" about the chest and waist, giving the sensation of something heavy tied round the chest. A well-marked phenomenon is the loss of ability to localise pain: if the patient is pricked in one limb he may say he feels it in the other. Reflexes diminish still further in this stage, and the eye symptoms become more marked; at the same time ataxia is very rare when optic atrophy exists.

In this stage the visceral symptoms are most remarkable, and consist of what are called tabetic crises, severe

paroxysms of pain referred to various viscera—laryngeal, gastric, nephritic, rectal, and urethral. Gastric crisis is the most common, there is intense pain in the stomach and vomiting of acid gastric juice; the attack may come on suddenly and last for some days. Paroxysms of pain in the rectum, accompanied or not by tenesmus, are common.

Trophic Symptoms.—Trophic changes are marked: sweating, shedding of the nails and teeth, herpes, and œdema. The perforating ulcer of the foot is a most characteristic phenomenon, commencing as a suppurating corn under the prominence of the first or fifth toe. The ulcer gradually eats its way through to the dorsum of the foot. It is in this stage that the condition known as Charcot's joint is to be seen: a huge painless swelling suddenly appears about the joint, such as the hip or knee, and in a few days may have altogether disappeared or suppuration taken place, with total disorganisation of the joint; this affection is very like chronic arthritis deformans.

The Third or Paralytic Stage.—In this all the symptoms deepen; progress is very slow as a rule. Ataxia becomes so marked that the patient is unable to stand, and later on he becomes quite bed-ridden. Incontinence or retention of urine sets up bladder or kidney mischief, which very often carries him off if pneumonia or cerebral apoplexy are not beforehand. The courses of the symptoms and duration of tabes are most variable: one patient may become hopelessly ataxic in a twelve-month, whereas another may be able to walk about and attend to his business for twenty or thirty years.

Diagnosis.—The presence of lightning pains when combined with any of the other signs is very distinctive, and the combination of any of the following signs is almost pathognomonic of tabes—*i.e.* absence of knee-jerk, "Argyll-Robertson pupil," lightning pains, visceral crises, atrophy of the optic disc, and Romberg's sign, and last, although not least, a history of syphilis. Wasserman's reaction test, together with cyto-diagnosis, may be of great value in doubtful cases.

Prognosis.—Complete recovery cannot be expected, but arrest of the process, with a marked amelioration of symptoms, is frequent. On the whole the prognosis of tabes is bad.

Treatment.—In treating tabes our object ought to be to arrest its progress and relieve symptoms, as we can never hope to restore to their normal condition the degenerated columns of the cord. For this purpose anti-syphilitic remedies are all-important; the treatment should be intensive, and for this purpose nothing is better than intramuscular injections of calomel, next to which comes inunction of mercury *à l'Aix*. Iodides given in intermittent courses in not less than 50 grains per day, and continued for not longer than ten days at a time, are very often very beneficial. Lightning and other pains are best relieved by phenacetin, antiebrine, or antipyrine; and gastric and other crises by hypodermic injections of morphia.

Bladder symptoms require constant care; when the organ cannot be perfectly emptied the catheter should be used.

GENERAL PARALYSIS

Like tabes, general paralysis is undoubtedly due to syphilis in at least 90 per cent. of cases. It occurs usually about the ages of thirty to thirty-five, and among those who live an active, busy life—hence is particularly liable to occur among active business men in large cities. Fournier maintains that the chief factor in the causation of general paralysis is insufficient treatment of syphilis. The predisposing causes are over-exertion and alcoholic and sexual excesses.

Symptoms.—These vary very much ; in some cases the mental and in others the motor-spinal or motor-cerebral symptoms predominate. The disease has been divided into certain stages, but these are ill defined, as the symptoms supposed to be peculiar to a particular stage may appear at any period of the malady. The importance of recognising the very earliest signs cannot be exaggerated.

Prodromata.—There may be some slight change in character which is often in the nature of an exaggeration of some peculiarity present in the individual: if he has been always quick in his temper he now shows unusual irritability ; his power of concentration may be weakened, or some feebleness may be noticed in his will. His affections may undergo some change, and moral perversions of various kinds may be noticed by his performance of acts which he formerly regarded as discourteous, dishonest, or indecent in others. Such acts may be first observed to occur after a dose of alcohol which formerly

had no effect upon his mental equilibrium. These fore-shadowings deepen into the symptoms of the real disease, any of which latter may also appear as the first warning to his immediate friends: thus his premonitory symptoms may be those of an abnormal idea of his own importance, wealth, and station; or indifference to business. Motor symptoms or restlessness, slight tremors of the lips and hands, difficulty in articulation or in letter-writing, may precede the mental warnings; pupillary rigidity or an unsteadiness in his gait may be the first sign that anything is wrong.

Mental Symptoms of the Established Disease.—

These consist of the exaggeration of the "warning symptoms"; the character of the patient becomes rapidly changed, he gets heartless and careless about his family and home duties, neglects his business—though his mind may be filled with schemes for making colossal fortunes—and he may take to the spending of money lavishly, and may at the same time not scruple as to how he obtains more. His will-power is markedly weakened; memory fails early, especially for recent events; he becomes unable to calculate, and may soon cease to remember the day of the week or the number of the year. Restlessness is marked, and there is a liability to violent outbursts of anger and jealousy, or to the performance of some indecent act.

As the mental deterioration increases towards dementia, delusions are common, the most characteristic type of which is the "grandiose," the patient fancying himself God, a king, or the possessor of boundless wealth: on

the other hand these grandiose ideas may be replaced by depression of spirits and melancholia; the patient often has the delusion that all food is poison, or else that it will "block up" his intestines.

Motor Symptoms.—The facial muscles are generally the first to show the serious nature of the disease. The face is flabby and expressionless, giving the idea of stolidity; in speaking there is a marked tremulous condition of the muscles, which show want of control; the lips and tongue are the seat of marked tremor; the tongue is protruded with difficulty and only with ataxic jerkings, and later on it is completely paralysed. Speech is markedly affected; it becomes halting, slow and drawling. The prominence of the cheeks is often noticed.

Handwriting.—Letters are unevenly formed, the strokes showing shakiness and unequal degrees of length and strength; but the most characteristic feature is the omission of letters, syllables, or complete words.

"Argyll-Robertson pupil" is marked in almost every case. The knee-jerks are also affected, being either exaggerated or the reverse. The movements of the limbs may be abnormal; the gait becomes unsteady, and may be typically tabetic, at other times it may be spastic.

In general paralysis there is a liability to paralytic seizures, which have a tendency to recur at short intervals, the patient being left hemiplegic, monoplegic, or aphasic. These paralytic symptoms usually pass off in a few hours, but each succeeding attack leaves a deepening of the mental weakness and muscular feebleness.

Sensory Symptoms.—These may consist of partial or total blindness, whilst the senses of smell and taste may also be lost; illusions and hallucinations, such as seeing faces or hearing noises, are common. Symptoms pointing to the connection between general paralysis and tabes are frequent—*e.g.* Charcot's joint affection, perforating ulcer, and spontaneous fracture of bones. Many authorities regard the essential features of tabes and general paralysis as identical, depending altogether on whether it be the cord or brain which is the seat of the process of degeneration.

Course and Duration.—The general average of cases run their course towards total dementia and death within a period of three years, and in rare cases a couple of months. The ordinary course is that as the patient proceeds towards complete dementia the paralytic symptoms deepen, he becomes bed-ridden, and is unable to articulate, the sphincters fail, and huge bed-sores form; he usually succumbs to some intercurrent affection, such as cystitis, diarrhœa, or general inanition.

Ætiology.—The same theories as to the pathogeny of tabes are held concerning general paralysis; the most likely being that the syphilitic toxin has so diminished the natural vitality or resistance of the entire nerve system that, certain tracts being exposed to "over-exertion," their nerve elements succumb to degeneration—a view which is supported by the fact that the disease is always more advanced in the cortex of the frontal lobes.

Prognosis.—The prognosis of general paralysis is bad; indeed, the affection may be looked on as incurable.

Treatment.—Nothing really can be done either to arrest or cure general paralysis, although if recognised very early anti-syphilitic measures should undoubtedly be given a chance.

EPILEPSY

The third parasyphilitic affection to be considered is epilepsy, which is of frequent occurrence in cerebral syphilis, and, like the non-specific variety, presents two forms—the “grand mal” and the “petit mal.” Headache, increasing in severity, always precedes an attack of syphilitic epilepsy. The epileptic aura and cry are absent as a rule. The attacks occur at intervals, and frequently with regularity every ten days or once a month. In some cases consciousness returns in a few minutes, whilst in others the patient remains in a stupid condition for hours and may remain so for some days. It is stated that the longer the prodromal stage the more severe will be the seizure, and *vice versa*.

In “petit mal” the paroxysm may begin either with a twitching of one side of the face, a turning of the tongue to one side, extreme giddiness, or cramps in the limbs; loss of consciousness and a slight convulsion follow. In a great number of cases there is no convulsion, but the patient, whilst talking or performing some act, becomes unconscious, and is seen to stare vacantly; if sitting he becomes motionless, and if conversing suddenly silent, and fails to comprehend questions addressed to him.

From simple epilepsy the specific form may be distinguished by the history of the case; simple epilepsy is

generally developed before puberty, whereas the specific form begins usually between twenty and thirty. The simple seizures are uninfluenced by mercury or the arylarsonates, whereas the specific forms respond to both.

Treatment of syphilitic epilepsy consists of mercury, arylarsonates, iodides, and of course bromides.

CHAPTER X

THE GENERAL TREATMENT OF SYPHILIS

UNTIL quite recently mercury was recognised as the only specific for syphilis, but now there is reason to believe that in the arylarsonates we are in possession of a second ; indeed, this is certain as far as concerns their power of preventing the occurrence of syphilitic symptoms and of causing their disappearance ; but whether they are capable of effecting an eventual permanent cure remains an open question, which can only be determined by time and further experience. At one time the iodides were supposed to be specific in their action, but for many years past they have been looked on as adjuncts only to mercury, and as possessing no specific power.

Abortive Treatment.—Many attempts have been made by cauterisation and excision of the primary lesion to prevent constitutional infection, but have invariably failed. Metchnikoff has endeavoured to destroy *in situ* the *Spirochæta pallida* by the application of a 30 per cent. calomel ointment, with a certain amount of success ; his experiments on monkeys proved successful in preventing the development of the disease when applied to the point of inoculation within an hour or two of infection, as also in the case of

the medical student already quoted, in whose case inoculation at the point of inoculation prevented further developments. Neisser says: "There is no doubt that by the application of strong mercurial ointments very many syphilitic infections could be avoided, and I hold it to be the duty of every doctor to publish this fact whenever he can, and to advise this individual prophylaxis." This question may, at present, be considered to be *sub judice*.

Specific Medication.—Many drugs have been used in the treatment of syphilis; among others sarsaparilla, guaiacum, sassafras, sulphur, arsenic, gold, silver, platinum, and many vegetable preparations; iodide of potassium, and last, but needless to say not least, mercury, and, as already mentioned, the arylarsonates. But most of these have long ago ceased to be employed in the treatment of syphilis. Sarsaparilla proves of benefit in syphilis under certain circumstances; but this is probably due more to its tonic and depurative effects than to any specific action. At one time iodide of potassium was believed to be a true specific in syphilis, but it has long ago been relegated to a position as a mere adjunct to the real specifics—mercury, and now the arylarsonates.

Mercury.—With the possible exception of quinine in malaria, no other drug is more worthy of the name "specific" than is mercury in its action upon syphilis; nevertheless it has had its ups and downs, at one time it was considered to be indispensable for the cure of the disease, at others it was looked on as useless, and at one period it fell into utter disrepute, as not only being useless,

but was accused of being the cause of half the misfortunes which had hitherto been attributed to syphilis itself. No doubt this was partially true, owing to the barbarous and unscientific way mercury was administered. It was during the Peninsular War that this state of things was first brought forward, principally by Guthrie; the position of mercury was seriously threatened, until it was in danger of being removed altogether from the category of syphilitic remedies. The situation was saved by William Ferguson, who calmly and lucidly explained the true position of affairs, and advocated the employment of mercury in doses sufficient to bring about its physiological effects short of the salivation which had previously been the custom.

It was many years before mercury recovered its good name, or rather lost its bad reputation; and even to this day it is a drug which is hated and detested by the general public as being the cause of unheard-of woes; and many a case of syphilis has been allowed to have its full swing owing to the refusal of the patient to undergo mercurial treatment through dread of its effects.

There is little cause for fear of mercury if administered properly and in therapeutic doses; at the same time there are undoubtedly certain dangers attaching to it—(1) salivation, (2) gastro-intestinal symptoms, (3) cutaneous eruptions, (4) disorders of nutrition.

Salivation.—The stomatitis seen to-day is generally of a mild type, and does not damage the teeth or jaws; but sometimes even now severe cases occur, varying in degree from slight swelling of the gums to intense inflammation of the whole buccal mucous membrane, accom-

panied by deep ulcerations, local gangrene, necrosis of the jaw, and loss of teeth. Salivation of this sort is nearly always the result of faulty methods of administration, or of neglect of buccal hygiene. A few cases, however, are due to some peculiar intolerance to mercury on the part of the patient.

Before beginning a course of mercury all old stumps should be extracted, and teeth freed from tartar and regulated as far as possible. Clear and concise rules should be given to the patient about the care of his teeth and gums whilst he is undergoing treatment by mercury; he should be warned as to the necessity of washing his teeth after each meal, and advised to use some mouth wash frequently during the day, such as chlorate of potash (5 grs. to the ounce), or better—

R	1.	2.
	Plumbi acetatis . . . ʒ j.	Aluminis sulph. . . ʒ j.
	Aquam, ad . . . ʒ v.	Aquam, ad . . . ʒ v.
	1 and 2 to be mixed and filtered.	

Or the gums may be painted two or three times a day with a solution of peroxide of hydrogen, or perhydrol, which is a 50 per cent. solution of peroxide of hydrogen, but which is quite non-irritating and most beneficial in keeping the gums healthy. Another excellent application in cases showing any tendency to pyorrhœa is powdered sulphate of copper applied to the roots of the teeth by means of a pointed stick or match. Should stomatitis of any severity occur, all mercury must be stopped, saline aperients freely administered, and a mixture of chlorate of potash (gr. xv) should be given three times a day.

Sweating should be induced by means of hot air or Turkish baths, and the patient kept as much as possible in the open air. The greatest attention must be paid to the teeth and gums in such cases, which latter ought to be painted frequently during the day with either perhydrol, solutions of chromic acid, or sulphate of copper.

Gastro-intestinal complications consist of pains in the stomach, colic, and diarrhœa; later on of dyspepsia and loss of appetite. Diarrhœa, although at first slight, may at times become very severe and assume dysenteric characters, with the passage of blood, slime, and mucus. A fatal result may follow. The gastro-intestinal disturbance is followed by anæmia, want of appetite, and emaciation.

METHODS OF ADMINISTERING MERCURY

Mercury is introduced into the system by different methods, the principal being—(1) by the internal or ingestion method; (2) by inunction; (3) by intramuscular injections. It is also administered by intravenous injection, by fumigation, by suppositories, and by inhalation with the aid of Wallender's bag.

The points to be considered in a choice of method are:

1. *Convenience of the patient.*—Which can be employed with the greatest convenience to the patient?

2. *Suitability to prolonged use.*—Which of them will best enable us to carry out the treatment over the lengthened period we know to be necessary to effect an eventual cure, or with a view to preventing future ravages of the disease?

3. *Regularity of treatment.*—Which of them will best ensure regularity of treatment?

4. *Rapidity of action in urgent cases.*—Which to adopt in severe cases of syphilis with urgent symptoms?

The Ingestion Method.—By the ingestion or internal method is meant the giving of mercury by the mouth, depending on the stomach and intestines for its absorption. It is the plan which even to this day is usually employed in British practice generally.

Before considering the technique of this method it will be well to see what are its advantages and disadvantages. First it is claimed that it is the easiest and most convenient method for the patient to carry out. Second, that it is free from certain dangers and inconveniences which are inherent in other methods—*i.e.* that it is much less likely to be followed by stomatitis, and that the latter when it does occur is far less severe than when produced by any of the other methods.

With regard to its being the easiest and most convenient method for the patient to carry out, in the writer's opinion, this will not hold ground at least with the plan of introducing mercury by intramuscular injections: surely an injection once a week is far preferable to being obliged to take medicine three, four, or perhaps five times a day for weeks and months at a time. As to stomatitis, this may be less severe than when it is produced by inunction or intramuscular injection, but it is none the less frequent—certainly not when compared with the intramuscular method.

The disadvantages of the ingestion method are: Firstly,

given in this manner there is no guarantee as to how much, if any, of the mercury is absorbed. Many cases are on record in which it has been shown that mercurial pills were passed through the intestinal tract unchanged in any way. One case is within the knowledge of the author of a patient taking grs. x of blue pill daily for a period of three months without any physiological effects having been produced. It was discovered later that the pills were regularly voided in the same condition in which they had been taken.

Secondly, sooner or later, in the majority of cases, mercury introduced by the internal method is more or less certain to produce gastric or gastro-intestinal irritation with all the concomitant effects—*i.e.* diarrhœa, debility, and anæmia. The mercury has to be withheld, and then the syphilitic virus gets the chance of reasserting itself. The third objection to the internal method is uncertainty as to its being carried out with anything like regularity, and this to the author's mind is the chief objection to the method.

The uncertainty as to regular administration may be due either to the patient's absentmindedness in forgetting to take his medicine, or, on the other hand, to his deliberately giving it up on the disappearance of active symptoms. To put the matter plainly, it is easy for the medical man to sit down and write a prescription for mixtures, pills, or powders, with instructions to his patient to take one of them three or four times a day for months at a time; but it is quite another thing to expect these instructions to be carried out with anything like regularity.

The conscientious patient, with the best intentions possible of adhering strictly to his instructions, places his medicine each morning in his pocket with the intention of taking it during the day; how often, when the end of the week comes, can he look back and say he has taken it regularly during every day of the week? Yet to be of any use we know that regularity in taking the mercury is an absolute necessity. On the other hand, the ordinary patient approaches the matter in a different spirit, and deliberately gives up his mercury as soon as the activity of the disease has ceased for any time.

Technique of the Ingestion Method.—In considering the technique of the internal method it is needless to say that the preparations of mercury used are innumerable. Here it will suffice to mention the chief of these mercurial compounds :

1. Metallic mercury, which is administered in different ways, and enters into some of the most famous preparations—*i.e.* “blue pill” :

R	Purified mercury	5 grms.
	Powdered liquorice	2½ ”
	Confection of roses	7½ ”

Divide into 100 pills, each containing 5 centigrams of mercury.

“Sedillot’s pills” :

R	Mercurial ointment	30 grms.
	Powdered soap	20 ”
	Powdered liquorice	10 ”

Misce et div. in pil. xx.

English "grey powder":

R	Mercury	1 part.
	Powdered chalk	3 parts.

This last is of all preparations of mercury the favourite one in England in the treatment of syphilis.

2. Calomel is not used very extensively internally, owing to its liability to bring on diarrhoea and stomatitis; it is chiefly given in the form of "Plummer's pills."

3. Biniodide of mercury is a very toxic agent, but is sometimes employed in conjunction with iodide of potassium.

4. Tannate of mercury "is not a definite compound," and in spite of the advantages claimed for it is not to be recommended.

5. Salicylate of mercury.

6. Proto-iodide and sublimate have proved the best and most reliable of all mercurial remedies given internally. Perchloride of mercury (corrosive sublimate) has been and is most popular in England. Among other celebrated preparations of which it is the basis Dupuytren's pills are perhaps the most famous. The formula is as follows:

R	Perchloride of mercury	cg. j (gr. $\frac{1}{6}$)
	Ext. of opium	cg. ij (gr. $\frac{1}{3}$)
	Ext. of guaiacum	cg. iv (gr. $\frac{2}{3}$)

It also enters into a very celebrated French preparation which is still extensively used in that country—viz. Van Swieten's liquor.

R	Bichloride of mercury	1 grm.
	Alcohol (90 per cent.)	100 grms.
	Distilled water	900 „

The strength is 1 in 1,000, so that each tablespoon contains exactly $1\frac{1}{2}$ cg. of corrosive sublimate. This preparation ought to be taken well diluted, and is best given in milk.

Van Swieten's liquor has not the same formula in all countries. Thus the French liquor is stronger than that of the Spanish pharmacopœia, and weaker than the English.

Sublimate also forms the basis of various other preparations: *e.g.* Hoffman's pills, which are composed of sublimate, distilled water, and breadcrumbs; Chomel's pills, consisting of equal parts of sublimate and extract of opium ($\frac{1}{2}$ cg. in each pill); and Baron Larrey's syrup, composed as follows:—

R	Sarsaparilla	} 500 grm.
	Guaiacum	
	Sassafras	
	Senna	
	Chiretta root	
	Elder	
	Bichloride of mercury	} āā cg. xxv.
	Ext. opii liq.	
	Hydrochlorate of ammonia	

Fournier suggests the following modification of Dupuytren's pills:—

R	Bichloride of mercury	} āā cg. j (gr. $\frac{1}{2}$)
	Ext. of opium	

for one pill, as containing less opium. These pills are best taken during or before meals.

Proto-iodide of mercury is a salt of greenish yellow colour, changing with the light, almost insoluble in water,

and insoluble in alcohol. It was introduced into therapeutics by Biett, and popularised by Ricord, whose celebrated pills have the following formula :—

R	Proto-iodide of mercury	.	.	gram. iij
	Ext. of thebain	.	.	„ j
	Theriaca	.	.	„ iij
	Confection of roses	.	.	„ vj
	Misce et div. in pil. lx.			

Each pill contains $\frac{1}{20}$ gram. of the proto-iodide.

There can be no doubt that for ingestion purposes corrosive sublimate and the proto-iodide are the best mercurial preparations to use. In France the proto-iodide is the most popular, whereas the perchloride is given the preference in England.

Both sublimate and the proto-iodide are excellent in their way, but one or the other may be more suitable under certain conditions: thus, proto-iodide is more likely to be followed by salivation than sublimate, which is probably the result of the proportionally larger dose of the former which is necessary in order to bring about physiological effects than is required in the case of sublimate.

Thus proto-iodide must be considered a salivating remedy, with a view to guarding against the occurrence of affections of the mouth which may result from it. No doubt it is less salivating than calomel, and also than mercurial inunctions; but it is salivating to a certain extent, which is the principal objection to its use, and it will be of the greatest importance to arrive at a more or less definite conclusion as to what is the buccal

tolerance dose of this remedy. With regard to the degree of buccal tolerance, excluding individuals with idiosyncrasies towards intolerance, there is a marked difference in the two sexes: a woman's mouth tolerates the proto-iodide much less than a man's.

For men we may say that a daily dose of $\frac{3}{4}$ gr. is absolutely inoffensive, and that in nine cases out of ten a dose of $1\frac{1}{2}$ gr. is tolerated without evil effect, provided that the mouth is in good order and is kept so during treatment.

It may be considered that a daily dose of $1\frac{1}{2}$ gr. of proto-iodide is the average dose of buccal toleration in men. Of course, much larger doses, up to 3 grs., are sometimes well tolerated.

As regards the other sex, there are few women in whom the mouth tolerates without irritation a dose of $1\frac{1}{2}$ gr., with which dose stomatitis is nearly always imminent, and seldom fails to occur if treatment is continued. The average dose of buccal toleration can be put down as 1 gr. of the proto-iodide.

Action on the Digestive Organs.—In this respect there are notable differences between the two preparations under consideration.

In therapeutic doses sublimate affects the stomach rather than the intestine, rarely producing diarrhœa, whilst, even in moderate doses, it often disturbs the stomach, causing cramps, pains, and strange sensations, often of such severity that treatment has to be suspended for a time at least. These pains are known as "sublimate gastralgia." Women suffer in this respect much more

than men—so much so that it is questionable if some other preparation of mercury should not always be preferred to the sublimate in the case of women.

Sublimate is tolerated by the stomach if care be taken not to prescribe too large doses of it, and not to continue it for too long a period, for even when well tolerated by the stomach, this is only for a time, after which it causes harm. Clinical experience taught me that from three to four weeks was the limit of this period, hence I made a rule never to prescribe sublimate for longer than a month at a time.

The proto-iodide seldom or never affects the stomach in any way, but in nearly every case proto-iodide is followed by slight attacks of colic and diarrhœa when first given: this is called “premonitory diarrhœa”; it soon passes off, and no further trouble may be caused during a long course of the salt. On the other hand, some patients are troubled with sudden attacks of diarrhœa varying in intensity from those lasting a few hours to those resembling dysentery, and threatening to become permanent. If we desire to produce therapeutic effects of any intensity the proto-iodide is far preferable to sublimate, because to bring about the same results with the latter it would be necessary to raise its dose to a dangerous degree.

Sublimate hardly ever affects the intestine or brings on diarrhœa.

From what has been seen as regards these two salts, it is hard to give preference to one over the other. They are both excellent remedies, each having its advantages

and disadvantages. All that can be affirmed with regard to the choice of either of them is that, as a rule, the proto-iodide ought to be given in the early secondary, and sublimate kept for the later secondary and tertiary stages. Sublimate administered in the first stage of the disease only exercises on secondary lesions an incomplete action—that is, it only brings them to an end slowly, and often allows them to be reproduced. An undoubted advantage that proto-iodide has over sublimate is that it can be continued over a much longer period without causing any trouble. On the other hand, sublimate is preferable to proto-iodide in the later stages owing to its undoubted greater influence over the late lesions, also owing to its combining better with iodide of potassium, which is of importance.

The pros and cons as regards the employment of these two salts may be summarised as follows :

1. With sublimate there is little salivation, but gastric intolerance is very frequent.
2. Gastric disturbances are infrequent with proto-iodide, but stomatitis and intestinal troubles are often caused by it.

It is needless to observe that the choice of either of these salts will depend a great deal on the nature and condition of the case. Thus for patients with bad teeth sublimate should be the chosen salt ; whereas in those inclined to suffer from dyspepsia and gastric troubles proto-iodide should be selected.

As to the best forms to order : sublimate is usually prescribed in solutions or in pills. A favourite solution,

especially in France, has been and is Van Swieten's liquor, whilst in pill form Dupuytren's pills (p. 118) are much in favour. As an improvement on that formula Fournier suggests the following :

R	Bichloride of mercury	.	.	} āā 1 cg. (gr. $\frac{1}{2}$)
	Extract of opium	.	.	

As a mixture, sublimate is generally ordered either in water or some tonic infusion. A stock mixture, which is a favourite one in English practice, is one containing liq. hydrarg. perchl. and iodide of potassium, and this is given for unlimited periods; but the less said about such a practice the better, except to condemn it freely.

Owing to its insolubility the proto-iodide can only be ordered in the form of pills, those of Ricord being still ever popular; but here again as an improvement Fournier suggests the following :

R	Proto-iodide of mercury	.	.	5 cg. ($\frac{5}{8}$ gr.)
	Extract of opium	.	.	1 „ ($\frac{1}{6}$ „)

as containing less opium than the original, and as affording greater scope for increasing or lessening the dose. A drawback to both Dupuytren's and Ricord's pills is that they contain opium, which is to my mind a mistake. Since opium has no curative action, what advantage is there in systematically combining it with mercury, and very often for the whole duration of the treatment? Personally I think it should only be added when required.

Dosage.—With regard to dosage it may be taken for granted that the dose of mercury ordered is, in nine cases

out of ten, lower than that consistent with the physiological effects which are necessary. This is generally the result of timidity—in other words, having to keep on the right side, which leads to insufficient treatment. It becomes all the more needful, then, for each individual case of syphilis to be studied separately, with a view, if possible, of arriving at some idea as to what dose can be ordered with safety—a dose which at the same time will be large enough to exert its full therapeutic effects. It may truly be said that no two cases of syphilis stand mercury alike, more especially when given by the internal method. It is almost impossible to lay down a rule as to what is the dose of either the bichloride or proto-iodide; it can only be surmised. As regards sublimate it can be considered as gr. $\frac{1}{2}$ daily for a man and gr. $\frac{1}{3}$ for a woman; the dose of proto-iodide, as already stated, is gr. $1\frac{1}{2}$ daily for a man and gr. 1 for a woman. These are the average doses, but the average dose is not always the most efficacious: not all manifestations of syphilis are equally influenced by the same dose of mercury. There are some which disappear with small doses, such as roseola or any of the generalised syphilides, while the same doses would have no effect whatever, on, for instance, cerebral syphilis. Again, it must ever be remembered that subjects respond differently to mercury, some to doses of the drug which would be too small to have the slightest effect on others, so that in giving mercury it behoves us to find out what is the “dose for the patient.”

Remarks on the Internal Method.—Personally, my experience of treating syphilis by the ingestion plan ex-

tended over a good many years, during which time I made use of most of the preparations above described. I found that, in the majority of cases thus treated, after mercury had been administered for a period of, say, a month or six weeks, it began to disagree in one way or the other. In some cases stomatitis appeared, the digestive system became impaired, and as a consequence the general condition of health began to suffer, a condition of malnutrition resulted, and the disease either remained *in statu quo*, or else further and worse outbreaks of it occurred; and in either case the drug had to be discontinued for a time at least. This same series of events went on, the patient gradually drifting into a chronic syphilitic state; he never got a chance of anything like a continued treatment, and consequently never got cured. Another lesson I learnt—that with this plan of treatment there was no certainty of the patient getting his medicine with any regularity; on the contrary, I had reason to suspect, and afterwards found out, that in the majority of instances this was the case, and in a great many the medicine was dropped altogether. The fact is, that as the taking of the medicine depends absolutely on the patient himself, he at times inadvertently forgot to take it; and if by chance he happened to be careless, he dropped it altogether when no urgent symptoms were present. This objection seemed to me to be so serious and insurmountable, as to be quite sufficient to put the ingestion plan of giving mercury out of court.

A third objection is that years ago clinical observation led me to suspect that in a great many cases treated by

this method, after the mercury had been taken for any length of time, the organism became as it were inured to it, and the drug apparently lost all its physiological effects; while in other cases it undoubtedly passed through the system unabsorbed.

CHAPTER XI

TREATMENT OF SYPHILIS (*continued*)

INUNCTION

The External or Inunction Method.—This is the oldest known method of administering mercury. It was employed in the fifteenth century against the ravages of what was called “mal français,” or the “new disease,” and is mentioned by Fracastor in his poem on syphilis. Popular before all other methods of giving mercury, the inunction plan, through the reckless manner in which it was carried out, gradually lost caste, and eventually died out. The reaction against it reached its highest point during the Peninsular War. Gaspard Torella, writing in 1497, says, “Avoid, like the plague, these murderous ointments which already have made so many victims ; it is they that killed Cardinal Segube, whose brother also owes his death to these ointments.”

The old plan of inunction consisted not only in a series of rubbings with mercurial ointment, but in addition purgation, bleeding, overheating, and dieting to the point of inanition ; these conditions were supposed to be absolutely necessary, as also was the production of stomatitis.

Here is a description of the inunction method as then carried out, in the words of Ulrich van Hutten (1488—1523): "Some used these anointings once a day, some twice, others three times and four times; the patient being shut up in a stove with continual and fervent heat some twenty, some thirty whole days; some laying in bed within the stove with many clothes, being compelled to sweat. Part at the second anointing began to faint; yet was the ointment of such strength that whatsoever distemper was in the upper parts it drew into the stomach and thence to the brain; and so the disease was voided both by the nose and mouth, and put the patient to such great pain that except they took good heed their teeth fell out, and their throats, their lungs, with the roofs of their mouths were full of sores; their jaws did swell, their teeth became loosened, and a stinking matter continually was voided from these places. What part soever it touched the same was strait corrupted thereby, so that not only their lips but the inside of their cheeks were grievously pained, and made the place where they were stink abominably; which sort of cure was indeed so terrible that many chose rather to die than to be eased thus of their sickness. Howbeit scarce one sick person in a hundred could be cured in this way, but quickly after relapsed, so that the cure held out but for a few days."

And in a later period Syme says as regards this form of administering mercury, "And the solitude of the syphilitic ward was only broken by the noise caused when the last tooth of one of the patients fell upon

the floor." The patients undergoing treatment as above described soon became debilitated and emaciated; some were reduced to a state of syncope, which, however, was regarded as a favourable sign; they were advised "not to become discouraged, and to look forward to an early cure."

Such treatment naturally caused severe salivation, but this was looked upon as being necessary, and the more profuse the salivation the better the outlook was; it was believed that the disease was evacuated by the mouth.

Fracastor exhorted his patients thus: "A truce to the disgust which this medication may inspire in you, for this is the price of your cure. Therefore spread this ointment on your body, and cover the whole skin, except the head and the region of the heart, with it. Bear this ordeal for ten days, the benefit of which will soon be felt. Soon, in fact, an infallible omen will announce the hour of your deliverance. You will soon feel the ferments of the disease dissolve in your mouth by an unclean slime, and you will see the virus evacuated at your feet in the saliva." The amount of salivation thought to be necessary was one which produced five or six pounds of saliva in twenty-four days, but the famous Dutch physician Boerhaave considered that a hundred pounds should be produced in thirty days.

Is it surprising, then, that under the above circumstances the inunction method became unpopular and fell into disrepute? It died out altogether, to rise again under happier auspices, and to become re-established in popularity. The methods of inunction to-day are very different

from those of yore. They simply consist of a certain amount of rubbings with a mercurial ointment of a known strength, combined with mild diaphoresis, good diet and hygiene, with a total absence of the purging, bleeding, and profuse sweating and salivation which had hitherto been considered necessary. However, popular as the inunction method became on the continent of Europe, it never appears to have attained the same repute in England even down to the present day, and this in the face of the teachings of some of her most famous syphilologists, notably John Hunter, who says: "When mercury can be thrown into the constitution by the external method it is preferable to the internal, as the skin is not nearly so essential to life as the stomach."

The main reason why the plan never became popular in England was, I believe, due to the ignorance that existed as regards its necessary technique; and it has always been an enigma to me why England has not taken example in this matter from Aachen (Aix-la-Chapelle), for there during the last century and a half the inunction method has flourished in the most successful way. Every nation has benefited more or less by it—none more so than England, for from this country syphilitic patients have gone to this place year after year, cases in which home treatment had signally failed, to return after a sojourn of a couple of months much improved.

MODERN TECHNIQUE OF THE EXTERNAL METHOD

This can best be given by describing the manner in which it is carried out at Aix-la-Chapelle, for there, as already said, it has been done for the last century and a half in such a thorough way as to make the place famous throughout the world as a resort for the successful treatment of syphilis, and to have led to hundreds of patients flocking there to receive that alleviation from their disease which they had before failed to obtain from perhaps one or two years of sporadic courses of treatment by the internal method. The routine treatment at Aix-la-Chapelle (Aachen) is as follows :

(1) A visit to a physician, who examines, weighs, and records case.

(2) The patient rises early each morning, goes to one of the mineral springs, where he partakes of one or two glasses of the sulphur water.

(3) Breakfast, consisting perhaps of one egg, bread, butter, and coffee.

(4) One or two hours later the patient proceeds to one of the many baths, and there has his bath, which consists of the natural sulphur water at a temperature of 39° C. In this he remains from twenty-five to thirty minutes ; when he leaves it he is well dried.

(5) Half an hour afterwards a professional rubber rubs into the patient's skin 75 grains of a mercurial ointment about the same strength as our Ung. hydrarg. (B.P.). Each rubbing lasts from fifteen to twenty minutes. To avoid

the effects of the friction caused by these rubbings, such as dermatitis, etc., the parts so rubbed are changed daily :

- 1st day, the arms ;
- 2nd day, the forearms ;
- 3rd day, the chest ;
- 4th day, the back ;
- 5th day, the thighs ;
- 6th day, the legs ;
- 7th day, the sides of the chest and loins ;

and on the eighth day the arms again, and so on, in rotation.

Composition of the Aachen Water.—The water from the Aachen springs contains from 22 to 28 grammes of chloride of sodium, 4 to 5 grammes of sulphates, and 8 to 12 grammes of carbonates in 10,000 c.cm., and their range of temperature for therapeutical purposes is from 38° C. to 72° C.

Gaseous Constituents.—Gases absorbed in water :

Nitrogen	9'00
Carbonic acid	89'4
Carburetted hydrogen	0'37
Sulphuretted hydrogen	—
Oxygen	1'23
							<u>100'00</u>
Nitrogen	66'98
Carbonic acid	30'89
Carburetted hydrogen	1'82
Oxygen
Sulphuretted hydrogen	0'31
							<u>100'00</u>

Total volume of absorbed carbonic acid, free and partly combined carbonic acid, 251'5.

The advantages claimed for these waters are that, since in the administration of mercury, remedies are required which will influence the whole organism as well as its individual parts, and thereby favour the general nutrition, the circulation, and the glandular activity, the water of Aachen fulfils these requirements in every way. In the first place, the drinking of 800 to 1,000 grammes of the sulphur water daily improves the appetite, increases the excretion of the kidneys, and regulates the bowels. The regular action of the bowels is maintained in almost every case, thus inflammation of the intestines consequent on the use of mercury is avoided.

The warm baths, on account of the quantity of soda which they contain, greatly facilitate the proper cleansing of the skin from excessive or diseased deposits from the epidermis and glands. By its warmth the water makes the skin pliable, opens its pores, and increases its normal action by stimulating the circulation. As a result, absorption and chemical transformation of the mercury in the ointment are facilitated.

Mode of Action of Inunction: How does Mercury penetrate the System?—The fact of absorption of mercury by the skin is proved in three ways: (1) by the appearance of mercury in the urine; (2) by the occurrence of the physiological effects of mercury, especially stomatitis; (3) by the production of therapeutic effects, which are often intense.

There are four theories as to the manner in which mercury penetrates the organism: (1) mechanical penetration in a state of fine division; (2) absorption in the

form of vapour ; (3) absorption by the hair follicles and sweat glands ; (4) some authorities maintain that mercury does not penetrate the skin at all, but is inhaled after volatilisation on the skin.

The majority of observers nowadays agree that most of the metal penetrates through the skin, only a small amount entering by the lungs. The idea that the curative action of inunction is due to the volatilisation of the mercury and its absorption by the lungs is based on the fact that mercury is much more volatile than was formerly supposed. However, if the mercury were absorbed by inhalation, hospital patients who are not taking mercury, and most certainly rubbers, would be mercurialised ; but this is not the case. It may be taken for granted that the amount of mercury which is absorbed by inhalation is but a negligible quantity.

Mercurial Ointments for Inunction. — In Aachen, generally speaking, the ointment used is the Ung. hydrarg. (G.P.).

Sometimes mercurial soaps are used, but these have the disadvantage of requiring a considerable time for absorption. On the other hand, they are said to be cleaner and also less irritating.

At the Military Hospital, Rochester Row, the following is the ointment used :

R

Ung. hydrarg.	50 grs.
Lanolin hydro.	25 „
Adipis benzoin.	25 „

Divide into two parts, and wrap in waxed paper.

Dosage.—No rules can be laid down as to the actual dose of ointment, as this depends on various factors, chief among them being the degree of tolerance of the patient. The average dose for an adult is ʒj, and this can be increased to ʒij, according to the tolerance of the patient. A somewhat smaller dose should suffice for a woman; in the case of an infant 15 to 30 grs. may be considered a safe dose.

The best time for inunction is the morning, as the movements caused by exercise favour absorption.

Mode of Rubbing.—The part rubbed on one day is not scrubbed until the morning prior to its being again utilised. The rubbing should, when possible, be carried out by trained rubbers; the rubbing should be done slowly, evenly, and with a good deal of pressure. The part, after being rubbed, if properly done, ought to look as if blacklead had been used—shiny, but not greasy. Each rubbing should last from fifteen to twenty minutes.

Effect on Rubbers.—It would be expected that the rubbers might be injuriously affected from inhalation or absorption of mercury, yet this is not the case; the writer has never seen any ill results to rubbers, although following the custom at Aachen, where no artificial protection to the hands is used. At Wiesbaden and other places glass balls and slabs are used in rubbing, but the experience at Aix, which coincides with that of the author, is that the rubbing can be done much more efficiently with the bare hand.

Number of Rubbings.—A course of rubbings at Aix lasts generally six weeks, during which period some forty

rubblings are administered ; but in England I think that thirty ought to be the maximum number, the greater number being permissible in the former case owing to the tolerance which is brought about by the use of the natural water, which of course is unobtainable for bathing purposes away from Aix. In my opinion all rubblings ought to cease after a maximum of thirty, followed by a rest of at least two months prior to a fresh course being commenced.

Necessary Precautions.—During a course of inunction, and for some time after, the greatest attention should be given to the hygiene of the mouth : the patient must be instructed to look to the state of his gums and the cleanliness of his teeth, and the latter should be well brushed after each meal with a fairly soft tooth-brush ; as a matter of routine some astringent mouth-wash should be used frequently during the day : a favourite one which is used at Rochester Row is—

Rx

Aluminis sulph.	. ʒ j.	Plumbi acetas	. ʒ j.
Aqua	. ʒ v.	Aqua	. ʒ v.

Mix and filter.

Should the gums show any tendency to soreness they may be painted two or three times a day with perhydrol or a solution of peroxide of hydrogen.

Diet.—The diet should be generous, the patient being told to live well and to drink freely of new milk. Spirits should be forbidden, but beer, claret, and hock allowed in moderation.

Exercise.—Exercise in the open air is to be very much encouraged; patients undergoing inunction should live and sleep in large, well-ventilated rooms.

Advantages of Inunction.—The advantages claimed for the inunction method are:

1. Therapeutic effects are far more marked than when the drug is given by the mouth. Undoubtedly in many cases inunction brings about a cure in which other methods failed; especially is it useful in all syphilitic sclerotic affections, such as the primary induration, sclerotic glossitis, and tabes, etc., in which cases, although the usual dose of the mercurial ointment may have to be raised, it very often proves most beneficial.

2. It does not affect the alimentary system. There is no doubt that mercury when administered by the skin, very rarely affects the digestive system, at any rate not nearly so frequently as when introduced by the ingestive plan. Valuable as this is in any case, it is much more so in the case of dyspeptic subjects, in those liable to diarrhoea, in subjects in whom it is important to support the general condition, and in infants and young children.

3. It leaves the stomach free for the administration of other remedies. This is certainly a great boon, for whilst the specific treatment is going on other remedies may be used, such as iodide of potassium, cod liver oil, tonics, etc.

Disadvantages of Inunction.—1. Treatment by the inunction method can only be of a very intermittent kind, which is opposed to our judgment as regards ultimate cure and prevention. What is meant by this

is that the courses of rubbings cannot be continued long enough, nor resorted to frequently enough, to enable us to carry out the chronic intermittent treatment.

2. It is very frequently followed by severe stomatitis, and often by diarrhœa and dermatitis. Although as a rule mercury when administered by the skin does not affect the alimentary canal, still at times it does so, causing pain, colic, and diarrhœa. Dermatitis is more common, and is usually limited to the sites of the inunction: it is in most cases the result of local irritation on a delicate skin, and in a few to some idiosyncrasy. In the former it generally occurs in the form of an erythema, either circumscribed or diffuse, whilst in the latter it may appear as an eczema, which consists in a deep red area of erythema covered with vesicles full of clear fluid which later on becomes turbid; this is accompanied by inflammation and swelling of the skin with heat and pruritus.

Stomatitis is far more common than diarrhœa or dermatitis; and it is certainly one of the chief objections to the inunction method that of all modes of introducing mercury into the system inunction is the most likely to cause stomatitis: some of the worst cases of this which the author remembers having seen occurred, either at Aachen or elsewhere, in patients whilst undergoing inunction. Moreover, the form of stomatitis resulting from inunction differs considerably from that produced by ingestion of mercury: it comes on more suddenly, without any warning; instead of beginning at some particular spot and spreading gradually, it is general and extensive from the first; it is more intense, salivation is considerable

and swelling of the salivary glands and ulceration of the gums are common.

4. It is dirty, inconvenient, and very difficult to have carried out with anything like efficiency under ordinary circumstances. That it is dirty goes without saying ; also it is undoubtedly inconvenient from two points—first because it necessitates the patient giving up at least an hour a day to it, and secondly it is compromising, as it stains linen, and servants and washerwomen soon get to know what is going on. These last objections may appear trivial, but they are not, as one soon finds out that for the efficient carrying out of the treatment the patient's feelings form an important factor. That it is difficult to have properly carried out is only too true, depending as it does on the capability and willingness of the rubber.

Conclusion.—Until recently I looked on the inunction plan as the most efficacious in removing certain signs and symptoms, and employed it extensively in cases such as for the removal of persistent induration at the site of infection, in all cases of syphilitic sclerosis, and in cerebro-spinal syphilis ; but at the present time intramuscular injections of calomel have quite taken the place of inunction in my practice when dealing with such cases, owing to its more rapid and intensive action.

The question to be considered is, whether the inunction method is suitable as a routine form of treatment, or whether it should be reserved for special cases ? As a routine treatment it is contra-indicated first because the treatment of syphilis is not a symptomatic one, but it

aims at extinguishing the virus both as a diathesis and as a possible source of future mishaps, which can only be realised by a treatment of long duration. It is obvious that the inunction method is not suitable for this purpose for certain reasons—*i.e.* it is open to accidents, as already seen, and is a method which is not easily carried out or agreeable to patients. For a treatment of long duration personal and social necessities must be taken into account, and from this point of view the inunction method is the most inconvenient. Undoubtedly if the patient tolerated inunction, and carried it out faithfully and regularly and for the whole of the necessary time, I am certain the result would leave nothing to be desired; but how often is such a patient to be found? As a routine practice the inunction method is to be condemned: it runs a very good chance of being badly performed; it may cause severe stomatitis; it is repugnant to the patient; it may end by discouraging and disquieting the patient with the treatment, and cause him to give up specific treatment altogether.

To my mind the inunction method should be reserved for particular cases: cerebral and spinal syphilis, cases which have proved refractory to other methods, cases of syphilis in the young; but, with the exception of the last, as already stated, even in these cases injections of calomel have taken its place.

CHAPTER XII

TREATMENT OF SYPHILIS (*continued*)—THE INTRAMUSCULAR METHOD

THIS method consists of injecting certain mercurial preparations into the muscles, with the view to their being absorbed by the circulatory system.

It was first suggested by Scarenzio, and was actively practised for a certain time: owing to certain accidents which appear to have almost invariably attended it, it had to be abandoned. The history of this method may be divided into three periods: (1) the period of Scarenzio; (2) the period of Smirnoff; (3) the period of Balzer.

The first period dates from 1864, when the treatment of syphilis by subcutaneous injections of calomel was introduced by Scarenzio, a professor in the University of Pavia. At first Scarenzio used yellow oxide of mercury, and later on, calomel; as an excipient glycerine was first employed, but being irritating, gum-water was afterwards substituted for it. He records having given eight subcutaneous injections of this, each of which was followed by an abscess. Ambrosoli of Milan published a series of sixteen cases, all treated by

the method recommended by Scarenzio, thirteen of which were followed by an abscess after each injection. Among the opponents of this method we find Professor Profeta, who writes of it: "I should never have recourse to the method unless all others failed, owing to the constant occurrence of abscesses at the site of injection." In spite of these accidents the method continued to be used in most of the capitals on the Continent, with varying fortunes in each country. In Italy, although it had some very enthusiastic exponents, its detractors numbered many men; among them, as already seen, was Profeta. Opinions concerning it were divided in France. At the St. Louis Hospital it was practised with much success by Hardy; and Liegois, substituting sublimate for calomel, was equally successful. On the other hand, Jullien was a strong opponent of the method. In England the system does not seem to have been practised at this period to any extent; indeed, there is little proof of its having been tried at all. In Germany and Austria opinions differed concerning it: we find Störk describing it as a "detestable" treatment, whilst Kölliker appears to have been in favour of it.

In three or four years the method had gradually died out, and we hear little of it until it was reintroduced by Smirnoff in 1882, in an interesting essay on the subject which was published in that year, in which he showed that with the help of antiseptic precautions, which by this time had become much better understood, injections could be given without the occurrence of abscesses. Smirnoff succeeded in reviving the subcutaneous method for a time; and

although abscesses became much rarer than formerly, still they were frequent enough to be the cause of the method becoming once more discredited.

For a third time it was reviewed: Balzer being the means of doing this in a paper which he read before the Société des Hôpitaux on May 11, 1888, entitled "Injections of Yellow Oxide of Mercury and Calomel in the Treatment of Syphilis," in which he explained that the chief causes of abscesses following the injections were because the latter were given into the subcutaneous tissue instead of into the deep tissues; secondly, owing to the unsuitability of the vehicles which had hitherto been in use. To remedy these defects he advocated deep injections into the muscles and the substitution of liquid paraffin as a vehicle for the mercury in place of gum-water, glycerine, and olive oil. These suggestions were followed by the best results, abscesses became rarer as time went on, and the intramuscular method became established in popular favour day by day until the present time, when it is certainly on the Continent the most popular mode of treating syphilis. Curiously it never seems to have been taken up in this country to any extent, and even in England to-day and in her world-wide Empire it is little known certainly amongst the civil medical profession. On the other hand, nowhere is the intramuscular treatment more popular than in the army, into which it was introduced in 1889, since which time it has been steadily gaining in favour among army surgeons. Brilliant results have attended its use, especially in India, where in the army the rates of invaliding and death from

syphilis have declined to about two-fifths of what they were prior to the introduction of the intramuscular method.

Advantages of the Intramuscular Method.—Like other methods of administering mercury, the intramuscular has its advantages and disadvantages, which must be carefully considered. Taking its advantages first, the following is a fairly complete list :

1. Convenience to the patient.
2. It insures regularity of treatment.
3. It leaves the stomach free for the reception of other remedies.
4. It ensures more accurate doses.
5. The absorption of mercury is much more certain.
6. It does not interfere with the gastro-intestinal system.
7. Less chance of toxic symptoms—stomatitis.
8. Both therapeutic intensity and physiological effects are much more marked and lasting.
9. It does not exaggerate the moral effect of the presence of syphilis upon the mind of the patient.

As regards convenience, I think it must be admitted that the only inconvenience which the intramuscular method entails is the occasional visit of the patient to his medical adviser to receive his injection; in the case where insoluble salts are used, there is an interval of at least a week and very often a fortnight: compare this with his having to take medicine three, four, or five times a day for months at a time, or with his being obliged to give up an hour or so a day for the purpose of inunction for periods varying from a month to six weeks.

There can be no question but that with the intramuscular method regularity and certainty of treatment is assured, and with it there is no fear of patients eluding such. This is a most important consideration, especially among hospital patients, who, owing to their horror of mercury, often do everything to try to avoid swallowing it.

The third advantage claimed for the intramuscular method—*i.e.* leaving the stomach free for the reception of other remedies and not irritating the digestive organs—is true; but the first part, avoiding the stomach, is not peculiar to it, as it is shared by the inunction method.

As regards accuracy of dosage, this is more apparent than real, for it assumes that the dose absorbed is always the same as that injected; and although I believe that in the majority of cases this is true, still it may sometimes be different—for instance, when the mercurial deposit becomes surrounded by inflammatory tissue, which prevents its absorption. Speaking generally, it will be allowed that, although not quite so accurate as is believed, the dosage of mercury given by injection can be gauged far more accurately than that given by either ingestion or inunction, for the reason that in the former case the dose of mercury which can reasonably be expected to be absorbed is known, whereas it is quite unknown in the case of ingestion or inunction. Absorption of mercury in a definite manner is ensured by the intramuscular method. Already we have seen that in the case of ingestion very little and sometimes no mercury may be absorbed; and by the inunction plan the amount of

absorption must of necessity be very uncertain, depending as it does, to a great extent, on the way the rubbing is done.

I have no hesitation in saying that the dangers of toxic effects are far less with the intramuscular method than with other plans, especially as regards stomatitis, provided the ordinary precautions are adhered to. I do not mean to assert that this never occurs; on the contrary, I have seen cases of very severe stomatitis following this method, although very rarely, and in my opinion in this respect it undoubtedly compares most favourably with the methods of ingestion and inunction.

All authorities, even those who oppose the intramuscular plan of giving mercury, are agreed as to its superiority in its therapeutic intensity and physiological effects on the symptoms of the disease. In this respect it has undoubtedly realised expectations; it is acknowledged on all hands to be a powerful form of mercurialisation, having an energetic action on most of the manifestations of syphilis.

With regard to the last advantage which I claim for the intramuscular method—*i.e.* its not emphasising the moral effect of the presence of syphilis on the mind of the patient—I would say that the mental condition ought to have a foremost place in our consideration. Those of highly-strung disposition are liable to suffer much from depression of spirits; the mere knowledge that they are infected induces in them a state of melancholy bordering on a condition known as syphilophobia, and this, in my

experience, is one of the greatest difficulties met with in treating syphilitic patients, especially among the educated and well-to-do classes.

The first thing to be done in such cases is to endeavour to divert the mind from the exciting cause. This we certainly do not do when treating the disease by either the method of ingestion or inunction, for when a patient has to take a pill, powder, or medicine three or four times a day, or to be daily rubbed, he is reminded each time of the "skeleton in his cupboard," whereas, whilst undergoing the intramuscular treatment, this reminder need only be given once a week, or even fortnight. This advantage may sound a trivial one, but I cannot lay too much stress on it, and I feel convinced that it has helped me over many difficulties; for with the mind depressed treatment of any kind is rendered all the harder to carry out to a successful issue.

The Disadvantages of the Intramuscular Method.—

The disadvantages of the intramuscular method are said to be the following :

1. Pain at the site of injection.
2. Nodosities and abscesses.
3. The occurrence of embolism.

Pain at the site of injection varies in different subjects and with the preparation of mercury used; it is, in fact, usually present when the soluble salts are employed; whereas, with the newer preparations of the insoluble salts, even calomel, it does not exist to any extent. I have met with two or three patients who complained of severe pain after injection, but those were neurasthenic

subjects, who would probably make a similar fuss if ordered to take medicine internally for any length of time. A few cases complain of slight, dull, aching pain, with some stiffness, lasting for one or two days; but the majority assert that pain either does not exist at all or is so slight as to be insignificant.

Nodosities and abscesses are things of the past, owing, no doubt, to improved technique. The former may certainly be sometimes seen even now, although very rarely. In former years I used to see them fairly often, but now they are very rare, this latter circumstance coinciding with the time I first began to use boiling oil as a steriliser for needles and syringes. In my opinion the occurrence of abscesses is due entirely to some neglect in carrying out the technique. As regards embolism, although cases are reported from time to time, I have never seen *one* in my long experience of this method.

The Two Methods of Intramuscular Injection.—The intramuscular methods are of two kinds—the frequent injection of soluble salts, and the infrequent injection of insoluble salts.

The method of frequent injections consists in a series of mercurial injections practised daily for five or six weeks. The preparations used for this purpose are nearly all soluble. The list of these preparations is innumerable, too long to produce here, also unnecessary; it will be sufficient to mention the principal:

Sublimate.

Double chloride of mercury and ammonium.

Peptonate of mercury.

Tannate of mercury.
 Cyanide of mercury.
 Biniodide of mercury
 Lactate of mercury.
 Urate of mercury.
 Benzoate of mercury.
 Acetate of mercury.
 Sozoiodolate of mercury.
 Succinimide of mercury.
 Chloro-albuminate of mercury.
 Alaniate of mercury.

All the above are mercury served up under different names, and from such a list of remedies it might be difficult to make a choice. However, the following are the forms in which they are generally prescribed :

℞ Hydrarg. perchloridi grs. iij
 Aquæ ʒj
 20 minims as a dose, by injection.

℞ Hydrarg. perchloridi grs. xxxij
 Ammon. chloridi grs. xij
 Aquæ ʒj
 Dose, 10 minims for an injection.

℞ Hydrarg. succinimate grs. ij
 Cocainæ hydrochloridi grs. iij
 Aquæ ʒij
 Dose, 10 minims for an injection.

℞ Hydrarg. cyanidi gr. j
 Cocainæ hydrochloridi gr. j
 Aquæ destil. ℥ 10
 Dose, 10 minims for an injection.

Peptonate of mercury is a solution in glycerine and water of a mixture of peptone, sublimate, and chloride of ammonium; it contains about one centigramme of bichloride in a centimetre of distilled water, and is said to be better tolerated than sublimate.

Benzoate of mercury is rendered soluble by chloride of sodium, and is prescribed thus for daily injection:

R Hydrarg. benzoat. }
 Ammon. benzoat. } āā gr. $\frac{3}{4}$
 Aquæ destil. ℥ iss

Biniodide of mercury oil was introduced by Panas:

R Hydrarg. Biniodide.
 Olei (sterilised).
 One c.c. contains $\frac{1}{16}$ grain of the biniodide.

Biniodide is an active and safe remedy, is well tolerated as an injection, and causes little pain or local trouble. Although an active remedy, it is one of only medium intensity, and in this respect cannot compare with either calomel or metallic mercury. The dose recommended (*i.e.* $\frac{1}{16}$ grain) is too small to produce therapeutic effects, for which purpose at least $\frac{1}{7}$ grain ought to be injected. The injections of biniodide should not be too concentrated; if so they are liable to produce much pain and nodosities.

Soziodolate of mercury is greatly prescribed for injection purposes, thus:

R Sod. iodi grs. x.
 Hydrarg. soziodol grs. v.
 Aquæ ℥ cc
 ℥ x to ℥ xii as an injection four or five times a week.

Like many of these preparations, when first introduced its praises were sung very loudly ; it was said to be a "perfect" remedy, free from any semblance of pain, and possessing rapid and powerful action in syphilis. When I was accustomed to use the soluble salts, I found it inferior to almost any of the other salts. Its therapeutic intensity appeared to be of the mildest kind.

Succinimide of mercury has also been highly recommended, and, indeed, it is freely used even now :

R	Hydrarg. succinim	grs. ij.
	Cocain. hydrochl.	grs. iij.
	Aquæ	℥ ij.

℥ x as an injection once daily.

Advantages and Disadvantages of Injection of the Soluble Salts.—Although at one time opinions were equally divided as to the merits of injection of the soluble salts of mercury and the insoluble, I think there can be little doubt that at the present time the advocates for the employment of the former are very few in comparison with those in favour of the insoluble salts. At the same time it cannot be denied that the daily injections of the soluble salts, especially of bichloride or biniodide, have a powerful anti-syphilitic action ; but there they end, as from the author's experience their curative or preventive action is very little. In other words, the soluble salts injected daily will remove the ordinary active early symptoms of syphilis, but have very little effect on lesions of the advanced stages ; and although one must never forget that recurrences may take place after the very best treatment, still it is an undoubted fact

that they are far more common after a course of the soluble salts than after one of inunction or injections of the insoluble salts. The real disadvantages of the method of frequent injections of the soluble salts are :

1. The injections are always more or less painful.
2. They are absorbed too rapidly, and, worse still, eliminated too quickly.
3. They require to be injected daily, or nearly so.

With regard to the pain, although this is never very great, still it is much more so than when the insoluble salts are used, and when I was accustomed to use these soluble salts I found that the pain they caused was a very great obstacle. As already seen, it has been claimed for some of these preparations that they cause little or no pain ; but this is not my experience, and I think I have employed most of them. That their absorption and elimination are far too rapid to have any lasting effect on the disease goes without saying, and this has become all the more apparent since the discovery of the *Spirochæta pallida*, which makes its reappearance very soon after the discontinuance of the injections.

The third disadvantage of the soluble salts is that to be effective at all they have of necessity to be injected daily, or very nearly so. From a practical point of view this is a great obstacle : in the first place, the patient not being able to give an injection to himself, it necessitates a daily visit to his medical adviser, which of itself is enough to condemn the method ; in any case, the vast majority of patients will object strongly to having an intramuscular injection daily.

In conclusion, I would say that, although formerly I believed that the frequent injections of the soluble salts were as good as, if not superior to, the insoluble salts in some few cases, time and experience have taught me that I was wrong, and I can honestly say that I do not know of any case in which they are not infinitely inferior to the latter, and that as a method of routine treatment they cannot be put on the same level.

THE METHOD OF INFREQUENT INJECTIONS OF INSOLUBLE SALTS

This method consists in a series of injections of insoluble salts of mercury at more or less long intervals. The rationale of such a method is based on our knowledge that, with a view to prevention and cure, syphilis is a disease which requires the administration of mercury for a period of at least two years intermittently, but in such a manner that the patient during the whole period is continuously under the action of mercury. Owing to their slow absorption and elimination, the insoluble salts are selected for this purpose.

Forms of Insoluble Salts used.—The two chief preparations of mercury which are used for carrying out the method of infrequent injections are metallic mercury itself and calomel, besides which, although not nearly so frequently employed, is salicylate of mercury. The insoluble salt originally used was the yellow oxide, which has long been superseded.

Metallic Mercury.—Metallic mercury for the treatment of syphilis by intramuscular injection was first intro-

duced by Lang, of Vienna. He brought it forward in the form of grey oil (*oleum cinereum*), which is a mercurial preparation consisting of mercury in a state of fine division, suspended in a liquid fat: it is a kind of liquid ointment, and contains 40 per cent. of mercury.

During the last five-and-twenty years the author has used metallic mercury in preference to all the other salts of the metal, such a preference being arrived at after ample opportunities of judging them side by side; and as years have gone on, and with increased experience, his faith has grown stronger than ever in it. To-day he maintains that, although its therapeutical intensity is certainly not so great as is that of calomel, its curative and preventive effects are far greater, and, as a consequence, that it easily holds premier place among the remedies for syphilis.

The Advantages of Metallic Mercury.—The advantages of metallic mercury are:

1. It is practically painless.
2. It is slowly absorbed and very slowly excreted.
3. It is less likely to produce stomatitis than other preparations.
4. It requires to be injected only at long intervals.
5. Therapeutic effects are far more lasting than those of any other preparation.

There is little doubt but that injections of metallic mercury are peculiarly free from pain as compared with those of other salts.

It is owing to the slowness of its absorption and elimination that metallic mercury is so superior in its lasting effects to the other preparations of mercury in the treat-

ment of syphilis; as a general rule it may be said that the preparations which are quickly absorbed are quickly eliminated. The rate of absorption of mercury given *per os* is uncertain; soluble salts of mercury given by injection are quickly absorbed and eliminated; salicylate of mercury is quickly absorbed and eliminated; calomel is slowly but powerfully absorbed, and eliminated fairly quickly; metallic mercury is very slowly absorbed and excreted.

The conclusion come to as regards the lasting effects of metallic mercury, has been further strengthened by observing the behaviour of the *Spirochaeta pallida* under its influence. At the Military Hospital, Rochester Row, it was found that, although those organisms disappeared with about the same rapidity under almost any form of mercurial injection, they reappeared at a much longer interval after the discontinuance of the metallic preparations than was the case under a similar discontinuance of any other form of mercury. This, needless to say, is a very important and significant fact, and a strong argument in favour of the metal itself in the treatment of syphilis.

Gagnière has studied the modifications in the blood caused by injections of metallic mercury, and has demonstrated that the corpuscles and the hæmoglobin increase after the second injection, and generally diminish after the fifth. It is accordingly indicated by him, not to give more than five consecutive injections.

With the single exception of calomel the therapeutic intensity of metallic mercury is greater than that of any other mercurial preparation; and, although inferior in this

respect to calomel, it is not only far better tolerated than that salt, but is far better than it as regards curative and preventive effects, which applies equally to all other preparations of mercury.

Clinical experience taught us that metallic mercury, by its slow absorption and elimination, is vastly superior to all other mercurial remedies in its lasting influence over syphilis—a lesson which the microscope and other bacteriological researches have confirmed.

It is needless to point out the very great advantage the insoluble salts have over the soluble—*i.e.* that it is only necessary to give injections of them at comparatively long intervals—at the most not oftener than once a week. This makes the plan less objectionable to the patient.

Preparations of Metallic Mercury.—As regards the preparations of either metallic mercury or of calomel, they must be homogeneous and capable of being injected, whilst at the same time they should be of such a consistence as to be able to hold the mercury in suspension. They should be non-caustic, unirritating, and sterile; they should not enter the organism as a foreign body, and should be chemically pure.

The preparations of metallic mercury which have been introduced from time to time have been numerous. Lang has modified the formula of his original “oleum cinereum” several times, the latest being:

R

Metallic mercury	2 parts
Sterilised anhydrous lanolin	1 part
Sterilised liq. paraffin	1 „
50 per cent. of mercury. Dose gr. $\frac{2}{3}$ of mercury.	

Lafay's formula :

R									
	Metallic mercury	40 parts
	Sterilised anhydrous lanolin	12 „
	Sterilised white vaseline	13 „
	Sterilised oil of vaseline	35 „
	40 per cent. of mercury. Dose gr. 1 to 2 grs. of mercury.								

Author's (original formula) :

R									
	Pure metallic mercury	3 j
	Anhydrous lanolin	3 iv
	Liquid paraffin (carbol. 2 %) ad	3 x
	By volume 10 per cent. of mercury. Dose 10 to 15 minims.								

The last is the mercurial cream which has been in use throughout the British Army both at home and abroad during the past ten years ; and although, generally speaking, it has given great satisfaction and has yielded brilliant results, I have always been conscious of a grave objection to which it, as well as all other preparations of the insoluble salts, was liable : it is, that, owing to the substances which have been employed in them as vehicles for the suspension of the mercury being *insoluble in the organism*, they entered the circulation as *foreign bodies*, and as such might possibly produce nodosities, abscesses and embolism. To overcome this grave objection had for years been my endeavour, until I eventually attained my object by substituting "palmitin" as the vehicle in place of lanolin.

Palmitin¹ is a neutral fat derived from palm oil, having

¹ In Stirling's work on Physiology, p. 29, it is stated that neutral fats of adipose tissues of the body generally consist of a mixture of stearin, olein, and palmitin. Prof. Halliburton, in "Essentials of Chemical Physiology," p. 15, states that the fat cells are composed

the same chemical composition as the palmitin of the human system. It is an ether glycerine of palmitic acid, is therefore easily saponified in the fluids of the organism, being converted into a soluble alkaline palmitate and glycerine, and thus it enters the circulation *not as a foreign body*, like all substances hitherto employed as vehicles. The advantages claimed for palmitin as a vehicle are :

1. It is non-irritant and non-toxic.
2. It is not so easily oxidised as the other compounds of human fat.
3. Being already a normal constituent of the human organism, it is easily saponified and soluble therein, and *does not* enter the circulation as a foreign body.
4. As a vehicle it makes a more homogeneous preparation for injection purposes than any other.
5. Its melting-point can be raised or lowered with the greatest facility.

Pure palmitin (which is the only preparation used) is a snowy-white flocculent powder, and great care is necessary to get it pure.

Analgesia.—The question of pain, although never amounting to anything serious so far as metallic mercury is concerned, still has been sufficient to constitute a grave objection to the practice of intramuscular injections of mercury, and is apt to bring about, what Fournier terms

of three different fats called palmitin, stearin and olein. Charles, "Physiology and Pathology," p. 84, says, palmitin is more abundant than stearin in human fats, and is the chief component of most animal fats.

"fear of the needle," with consequent desertion and non-attendance for further injections on the part of patients; in the case of calomel pain used to be the *chief objection* to its use for injection purposes.

With a view, if possible, to abolish pain altogether after injections, various substances have been introduced from time to time into the mercurial preparations used for that purpose—*i.e.* morphia, cocaine, β -cocaine, etc.; these, acting as they do almost at once, will assuage any pain which may follow immediately after the injection. But unfortunately, this is not the kind of drawback we have as a rule to deal with, as the pain which troubles us is one which comes on the second or third day after the injection, when all local anæsthetics like the above are useless. This is a very serious matter, but more so as regards injections of calomel, for the pain is most marked and severe with this drug. The consequence was that hitherto, not being able to cope with it, injection of calomel had to be abandoned and only resorted to in some grave case where pain was a matter of secondary consideration; thus perhaps our strongest weapon for dealing with syphilis was practically lost to us.

To obviate this pain, I added to my latest mercurial preparation equal parts of absolute creosote and camphoric acid—a combination which has proved altogether a complete success, as it renders the injections even of calomel quite painless. This combination of creosote and camphoric acid possesses other attributes: *i.e.* it is non-toxic, strongly antiseptic, and, being viscid, is a valuable adjuvant to the palmitin in making up a homogeneous vehicle.

The following is the formula for the metallic cream :

R	Hydrarg. pur	10 grms.
	Creo-camph. ¹	20 c.c.
	Palmitin bases ad	100 c.c.

m x contain 1 grain of metallic mercury.

The greatest care ought to be exercised in seeing that the cream is of proper consistence. It should be kept in wide-mouthed glass bottles, and only removed from them when required for injection purposes. No attempt should be made to sterilise the cream, as it is already sterile;² before use it should be well stirred up with a glass rod. In cold climates the cream is liable to become semi-solid, and it may require slight heating in a warm-water bath; in the tropics the reverse occurs, and there the bottle containing the cream should *always* be kept in an ice-chest until it is required for use, when it can be transferred to some crushed ice.

It is advisable that the melting-point of this cream should be regulated to suit the climate. In the case of the cream used in England at present, we find 35° centigrade the best; in the creams sent to the tropics, it is raised by 3° centigrade.

Disadvantage.—Metallic mercury has only one real disadvantage, which is, that should salivation take place after an injection it is a difficult matter to prevent matters getting worse, unless the mercury can be removed by

¹ Equal parts of absolute creosote and camphoric acid.

² Leishman reports that "this preparation is sterile and bacteria will not grow in it."

operation. I have never seen a case requiring so severe a measure, and cannot help thinking that the reported cases were the victims of too large a dose; so long as the latter does not exceed $1\frac{1}{2}$ gr. per week these cases will not occur.

Calomel.—Calomel has long ago proved itself to be the most potent salt of mercury in its power over syphilis in all its stages. It is more active and energetic than any other preparation of mercury, acting promptly in acute cases, as well as clearing up old-standing ones.

In spite of this, as already stated, owing to the pain which followed calomel injections, it has been limited to the treatment of certain special cases.

This pain at times was almost intolerable, and at one period I used to give injections of calomel with much hesitation, reserving them for exceptional cases where symptoms were of such urgency that pain could not be taken into account. However, by the help of the combination of creosote and camphoric acid (already described) the pain has been entirely overcome, and for the past three years I have been using calomel with impunity.

The following is the formula for calomel cream :

R	Calomel purified	5 grms.
	"Creo-camph." ¹	20 c.c.
	Palmitin bases ad.	100 c.c.

℥ x equals calomel $\frac{1}{2}$ gr. Dose ℥ x to xv per week.

Calomel and Metallic Mercury.—It has been observed long ago by others, as well as by the author, that the action of calomel on syphilis, although remarkably

¹ See footnote, p. 161.

energetic and rapid, is short-lived when compared with that of metallic mercury. Hence it will never take the place of the latter in the routine treatment of the disease, but will be reserved more for dispersing early symptoms and signs of the disease, and for those cases where symptoms call for rapid action, *i.e.* cerebral and spinal syphilis, etc. Even in such cases metallic mercury will have to be reverted to, to effect a permanent alleviation.

CHAPTER XIII

TECHNIQUE OF THE INTRAMUSCULAR METHOD

THE technique of the intramuscular method of introducing mercury into the organism is simple, but the following rules concerning it, although some may appear too insignificant to be remembered, are all of the greatest importance, and should be strictly adhered to.

Instruments.—1. The syringe should be all glass, so that it can be sterilised throughout.

2. The needles must be of either platino-iridium or gold : maximum length $1\frac{1}{8}$ in.

3. The points of the needles to be kept as keen as possible, to facilitate penetration and thus lessen pain.

4. Steel needles not to be used, as they are apt to snap.

5. Both needles and syringe to be thoroughly sterilised in oil heated to 160° F.

6. "Injections to be given into the muscles," and not subcutaneously.

7. The skin over the site of injection to be swabbed over with some antiseptic solution prior to puncture.

8. A cloth, wrung out of carbolic acid solution 1 in 20, to be spread on a table to lay the syringe on.

9. No cotton wool or anything "fluffy" to be brought near or used to wipe the needles, pieces of sterilised linen or gauze being used for this purpose.

10. The best sites for injection are (1) upper third of buttock; (2) the retro-trochanteric fossa; (3) the lumbar muscles.

11. The operation of injection to be completed in one stage.

12. In the case of the insoluble salts of mercury injections should be given at most once a week.

Salicylate of Mercury.—The salicylate of mercury is used on a large scale on the Continent, especially in Germany. For some time I employed it fairly extensively, giving $\frac{1}{2}$ gr. suspended in liquor paraffin, twice a week, but on the whole found it very inferior to either mercury or calomel.

SOME POINTS TO BE CONSIDERED IN THE TREATMENT OF SYPHILIS BY THE INTRAMUSCULAR METHOD

As to dosage, no definite rule can be laid down, for, as already pointed out, each patient tolerates mercury to a different degree. What the latter is can only be arrived at by a personal study of each individual case; hence the great necessity of treating cases on their merits.

The following circumstances govern, to a great extent, the dosage:—

1. The type of syphilis: as pointed out, the dose of mercury which will dissipate an ordinary roseolar rash

will probably have no effect on a papular or pustular eruption.

2. The condition of the patient: a strong, healthy individual will, as a rule, require a larger dose than a weakly one.

3. Cases of "malignant" or "virulent" syphilis require smaller doses than ordinary ones.

Maximum Dose.—Of the metallic mercurial, I find that the maximum dose should not exceed $1\frac{1}{2}$ gr., or \mathfrak{m} . xv of the cream. I get far better results using this reduced dose than I formerly did when employing the larger ones. The fact is, that under large doses of mercury the blood after a time deteriorates, but that when smaller doses are given the metal acts as a blood tonic.

The maximum dose of calomel which I give is $\frac{3}{4}$ gr. (\mathfrak{m} xv of the calomel cream); this is given once a week, and is seldom continued longer than the fourth injection, when metallic cream is resorted to.

Treatment should be of an intermittent character—that is, injections should be given in courses, with certain intervals when none are given; these "rest-intervals" being gradually increased in length as the case goes on.

Although no arbitrary rule can be laid down as to dose, intervals between injections, intervals of rest and length of treatment, it is a safe and prudent proceeding to have a certain plan to follow, and this is my own.

PLAN

1. A course of six weeks' treatment, which involves six mercurial injections (four of which are calomel).

2. Two months' interval without injections.
3. Two months' treatment: eight mercurial injections (metallic).
4. Four months' period of rest.
5. Two months' treatment: eight mercurial injections (metallic).
6. Six months' period of rest.
7. One month's treatment: four mercurial injections.
8. Four months' period of rest.
9. Two months' treatment: eight mercurial injections.

In giving this tabular statement it cannot be too strongly impressed on the reader that it is absolutely impossible to lay down any stock plan of dealing with a disease like syphilis.

In former years it was my custom to begin treatment with inunction of mercury (30 rubbings à l'Aix); but now that I am enabled to use calomel with impunity I begin the treatment with it in preference to inunction, as there is no comparison between the two as regards rapidity and energy of action; after four injections of calomel I resort to metallic mercury, which is probably employed during the remainder of the treatment.

How Long should Treatment be continued?—Although one can never say for certain how long treatment should be continued, or when a patient can be considered cured of his disease, still treatment cannot go on for ever, and a decision will most certainly be asked for and will have to be given sooner or later. Up to recent years the only means we had to enable us to form a definite opinion on this subject was

long experience of treatment and observation of numbers of cases; however, the introduction of Wassermann's reaction test bids fair to put us in a far stronger and better position in coming to a definite decision as to whether a case may be considered cured or not: and I think we have every right to believe that a case which has had two years' thorough treatment, and which at the end of that time gives repeated negative reactions with Wassermann's test, is one which, to say the least, needs no further treatment. As regards this test, one cannot help feeling that its importance in solving the questions of "how long should treatment be continued," or "when the patient may be considered cured" cannot be exaggerated.

Precaution.—It is unnecessary to say that before the injection of mercury is given all the precautions as regards the hygiene of the mouth and teeth, as already described (p. 113), should be rigidly adhered to.

Contra-indications to Mercury.

Albuminuria.—Many cases of syphilis exhibit albuminuria in their early stages, due probably to tubal nephritis of a syphilitic nature, which will disappear under mercury. On the other hand, the metal must be given carefully and in reduced doses where organic disease of the kidneys is due to some other cause.

Malaria adds very much to the seriousness of an attack of syphilis, as patients suffering from it stand mercury badly and become easily salivated. Before being subjected to mercury such patients should have a thorough course of quinine.

OTHER METHODS OF ADMINISTERING MERCURY

Fumigation was used frequently in days of yore, but fell into disrepute for many years until it was partially revived by Henry Lee. It is little practised now, as it often produces salivation, anæmia, and general debility.

Intravenous Injection, introduced by Baccelli in 1893, consists of the introduction of mercury into the circulation through a vein; the advantages claimed being that it is painless, and that physiological effects are brought about much quicker than when other methods are employed. The objections to it are difficulties of technique, thrombosis, embolism, and phlebitis.

Zittmann's Treatment consists of treating chronic and refractory cases of syphilis by eliminating the poison from the system by sweating, purging, and the administration of mercury in infinitesimal doses, the latter being combined with tonic decoctions. The course of treatment lasts fourteen days, during which time the patient is kept in a temperature of 80° F.

CHAPTER XIV

FURTHER DEVELOPMENTS IN THE TREATMENT OF SYPHILIS, INCLUDING THE "EHRlich-HATA-No. 606 PREPARATION"

AS a result of the beneficial effects which had been obtained from the use of "Atoxyl" in Sleeping Sickness, and from his own researches as regards its action in fowl spirillosis, Uhlenhuth suggested that the same drug might be useful in Syphilis, the latter being, like Trypanosomiasis, a protozoal disease. Hallopeau and Salmon in France and the author in England made experiments according to this suggestion with much success, other observers also reporting favourably on it. On the other hand, from different sources came records showing symptoms of toxicity from its use—*i.e.* gastro-intestinal pains, malaise, nausea, and vomiting, and more serious still, of total blindness from optic atrophy. These adverse reports resulted in Atoxyl being dropped; in England in its place a preparation of arsenic named Soamin (para-amino-phenyl-arsonate) was adopted; this is analogous to Atoxyl, but is a known staple preparation. It had one great disadvantage—*i.e.* that its solutions decomposed on keeping, and were thus rendered dangerous.

Dose.—Given by intramuscular injection, I gave 10 grs. every other day until a total of 100 grs. had been given, and the course was repeated in a month's time with this preparation. I had much success in the early stages of syphilis, more especially in cases with mouth and throat lesions.

"Arsacetin"

The next Arylarsonate preparation used was "Arsacetin," introduced by Ehrlich. This was spoken of very highly by Neisser before the Dermatological Clinic at Breslau. Arsacetin is described as Sodium Acetyl-phenyl-arsonate. Of this Neisser says, "In accordance with this experience gained with animals, we have now for some months treated the greater number of our syphilis patients with Arsacetin, and I believe that I can recommend it as a very useful preparation." In the writer's hands it proved a great success in some two hundred cases of both early and late syphilis.

Dose.—Given intramuscularly in 10 per cent and 15 per cent solutions in courses of 100 grs., like Soamin. Its great advantage is that its solutions never decompose.

Arseno-phenyl-glycin

Another preparation, also introduced by Ehrlich, is Arseno-phenyl-glycin. This preparation was proved to be the most highly trypanocidal of all Arylarsonates, and it was hoped that it would prove equally so to the *Spirochaeta pallidum*. These hopes have not been fulfilled, and in

the author's estimation it is not nearly so efficacious as Arsacetin; besides, it has the great disadvantage that exposure to air causes decomposition, when the drug becomes poisonous.

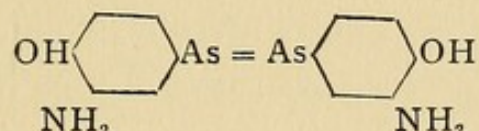
Conclusions as regards Arylarsonates

That the Arylarsonates have a distinct specific effect in clearing up syphilitic symptoms, both in early and late syphilis, there can be no doubt whatever, and up to within eighteen months ago one had much hope of their being able to effect a final cure; however, since Wasserman's reaction test became more familiar to us, this assumption, to say the least, has become doubtful. It is found that whereas in many cases they do not appear to affect the reaction at all, in others a negative one is brought about much more slowly when they are used than is the case when mercury is employed, and what is of still more significance is that a positive reaction returns very quickly after their discontinuance.

"Hata," or No. 606

Ehrlich, who has been the foremost worker for years in the study of the curative values of innumerable synthetic organic bodies, observes "that it is not an unusual phenomenon that a substance which is inimical to an organism in a large dose is favourable to its growth in a small one, and in those instances in which a 'contrary effect' is observed, the quantity of the chemical reagent

which the parasite fixes is so small that it is sufficient to stimulate it, but not to destroy it." Ehrlich therefore inclines to his "*Therapia magna sterilans*." He would introduce into the body one, and only one, massive dose of the parasitotropic chemical substance, which would free it, once and for all, from its invading parasitic foes." With this object in view he has introduced the now well-known preparation dioxy-diamido-arseno-benzol ; this has been investigated by Hata, hence it is called by his name, or by the number 606, for which the following is the formula :



"Hata" appears as a yellowish powder, and each dose is contained in a glass capsule sealed in vacuo. Before commencing treatment by No. 606 the patient should be kept in bed, a pulse and temperature chart kept, and every means taken to ascertain whether the patient is free from degeneration of liver and kidney.

Method of Administering the Drug

The method adopted for the preparation of the emulsion of "Hata" at the Military Hospital, Rochester Row, London, is as follows: 0.6 gramme of the powder is shaken into 30 c.c. of sterile water heated to 50° C. contained in a sterile vessel. Solution is effected with the aid of a glass rod ; 6 c.c. of $\frac{\text{N}}{\text{I}}$, NaOH are slowly added

—a lumpy precipitate falls, which re-dissolves in the excess of the alkali. $\frac{N}{I}$ acetic acid (prepared by mixing 1 c.c. of glacial acetic acid with 16.6 c.c. of sterile water) is dropped in until neutrality is restored ; 3.25 c.c. is the theoretical amount of $\frac{N}{I}$ acid required. The “Hata” salt is again precipitated, but this time in a very fine form, which can pass with ease through the needle of the syringe. By using the exact quantities given above, the “606” becomes suspended in a solution of sodium chloride and acetate, which is isotonic with physiological saline fluid—pain is thereby avoided. The whole is then injected either into the glutei or subcutaneously beneath the scapula. The pain of the injection is trifling at the time, but shortly afterwards may be severe. On the third or fourth day it may be aggravated by the infiltration which is produced ; this may be relieved by warm baths and fomentations, but morphia is sometimes required.

The temperature as a general rule rises to 100° F. on the night of the injection, to become normal after 48 hours. In a number of cases induration remains for some time at the site of injection.

With regard to “Hata” in the treatment of syphilis, Neisser has given the following pronouncement :—

“I have injected ‘Hata’ in 126 cases, and find that the preparation is very highly spirochætotropic. In almost every instance where manifest lesions existed, the lesions subsided in a startling manner. Primary sores lost their hardness and healed, whilst the *Treponemata* in Chancre

and Condylomata disappeared in twenty-four hours. Muscular and papular eruptions became stains in a day or so. Mucous patches went ; shotty glands subsided ; gummata melted away ; tertiary ulcers of malignant syphilis cleaned and cicatrised in a few days ; the paralyses and pains of cerebral syphilis disappeared sometimes in an hour or so."

Action in the Wasserman Reaction.

As to the influence of the new remedy in changing a positive Wasserman reaction into a negative, Neisser observed this in 44 per cent of his cases. Gerome found negative reactions in 60 per cent of his ; Schrubert in 80 to 90 per cent ; and Wechselmann in 100 per cent of his. In 270 cases treated with "Hata" by Lange, 57 per cent reacted negatively four or five weeks after the treatment.

McDonald reporting on 20 cases treated by "Hata" says : "Beyond the improvement observed by the naked eye, I was very much struck by the extraordinary change for the better in almost every patient's general condition ; they not only appeared brighter, but felt ever so much better and put on weight."

Toxicity.—Neisser states that 2,500 patients have been treated with "606" without any toxic effects, and disorders of vision and optic atrophy have never been observed.

Final Remarks.—At the Frankfort Congress of the German Dermatological Society in 1907, Ehrlich when introducing "Arsacetin" as an improved remedy for Syphilis, remarked thus :

"But even if this material should prove unsuitable for human use, we must not throw up the cards and abandon hope of something better. Then must we advance further along the road which now stretches clear before us."

True to this advice, Ehrlich has continued the hard fight until he is about to reap his reward by producing "Hata" or "No. 606," which apparently has a wonderful future before it in the treatment of Syphilis.

AUXILIARY MEANS OF TREATMENT

Although mercury and the arylarsonates form the main part of the treatment of syphilis, there are auxiliary means which are also very necessary—viz. hydrotherapy, iodide of potassium, and various tonics; besides these care in living and dieting is most desirable.

Second only to specific medication do I consider hydrotherapy, for hot baths of all kinds favour the elimination of mercury, and, what is of greater importance, increase and maintain metabolism generally. Hot-air baths are best, then Turkish baths, and last hot-water baths. At Rochester Row every patient undergoing either mercurial or arylarsonate treatment for syphilis sits in a hot-air bath at a temperature of 300° daily for ten minutes.

Iodide of Potassium.—Iodide of potassium at one time was supposed to have a specific action on syphilis; but for many years it has been regarded not as a specific, but as a valuable adjunct to mercury. In the early stages of the disease it is of little value, its therapeutic efficiency increasing in direct ratio with the age of the disease. It acts by promoting fatty degeneration and absorption of the imperfectly organised exudates.

As a rule, iodide of potassium is unnecessary in the early stages, except to relieve nocturnal headaches and periosteal pains generally. In such cases it is most successful, given in 5-grain doses three times a day.

In the later stages iodide of potassium, either given alone after a thorough course of mercury, or in combination with the latter, produces results which are sometimes

marvellous. On the other hand, when given in an unscientific manner the iodides lead to grave consequences. They act on the system as depressants, lowering it to such an extent that it is left an easy prey to the further ravages of syphilis. At other times iodism is produced, represented by gastro-intestinal irritation, coryza, pustular and other forms of skin eruptions, various forms of neuritis, and acute œdema of the larynx.

In ordinary doses most patients will exhibit no symptoms whatever from the use of the iodides. A small proportion may suffer from a coppery taste in the mouth, coryza, and perhaps some gastro-intestinal catarrh. A still smaller proportion may be entirely intolerant of iodide of potassium, and will suffer from swelling of the mucous membranes, especially of the larynx and pharynx.

Rules for giving Iodide of Potassium.

1. The drug ought to be given well diluted.
2. Excipients facilitate absorption.
3. It should be given about an hour after meals.
4. It should be given in intermittent courses of increasing doses, never for longer than ten days at a time, after which there should be a week's interval before it is resumed.

Dosage.—In the early stages, if required, the average dose is gr. v three times a day; in the later stages gr. x three times a day, increasing up to gr. xxx three times a day; so that by the end of a course of ten or fourteen days the patient will be taking 3 ij per day: as much as 3 ij three times a day may be found necessary in some cases.

Manner of Giving Iodides.—They may be given in the form of a saturated solution, one drop of which represents approximately gr. j of iodide of potassium :

R Iodide of potassium ʒ v
 Aquæ ad. ʒ j

Dose : ʒ v to ʒ x in a glass of milk and water three times a day.

If this disagrees, 5 to 10 grains of pepsin may be added.

The great thing to remember in giving iodide of potassium internally, is to give it well diluted. It can be taken in milk, beer, wine, or in any liquid.

The drug can be given by enema when necessary. When thus administered the intestine should first be evacuated by a simple enema. Then an enema of iodide of potassium, gr. xxx to gr. xl dissolved in ʒ ij of water with a few drops of laudanum, may be given.

Hypodermic Injection.—Hypodermic injection of potassium iodide is sometimes resorted to. This mode cannot be recommended owing to the frequent occurrence of abscesses and sloughing.

Iodipin.—Iodipin is a combination of iodine and sesame oil, and is prepared in two strengths, *i.e.* 10 % and 20 %, the former for internal medication, the latter for injection purposes. Although the desired therapeutic effects can be brought about by giving it internally, this manner is not recommended, as it is apt to bring on dyspepsia. Given hypodermically and intramuscularly, the dose is : from c.c. x to c.c. xx for ten consecutive days. The syringe should be capable of holding at least 10 c.c. The needle should be $2\frac{1}{2}$ in. long, and have a large bore.

Injections are best given in the loose tissues of the loins. Iodipin is a viscid fluid, and requires heating to at least body temperature to bring it to the proper consistence for injection purposes. The advantages claimed for iodipin over iodide of potassium are that it is more slowly absorbed and excreted than the latter; that it is non-depressent, and does not interfere with the digestion. I have used iodipin very extensively, and can recommend it as a substitute for potassium iodide in all cases where the latter is inadmissible. It has one objection—*i.e.* the large bulk it is necessary to inject at a sitting.

Iodism.—The treatment of iodism will depend on the severity or otherwise of the symptoms. When these are mild, and it is important to continue the drug, the iodide may be given in increased doses; but when severe, discontinuance of the drug is imperative.

The character of the iodide rash is important:

1. Rapidity of invasion.
2. Begins as a vesicle, and runs speedily through a pustular stage.
3. The margins are inflamed with a bright red areola.
4. The base is soft.
5. The suppression of the drug causes the disappearance of the rash.

CHAPTER XV

MODERN AIDS IN THE DIAGNOSIS OF SYPHILIS

SCHAUDINN in 1905 discovered the *Spirochæta pallida*, and from various experiments was led to believe that this spirochæte was the true cause of syphilis—a belief soon to be fully confirmed by some of the greatest pathologists of the day, notably Metchnikoff, Levaditi, Roux and Koch, and to-day it is the generally accepted fact.

Since a positive diagnosis can only be obtained by finding the *Spirochæta pallida*, the importance of this discovery of Schaudinn can easily be imagined. It is of greater value in the primary stage of syphilis than at any other. In no stage of the disease is diagnosis so important. Seen early, some chancres defy the most experienced in coming to a conclusion as to their real nature, with the result that one of two courses is usually adopted—either the patient is given mercury with a three or four years' treatment to look forward to, and the constant thought of suffering from a disease of which he may be entirely innocent, or he is given no treatment until the whole system is infected and secondaries are obvious. Thus the most valuable time for grappling with

the disease is lost, for it is an undoubted fact that the earlier treatment is begun, and the more vigorously it is carried out in the primary stage, so much the sooner may a cure be looked for and further developments prevented.

To demonstrate the *Spirochæta pallida* the specimen should be examined by the "dark ground illumination." This latter is obtained by using a condenser, which allows no rays of light to reach the eye except those reflected by certain objects, such as the *Spirochæta pallida*, which appears as a delicate, attenuated, brightly illuminated silvery corkscrew standing out in beautiful contrast on a dark or intensely black field. The necessary apparatus for the "dark ground illumination" can be adapted to any microscope at a comparatively small cost, and the technique for setting up the specimen is extremely simple. By its means a diagnosis can be established in the case of an untreated syphilitic sore in a very few minutes.

It is of course necessary for the observer to familiarise himself with the appearances of the various spirochætes under this method of examination, but when the characteristic appearance of the *Spirochæta pallida* has been once mentally fixed, no mistake should occur. In lesions of the genital organs the spirochætes which are likely to cause confusion at first are the finer forms of *Spirochæta refringens*, amongst which, without committing oneself to any definite opinion as regards their relationship to the form originally named by Schaudinn and Hoffman as *S. refringens*, may be mentioned *S. balanitidis* and the spirochætes of ulcerating cancers and

papillomata. In general these differ from the *S. pallida* by their greater thickness, irregularity of undulations and the wider spacing of the latter, while they are to be found on the surface rather than in the depths of the sore, and in the ulcerated area rather than the indurated margin.

The beginner at this method of examination is strongly urged to make himself familiar—by taking specimens from the surface of syphilitic sores, from the deeper layers of epithelium at the indurated margin, from the secretion of cases of balanitis, and from other than syphilitic lesions—with the appearance of the various spirochætes found in these conditions. He will find half an hour's work in this direction of more value than pages of description.

Burri's Method¹ consists of demonstrating the *Spirochaeta pallida* by means of Chinese ink. A platinum loopful of secretion from a sore is placed upon a slide, surrounded by seven or eight loopfuls of distilled water and the same quantity of a solution of Chinese ink. The whole is mixed and spread out upon a slide, or a blood film is made, allowed to dry, and examined with an oil-immersion lens. The ink produces a dark background, and the objects under examination stand out white.

Giemsa's Stain.—At one time it was believed that, whereas all other spirochætes stained blue with Giemsa's stain, the *Spirochaeta pallida* stained pink; but now it is known that the latter sometimes stains blue, so that staining is not really a very strong point.

¹ The *Journal of Clinical Research*, May 1910, p. 59, has a note on this method.—[Ed.]

Excision of Chancres.—Neisser's experiments on the infectivity of organs of syphilised monkeys at different periods after inoculation, show that by the time the chancre has appeared (in fact long before), the spirochæte has already established itself in the hæmopoietic organs and blood, so that excision of the chancre is theoretically not sound. Levaditi and Koch condemn it.

The Spirochaeta Pallida.—That the *Spirochaeta pallida* is the true organism of syphilis has been established beyond a doubt from the following :

It is found only in syphilitic lesions.

It has been found in the blood of syphilitics.

It has been found in the blood and viscera of syphilitic infants.

Metchnikoff and Roux found it in lesions in monkeys caused by inoculation from syphilitic men and monkeys.

Wassermann's Serum Reaction Test.¹—Of recent advances in medicine none can claim to be of so much importance as the serum diagnosis of syphilis, a test based on what is known as the Bordet-Gengou reaction. The latter is a binding of the complement which takes place when an antigen meets with its homologous inactive immune serum, erythrocytes and hæmolytic serum (which has been inactivated in order to rob it of its complement). No hæmolysis can occur if the complement has become bound, because the hæmolysin has no free complement. Founded on this, Wassermann discovered that a positive

¹ A useful article on "The Serum of Diagnosis of Syphilis" will be found in *The Practitioner*, September 1909 [Ed.], also see E. Merck's Annual Report, Vol. XXII.

reaction could be obtained by the bringing together of bacterial extracts and immune serum, and later on proved that extracts of organs behaved as the antigen, and that in the serum of apes, which had been treated with syphilitic extract, substances appeared which brought about fixation of the complement. Finally he found the same substances in serum of human syphilitics.

In Wassermann's test the *antigen* is obtained from the liver or spleen of an hereditary syphilitic infant ; the *anti-serum* from the blood of the patient ; the *complement* from guinea-pig serum ; the *erythrocytes* from sheep's blood ; and the *hæmolytic serum* from an immunised rabbit.

The technique of Wassermann's test is certainly very intricate, and can only be satisfactorily carried out in a well-equipped laboratory and by an expert, and, as at present instituted, can never come within the range of the general practitioner. Of late years many workers have endeavoured to modify and simplify the test, but have not succeeded, and at the present moment Wassermann's original method still holds its ground as the most approved and most reliable of all.

The value of Wassermann's reaction varies according to the stage of the disease. In the primary stage a positive result is not obtained in more than 40 per cent. of cases. In the secondary stage a positive reaction is obtained in 85 per cent. of all cases, whether showing secondary manifestations or not, and where the patient is undergoing treatment. When there are secondary signs present, such as rash, and where the patient has not yet had any mercury, 97 per cent. give a positive Wassermann.

Treatment, of course, influences the results of Wassermann's test. Directly after a course or courses of intermittent treatment the reaction is usually negative, but when the mercury becomes eliminated the reaction resulting is positive. The greater the number of courses the more likelihood there is of a negative result, which in time may become permanent; and herein lies a most important point in connection with the Wassermann test. Should a case which has undergone a thorough treatment give a negative reaction three, six, or nine months after the cessation of all treatment, is it then justifiable to give an opinion that a cure has been established? This would indeed be a great advance; but at present the reaction is not certain enough to justify such an opinion; time and further experience of the test can alone tell us.

Two facts which Wassermann's test has taught us are: the enormous benefit which arises from an early and vigorous treatment; and the advantage of injections and inunction over the oral administration of mercury.

Whatever time may tell us as to the value of Wassermann's test in enabling a definite opinion to be given as to cure or not, there can be no doubt as to its present-day value to the clinician, in not only enabling him to diagnose syphilis, but also to differentiate between it and other diseases.

1. Take a very common instance—that of a patient who gives a history of a sore which appeared a few days after connection, and disappeared within ten days to a fortnight. No notice is taken at the time, but some months later a few spots appear on the body, and a medical opinion

is sought, but no definite conclusion can be arrived at. With such a history and a "positive" Wassermann there cannot be any doubt as to the nature of the disease, and treatment should be commenced forthwith.

2. Differential diagnoses between various ulcers and syphilitic ones.

3. Gummatous periostitis and sarcoma.

4. Gummata of the testes, tubercle, and new growth.

5. Gumma and malignant growth of the liver.

6. Syphilitic ulceration of the tongue and epithelioma.

The author had a case which was under orders to have excision of the tongue for cancer. There was no evidence of acquired syphilis, but slight of hereditary disease. Wassermann's test gave an undoubted positive reaction. The patient was put on atoxylate of mercury injections, which cleared up the local affection at once.

7. Between general paralysis of the insane and other cerebral affections, 100 per cent. of cases of general paralysis give a positive reaction.

8. Tabes, in which 70 per cent. of the cases give a positive reaction.

9. In cases of repeated abortions.

10. Between cases of hereditary syphilis and tubercle.

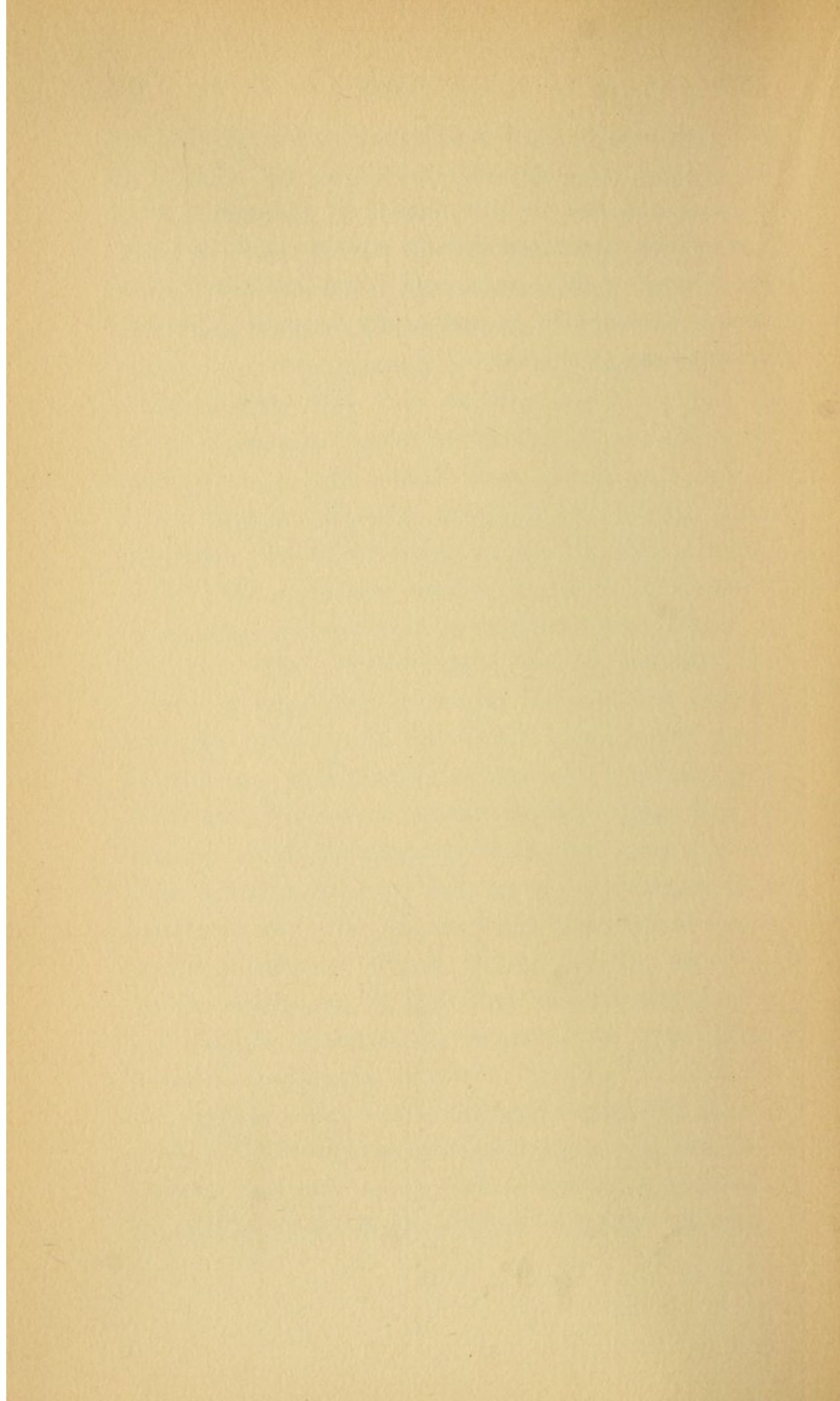
11. Syphilitic affections of the eye, and those due to some other cause.

Some two years ago a case was sent to the author, the patient a male, aged fifty-five, who had suffered for thirty years from rheumatic arthritis and periodic attacks of what was considered rheumatic iritis. The oculist who sent the case wanted to see how these attacks

behaved under metallic mercurial injections. Although there was no history nor sign whatsoever of either acquired or hereditary syphilis, the patient's blood when subjected to Wassermann's test gave an undoubted positive result. The case was treated accordingly, since which time there has been no recurrence of iritis, and now the reaction has been negative for the last four months.

Conclusion.—The value of these two discoveries—*i.e.* of the *Spirochæta pallida* by Schaudinn, and the serum reaction test by Wassermann—have opened up a new era in the clinical study and treatment of syphilis. Their importance cannot be exaggerated. The former enables us to give a definite opinion as to the character of the primary lesion, which in itself is a tremendous advantage; whilst Wassermann's reaction test has been proved by experience in several thousands of cases all over the world to be one which is practically specific for syphilis. It is therefore an addition to the diagnostic armament of the very highest value. Apart from its value as an aid to diagnosis in obscure cases, I believe there is reason to hope that by it we may gain some knowledge as to the progress which treatment is making against the disease. Though the reaction is of too recent date to enable one to make any definite statement on this question, it seems to be undoubted that efficient treatment does tend to convert a "positive" reaction into a "negative" one; and in the great majority of cases the occurrence of a negative reaction in cases of syphilis after efficient treatment appears to be the more frequent as the clinical signs indicate a return to health. Whether it

will eventually be possible to determine from a succession of negative reactions that treatment has effected its purpose and can be discontinued is a question which can only be determined after the lapse of many years, when the history of the cases whose blood has already been tested and found to be persistently "negative" has been followed out to the end.



INDEX

(Authorities in Italics)

Aachen, method of, 121, 122 | Arteritis cerebral, 80

ERRATA TO INDEX

Omit—

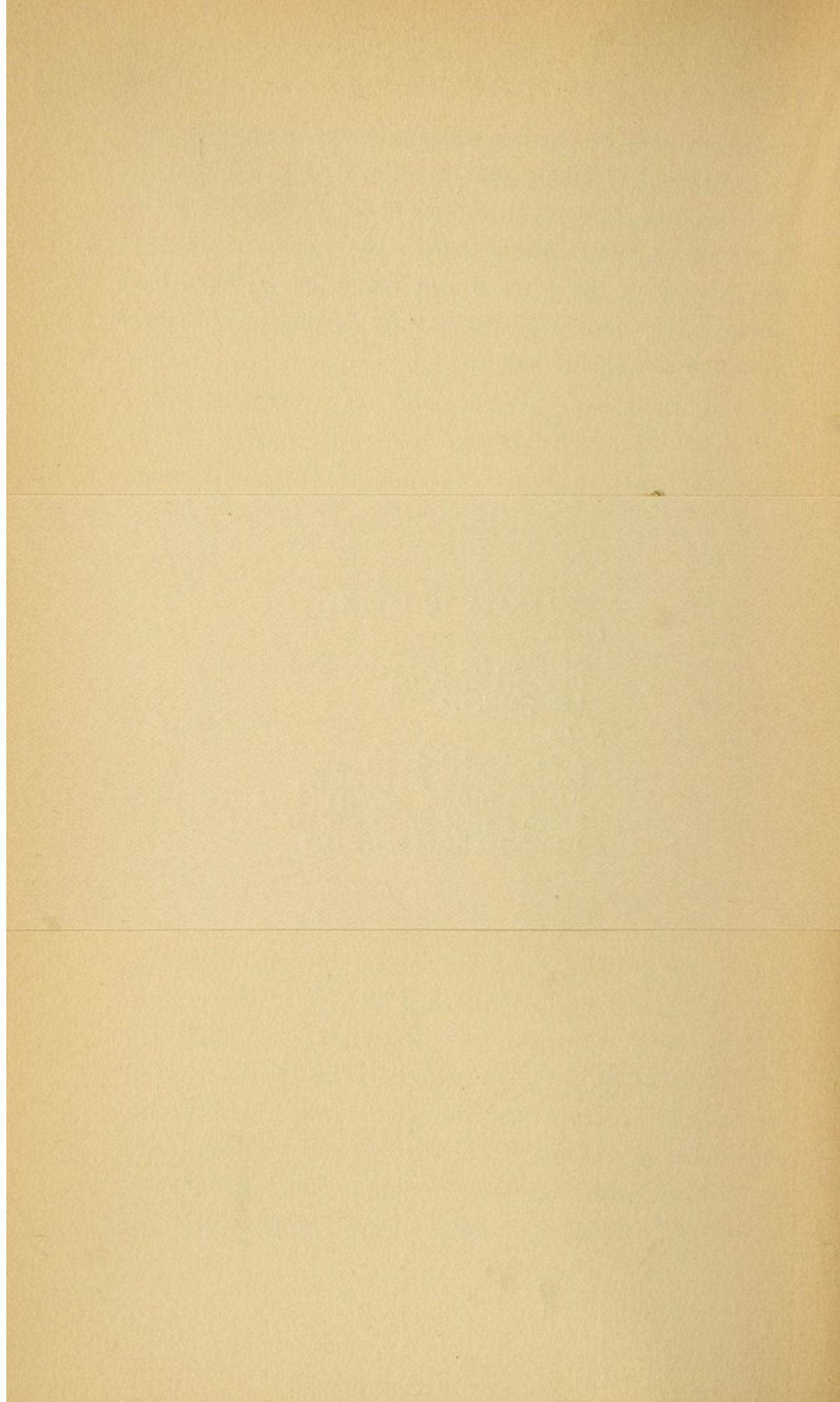
Arsonates, 170
Glossitis, sclerotic, 173
Leucoplakia, 172

Add—

Arseno-phenyl-glycin, 171
Dioxy-diamido-arseno-benzol, 173
"Ehrlich-Hata-No. 606," 172
Sodium acetyl-phenyl-arsonate, 171
Wasserman's Reaction, 172-174B

Antigen, 182
Antipyrin, 103
Antiquity of syphilis, 4
Anti-serum, 183
Anti-syphilitic serum, 14
Anus, chancres of, 25
Aortic regurgitation, 86
Aphasia, 66
Aphonia, 78
Argyll-Robertson pupil, 96, 99, 106
Aristol, 42
Arsacetin, 171
Arsenic, 111
Arsonates, 170
Arsonic acid, 170
Arterial system, tertiary affections
of, 86
Arteritis, 86

Bimouide of mercury, 110
Black wash, 42, 60
Blood, changes caused in, by mercury,
156
Blue pill, 117
Boerhaave, 130
Bones, secondary affections of, 66
— tertiary affections of, 83
Borax, 58
Bordet-Gengou reaction, 182
Boric acid, 42, 59, 60
Breast, chancre of, 36
Bromides, 109
Buccal hygiene, 131, 137
— tolerance, sex differences, 121
Burri's method (*Chinese ink*), 181
Bursæ, secondary affections of, 67
— tertiary affections of, 82



INDEX

(Authorities in Italics)

- Aachen, method at, 131, 132
 — water, composition, 133
 Acid, chromic, 44, 58, 62, 76, 114
 —nitrate of mercury, 60
 Acne, 51
 Aix-la-Chapelle, *see* Aachen.
 Albuminuria, 49, 66, 80, 168
 Alcohol, rules during inunction, 137
 Alimentary system, tertiary affec-
 tions of, 72
 Alopecia, 60
 Alphyl, 170
Ambrosoli, of Milan, 142
 American origin of syphilis, 5
 Ammonium chloride, 150
 Amyloid degeneration of kidney, 81
 — — of liver, 79
 Anæmia, 56
 Analgesia, 159
 Aneurysm, 86, 89
 Angina pectoris, 49
 Aniline, 171
 Ankylosis, 84
 Annular chancre, 19
 Antifebrin, 103
 Antigen, 182
 Antipyrin, 103
 Antiquity of syphilis, 4
 Anti-serum, 183
 Anti-syphilitic serum, 14
 Anus, chancres of, 25
 Aortic regurgitation, 86
 Aphasia, 66
 Aphonia, 78
 Argyll-Robertson pupil, 96, 99, 106
 Aristol, 42
 Arsacetin, 171
 Arsenic, 111
 Arsonates, 170
 Arsonic acid, 170
 Arterial system, tertiary affections
 of, 86
 Arteritis, 86
 Arteritis, cerebral, 89
 Arthritis, gummatous, 84
 — secondary, 67
 — tertiary, 84
 Arylarsonates, 75, 109, 110
 — treatment by, 170
 Ascites, 80
 Atheroma, 88
 — of aorta, 86
 Atoxyl, 170, 172
 Atoxylate of mercury, 173, 185
 Atropine, 63
 Auto-inoculation, 30
 Auxiliary means of treatment, 175
 "Ayurvedas," 2
 β -cocaine, 160
Bacelli, 169
 Bacillus paralyticans, 98
 Bacteriology of syphilis, 11
Balzer, 144
 Baron Larrey's syrup, 119
 Baths, hot-air, 114, 175
 — Turkish, 114, 175
Bielt, 120
 Biniodide of mercury, 118
 Black wash, 42, 60
 Blood, changes caused in, by mercury,
 156
 Blue pill, 117
Boerhaave, 130
 Bones, secondary affections of, 66
 — tertiary affections of, 83
 Borax, 58
 Bordet-Gengou reaction, 182
 Boric acid, 42, 59, 60
 Breast, chancre of, 36
 Bromides, 109
 Buccal hygiene, 131, 137
 — tolerance, sex differences, 121
 Burri's method (*Chinese ink*), 181
 Bursæ, secondary affections of, 67
 — tertiary affections of, 82

- Cachexia, syphilitic, 47
 Calomel, dry dressing, 43
 — dusting powder, 60
 — injections, 75, 95, 103, 144, 156, 162
 — — formula for, 162
 — — pain after, 160
 — ointment (Metchnikoff), 43
 Camphoric acid, 160
 Cancer of lip, 32
 — of tongue, 74
 Carbolic acid, 43, 58, 60,
 — lotion, 42
 Castellani, 31
 Cautery, actual, 44
 Central America, 1, 4
 Cephalalgia, 64
 Cerebral syphilis, statistics, 91
 Cerebro-spinal fluid, leucocytosis of,
 94, 96
 — syphilis, 94
 Chancre, description of, 17
 — indurated, 10
 — prognosis of, 37
 — seats of, 21
 — — anus, 25
 — — base of penis, 23
 — — breast, 36
 — — concealed, 24
 — — extragenital, 32
 — — eye, 34
 — — face, 35
 — — finger, 35
 — — general integument, 36
 — — genital, 22
 — — groin, 25
 — — lip, 32
 — — preputial, 24
 — — scrotum, 23
 — — sub-preputial, 24
 — — tongue, 33
 — — tonsil, 34
 — — urethra, 22
 — — urinary meatus, 22
 — structure of, 18
 — treatment of, 40
 — varieties of, 19
 — — annular, 19
 — — ecthymatous, 19
 — — dry papule, 19
 — — false relapsing, 21
 — — mixed, 20
 — — phagedænic, 43
 — — recurring, 20
 — — silvery spot, 19
 — — true relapsing, 21
 — — vaccination, 36
 Chancroid inflammation, 26
 Chancrous erosion, 18
 Charcoal poultices, 44
 Charcot's gait, 87
 — joint, 102, 107
 Charles (Physiology), 159
 — V., Emperor, 6
 Charles VIII. of France, 4, 6
 Chimpanzee, inoculation of, 14
 Chinese ink method, 181
 — knowledge of syphilis, 2
 Chlorate of potash, 58, 113
 Chomel's pills, 119
 Chorea, 90
 Choroiditis, 63
 Chromic acid, 44, 58, 62, 76, 114
 Circinate syphilide, 54
 Circulatory system, tertiary affec-
 tions of, 86
 Cocain hydrochlorat., 150, 160
 Collins, 97
 Columbus, sailors of, 4
 Concealed chancres, 24
 Condylomata, 59
 Conjunctival chancre, 34
 Copper, sulphate of, 113, 114
 Coryza, 176
 Creo-camph., 161, 162
 Creosote, 160
 Cyclitis, 63
 Cyto-diagnosis, 103
 Cytoryctes luis, 12
 Dactylitis syphilitica, 85
 Dark-ground illumination, 180
 De Lisle, 12
 Depression, mental, 66
 Dermatitis during inunction, 139
 — secondary, 49
 — tertiary, 70
 Dermatol, 42
 Destruction of syphilitic virus, 41
 Diagnosis, differential, 28, 184
 — of chancre, 27
 — modern aids to, 179
 Diarrhoea, 139
 Diaz de Isla, 5, 6
 Diet during inunction, 137
 Diffuse paronychia, 61
 Digestive organs, action of mercury
 preparations on, 121
 Dosage of mercury, 124
 Dose, maximum for injection,
 166
 Dry papule, the, 19
 Ducrey, 8
 Dupuytren's pills, 118, 124
 — — Fournier's modification of, 119,
 124
 Duration of treatment, 167
 Dystrophy of the neurones, 96
 Eburnation of bony tissue, 83
 Ecthymatous chancre, the, 19
 Eczema, 35
 Edinburgh, syphilis in, 7
 Ehrlich, of Frankfort, 171
 Embolism, 148
 Endarteritis obliterans, 86
 Endoperiarthritis, 86
 Enema of potass. iodid., 177

- England, introduction of syphilis into, 6
 Epididymis, secondary affections of, 68
 Epilepsy, 66, 108
 Epithelioma, diagnosis of, 32
 Erb, 97
 Eruptions, secondary, 49
 — tertiary, 70
 Erythema of larynx, 60
 Erythematous syphilides, 51, 52
 Europhen, 42
 Exercise during inunction, 138
 Exostoses, 83
 External method, 128
 Extragenital chancres, 31
 Eye, chancre of, 34
 — secondary affections of, 62

 Facial chancre, 35
 False relapsing chancre, 21
 Ferguson, William, 112
 Ferrier, 98
 "Ficus," of the Romans, 2
 Finger, chancre of, 35
 — tertiary affections of, 85
 Follicular syphilides, 51, 52
 Fournier, 10, 90, 96, 97, 160
 Fournier's modification of Dupuytren's pill, 119, 124
 Fracture, spontaneous, 107
 Fumigation, 169

 Gagnière, 156
 Gaseous constituents of Aachen water, 133
 Gastro-intestinal irritation, 176
 General paralysis, 104
 Genital chancre, 22
 — organs, mucous patches of, 59
 Giemsa's stain, 12, 15, 181
 Girdle pain, 93
 Glands, enlargement of, 46
 Glossitis, gummatous, 73
 — sclerosing, 73
 — sclerotic, 173
 — superficial, 72
 Glycerin, 144
 Gold, 111
 Gowers, 97, 99
 "Grand mal," 108
 Grandiose delusions, 105
 Grey oil, 155
 — powder, 118
 Groin, chancre of; 25
 Guaiacum, 111
 Guillain, 98
 Gumma, structure of, 9
 Gummata, subcutaneous, 71
 Gummatous syphilides, 71
 Gum-water, 144
 Guthrie, 112

 Hæmolytic serum, 183
 Hæmoptysis, 79

 Hair, affections of the, 60
 Haiti, 4, 5, 6
 Halliburton, 158
 Hallopeau, 170, 171
 Hardy, 143
 Headache, nocturnal, 64, 175
 Hebrew knowledge of syphilis, 3
 Hemiplegia, early, 64
 — syphilitic, 92
 Hepatitis, 79
 Hippocrates, 2
 Hoang-ti, Emperor, 2
 Hoffmann, 13, 180
 Hoffmann's pills, 119
 Hot-air baths, 175
 Hot compresses, 63
 Hot-water baths, 175
 Hunter, John, 7, 131
 — — experiment of, 7
 Hutten, Ulrich van, 129
 Hydrocele, 85
 —, tapping, 86
 Hydrotherapy, 175
 Hydroxyl group, 170
 Hygiene of mouth, 113, 137
 Hyperæmia of pharynx, 48
 — of tonsils, 48
 Hypodermic injection of potass. iodid., 177

 India, syphilis in, 2
 Indian (W.), source of syphilis, 5
 Indolent paronychia, 61
 Indurated chancre, 10
 Induration, description of, 17
 Injection, intramuscular, 142
 — sites for, 165
 — intravenous, 169
 Insoluble salts, injection of, 154
 Internal method, remarks on, 125
 Interstitial nephritis, 81
 Intramuscular method, 142
 — — advantages of, 145
 — — disadvantages of, 148
 — — points in, 165
 — — stomatitis after, 147
 — — success of, 144
 — — technique of, 164
 Intravenous injection, 169
 Inunction, cases for, 141
 — diet during, 137
 — disadvantages of, 138
 — exercise during, 137
 — mercurial, 95
 — method, 128
 — mode of action, 134
 — ointments for, 135
 Iodide of potassium, 72, 75, 175
 — — manner of giving, 177
 — — rash, 178
 Iodine, solutions of, 77
 Iodipin, 72, 177
 Iodism, 176, 178
 Iodoform, 42, 59, 60, 62, 72

- Iridectomy, 63
 Irido-choroiditis, 63
 Iritis, 62

 James IV. of Scotland, 7
 Japanese knowledge of syphilis, 2
 Jaundice, 66, 80
 Joints, secondary affections of the, 67
 — tertiary affections of the, 84
Jullien, 143

 Kidney, amyloid disease of, 81
 — granular contracted, 81
 — secondary affections of, 49
 — tertiary affections of, 81
 Knee-jerks, 100
Koch, 171, 179, 182
Kölliker, 143

 Labial chancre, 32
 — epithelioma, 33
 Lafay's formula, 158
 Lambkin's original formula, 158
Lancereaux, 2
Lang, of Vienna, 154, 157
 Larrey's syrup, 119
 Laryngitis, early, 60
 Larynx, affections of, 60
 — erythema of, 60
 — œdema of, 176
 — tertiary affections of, 78
Las Casas, 5, 6
Lee, Henry, 169
 Leeches, 63
Leishman, 161
 Lenticular syphilides, 51, 53
 Lepa, syphilitic, 54
 Leprosy, Biblical account of, 3
 Leucocytosis of cerebrospinal fluid, 94, 96
 Leucoderma, 56
 Leucoplakia, 58, 172
Levaditi, 9, 14, 179, 182
 Lichen, 50
Liegeois, 143
 Lightning pains, 99
 Lips, chancre of, 32
 — tertiary lesions of, 72
 Liver, congestion of, 66
 — tertiary affections of, 79
 Locomotor ataxia, 96
 Lungs, tertiary affections of, 78
 Lupus, differential diagnosis, 77
 Lustgarten's bacillus, 12
 Lymphangitis, inflammatory, 39
 — specific, 39
 Lympho-angiotic theory of tabes, 98
 Lymphocytosis, 97

Magrath, 98
 "Mal français," 128
 Malaria, 168
Maries, 98

 Melting-point of mercurial cream, 161
 Meningitis, 91
 — spinal, 93
 Meningo-myelitis, 93
 Mental depression, 66
 Mercurial cream, 158
 — ointment, 46, 72
 — plaster, 86
 — soaps, 135
 Mercury, 111
 — acetate of, 150
 — acid nitrate of, 60
 — alanate of, 150
 — and ammonium, double chloride of, 149
 — atoxylate of, 173, 185
 — benzoate of, 150
 — bichloride, 61-3, 152
 — biniodide, 118, 150
 — — oil, 151
 — chloro-albuminate of, 150
 — contra-indications, 168
 — cyanide of, 150
 — dosage of, 124
 — ingestion method, 115
 — intramuscular method, 142
 — lactate of, 150
 — metallic, 154
 — — advantages of, 155
 — — disadvantages of, 161
 — methods of administering, 114
 — oleate of, 43
 — peptonate of, 149, 151
 — perchloride, 118: *see* bichloride
 — preparations of, 157
 — proto-iodide, 119
 — salicylate, 118, 154, 156, 165
 — sozoiodolate of, 150, 151
 — succinimate of, 150, 152
 — tannate of, 118, 150
 — urate of, 150
 — yellow oxide of, 144, 154
Melchnikoff, 8, 14, 41, 110, 179, 182
 — ointment, 41, 43, 110
 Methods, ingestion, 115
 — intramuscular, 142
 — intravenous, 169
 — inunction, 128
 Microbiology of syphilis, 11
 Migraine, 90
 Mixed chancre, 20, 26
 Modern aids in diagnosis, 179
Moebius, 97
 Monkeys, inoculation of, 14
 Morphia, 160
 — hypodermic, 68, 103
 Motor paralysis, 64
Mott, 96
 Mouth, hygiene of, 113, 137
 — wash, 137
 Mucous membranes, secondary affections of, 57
 — patches, 58

- Mucous membranes, patches of
 genital organs, 59
 Muscles, tertiary diseases of, 82
 Myelitis, 93
 Myositis, chronic infiltrative, 82
 — gummatous nodular, 82
 — hyperæmic, 82

 Nails, secondary affections of, 61
 "Needle, fear of the," 160
 Needles, 164
 Neisser, 111, 172
 — experiment, 181
 Nephritis, 49
 — interstitial, 81
 Nervous system, secondary affec-
 tions of, 64
 — tertiary affections of, 90
 Neuralgia, 64
 Neuritis, optic, 66
 Neurones, dystrophy of, 96
 Nitrate of silver, 58, 60
 Nitric acid, 43, 44, 60, 62
 Nocturnal headaches, 64, 175
 Nose, syphilitic affections of, 59

 Ocular chancre, 34
 Ointment, mercurial, 46, 72
 — — Metchnikoff's, 41, 43, 110
 — white precipitate, 61
 Okamura, 2
 Oleate of mercury, 43
 Olein, 158
 Oleum cinereum, 155, 157
 Olive oil, 144
 Onychia, 61
 Opaline patches, 57
 Optic atrophy, 103
 — neuritis, 66
 Orchitis, 68
 Osteoperiostitis, 83
 Osteotic pains, 47
 Oviedo, 5, 6

 Pain after injection, 148, 152, 155,
 159
 Pains, neuralgic, 47
 — osteotic, 47
 — periosteal, 175
 — rheumatic, 48
 — rheumatoid, 67
 Palate, gumma of, 76
 Palmitin, 158, 159
 Palpebral chancre, 34
 Panarteritis, 86
 Panas, 151
 Papular syphilides, 51, 53
 Paraffin, liquid, 144
 Paralysis, general, 104
 — motor, eye and face, 64
 Paraplegia, 92, 93
 — early, 64
 Parasyphilis, 10, 96
 Parchment-like sore, 18

 Parenchymatous iritis, 62
 Parenga (Yaws), 31
 Paronychia, 61
 Pasteur, 11
 Patellar bursæ, 82
 Pathology of syphilis, 9
 Peninsular War, 112, 128
 Penis, chancres of, 23
 Perforating ulcer, 107
 Perhydrol (Merck), 43, 58, 72, 76,
 77, 113, 114
 Peri-arteritis, 10, 86
 Perihepatitis, 79
 Periosteal pains, 175
 Periostitis, 66
 Peroxide of hydrogen, 59, 76, 113
 — — lotion, 42
 — "Petit Mal," 108
 Phagedænic chancres, 43
 Pharynx, hyperæmia of, 48
 — tertiary affections of, 77
 Phenacetin, 103
 Pian (Yaws), 31
 Pigmentary syphilides, 56
 — — retiform, 56
 Plan of treatment, 166
 "Plaques," 48, 58
 Plastic iritis, 62
 Platinum, 111
 Pleural effusion, 66
 Plummer's pill, 58
 Potassium, chlorate of, 58, 113
 — iodide, 95, 103, 109, 111, 175
 — — rules for, 176
 Prehistoric existence of syphilis, 2, 3
 Prepuce, chancres of, 24
 Prescriptions, 76, 113, 117, 118, 150,
 151, 157, 158, 161, 162
 Profeta, 143
 Proto-iodide of mercury, 118, 119
 Psoriasis, 50
 — of the tongue, 58
 Pupil, Argyll-Robertson, 96, 99, 106
 Pustular syphilides, 55

 Quaternary syphilis, 96
 Quinine, 168

 Ravant, 94, 97
 Rectum, tertiary affections of, 81
 Recurring chancre, 20
 Relapsing chancre, 21
 Resorcin, 60
 Retiform pigmentary syphilide, 56
 Retinitis, 63
 Reuter, 13
 Rheumatic pains, 48
 Rheumatoid pains, 67
 Ricord, 7
 Ricord's pills, 120
 — — Fournier's modification of, 124
 Robertson, Argyll-, pupil, 96, 99,
 106
 Robertson, Ford, 98

- Rochester Row, formulæ at, 135, 137
 Romberg's sign, 100
 Roseolar syphilides, 52
 Roux, 8, 14, 179, 182
 Rubbing, mode of, 136
 Rupia, 55

 Salicylate of mercury, 118, 165
 Salivation, 112, 129
 Salmon, 170
 Sarsaparilla, 111
 Sassafras, 111
 Scarenzio of Pavia, 142
 Schaudinn, 8, 12, 13, 179
 Scotland, syphilis in, 7
 Scrotum, chancre of, 23
 Secondary period affections, 45
 albuminuria, 49
 angina pectoris, 49
 cachexia, 47
 eruptions, 49
 eye, 62
 glandular, 46
 hair, 60
 joint, 67
 laryngeal, 60
 mucous patches, 59
 nerve, 64
 nose, 59
 onychia, 61
 orchitis, 68
 paronychia, 61
 periostitis, 66
 syphilides, 49
 tenosynovitis, 68
 tongue, 57
 tonsils, 48
 visceral, 66
 Sedillot's pill, 117
 Seigel, 12
 Senarega, 6
 Serum, anti-syphilitic, 14
 Sicard, 97
 Silver, 111
 Silvery spot, the, 19
 Sites for injection, 165
 Sleeping sickness, 170
 Smirnoff, 143
 Soamin, 171
 Sodium chloride, 151
 — iodide, 151
 — paraminophenylarsonate, 171
 Soft chancre, diagnosis of, 28
 Soluble salts, injection of, 152
 Spinal cord, tertiary syphilis of, 93
 Spirochæta balantiditis, 180
 — pallida, 8, 12, 14, 27, 70, 110, 180
 — examination for, 15
 — refringens, 12, 180
 Spitz, 13
 Spleen, tertiary affections of, 80
 Spondylitis, syphilitic, 83
 Spontaneous fracture, 107
 Squamous syphilides, 51, 54

 Starch, 60
 Stärk, 143
 Statistics, cerebral syphilis, 91
 Stearin, 158
 Stewart, Purves, 98
 Stirling, 158
 Stomach, tertiary affections of, 81
 Stomatitis, 112, 129
 Stricture of rectum, 81
 Sublimate, 118, 149, (*see* Mercury bichlor.)
 — gastralgia, 121
 — solution, 42
 Sub-preputial chancres, 24
 Sulphur, 111
 Susrutas, 2
 Sycosis, 35
 "Sykos" of the Greeks, 2
 Syme, 129
 Synovitis, secondary, 68
 — tertiary, 84
 Syphilides, 49
 Syphilis, history of, 1
 — pathology of, 9
 — prehistoric, 3
 Syphilo-dermata, 49
 Syphilophobia, 147

 Tannate of mercury, 118
 Tattooing, infection by, 36
 Taylor, 19
 Technique of the external method, 132
 — of the intramuscular method, 164
 Tendons, secondary affections of, 68
 — tertiary diseases of, 82
 Teno-synovitis, 68, 82
 Tertiary affections:
 alimentary system, 72
 arteries, 86
 bones, 83
 bursæ, 82
 circulatory system, 86
 fingers, 85
 joints, 84
 kidneys, 81
 larynx, 78
 lips, 72
 liver, 79
 lungs, 78
 muscles, 82
 nervous system, 90
 palate, 76
 pharynx, 77
 rectum, 81
 skin, 70
 spinal cord, 93
 spleen, 80
 stomach, 81
 tendons, 82
 testes, 85
 toes, 85
 tongue, 72
 trachea, 78

- Tertiary syphilis, 69
 Testicle, secondary affections of, 68
 — strapping, 86
 — tertiary affections of, 85
Thucydides, 2
 Tinea circinata, 54
 Toes, tertiary affections of, 85
 Tongue, cancer of, 74
 — chancre of, 33
 — fissures of, 75
 — gummata of, 74
 — superficial affections of, 57
 — tertiary affections of, 72
 — ulcers of, 75
 Tonsils, chancre of, 34
 — hyperæmia of, 48
Torella, Gaspard, 128
 Trachea, tertiary affections of, 78
 Treatment, duration of, 167
 — plan of, 166
 — Zittmann's, 169
Treponema pertenue, 31
 True relapsing chancre, 21
 Tubercle, differential diagnosis, 77
 Turkish baths, 114, 175

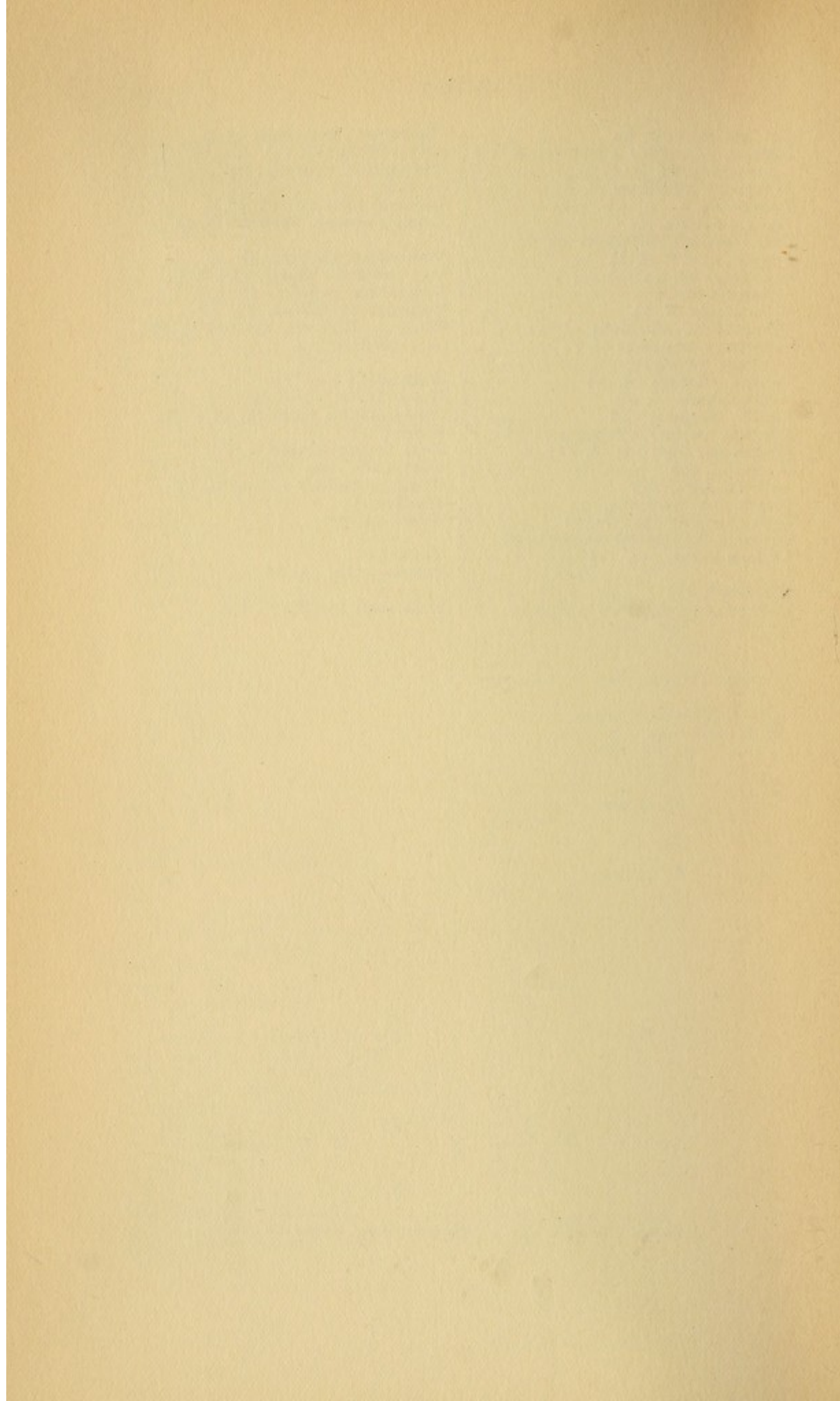
Uhlenhuth, 170
 Ulcerative gummatous syphilides, 71
 Ulcerative paronychia, 61
 Ulcers of tongue, 75
 Unguentum hydrarg., 43
 — G.P., 135
 Urethra, chancres of, 22
 Urinary meatus, chancres of, 22

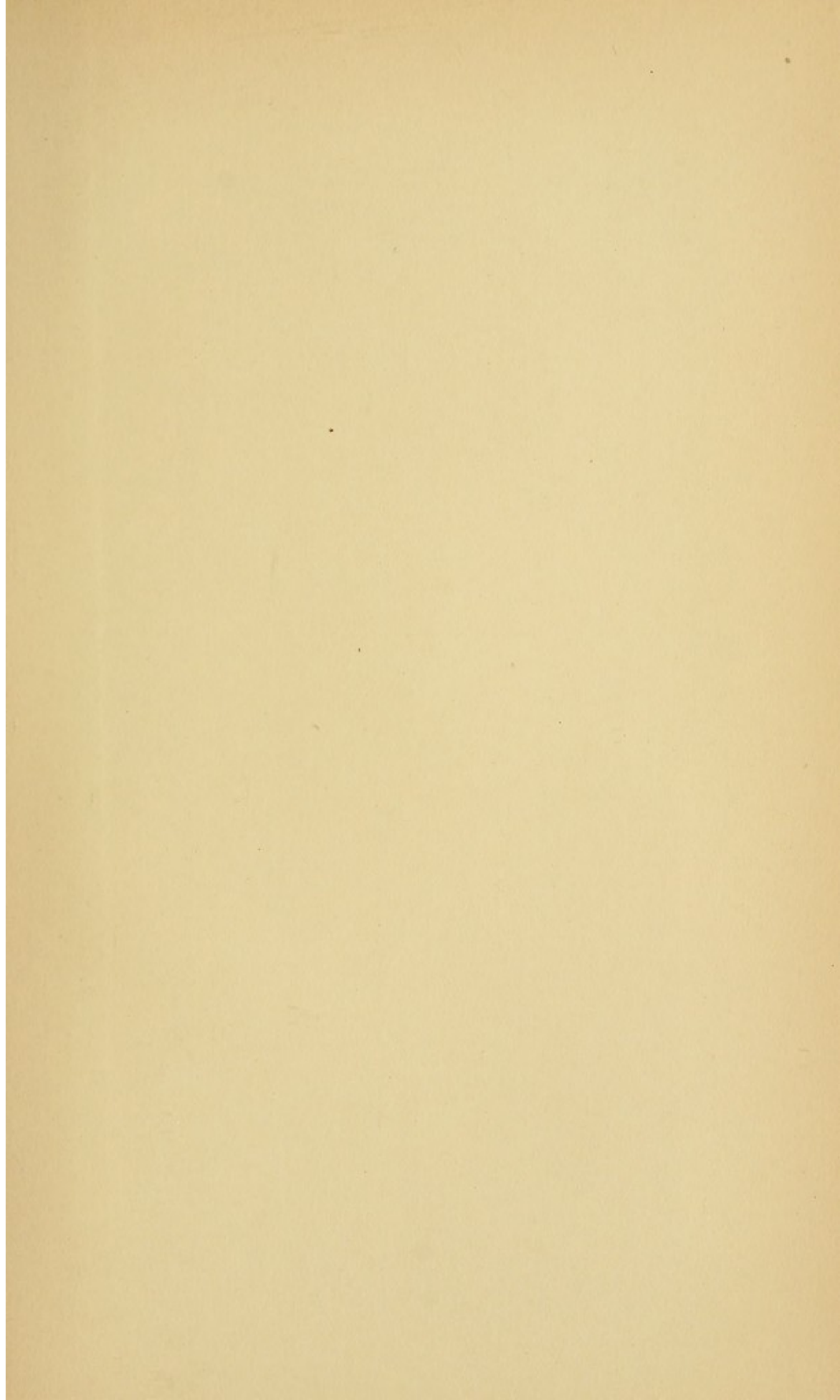
 Vaccination chancre, 36
 Van Swieten's liquor, 118, 124
 Vegetating papules, 59
 Vesicular syphilides, 51, 55
 Visceral affections, secondary, 66
 — — tertiary, 79

 Wallender's bag, 114
Ward, Major, 170, 173
 Wassermann's reaction, 103, 182
Weigert, 12
 West Indian Islands, 1, 5
 Westphal's sign, 100
 White precipitate ointment, 61
 Whitlow, 35
Widal, 94, 97

 Yaws, 31
 Yellow wash, 42, 60

 Zittmann's treatment, 169





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