The treatment of syphilis / by F.J. Lambkin.

THE TREATMENT OF SYPHILIS

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CHAPTER XVI

PRELIMINARY

Is it necessary to treat Syphilis?

If we mean by this, Can a patient recover from syphilis without any specific treatment? then the answer is, that this is quite possible, although improbable. Given a good, robust, and resistant constitution, an attenuated virus, and life under the best hygienic conditions, it is quite possible for the system to rid itself of the disease without any treatment. Personally, I have seen at least four such cases in which there was a history of undoubted syphilis (chancre, adenitis, and roseola), with absolutely no treatment whatsoever; and in the course of five-and-twenty years later there had been no further sign of the disease. Three of the four cases married and had families, which were apparently perfectly healthy.

On the other hand, it has been my lot to have met with thirty-two similar cases about which a very different account must be given. Out of this number, six developed cerebral syphilis within the first ten years; twelve, paralyses of different kinds before the fifteenth year; and the remainder have been affected with various sorts of tertiary manifestations.

If the question as to the possibility of a community becoming immune from the disease is asked, the answer to this, although being in the affirmative, will require to be very qualified. Experience shows that, like all other diseases in communities, when syphilis has existed and has been more or less allowed to run its course, it tends to exhaust itself and becomes weaker, reproducing itself in a benign manner; but if transferred to fresh ground, it again becomes as virulent as in the beginning. Innumerable examples of this are on record, notably those in the description by William Fergusson in the 'Medico-Chirurgical

Transactions', vol. iv, of June 12, 1812, about the state of Portugal during the Peninsular War as regards syphilis. At that time he found that, whereas the British soldier suffered terribly from mutilations and disfigurements and other dreadful ravages of syphilis during the four years' occupation of the country, the disease existed in the mildest form among the inhabitants. He added, 'that the virulence of the disease has become so much mitigated by reason of general and inadequately resisted diffusion, or other causes, that after running a certain (commonly a mild) course through the respective order of parts, according to the known laws of its progress, it exhausts itself and ceases spontaneously.' But at what expense was this state of things brought about? Fergusson (page 14) says: 'The Portuguese, through apathy, and at a dreadful price levied on the generations that are past, and never in all probability to be redeemed by their descendants, appear to have gained a great exemption from their immediate effects; but the price was too high, and God forbid that we, in despite of the faculties with which we have been gifted to preserve ourselves and others, should ever offer up our bodies to be the unresisting subjects of disease, the fatal consequences of which, though they might go to extinguish one or two ills, would be felt in the deterioration of our race to the most distant ages.' Such were the words of William Fergusson, the Inspector-General of Hospitals to the Portuguese Army in 1812, and they seem prophetic.

Prof. Fournier says: 'What I have seen, like every one else, and what I see every day, is this: cases of syphilis, which are abandoned to their own evolution, lead at first to a group of lesions, which although not serious, are none the less important, and later on to more serious lesions, often grave and sometimes fatal, constituting tertiarism.' Again, in answering the question as to whether every case of syphilis left to its own evolution ends in tertiary symptoms, he says: 'I know hardly any example of syphilitic subjects who, having abandoned their disease to its spontaneous evolution, have not sooner or later paid for their imprudence by some tertiary lesion more or less serious. I have met with two hundred and forty-one subjects who, having never undergone

any treatment for their syphilis, have all been affected with tertiary manifestations of various kinds.'

The answer to the question then, as to whether it is necessary to treat syphilis, is most certainly in the affirmative, as in ninety-nine cases out of a hundred syphilis, when abandoned to its own evolution, is a disease which is prolific in dangers of many varieties.

In connexion with the above, one very important question, which has been the subject of much dispute, will have to be alluded to here, i.e. Granted that, generally speaking, it is necessary to treat syphilis, are there exceptions to the rule, and is it necessary to treat all, even the mildest cases? To my mind this resolves itself into the question, Can we draw any definite line between mild and severe syphilis? In answer to this, I should say, How are we to determine as to the quality of a case of syphilis in its early stages, or what it is likely to be in ten or fifteen years hence?

Have we any solid grounds for believing that what we term 'benign' syphilis is less likely to be followed by tertiary manifestations than the severe form? This is the crux of the whole question; and as far as statistics go we have no reason whatever for believing that this may be the case. Available figures, on the contrary, go to prove the reverse, but this may possibly be the consequence of the scanty treatment which the mild form is likely to receive when compared with the more severe type. There is nothing, one way or the other, in the early stages to guide us as to what the ultimate progress of a case may be. The source of origin, period of incubation, character of the primary sore, or early eruption, will not help us in the least. One thing should always be remembered, viz. that syphilis which 'begins well may end badly'.

As regards this question Fournier gives the following statistics where tertiary lesions occurred in cases with the undermentioned antecedents:—

Benign secondaries	1,424	times
Secondaries of average severity	131	,,
Severe secondaries	54	,,
Early malignant syphilis	64	,,
	1,673	,,

Thus in the majority of cases (1,424 out of 1,673) tertiary manifestations followed secondary syphilis of benign character, showing that nine times out of ten, tertiary symptoms result from syphilis that was originally benign. In my opinion, to leave a patient untreated, or, in fact, to make any difference in the amount of treatment, because he happens to be suffering from 'benign' syphilis, is to abandon, or subject him to the gravest possibilities in the future.

Abortive Treatment

Attempts have been made hundreds of times by cauterization and total excision of the chancre to prevent constitutional infection; but these efforts have invariably failed. Even although these failures may have been the result of the operation not having been thoroughly done, the continuance of such treatment can hardly be justified. Lately, Metchnikoff has endeavoured to destroy the *Spirochaete pallida* by the application of a 30 per cent. calomel ointment in, and about, the site of inoculation. His experiments on monkeys proved successful in that inunction at the point of inoculation, within an hour or two after it, prevented the development of the disease. He was enabled to carry out a similar experiment (see p. 180) on a medical student who voluntarily offered himself. In the case of the latter, inunction at the point of inoculation prevented further developments. However, Neisser's experiments on the same lines do not confirm Metchnikoff's views. The question may, at present, be considered to be *sub judice*; but to my mind it appears to hold out some hope of good results in future.

Specific Medication. By this is understood, medication with substances which are supposed to have the power of attacking the cause of the disease in such a way as to be directly curative. In the case of syphilis these substances are innumerable, and great promises have been made from time to time for each of them. The following are the names of a few: guaiacum, sarsaparilla, sassafras, sulphur, arsenic, gold, silver, platinum, and many vegetable preparations of lobelia, hops, and chicory; last, but not least, come iodide of potassium and, of course, mercury.

Most of these have long ago sunk into the oblivion they deserve. One of the exceptions is sarsaparilla, which in the sixteenth century had a great reputation as an antisyphilitic, and formed the basis of many 'well-known certain cures'. However, its reputation gradually waned until it appeared at one time to be totally forgotten. During late years it has been revived to a certain extent, and principally through Zittmann, of whose celebrated decoctions (pp. 249 and 305) it forms the staple part. There is no doubt whatever that, under certain circumstances, sarsaparilla and some of the above-named substances have a beneficial effect in cases of syphilis; but that this is due to their tonic and depurative effects, rather than any specific action, is also certain. There is no reason to believe that they have any true specific action on the syphilitic virus. At one time, indeed up to a comparatively recent date, iodide of potassium was believed to be a true specific in syphilis, come to oust mercury from that position, or at least to compete successfully with it; but, as will be seen later on, it has been relegated to a second place as a mere adjunct to mercury.

CHAPTER XVII

MERCURY

After having been employed in the treatment of syphilis for at least four hundred years, and having passed through the furnace of fierce and heated discussions, mercury is now firmly established in the estimation of all syphilologists as the true specific and antidote for syphilis; and, since the discovery by Schaudinn of the *Spirochaete pallida*, observations of the action of mercury on the latter have strengthened more than ever the position of that metal as a specific.[1] Personally, I would say that in the whole category of therapeutics there is—with the possible exception of quinine in malaria—no other drug more worthy of the name 'specific' than mercury. This position, which has been attained and preserved in the face of extraordinary vicissitudes, will, I believe, always be maintained, owing to its powerful action on the disease, which must be evident to every observer, and cannot be denied.

Mercury fell into utter disrepute in the treatment of syphilis at one period, and it was accounted as being the cause of half the misfortunes which had hitherto been attributed to the disease itself. No doubt it was owing to the barbarous treatment to which syphilitic patients were formerly submitted, when the virtues of the remedy were attributed to its salivating action, and when unfortunate patients were condemned to continued salivation. Donald Munro, writing in 1780, says: 'Where there are evident symptoms of a confirmed pox, the only method of cure

[1] This was written prior to the completion of a series of experiments which I was making at the Military Hospital, Rochester Row, with reference to the treatment of syphilis with the meta-arsenic-anilide salts, the completion of which have convinced me of the important fact that we have in these salts an undoubted second specific for the disease. Whether they will eventually prove as efficacious or more so than mercury time and experience can alone tell (see pp. 308–11).

that has hitherto been found effectual is to throw in such a quantity of mercury, either by the mouth or by inunction, as will bring on more or less salivation, and to keep that up until most of the venereal symptoms disappear.' He goes on to describe the ways of doing this: 'The patient ought to have 2, 3, or 4 grains of calomel, or 6–7 grains of metallic mercury killed with honey twice a day. One of these methods to be continued until the breath begins to smell and a bad taste is perceived in the mouth, and the gums to swell and become painful.'

It was during the Peninsular War that this state of affairs first became manifestly apparent, and through the writings of G. J. Guthrie (1785–1856) and other army surgeons the position of mercury was seriously threatened, but was saved by William Fergusson, 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.

But the bad name then acquired by mercury has never been entirely removed, and to this day it is a drug hated and detested by the general public, as being the cause of ulceration, gangrene, severe bone lesions, paralysis, and—of course—alopecia; in many a case syphilis has been allowed to have its full course owing to the absolute refusal of the patient to undergo mercurial treatment, solely on account of this loathing.

Although there is little fear of mercury producing any ill effects when administered therapeutically, there are undoubtedly certain dangers attached to it. These may be divided into four classes: (1) salivation, (2) gastro-intestinal symptoms, (3) cutaneous eruptions, (4) disorders of nutrition.

Salivation may occur in the form of stomatitis, varying in degree from slight redness and swelling of the gums to intense inflammation of the whole buccal mucous membrane, accompanied by deep ulcerations, local gangrene, necrosis of the jaw, and loss of teeth. Such cases, however, belong to days gone by, and happily seldom, if ever, occur at the present time. The stomatitis we come across now is only partial, and does not damage the teeth or jaws. Severe salivation is nearly always the result of

negligence, either in the way mercury is administered, or from neglect in carrying out the ordinary precautions which are always necessary when a patient is undergoing mercurial treatment, viz. hygiene of the mouth. Too much attention cannot be paid to this, and mercurial treatment should never be commenced without previously ascertaining if the mouth is in a condition to permit of it. If possible a visit to the dentist ought to be made, all teeth regulated as well as possible, and old stumps removed. At the same time the patient should be warned that he is undergoing mercurial treatment, and without alarming him he should be instructed as to the absolute necessity of keeping a strict watch over his mouth and teeth, special emphasis being laid on the brushing of the latter after each meal. He should always be given a mouth-wash to use frequently during the day. This may consist of either chlorate of potash, gr. 5 to the ounce, or, better still :—

R (1)	R (2)
Plumbi acetatis, ℥ i	Aluminis sulphatis, ℥ i
Aquam, ad ℥ v	Aquam, ad ℥ v

Sig.

(1) and (2) to be mixed and filtered.

The gums should be painted two or three times a day with borax and glycerine, or with peroxide of hydrogen, or better still with perhydrol (Merck), which is a 50 per cent. solution of peroxide of hydrogen, and is quite non-irritating.

There are, of course, cases where some peculiar intolerance of mercury cannot be foreseen, and then extra care is necessary. Should stomatitis of any severity come on, in spite of every care, it is needless to say that all mercurial medication must cease. Saline aperients should be freely given, and the patient should be ordered a mixture containing potassium chlorate in 15-grain doses to be taken every second or third hour. Hot-air baths should be administered frequently, and if sweating be profuse, atropine should be given subcutaneously in doses of gr. $\frac{1}{100}$. At the same time the mouth and gums should be swabbed out frequently during the day with perhydrol, or with a solution of chromic acid, and strongly astringent mouth-washes.

Gastro-intestinal complications. These consist at first of pains in the stomach, colic, and diarrhoea; at a later period, dyspepsia and loss of appetite. These are generally the sequelae of the ingestion of mercury, and, although with the view of preventing them certain drugs have been recommended to be added to the mercury —such as opium and extracts of thebain—my advice is that when once they show themselves, methods of giving mercury other than by the mouth should be tried. At the same time, although these symptoms are generally the results of taking mercury internally, it must be recognized that gastro-intestinal symptoms of a far severer kind have been known to follow inunction and intramuscular injections, some of the cases reported having presented dysenteric symptoms—the passage of blood, slime, and mucus—whilst one or two have ended fatally.

Cutaneous complications. These are, in my experience, very rare, although Fournier and other French writers consider them more frequent. The most common is a form of desquamative dermatitis, resembling erysipelas, whilst others simulate scarlatina and urticaria.

Nutritive complications. It may be assumed that anything producing gastro-intestinal disturbance will be followed by languor, anaemia, want of appetite, and emaciation; but even in the absence of these there is undoubtedly such a thing as the 'high-water mark', beyond which trouble follows if mercury is continued. Experience shows that after a few weeks the strongest stomach may become fatigued by the remedy, and even suffer damage.

Hence the necessity of allowing intervals during treatment, when all mercury is suspended.

Therapeutic Actions of Mercury

Action on the syphilitic virus. 1. It has long been supposed that mercury has a bactericidal action on the micro-organism of syphilis, and from what we now know as regards its action on the *Spirochaete pallida* there is every reason to believe that this is true. Two years ago I found that one intramuscular injection

of gr. 1 of metallic mercury caused the disappearance, in about two days, of these organisms in a case in which they had been numerous before the injection ; and I may here note that nothing has struck me more than finding how small a dose of mercury is sufficient to cause the disappearance of the spirochaetes. Surely then we have *a priori* grounds for believing in the theory of the direct destructive property which mercury has on the syphilitic virus, believing—as we do now—that the *Spirochaete pallida* constitutes this virus!

2. It is supposed that mercury, by its action on the syphilitic virus, forms alexins, i.e. substances furnishing the organism with the power of defence by neutralizing the pathogenic agents.

Two important actions. Two important actions are claimed for mercury :—first, that it is curative ; second, that by its action it influences syphilis both as a whole, and in the future of the disease.

The curative action of mercury must be self-evident to the most casual observer. Note how syphilitic lesions are cut short : how, for instance, a papulo-squamous syphilide which, before the administration of mercury had remained *in statu quo* for months, disappears under the influence of the specific in as many days ; and again how some syphilitic lesions, which tend to destroy an organ, rapidly disappear under mercury. There are numerous other instances which occur daily to the casual observer, but which are none the less expressive of the curative action of mercury ; of these none are more striking than those vague cerebral cases—with resulting nervous disorders of all kinds—which, having resisted all other treatment, begin to clear up when diagnosed as syphilitic and treated with mercury. Secondly, the action of mercury on syphilis as a whole, and in its future. In this connexion the question may be asked whether, as some believe, mercury acts only on the lesions and symptoms of syphilis, or whether this action extends to the disease itself. I have always believed that the second represents the true state of the case, and do so more firmly the oftener I see the way it influences the *Spirochaete pallida*. This being so, we have every ground for believing that, when administered long enough, mercury exerts

a general influence on the disease as a whole, and will eventually result in cure.

That it exerts a preventive action on the secondary period is illustrated every day when we see secondary syphilis, in subjects who have been treated with mercury from the beginning, nearly always reduced to lesions of a superficial and benign character, and compare them with cases which have gone untreated. In the latter we see cutaneous syphilis of different kinds—from roseola to the pustular and pustulo-crustaceous, deep ulceration of the tongue and throat—with various other lesions of a more or less severe character. When treated, syphilis undoubtedly becomes attenuated, atypical, and benign.

In the tertiary period the action of mercury is still more marked; this is proved by the frequency of tertiary lesions in syphilitic subjects who have not been treated at all, or who have been insufficiently dealt with.

The following tables are taken from 100 cases of cerebral syphilis :—

After thorough mercurial treatment	5 cases
After moderate, but insufficient treatment	6 ,,
After only 7–18 months' treatment	10 ,,
After only 6 months' treatment	70 ,,
After no treatment	9 ,,
	100 ,,

Therapeutic antecedents of 1,703 cases of tertiary syphilis :—

No treatment at all	217 cases
Treatment for less than a year	1,162 ,,
Treatment for one or two years	265 ,,
Treatment for over two years	53 ,,
Treatment for more than three years	6 ,,
	1,703 ,,

Thus, out of 1,703 cases of tertiary manifestations, 59 occurred after treatment, which might be considered sufficient ; and 1,644 followed insufficient or simple expectant treatment.

Methods of administering Mercury

There are three principal methods by which mercury is introduced into the system :—

1. The internal, or ingestion method.
2. The external, or inunction method.
3. The method by intramuscular injection.

Two others are less often used, i.e. the method of fumigation, and the method of intravenous injection.

In making our selection as to which of these plans is to be employed, we must be guided by certain conditions and circumstances, and should not rush blindly into conclusions without carefully weighing the following :—

(1) Which of the above methods can be employed with the greatest convenience to the patient.

(2) 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 of preventing the future ravages of the disease.

(3) Which of these plans will best ensure regularity of treatment.

(4) The best method to adopt in cases of severe and urgent syphilis.

These are the chief considerations which ought to guide us in making our selection, but there are others of minor consideration which will, no doubt, also influence us—such as the state of the patient's digestion—and last, but not least, private considerations which may contra-indicate certain methods.

The Ingestion Method

This consists in the absorption of mercury by the stomach and intestines. It is the plan which has usually been employed up to late years, until better and more convenient methods entered the list ; and indeed even now it is the one which is most popular in England. The reasons why the internal method was preferred is not far to seek, i.e. convenience for both physician and patient

over the method which had hitherto existed. This is undoubtedly the sole and real reason, because its therapeutic effects are far inferior to those of the inunction method, which was practically its sole competitor; besides, it was at least equally liable to all the dangers and accidents which were found in connexion with the other plans.

The disadvantages of this method have become very palpable of late years, so much so that it is gradually dropping out from amongst the different plans for carrying out the treatment of syphilis. This of course applies in a special manner to the continents of Europe and America. Its disadvantages are :—

First. It is particularly liable to irritate the gums, and to bring about gastro-intestinal disorders of all sorts. This is a serious objection, as it necessitates the treatment being abandoned for a time at least, in which case the disease gets a further hold on the system; and if persisted in, emaciation, debility, and anaemia are brought on, thus placing the patient in the very worst position to resist the disease.

Secondly. Uncertainty as to its being carried out with anything like regularity. This, to my mind, is the chief objection to the ingestion method. The uncertainty of regularity is the result either of the patient's absentmindedness in forgetting to take his medicine, or, on the other hand, to his deliberately giving it up on the first disappearance of the morbid symptoms of the disease. To put the matter concisely, it is easy for the physician or surgeon 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 perhaps months at a time; but it is quite another thing to expect (even if all goes well as regards toleration) that there is any chance of these instructions being carried out with anything approaching to 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 idea of taking it during the day; but I wonder how often, when the end of the week comes, he can look back and say he has done so regularly during every day of that week. Yet to be of any use we know that regularity in

taking the mercury, or something approaching it, is necessary. On the other hand, the ordinary patient, in nine cases out of ten, 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. This second objection is enough to put the internal method entirely out of court as a routine plan of treatment, as it is impossible to have it carried out.

Thirdly. That it is inconvenient. Oddly enough, the contrary is claimed for it by its adherents, such as Fournier, who puts it—'What is more simple than to swallow every day one or two pills, or one or two spoonfuls of a mixture ? This is neither troublesome nor embarrassing. Compare this ideal simplicity with the practice of inunction or injection—the former with its daily rubbings, the latter with its weekly visit to a physician. What a waste of time ! What tediousness !' I quote this as the argument appears to me to condemn itself. It may be easier, certainly, to take medicine or pills two or three times a day than to submit to a daily rubbing ; but who will be so bold as to argue that it can be done with as great facility as a visit once a week to a physician, for the purpose of receiving an injection ?

Fourthly. Uncertainty as to the dosage. By this is meant the uncertainty which always exists as to the amount of mercury which is taken, i.e. actually absorbed. Many cases are on record where mercurial pills taken by the mouth have passed through the gastro-intestinal system, and have been voided per rectum in exactly the same condition in which they were taken, absolutely none of the mercury having been absorbed. It is needless to point out the seriousness of such a state of things as this.

The advantages claimed for the internal method are :—

First, convenience to the physician.

Secondly, convenience to the patient.

Thirdly, that any salivation which may accompany it is more easily cut short than when it follows on the use of any of the other plans.

The first of these two have already been considered, and, I think, proved to be just the other way. As regards the third advantage it can, I think, be upheld.

Technique of Internal Method

It is now necessary to give the technique with the different preparations used for ingestion. Needless to say, that the number of preparations of mercury used for this method are innumerable ; to give a list of them would be almost impossible (see also p. 192). It will suffice to mention the chief of these mercurial compounds.

1. Metallic mercury, which is administered in different ways and enters into the formation of some of the most famous preparations, i.e. English ' blue pill '.

℞

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

Sig.

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

Sédillot's pills.

℞

Mercurial ointment	30 grms.
Powdered soap	20 ,,
Powdered liquorice	10 ,,

Misce et div. in pil. 20.

English ' grey powder '.

℞

Mercury	1 part
Powdered chalk	3 parts

2. *Calomel* has had its ups and downs. It is not at present used very extensively internally, as it is apt to bring on diarrhoea and stomatitis. It is chiefly given in the form of Plummer's pills.

3. *Biniodide of Mercury* is still used sometimes in conjunction with iodide of potassium ; it is inclined to be toxic and cause stomatitis.

4. *Tannate of mercury.*

5. *Salicylate of mercury.*

6. *Perchloride of mercury.*

7. *Proto-iodide of mercury.*

Tannate of mercury is not a definite compound, and is therefore unreliable.

Salicylate of mercury has, from time to time, been highly extolled, but its therapeutic intensity is very mild indeed.

Perchloride of mercury (corrosive sublimate) has been the favourite of all the salts used internally, with the possible exception of the proto-iodide and sublimate. Among other celebrated preparations of which it is the basis, Dupuytren's pills are perhaps the most famous. These consist of

Perchloride of mercury	1 cgr. (gr. $\frac{1}{6}$)
Ext. of opium	2 cgr. (gr. $\frac{1}{3}$)
Ext. of guaiacum	4 cgr. (gr. $\frac{2}{3}$)

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

℞

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

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

Proto-iodide of mercury is a salt of greenish-yellow colour, and very faintly soluble. Hence it is always ordered in pill. It is very much used in France, where it was popularized by Ricord when he introduced it in his well-known pills, the formula for which is :—

℞

Proto-iodide of mercury	3 grms.
Extract of thebain	1 ,,
Theriaca	3 ,,
Confection of roses	6 ,,

Misce et div. in pil. 60.

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

There can be no doubt, for ingestion purposes, corrosive sublimate and the proto-iodide are the best preparations of mercury to use. The question is, Which of them is to be preferred? As already stated, in France the proto-iodide is

appreciated most, whereas the perchloride is preferred in England, but there is something to be said for and against both of them. Let us compare them :—

Proto-iodide is more likely to be followed by salivation (stomatitis) than sublimate. This appears to be certain, and is probably the result of the proportionately larger dose of the former which must be given in order to bring about physiological effects than the amount necessary in the case of sublimate.

Perchloride is more likely to be followed by gastric trouble than the proto-iodide if given for any length of time; it is very apt to cause constant pains in the stomach (sublimate gastralgia).

On the other hand, proto-iodide irritates the intestine more than does sublimate, and is far more likely to bring on diarrhoea than the latter.

In nearly every case proto-iodide is followed by slight attacks of colic and diarrhoea when first given: this is called 'premonitory' diarrhoea. This 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 diarrhoea, 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, as a good effect can be realized much better through it, owing to the fact that its dose can be raised with safety; whereas in the case of sublimate this cannot be done without running the risk of salivation and other toxic effects. 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 these salts is, I should say, that, as a rule, the proto-iodide ought to be given in the early secondary, and sublimate in the later secondary and tertiary stages. One undoubted advantage which proto-iodide has over sublimate is that it can be continued over a much longer period without causing any trouble. Of course, either of these salts must be prescribed according to the case and its conditions. Thus for patients with bad teeth, sublimate should

be the salt chosen; whereas in those inclined to suffer from dyspepsia and gastric troubles, proto-iodide should be selected. As to the best forms to order: sublimate can be given in either mixture or pill, of these I used to prefer the latter, especially in the form above described (page 270) as Dupuytren's pills. As an improvement on that formula, Prof. Fournier suggests the following:—

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

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

As a mixture, sublimate is generally ordered either in water or some tonic infusion. A stock mixture, which is in habitual use in England, is one containing liq. hydrarg. perch. and iodide of potash: this is given for indefinite periods. The less said about this practice the better, except to condemn it freely.

Proto-iodide of mercury can only be given in the form of pills. Being insoluble, it cannot be ordered in mixture or solution. The ever popular 'Ricord' pills are still much used, and here again, as an improvement, Fournier suggests the following:—

℞

Proto-iodide of mercury . . .	5 cgm. (gr. $\frac{5}{6}$)
Extract of opium	1 cgm. (gr. $\frac{1}{6}$)

as being easier to increase and decrease the dose, and as containing less opium.

Dosage. With regard to dosage, it can be taken for granted that the dose of mercury ordered is, in nine cases out of ten, lower than that consistent with its physiological effects. This is generally the result of timidity—in other words, having to keep on the right side. This leads to inefficient 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 be truly 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 bi-chloride or proto-iodide; but we can surmise as to what might be considered an average one. With regard to sublimate, this can be considered as gr. $\frac{1}{2}$ daily for a man, and gr. $\frac{1}{3}$ daily for a woman; whilst that of the proto-iodide may be taken as gr. $1\frac{1}{2}$–2 and gr. 1–$1\frac{1}{2}$ respectively as a daily average dose. At the same time, it is well to remember that an early and mild lesion is acted on more easily by a weak dose than is a later and more severe one. In other words, the dose which will be sufficient to remove a mild roseolar rash will not make the slightest impression on a case of syphilitic papular eruption, and it would be absurd to trust to this same dose in the case of cerebral or spinal syphilis.

Remarks as to the Internal Method

My personal experience of treating syphilis by this method has extended over a good many years, during which time I have used all methods as well as most of the preparations that have been recommended. I found, in the majority of cases, after mercury had been administered by the mouth for six weeks or two months, it began to disagree in one way or another. Stomatitis appeared, and the digestive system becoming impaired, the general condition of health naturally began to suffer. A condition of malnutrition set in, and the disease remained either *in statu quo* or else further outbreaks took place. In either case the drug had to be discontinued for a time, to be recommenced again later on. The same series of events went on, and the patient gradually drifted into a chronic syphilitic state. Another and far more serious lesson I learnt—that with this plan of treatment there was no certainty that the patient ever got his medicine with any sort of regularity, and in many cases the chances were that he never got it at all. The fact is, that as the administration of the medicine depends absolutely on the patient himself, I found that, no matter how keen he was to get rid of his disease, he at times inadvertently forgot to take the medicine; 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, that finally I came to the conclusion —which I have since had no reason to change—that it alone is sufficient to put the internal method out of court altogether as a plan of routine treatment.

Again, years ago, clinical observation led me to suspect that in a great many cases treated by this method, after mercury had been taken for any length of time, the system 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. The experience of later years has merely served to confirm this conviction.

The External, or Inunction Method

This is the oldest known method of administering mercury. There are evidences of its having been used in the earliest periods in the history of syphilis. In the fifteenth, sixteenth, and seventeenth centuries it flourished, and during the sixteenth century it was by means of this method that mercury was introduced in dealing with what was known as the ' new disease ' (syphilis) which was then rampant in Europe. Popular beyond all other modes of administering mercury, the inunction method, through the reckless manner in which it was carried out, gradually died out and a violent reaction set in against it, the height of which was reached during the Peninsular War.

It is now well known that up to a certain date the idea of being able to cure syphilis without inducing salivation was not thought possible, but, on the contrary, it was held that salivation was absolutely necessary ; it can be imagined that for this purpose no method of administering mercury lent itself better than did that of inunction.

The old method of inunction consisted not only of a certain number of rubbings, but, in addition, purgation, bleeding, and over-heating in a specially prepared hot chamber were employed, (p. 201), and during the time of treatment the patient was kept on a restricted diet. It can be imagined what was the effect of

inunction practised in this manner, and the wonder is that the patient survived, say, thirty to forty days of a course of such treatment. However, things have changed much since those days, and the method by inunction to-day is now very different. It simply consists of a certain number of rubbings with a mercurial ointment, the strength of which is at least known, combined with mild diaphoresis, good diet and hygiene, and a total absence of the purging, bleeding, and profuse sweating as above described. Popular as the inunction method undoubtedly was on the continent of Europe, it never appears to have attained a vogue in England even down to the present day, and this in the face of the writings of some of her most famous syphilogists, including 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 due, I believe, to the ignorance that existed as regards technique; this same ignorance has remained to the present day. It has always been an enigma to me why England has not taken example in this matter from Aachen, or Aix-la-Chapelle, for there, during the last century and a half, the inunction method has flourished in the most successful manner. Every nation in the world 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. I fear it is only one more proof of that Conservatism in our profession in England which prevents it from adopting anything new.

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 I have 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 have before failed to obtain from perhaps one or two years of sporadic courses of treatment by the internal method. The routine treatment at Aachen is as follows: First of all the patient calls upon his doctor, who examines him and takes his weight, which he carefully records. If it be an ordinary case, after further instructions as to the treatment he is about to go through, the patient is told to come and see the medical man in a week's time. During the interval his treatment is this :—

He rises early each morning and walks to one of the mineral springs—a matter of perhaps a quarter of a mile, then he partakes of one or two glasses of the sulphur water.

Then follows a light breakfast, consisting perhaps of one egg, bread, butter, and coffee.

One to two hours later he goes to one of the many baths, and there proceeds to have his bath, which consists of warm sulphur water at 39° C. The patient sits immersed in this for 25 minutes, when he leaves it and is well dried. Half an hour afterwards a professional rubber rubs into his skin 75 grains of a mercurial ointment, which is slightly stronger than the ung. hydrarg. (*B. P.*). The rubbing lasts from fifteen to twenty minutes.

The parts of the body into which the ointment is rubbed are changed daily, so as to avoid the effects of friction, such as dermatitis, &c.

First day, the arms; second day, forearms; third day, the chest; fourth day, the back; fifth day, the thighs; sixth day, the legs; returning on the seventh day to the arms. The ointment is rubbed dry, until it looks more like black-lead than anything else, and the part of the body rubbed is not washed or scrubbed until the morning of the day it is its turn to be rubbed again. The professional rubbers at Aix use no artificial protection to the hands against the chance of absorption of mercury themselves. At Wiesbaden and other places glass balls and slabs are used in rubbing. The Aix rubbers never suffer from any sign of salivation, and they maintain that the rubbing can be far more effectually done by the bare hands than by any artificial means. I may here say that our experience at the Military Hospital, Rochester

Row, London, where the Aix treatment is carried out as nearly as possible, our experience is the same; and I have never seen any bad effects to the rubbers. Whilst the course of treatment is going on, the patient is warned to pay strict attention to the state of his gums and the cleanliness of his teeth, and to use frequently during the course of the day a mouth-wash of alum and lead, the composition of which has already been given (vol. i, p. 216), well brushing the teeth after each meal. The diet is not restricted to any marked extent: the patient is advised to live well and to drink freely of new milk. Spirits are forbidden, but beer and the light Rhenish wines are allowed in moderation. Mental and bodily exercises are encouraged, and the patient is advised to spend as many hours as possible in the open air during the day. Of course all precautions against cold and chill have to be taken, and flannel worn next to the skin. In any case, at the end of each week the patient pays a visit to his medical adviser, who again records his weight, and notes the progress which has been made.

The course of treatment usually lasts six weeks. The patient is then allowed to leave Aachen, but is advised to return in not less than a year's time for a further course.

As already mentioned, the above technique of the inunction method is imitated as closely as possible at the Military Hospital, Rochester Row, London, whenever this particular plan of treatment is adopted, and up to the last year these occasions were fairly frequent in cases when greater therapeutic intensity was desired; but since the time that I have been able to use calomel by injection with impunity, injections have given place altogether to calomel, which brings about the desired effect much more readily.

Advantages of the Inunction Method

1. Therapeutic effects are far more marked than when the drug is given by the mouth.

2. It does not affect the alimentary canal.

3. It leaves the stomach free for the administration of other remedies.

Disadvantages

1. Treatment by this method can only be of an intermittent nature, and this is opposed to our judgement as regards ultimate cure and prevention.

2. It is very frequently followed by a severe form of dermatitis.

3. It cannot be resorted to in certain cases, as, for instance, where there are severe cutaneous lesions scattered over the body.

4. It is dirty, inconvenient, and *very* difficult to have carried out with anything like efficiency under ordinary circumstances.

5. It is far more likely to be followed by stomatitis and salivation of a peculiarly severe type than is any other method.

Until recently I looked on the inunction method of treatment as the most efficient in removing certain signs and symptoms of syphilis, and I employed it extensively in some cases, such as, for the removal of persistent induration round the site of a chancre, in skin eruptions like papular psoriasis, in all cases of syphilitic sclerosis, commencing locomotor ataxia, and in cases of cerebral sclerosis. In such cases I invariably put the patient through a full course of inunction, but at the present time the intramuscular injection of calomel has entirely taken the place of inunction in such cases.

It would be well to remember one other drawback to inunction —the nature of the method is such that it can be carried out in private practice only with the greatest difficulty, as it necessitates the patient giving up at least an hour a day to it, and doing away with any chance of secrecy as regards the nature of the disease from which he is suffering. This latter may appear insignificant; but nevertheless it is an objection to this method of treatment which is sometimes insurmountable.

CHAPTER XVIII

THE INTRAMUSCULAR METHOD

We now come to the third method of administering mercury in the treatment of syphilis.

It is known as the intramuscular method, and consists in the introduction of certain mercurial preparations by intramuscular injection for absorption by the circulatory system.

The idea was first suggested by Scarenzio in 1864, and was actively practised for a certain time; but owing to certain accidents which generally followed 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, or that of Scarenzio, dates from 1864, when the treatment of syphilis by hypodermic injection of mercury was introduced by that surgeon, a professor in the University of Pavia. At the same time, it appears to have been previously suggested by Berkeley Hill, of London, in a paper which he wrote to the 'Lancet' in the year 1866 (vol. i, p. 498), but who, up to then, had never actually practised it. Scarenzio at first used the yellow oxide of mercury, and later on, calomel; as an excipient he used glycerine, but finding this very irritating he substituted gum-water. He records having given eight subcutaneous injections, each of which was followed by an abscess. Ambrosoli,[1] of Milan, published a series of sixteen cases, all treated by Scarenzio's method, thirteen of which, although benefiting much by the treatment as far as the disease was concerned, were all followed by abscesses. On the other hand, we find Professor Profeta writing of the method thus: 'I should never have

[1] Ambrosoli's paper published Ann. de derm. et de syphil., 1866, p. 347.

recourse to the method unless all others failed, owing to the constant recurrence of abscesses at the site of injection.'[1] The method was persisted in, although to a very limited extent, in most of the capitals on the Continent for a few years. In Italy it had enthusiastic exponents, but far more detractors, chief among the latter being Profeta.

In France opinions were very much divided about it. Hardy practised it with much success at the St. Louis Hospital. Liegois used sublimate instead of calomel, and had a certain amount of success, whereas Jullien was an opponent of the plan. Belgium and England did not trouble themselves about it one way or the other, indeed we have little proof that the method was ever tried in either country at this time.

Essays were numerous regarding the subcutaneous method both in Germany and Austria, opinions being, on the whole, hostile to it. Störk, for instance, described it as a 'detestable' treatment, whilst Kölliker appears to have been in favour of it. However, this plan of treatment gradually died out in three or four years after its introduction, and was not renewed until we come to the *second* period, or that of Smirnoff, who, in 1882, published an interesting work on the subject, in which he endeavoured to revive the treatment. He maintained that with the help of antiseptic precautions, which by that time were much better known, it was quite possible to give injections without abscess formation as a result, and he succeeded in his endeavours.

Although abscesses became much rarer, still they continued to appear now and then, and the method was again dropped, remaining in abeyance until the appearance of a paper by Balzer, which he read on March 11, 1888, before the Société des Hôpitaux, on 'Injections of yellow oxide of mercury and calomel in the treatment of syphilis'.

The *third*, or what I term the period of Balzer, dates from the final introduction of the treatment up to the present time. Balzer pointed out that the chief cause of the abscesses which had hitherto always followed the injection of mercury was first, because it was

[1] Ancora della cura mercuriale ipodermica della sifilide (Clin. dermo-sifil. di Palermo, 1878, pp. 150–66).

given into the subcutaneous tissue, and second, owing to the unsuitability of the vehicles which had hitherto been in use, i.e. gum-water, glycerine, and olive oil.

As a remedy he suggested giving the injections intramuscularly, and employing liquid paraffin as a substitute for the older vehicles. Good results followed almost immediately, and abscesses became rare. From this time the intramuscular method of treating syphilis gradually grew in favour, until to-day it is undoubtedly the most popular method in Europe and America. The same cannot be said of it in England and her world-wide Empire, where it is still little known, the exception being in her army, where, since the year 1889, it has been gradually pushing its way and gaining in favour through the brilliant results which have been attained, especially in India, where, during the last decade, admission to hospital for syphilis among British troops has fallen from 400 per 1,000 to 110 per 1,000, and invaliding—for the same cause—from 14 per 1,000 to ·92 per 1,000, in 1906. This result is due, almost entirely, to the adoption of the intramuscular method of administering mercury.

Advantages and Disadvantages of the Intramuscular Method

It is now necessary to carefully consider what are the advantages and disadvantages of this method.

Advantages

1. Convenience to the patient.
2. It ensures the patient getting the treatment regularly.
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. There is less chance of toxic symptoms—especially of stomatitis.
8. Both therapeutic intensity and physiological effects are

much more marked and lasting when introduced by this method than by any other.

Let us consider these seriatim :—

As regards *convenience*, I think this must be admitted, as all the inconvenience which the intramuscular method causes to the patient is an occasional visit to his medical man, which, in the case where an insoluble preparation is used, is generally once a week, and often not more than once a fortnight. Compare this with having to take medicine two, three, or four times a day for perhaps months at a time ; or, again, having to give up an hour a day, for perhaps a month or six weeks at a time, for inunction. In the case of the injection method the patient receives his treatment once a week or a fortnight, as the case may be, and has no reason to think any more about it until the time comes round for the next visit. This is a very great advantage in those cases where it becomes a matter of importance that the patient should think as little as possible about his disease.

By the intramuscular method regularity and certainty of treatment are ensured, as the treatment is entirely in the hands of the medical attendant, who knows for a certainty that the amount *is* given, and *when* it is given, and that it is not—as in the case of the internal method—left to the will, or memory, of the patient himself ; or, as in the case of inunction, left to the rubber. The third advantage is apparent : as the drug does not enter the stomach, it leaves this organ free to receive other remedies.

As regards the fourth advantage—more accurate dosage—it is certain that by the intramuscular method the amount of mercury introduced can be made mathematically correct.

Absorption of mercury in a definite manner is ensured by this method. We have seen already that in the case of the ingestion plan the actual amount of mercury which is absorbed is most uncertain, and that in some cases little, if any, may be absorbed. On the other hand, by the inunction method, the amount of absorption must of necessity be very uncertain, depending as it does to a great extent on the way the rubbing has been done. We know that, when given by the intramuscular method, mercury does not interfere with the gastro-intestinal system ; this, needless

to say, is a priceless advantage held by this plan over the internal method.

With regard to the seventh advantage, i.e. less chance of being followed by stomatitis and salivation than when given otherwise, I came to this conclusion many years ago, and time has only confirmed me in my opinion.

The latest proof I have had has been during my recent visit to the Uganda Protectorate (see also pp. 339–55) to inquire into the state of syphilis there. On my arrival in that country I was informed by every medical man that the natives were peculiarly susceptible to mercury, becoming salivated after extraordinarily small doses. I was assured that one grain of metallic mercury given by the mouth brought on immediate salivation. Some of the medical men said that it was with a certain amount of trepidation that they ever ordered mercury; and Dr. Cook, of the English Mission there, who has had a very great experience among the natives, informed me that he never gave more than gr. $\frac{1}{12}$ of metallic mercury to any natives, for fear of trouble. He instanced many cases which had become severely salivated after what, elsewhere, would have been considered absurdly small doses. The profession was equally strong as regards the occurrence of salivation after inunction. I also learnt from the French Mission, the White Fathers, that at many of their out-of-the-way stations, where there is not a medical man for miles, they have to treat the natives themselves, and in the case of syphilis, which I may say is rampant throughout the land, their favourite remedy is Van Swieten's liquor, but they are afraid to give it in anything like its ordinarily supposed safe dose, owing to the number of cases of severe salivation that occur from time to time. The medical profession, both in East Africa and Uganda, were more than interested to see how the patients would stand mercurial injections. I began by giving half my usual dose of metallic mercury, i.e. half a grain per week. This was readily tolerated, and it was not long before I gave full doses of the same. Although these injections were given in a series of 200 cases whilst I was in the country, not one case either of stomatitis or of any other toxic symptom was noticed. When I left the country the intramuscular method of

treating syphilis was being taken up enthusiastically, and the injections were also being given in great numbers for 'sleeping sickness' after atoxyl, in the various sleeping-sickness camps.

This tolerance of mercury by the natives when given in this manner was, I could see, a great surprise to the medical profession out there, but, personally, I was not astonished in the least, as it simply bore out my experience of years, i.e. that patients who are the most susceptible to mercury will stand it when given by the intramuscular method, although they would at once suffer from toxic symptoms if it had been given in any other manner.

I think it is generally admitted that therapeutically its action is far more intense than when given by other methods; this is more especially the case with calomel.

Disadvantages

The disadvantages which are alleged against the intramuscular method are as follows :—

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

Pain at the seat of the injection depends altogether on what preparation of mercury is 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.

The occurrences of nodosities and abscesses may now be considered as ancient history, owing, no doubt, to improved technique. As regards abscesses, I may say that in my *own practice* I have never seen one. In former years I was accustomed to come across a number of painful nodosities at the site of injection, but during the last few years they have become rare, and this rarity, I think, has coincided with the time I first began to use boiling oil as a sterilizer. As regards embolism, although cases have been reported time after time, it has never been my lot to come across one.

Two Methods of Intramuscular Injection

The intramuscular method is of two kinds, i.e. the *frequent* injection of soluble salts, and the *infrequent* injection of insoluble salts.

Method of Frequent Injection of Soluble Salts.

These consist of a series of mercurial injections practised daily for from three to four weeks at a time. The list of preparations which have been used for this purpose is innumerable, the principal being: sublimate, sozoiodate, succinimate, cyanide, biniodide, lactate, and numerous others; these, however, are the best. The following are the forms in which they are generally prescribed :—

℞
Hydrarg. perchloridi . . . . . grs. 3
Aquam . . . . . oz. 1
Dose, minims 20 for an injection.

℞
Hydrarg. perchloridi . . . . . grs. 32
Ammon. chloridi . . . . . grs. 12
Aquam . . . . . oz. 1
Dose, minims 10 for an injection.

℞
Hydrarg. succinimate . . . . . grs. 2
Cocainae hydrochloridi . . . . . grs. 3
Aquam . . . . . oz. 2
Dose, minims 10 for an injection.

℞
Hydrarg. cyanidi . . . . . gr. 1
Cocainae hydrochloridi . . . . . gr. 1
Aquam distil. . . . . m. 10
Dose, minims 10 for an injection.

The technique as regards actual injection is exactly the same for both methods; but looked at practically from every side there is no comparison between them, either in effecting an ultimate cure or from a preventive point of view.

The method of frequent injections of the soluble salts of mercury has the following grave objections :—

1. The injections are always more or less painful.

2. The injections are absorbed too rapidly, and, worse still, eliminated even more rapidly.

3. They require to be repeated daily, or nearly so.

One of my first reasons for abandoning this method was on account of the pain which invariably followed each injection, and this fact can be easily proved.

It has been claimed that some of these solutions are less painful than others ; personally, I do not consider that such is the case, and I think that I have employed most of them.

That they are absorbed and eliminated too rapidly accounts for the inevitable occurrence of the disease, and still more for the rapid reappearance of the *Spirochaete pallida* unless the injections are kept up daily, or nearly so. The very fact of having to repeat the injections so frequently condemns this method when compared with that of the next, to be here described.

The Method of Infrequent Injections of Insoluble Salts.

The two great preparations of mercury which are used in carrying out this method are metallic mercury itself and calomel. There is a third which is far less frequently employed—salicylate of mercury.

The insoluble salt originally used for this purpose was yellow oxide, but this has long been superseded by the two above mentioned, owing to their vast superiority in every way.

Metallic mercury was first proposed by Lang, of Vienna, to be used intramuscularly in the treatment of syphilis. Lang introduced it in a preparation consisting of mercury in a state of fine subdivision suspended in liquid fat. This preparation goes by the name of 'oleum cinereum' and contains 40 per cent. of mercury.

For the past twenty years the author has been using the metal itself in preference to all the other salts of mercury, and as

years have gone on, and increased experience has been obtained, his faith in it has grown stronger and stronger; to-day, therefore, he maintains that, although the therapeutic intensity of metallic mercury is probably not as great as that of calomel, its curative effects are far more certain and lasting than those of any known salt of mercury; and that it easily holds premier place in the treatment of syphilis both from a curative and preventive point of view.

The advantages of metallic mercury—which to a certain extent also apply to calomel—are :—

1. It is practically painless. (This does not apply to calomel.)
2. Slow absorption, and equally slow elimination.
3. Less likely to produce stomatitis than any salt of mercury. (This does not apply to calomel.)
4. Needs only to be injected at long intervals—at most once a week.
5. Therapeutic effects are far more lasting than those of any other salt.

Experience has long taught us these facts as regards metallic mercury ; but until recently the reverse was the case with calomel ; at the present time, however, the pain, which is so marked after the use of this drug, has been overcome.

In its slow absorption and elimination lies, in my opinion, the secret why metallic mercury is so superior in its lasting effects in the treatment of syphilis over all other salts, and this conclusion has been further strengthened by observing the behaviour of the spirochaete under its influence.

At the Military Hospital, Rochester Row, it was found that, although these organisms disappeared with about the same rapidity under almost any form of mercurial injection, they reappeared at a longer interval after the discontinuance of the metallic preparations than was the case under a similar discontinuance of any salt 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 demon-

strated that the corpuscles and haemoglobin increase after the second injection, and generally diminish after the fifth. It has also been proved that although mercury appears in the urine (see p. 213) within an hour of the injection of metallic mercury, it continues to be excreted in it for two months after the sixth injection of one grain. Radiographs also show spindles of mercury at the seat of injection up to the fifth day. That mercury, given by intramuscular injections, is less likely to be followed by toxic symptoms—such as stomatitis—has been my opinion for many years, and this fact has lately been strikingly illustrated by my experience of it in the Uganda Protectorate as subsequently related (Chapter XXV).

The fact that it is only necessary—in carrying out the intramuscular method with the metal itself, and with all the insoluble salts—at the most to inject not oftener than once a week, is a very great advantage if only for a single reason : it makes the plan less objectionable to the patient.

Recurrences after a course of injections of the insoluble salts are undoubtedly less frequent than after a similar course of the soluble preparations of mercury, and this is most marked when metallic mercury has been employed. I have long noticed, as between the two—metallic mercury and calomel—that whereas the superiority of calomel as regards therapeutic intensity is undoubted, the metal is tolerated much better, and its lasting effects are much more marked. Hence, as a routine method of treatment, injections of metallic mercury are much to be preferred. The fact is that calomel is an intensive remedy of the first order, the other of relative medium activity. In other words, mercury is slower in action, but is more sure and certain from a curative and preventive point of view.

Technique of the Intramuscular Method

We must now proceed to describe this important subject, and the description which follows applies equally to injections of either the soluble or insoluble salts.

1. As to the mercurial preparations which are used. These

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.

2. *Instruments.* The syringe used should be made entirely of glass so that all its parts can be separately sterilized.

3. The needles must be made of platino-iridium or gold; they need not be longer than $1\frac{1}{8}$ inch.

4. The points of the needles must be kept as keen as possible, so as to allow of easy penetration.

5. Both the syringe and needles should be sterilized thoroughly in boiling olive oil before use.

6. *The injections must be given into the muscles, not subcutaneously.*

7. The skin over the site of injection ought to be swabbed over with an antiseptic solution of either carbolic acid, alcohol, or perchloride of mercury before the operation.

8. A cloth wrung out of carbolic acid solution 1 in 20 should be spread on a table close at hand, to lay the syringe or syringes on during the injections.

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

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

11. The operation of injection should be completed in *one* stage.

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

The above rules, although some of them may appear almost too insignificant to remember, are all of the greatest importance and should be strictly adhered to. I discuss them in detail at p. 295.

Salicylate of Mercury

This salt was, and is still, very much used in Germany. I have myself used it fairly extensively suspended in liq. paraffin, giving

gr. ½ twice a week. I have, however, long since given it up as being far inferior in every respect either to metallic mercury or calomel.

Mention has already been made of various soluble solutions of mercury ; it is necessary now to allude to the insoluble preparations, and first of all those of metallic mercury itself. Lang has modified the formula of his original ' oleum cinereum ' several times, the latest being :—

℞

Metallic mercury	2 parts
Sterilized anhydrous lanolin . .	1 part
Sterilized liq. paraffin . . .	1 part

50 per cent. of mercury. Dose gr. ⅔ of mercury.

Lafay's formula :—

℞

Metallic mercury	40 parts
Sterilized anhydrous lanolin . .	12 parts
Sterilized white vaseline . . .	13 parts
Sterilized oil of vaseline . . .	35 parts

40 per cent. of mercury. Dose gr. 1 to grs. 2 of mercury.

Author's (old formula) :—

℞

Pure metallic mercury . . .	oz. 1
Anhydrous lanolin	oz. 4
Liquid paraffin (carbol. 2 per cent.) ad .	oz. 10

By volume 10 per cent. of mercury. Dose 10 to 15 grs.

This last is the cream which has been in use throughout the British army both at home and abroad during the past seven years, and although, generally speaking, it has given great satisfaction and has yielded brilliant results, I have always been conscious of a grave objection which it possessed together with all other preparations of the insoluble salts hitherto used : that owing to the substances which have been employed in them as vehicles to suspend the mercury being insoluble in the organism, they entered the circulation as foreign bodies, and as such might possibly produce nodosities, abscesses, and embolism. This, of course, is

a most grave objection. To obviate this, I have now substituted palmitin as a vehicle.

Palmitin is a neutral fat derived from palm oil, having the same chemical composition as the palmitin of the human system. It is an ether glyceride of palmitic acid and is therefore easily saponified in the fluids of the organism, being converted into a soluble alkaline palmitate and glycerine, which does not enter the circulation as a foreign body like all the substances hitherto used as vehicles.

The advantages claimed for palmitin as a vehicle are :—

1. It is non-irritant.

2. It is not so easily oxidized as the other components of human fat.

3. Being already a normal constituent of the human organism, and thus being easily saponified and soluble in the body, it 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 and lowered with the greatest ease.

Analgesia

The question of pain, although never amounting to anything serious as far as metallic mercury is concerned, slight as it always is, constitutes a grave objection to the practice of intramuscular injections, and, more especially in the case of calomel, practically renders the use of this form prohibitive.

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, cocain, beta-eucain, &c. 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 trouble we have, as a rule, to deal with, as the pain usually comes on two or three days after the injection, when all local anaesthetics are useless. This is a very serious matter in any case, but more so as regards injections of calomel, for the pain is most marked and

severe with this drug. The consequence is that, having been hitherto unable to cope with it, we have been forced more or less to abandon injections of calomel as anything like a routine method of treatment, and have only employed it under exceptional circumstances when pain is a matter of secondary consideration. For this reason, perhaps the strongest weapon for dealing with syphilis has been almost lost to us.

For the purpose of avoiding this pain, in my own latest mercurial preparation I have added equal parts of absolute creosote and camphoric acid. This combination has been most successful, and renders injections not only of metallic mercury but even of calomel absolutely painless.

Another advantage is that the creosote possesses double the bactericidal effects of pure carbolic acid when tested by the Rideal-Walker process.

This combination of pure creosote and camphor possesses other advantages besides its analgesic powers, i.e. it is non-toxic, and this is not wholly true of other suggested local anaesthetics, it is strongly antiseptic, and, being a viscid body, is a valuable adjuvant to the palmitin in making up a vehicle, which will hold metallic mercury or calomel in suspension ; in fact, the combination forms a most homogeneous preparation.

The following is the formula for the metallic mercurial preparation which I now use for intramuscular injection :—

℞

Hydrargyrum Pur.	10 grms.
'Creo-camph.'[1]	20 c.c.
Palmitin basis to	100 c.c.

10 m. contains 1 grain of metallic mercury.[2]

The greatest care ought to be exercised in seeing that the mercurial cream is of proper consistence. It should be kept in a wide-mouthed glass-stoppered bottle from which it ought never to be removed except for injections, and before use should invariably be stirred up by means of a glass rod, rendered sterile by being

[1] Equal parts of absolute creosote and camphoric acid.

[2] Leishman reports that 'this preparation is sterile, and bacteria will not grow in it'.

dipped into boiling oil. In cold climates the cream is liable to become semi-solid, and may require heating in a warm bath; in the tropics, on the other hand, the bottle containing the cream should always be kept in the ice chest until it is required for use, when it can be transferred to some crushed ice.

Injections are made on an average once a week, with doses of 10 mg., but of course the dose must vary according to circumstances.

To recapitulate. *The advantages* of metallic mercury are: (1) that it is painless; (2) that it is tolerated better than any preparation of mercury; (3) that its therapeutic effects, although not so intensive as calomel, are more so than any other known form; (4) that its physiological effects are *far* more lasting than is the case of any salt of mercury, calomel included, thus making it *par excellence* the form to be preferred in the routine treatment of syphilis.

Disadvantages. Its one disadvantage is that should salivation take place after an injection, it is a difficult matter to prevent the symptoms getting worse unless the mercury is removed. This has been done by excision, but the operation to effect this is as difficult as it is serious.

Calomel

Syphilographers the world over have long considered calomel to be the most potent salt of mercury in its power over syphilis in all its stages, its action in this respect being truly remarkable. It is more active and energetic than any known salt of mercury, acting promptly in acute cases, as well as clearing up old-standing ones which may have resisted and baffled all other treatment. Nevertheless, in spite of all this, calomel has been limited to the treatment of certain cases, and the idea of employing it in anything like a systematic manner was long ago abandoned, owing to one great drawback, i.e. the intense pain which was liable to follow its use as an injection, coming on about the second or third day after inoculation and lasting with more or less severity for three or four days. I have seen so many cases in which this pain

has been almost intolerable, that, as years went on, I gave intramuscular injections of calomel with more or less dread, and reserved them for cases the urgency of which called for their employment in spite of the pain which was sure to follow. However, by introducing the combination of creosote and camphor (see p. 292) into the following preparation, I am now enabled to use calomel with impunity, so great has been the success of this compound as an analgesic.

The following is the formula :—

R.

Calomel	5 grms.
'Creo.-camph.'[1]	20 c.c.
Palmitin basis to	100 c.c.

10 min. equals calomel ½ gr. Dose 10 to 15 min., as an injection once a week for not more than four weeks in succession.

The precautions to be taken in the use of this mixture are the same as those required in the case of the metallic cream.

Those who know the remarkable therapeutic attributes which calomel possesses in dealing with the symptoms and lesions of syphilis, but who have had to abandon it with regret, time after time, owing to pain, will thoroughly appreciate the advantage which this preparation affords, as they can now use the salt at will without any fear of pain.

But the question that remains is, Ought calomel to be preferred to metallic mercury as a matter of routine ? I think the answer is in the negative, nor do I think that it will ever be so used. With reference to this, I would remark that it has been long since observed by others as well as by myself, that the action of calomel on syphilis, although it is so remarkably energetic and rapid, is short-lived when compared with that of metallic mercury. Therefore I think that, in spite of our now being able to use calomel without let or hindrance, it will never take the place of mercury itself in the routine treatment of syphilis, but will be reserved more for dispersing early symptoms and signs of the disease, and that after this has been done we shall revert to the use of metallic mercury again. Even this is of the greatest

[1] Equal parts of absolute creosote and camphoric acid.

advantage, as I will subsequently endeavour to show. Of course it will be employed more than ever in all very urgent cases, as in iritis, and in cerebral and spinal cases.

To return to other considerations of the technique of the intramuscular method :—

The advantage of the ' all-glass ' syringe is obvious for the purpose of sterilization. The syringe I use is capable of containing 40 min., the reason for this being that four full doses can be given without the necessity of recharging the syringe. This is an undoubted advantage, especially when there are a number of patients to be injected.

To recharge the syringe the needle must be detached.

The object of having a platino-iridium needle, in preference to one of steel, is that the latter is apt to snap, an awkward accident which I have seen happen on more than one occasion. This is more especially the case when the soluble salts are employed, as they corrode the steel in time.

The necessity of keeping the point of the needle as keen as possible is to render its penetration all the more easy and painless, a most important consideration from the patient's point of view; as Fournier says, in a great many cases it is ' fear of the needle ' that drives the patient away from this plan of treatment.

Sterilization in boiling oil both of the syringe and needle is of he greatest importance. The oil should be boiled in a porcelain (not in an earthenware) crucible, all parts of the syringe being placed in it before injections begin, and the needle ought to be dipped therein between each injection. Before filling the syringe with mercurial cream, care should be taken to allow the former to cool, otherwise the mercury will separate in the syringe.

The reason for not allowing any cotton wool or fluffy material near the needle is to obviate the chance of any of the fibres or fluff finding their way into the lumen of the needle, as by doing so they might be injected together with the cream and become a focus of inflammation. It is absolutely necessary that the injections be given into the muscles themselves, and not subcutaneously, as long experience has taught us that when given into the subcutaneous tissue, abscesses are very liable to follow.

I have found the measures before recommended (see p. 289) for sterilizing the skin at the seat of injection to be quite sufficient, and I do not think that, practically speaking, it is at all necessary to undertake fuller measures to sterilize the skin.

As regards the site of injection, most syphilographers are agreed that, generally speaking, the buttock is the best, taking care to use each buttock alternately. As to the actual point of injection they disagree, and much ingenuity has been exercised in drawing parallel and horizontal lines to define a safe region. Personally, I almost invariably give the injections anywhere in the upper third of the buttock, and have never had reason to regret so doing; besides being safe as regards the great vessels and sciatic nerve, this region is free from the pressure caused by sitting or riding. The lumbar and deltoid muscles may also be utilized, if for any reason the buttocks are not available.

Most textbooks recommend that the injections should be done in two stages, thus: The needle with the empty syringe attached is thrust into the muscles, the piston of the syringe being then slightly withdrawn, and should any blood now well up, it is supposed to indicate that some vessel has been wounded; to avoid injecting into it, and risk the chance of embolism, the needle is now withdrawn and reinserted somewhere else—a procedure which might go on *ad infinitum*. The above precaution may be theoretically correct, but in my opinion it is, practically speaking, quite unnecessary, and is counterbalanced by the fact that at one sitting a patient may have to undergo half a dozen stabs before the presence of blood is eliminated, a result which will scarcely tend to popularize the method in his eyes, nor to get rid of the 'fear of the needle'.

Personally, I have always carried out the injections in one stage, and have never yet as much as seen an embolism or abscess in my own practice. My procedure is as follows: Having filled the syringe and fixed the needle, I insert the latter with one thrust into the muscle, inject slowly, and withdraw the needle quickly; the latter manœuvre is done so as to avoid any of the cream which may have remained in the needle being allowed to get into the track of the latter.

Points to be considered in carrying out the Intramuscular Treatment of Syphilis by the Insoluble Salts

No definite rule as to dosage can be laid down in employing this method of treatment, for it has to be remembered that, as already pointed out, each patient tolerates mercury to a different degree, and that this degree of tolerance can only be arrived at by a personal study of each individual case; also that the type of syphilis we may have to deal with may require either a larger or smaller dose, as the case may be; for instance, as already pointed out, the dose of mercury which will dissipate an ordinary roseolar rash will probably have no effect whatever on a papular or pustular eruption. Hence the further necessity of each case being treated on its merits. In any case, it can be truly said that, if it is easy to increase or lessen the dose when treating the disease by the ingestion method, it is far easier to do so by means of the intramuscular, and furthermore, that the dose can be more easily gauged when it is given by injection.

Another circumstance which governs the dose is the actual condition of the patient, because a strong healthy individual requires as a rule a larger dose than a weakly and ill-conditioned one. Again, cases of what is called 'malignant' or 'virulent' syphilis ought, as a rule, to receive much smaller doses than patients who are suffering from the more usual form of the disease.

It should always be remembered that, whatever dose is decided on, it can be far better regulated by means of the intramuscular than any other method.

As regards the maximum dose—here we can form a more definite opinion. Of late years the tendency among the most experienced has been to treat syphilis with very much smaller doses than in times past; my own personal experience agrees with this. The original mercurial cream which I used contained 30 per cent. of mercury, and the amount I was in the habit of injecting was equivalent to grs. iij of mercury. I found that this amount was unnecessarily large, and gradually reduced it to its present strength, i.e. 10 per cent.; of this I consider the usual maximum dose to be

min. x or gr. j of mercury, although in exceptional cases I go up to 1½ grs. (15 min.). During the last ten years I have been using this very much reduced dose, and from the first I got not only as good, but on the whole, far better results. This has been explained since the time that we have been able to watch the effects of mercury on the *Spirochaete pallida*, as the organism is seen to disappear as quickly under the small dose as with the larger ; moreover, research has shown that, whereas mercury in large doses causes a decrease in the red corpuscles after a time, the corpuscles actually increase in number when the smaller dose is employed. The fact is, that under large doses of mercury the blood deteriorates, but that when given in smaller doses the metal acts as a blood tonic. No wonder, then, that my cases have done so much better since I adopted these reduced doses. The advantage of being able to deal successfully with syphilis by these smaller doses is great.

The maximum dose of my preparations above described, i.e. 1 gr. of mercury once a week, will be found sufficient in nine cases out of ten.

Although one can never say for certain as to how long treatment should be continued, or as to the time when a patient can be considered free from 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. The only means which can enable us to form a definite opinion on this vexed question is long experience of treatment and observation of a great many cases. My own experience enables me to say that two years' treatment, including intervals of rest, is in most cases sufficient. This time, I am aware, is shorter than that laid down by some of the greatest authorities, including Prof. Fournier himself. The latter says four to five years, but then Prof. Fournier employs almost entirely the ingestion method, which will certainly account for the opinion he has formed.

As to calomel, the maximum dose which I give is gr. ¾ (min. xv) of the calomel cream ; this is given once a week, and is never continued for longer than the fourth injection.

As to the interval which ought to be allowed to elapse between

each injection: a ruling as to this, again, can at the present time be more or less definitely laid down, assisted as we are by the more perfect qualitative analysis of urine (p. 211), and to a certain extent by radiography, but most of all by personal observation of a large number of cases. On this basis I have been led to conclude that a week is the interval which should be generally allowed to elapse. This should seldom if ever be extended; at any rate, in the case of metallic mercury, which, we have already seen, the radiograph shows to be present in the muscle up to six or seven days after injection; at a late period in the disease the interval can generally be extended to once a fortnight.

The treatment must be of an intermittent character—that is, that the injections are given in courses, with certain intervals when no injections are given; these 'rest intervals', as they are called, gradually increase as the case goes on.

Although we cannot and ought not to lay down any arbitrary rule as to dose, intervals between injections, periods of rest, and length of treatment, it is both prudent and a safe and convenient proceeding to have a certain plan to go on, and my own, or rather the one I generally adopt, is as follows:—

At first a course of six weeks' energetic treatment is given, which involves six mercurial injections. On finishing this course the patient is allowed an interval of two months without any treatment, but during that time is seen once a week, or fortnight at least. Should he remain free from syphilitic manifestations for two months, he is then ordered a further course of four injections once a fortnight. If fresh symptoms appear, a second course of six injections weekly is given, followed by a two months' interval. If free from signs of the disease, the next interval is increased to four months, followed by a course of four injections. The succeeding interval may be increased to six months, followed by four injections, one each month.

In a tabular form this reads:—

1. Six weeks' treatment; 6 mercurial injections (4 of which will probably have been calomel, the remainder metallic mercury).
2. Two months' period of rest.
3. Two months' treatment; 4 mercurial injections (metallic).

4. Four months' period of rest.
5. Two months' treatment ; 4 injections (metallic mercury).
6. Six months' period of rest.
7. Four months' treatment ; 4 injections (metallic mercury).
8. One month's period of rest.
9. Two months' treatment ; 4 injections (metallic mercury).

Total 24 months' treatment. With 22 intramuscular injections, 4 of calomel and 18 of metallic mercury.

The above will, of course, only apply to patients who have had no further relapse ; for those who have had relapses, treatment must be extended accordingly.

In giving this tabular statement it cannot be too strongly impressed on the reader once more, that no actual plan of treatment can be laid down when dealing with a disease like syphilis, but that every case should be judged of and treated on its merits.

In looking at the above it will be noticed that I now treat all my cases at the beginning with calomel injections, but *never* give more than four of these ; after the fourth, metallic mercury is substituted ; indeed, all the cases do not get even as many as four, because the metal is given as soon as all very marked symptoms have disappeared. This disappearance may occur very rapidly under the influence of calomel. I may say here that since I have adopted this line of treatment at Rochester Row Military Hospital, the number of days spent as in-patients there for syphilis has been reduced from 33 days (when metallic mercury was given from the commencement) to 17 days at the present time. I need not repeat that calomel is given in all urgent cases.

Precautions to be Adopted

It is unnecessary to say that before an injection of mercury is given the hygiene of the mouth and teeth must be looked to, as already advised (p. 262) ; this cannot be too strictly carried out. Among careful patients this can be done easily ; careless persons ought to be seen more frequently, simply for the purpose of examining the state of their mouths. The patient's weight must be taken, and carefully recorded at the commencement, as it will

be a very certain indication afterwards as to whether mercury is agreeing with the patient or not. The urine must be examined for albumen and sugar.

The patient's previous history as to his life, habits, and as to any illness he may have had, when he has resided in the tropics, must be found out and noticed.

Contra-indications to Mercury

Carmichael, of Dublin, than whom in his day there was no greater authority on syphilis, taught that mercury was contra-indicated in cases of syphilis accompanied by rupia. Undoubtedly in this he was mistaken, and some of my most successful cases have been cases of rupia in the early and later stages treated by the intramuscular method. But there are cases in which mercury, if not entirely contra-indicated, must be given with care and circumspection. The chief of these are when the patient suffers from chronic albuminuria, or is tainted with malaria.

Albuminuria. As regards albuminuria, everything will depend on the nature and cause of the condition. If it be of a transitory nature, and there is no reason to think that true kidney mischief exists, the mercurial course can be undertaken. In this connexion it may be observed that many cases of early syphilis have albuminuria, and that this begins to clear up directly mercury is exhibited. This would appear to be due to some tubal nephritis, the result of the syphilitic poison.

When, however, there is evidence of permanent organic change in the kidneys, the question of giving or withholding mercury must always prove a difficult one to decide, and it behoves us to proceed with care, for undoubtedly its administration under the circumstances is fraught with many dangers. Personally, I have treated many cases of syphilis complicated with Bright's disease, and with favourable results; on the whole, I am distinctly in favour of not withholding mercury, but it must be given in very minute doses, and the action of the skin must at the same time, even more than in ordinary cases, be encouraged by the constant use of Turkish and hot-air baths.

Malaria

I do not think that, hitherto, malaria has been generally regarded as a contra-indication to giving mercury. My own experience, however, is that a malarial taint adds very much to the seriousness of an attack of syphilis. Patients suffering simultaneously from malaria and syphilis stand mercury badly, and become salivated easily. They are, too, more prone than others to suffer from syphilis in its more aggravated and serious forms. In such cases mercury must be given, but with much care ; as a preliminary measure, the patient should be subjected to a thorough course of quinine, both before and during the mercurial course. All cases of syphilis complicated with malaria ought of necessity to be removed from unhealthy districts into elevated healthy spots.

CHAPTER XIX

OTHER METHODS OF ADMINISTERING MERCURY

Fumigation

Is nearly as old as the inunction method. Formerly it was done in a very rough and ready manner, besides which the preparations of mercury which were used for this purpose were most unsuitable: cinnabar, grey oxide, and impure calomel were first employed. Innumerable cases of fatal poisoning resulted, and the treatment was gradually abandoned.

The method of fumigation as now practised is as follows: The patient, seated on a wooden chair, is enveloped up to the neck in a sheet, which extends to the ground. The vaporizing apparatus is placed under the chair; it consists of a spirit lamp, a tripod, and a circular basin forming a water-bath, with a cup placed in its centre. The lamp is lighted under the tripod, which supports the basin full of water, and this volatilizes the calomel, of which 15 to 60 grains is placed in the cup. The head is protected from the mercurial fumes, so that inhalation cannot take place. The volatilization of the calomel is complete at the end of a quarter of an hour. The lamp is now extinguished, and the patient is left for another ten minutes in the vapour. After this he is put to bed still enveloped in the same covering, and there remains for an hour. This process is repeated every day, every second day, or once a week, as the case may be. The calomel used is the purest which can be obtained; it will only volatilize in the presence of water (steam).

The adherents of this method, including Lalonette in France and Henry Lee in England, claim for it—

1. That it does not interfere with the gastro-intestinal functions.
2. That it is easy and convenient.
3. That its therapeutic effects are very active.

On the other hand, its opponents maintain—

1. That it often produces stomatitis, anaemia, and general debility, these being no doubt the result of repeated and profuse diaphoresis. (My own experience most certainly bears this out.)

2. That it is uncertain, because with this method we can never know how much or how little of the calomel will be absorbed.

3. Outside hospitals and public institutions it is impracticable.

My own conclusions as regards fumigation are that it may possibly be useful in dealing with certain obstinate eruptions because of its local effects, but that, as a matter of routine treatment in syphilis, it is not to be considered.

Intravenous Injections

This method was introduced by Baccelli in 1893. The technique is easy—in theory : a prominent vein, one near the bend of the elbow for choice, is selected and made to project by compression as in venesection ; the puncture is now made holding the needle parallel with the vein ; the obstacle to the return circulation is removed, and the solution is injected into the vein. The salts used are sublimate, cyanide, and the benzoate of mercury. Of these the cyanide is the favourite ; this is given in doses up to gr. $\frac{1}{6}$.

The injections are given every day, or every other day, in courses of from twenty to thirty.

The advantages claimed for this method are :—

1. Its painlessness.
2. The absence of local trouble.
3. The absence of toxic effects.
4. Instantaneous introduction into the blood.

Unfortunately, in most cases this method has been tried more or less as an experiment, and it has been soon abandoned for the following reasons :—

1. Because of technical difficulties. It is easy to miss the vein, to go to one side of it, or through it ; again, in women and fat persons it is very often hard to find a suitable vein. Lastly,

after a certain number of injections, infiltration of blood into the surrounding tissues causes much difficulty in finding the vein.

2. Thrombosis, embolism, and phlebitis of a severe character may sometimes follow an injection.

3. Its therapeutic effects are unsatisfactory. The drug when given in this way is too rapidly absorbed and eliminated, and in intensity does not compare with intramuscular injections, either of calomel or of metallic mercury.

4. Fear of carrying it out on the part of the surgeon, to whom it may not seem altogether right to place the endocardium in direct and sudden contact with a toxic agent.

My own experience of the intravenous method of administering mercury is that, whilst there are undoubtedly both dangers and difficulties in the method, I cannot see one single point in its favour, and no one would, I am sure, suggest it as a routine method for carrying out the necessarily prolonged treatment of syphilis.

Zittmann's Treatment

This is a plan for treating chronic and refractory cases of syphilis. The principle of the treatment apparently consists in eliminating the poison from the system by sweating, purgation, 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 confined to a room the temperature of which is kept at 80° F. The evening before commencing the treatment, two of the following pills are taken :—

℞

Hydrarg. subchlor.	grs. 2
Ext. colocynth. co.	grs. 5
Ext. hyoscyami	grs. 2

Ft. pil. 2.

The diet consists of, *for breakfast*, boiled egg or bacon, tea, no sugar or spices.

Lunch. Meat, vegetables, no fruit.

Dinner. Soup, fish, poultry.

For the first four days of the treatment, the patient drinks a half-pint of the following decoction, as hot as possible, at 9 a.m., 10 a.m., 11 a.m., and noon :—

Decoction No. 1.

℞

Rad. sarsae contus	℥iv
Sem. anisi contus Sem. foeniculi contus	āā gr. 80
Fol. sennae	℥j
Rad. glycyrrhiz contus	℥iv

Add in a linen bag :

Sacch. alb. Alum sulph.	āā ℥ij
Hydr. subchlor.	gr. 80
Hydr. bisulph. rub.	gr. 20
Aquam	3 gallons

M.

Boil gently down to 1 gallon, strain and put into four 40-ounce bottles. Label 'The Strong Decoction'.

On the same days at 3 p.m., 4 p.m., 5 p.m., and 6 p.m., the patient drinks a half-pint of the following decoction, No. 2, which is taken cold :—

Decoction No. 2.

℞

To the dregs of No. 1 add :—

Rad. sarsae contus Semin. cardam. contus Cortex limonis contus Rad. glycyrrhizae contus	of each 60 grains
Aquam	3 gallons

Boil gently down to 1 gallon, strain, and put in four 40-ounce bottles, and label 'The Weak Decoction'.

The patient is kept in bed except for one hour every evening, when he may sit up.

In the evening two pills are administered, the patient starting the decoctions again next day, as before. This treatment goes on in the same way until the fifteenth day, when it is discontinued.

No claim whatever has been made for Zittmann's method as a routine one for the treatment of syphilis; it is entirely a special mode of treating chronic refractory cases of tertiary disease, and it would not have been noticed in so much detail in this article but for the fact that the author has had some considerable experience of it in such cases, as well as ample opportunities of judging as to its merits. The patients I have seen treated with it were cases of long-standing tertiary syphilis from India; some of these had from two to four and five courses of the above, and I am unable to say that they were permanently benefited, although they were certainly temporarily relieved. All these cases were subsequently permanently benefited by intramuscular injections of small doses of metallic mercury, hot-air baths, and generous diet and tonics; and I consider that the good effects claimed for Zittmann's method can be brought about by these means alone with greater facility, and certainly in a far less disagreeable manner.

Welander's Bag

This is a method introduced by Welander, who depends on the absorption of mercurial vapour for the administration of mercury. The bag consists of a double piece of flannel which is impregnated with mercury (mercurial ointment), and is worn round the chest; it has but a feeble therapeutic action.

Serum Treatment

Many attempts have been made to institute a serum treatment for syphilis, but so far these have not been successful. All that need be said here, or indeed can be said, is, that the whole question of sero-therapy in syphilis has been revolutionized by the successful inoculation of monkeys with syphilis. Research has not yet given any satisfactory results, and the question may be considered for the present to be *sub judice* (see also vol. i, p. 171).

CHAPTER XX

THE ORGANIC COMPOUNDS OF ARSENIC IN SYPHILIS

Arylarsonates in Syphilis

The efficacy of atoxyl in sleeping sickness, a disease caused by an organism in many ways closely resembling the organism of syphilis, led to the conclusion that the remedy might be equally successful against a similar malady, and as the nature of syphilis has been acknowledged since the discovery of the *Spirochaete pallida*, atoxyl has been tried as a remedy for this disease also.

Working from a prophylactic point of view, Metchnikoff has investigated the drug,and at the International Congress of Hygiene, Berlin, 1907, he gave the result of his researches. In the first part of his research he had given a succession of doses of atoxyl subcutaneously at intervals of a few days, and succeeded in warding off the disease. Next he tried the effect of giving a single dose only in two cases as long as fifteen days after inoculation with the syphilitic virus, and again the result was successful. Control monkeys infected with the same material developed a sore after the usual incubation period. From further experiments he concluded that the immunity conferred by atoxyl is not of long duration, and further, that the treatment does not lead to any generalization of the virus in the system.

He suggests the injection into the muscles of two doses of grs. 7 of atoxyl at intervals of 48 hours up to 14 days after the exposure to infection. With a view to determine this question experiments are now being carried out on a large scale in the military hospitals in England, where it is proposed to subject all men who report a venereal sore of any description to two injections of atoxyl of grs.10, each at an interval of four or five days; by these means it is hoped that some definite conclusion may be arrived at as to its abortive power.

Internally, in the general treatment of syphilis, atoxyl has been spoken of favourably by Hallopeau and Salmon in France. The latter advises it to be used as follows: first, 0·75 grams; two days later, 0·60 grams; and three days after, 0·50 grams. He does not recommend the drug to be pushed till all syphilitic symptoms have disappeared, but considers that it attenuates the disease. He stated that he had sometimes met with cases showing signs of gastro-intestinal disturbance after the fourth injection, and advises a pause after the third injection for this reason.

During the last twelve months the arylarsonates have been used very extensively at the Military Hospital, Rochester Row, London, in the treatment of syphilis by the author, who published a paper on the subject in the 'Journal of the Royal Army Medical Corps', December 1907. The results therein recorded were sufficiently encouraging, and experiments were proceeded with. Since then some seventy cases of syphilis have been treated solely by atoxyl or one of its compounds. All these cases have done well; they have gained in weight almost immediately after coming under treatment. The beneficial effect of the drug appears to be most marked in those cases where there is ulceration of the mouth, throat, or tongue; there has been a noticeable absence of severe sore throats in the hospital since the treatment by atoxyl began. The action of the drug was perhaps even better marked in three cases of vegetating condylomata, which improved rapidly under its influence.

The action of the drug on the rashes of syphilis would appear to be rather to exaggerate them. This is probably due to the hyperaemic effect of the arsenic. A rose-coloured papular eruption very often follows its use, but this can easily be distinguished from a specific rash.

What are Arylarsonate Salts? [1] Atoxyl, another of the pre-

[1] The term 'arylarsonates' indicates those arsonates to which an aryl group is attached. The arsonic acids may be considered to be derived from arsenic acid by the replacing of the hydroxyl group by an organic radicle. The organic radicle may be a member either of the fatty or paraffin series, such as methyl, ethyl, &c., or of the aromatic or benzene series, as phenyl. The radicles of the former are known as 'alphyl', and an arsenic acid of this type would be known as 'alphylarsonic' acid. When the radicle belongs to the aromatic or

parations of arylarsonates used, is said to be a meta-arsenic anilide, containing 37·69 per cent. of arsenic. It was highly praised by the manufacturers, on the ground that it provided a means of administering, apparently, unlimited amounts of arsenic without producing toxic effects. Analysis has subsequently shown that atoxyl contains 25·7 per cent. of arsenic. Unfortunately, during the last two years a number of cases have suffered from serious toxic symptoms after the administration of atoxyl. A great many of these have occurred in Uganda and German East Africa, where the drug has been largely given for sleeping sickness; of these the principal and most serious was a form of blindness, many cases of which have been recorded by Koch and others. Whether these toxic effects have been caused by the rather impure preparations of atoxyl which have recently been put on the market, or by the increase in dose of the drug given, is not certain; the probability is that both have been causes in producing the same effect.

At the Military Hospital, Rochester Row, we have been using a preparation made by Messrs. Burroughs & Wellcome, of London, which they obtain from aniline and arsenic acid, and which they called ortho-arsenic-anilide. The corrected and final formula and name for the salt is

$$NH_2\,C_6\,H_4\,As\begin{matrix}/OH\\=O\\\backslash ONa\end{matrix} + 5\,H_2O$$

Sodium-para-amino-phenyl-arsenate.

This is the salt which has been used so extensively at Rochester Row in the treatment of syphilis, instead of the compound called atoxyl; it is known as sodium-para-amino-phenyl-arsenate. The manufacturers have named this compound 'Soamin'.

Up to the present time some 70 cases of well-marked syphilis have been treated with this compound, each patient getting an average of grs. 90 to grs. 100 (grs. 10 every second day).

It was difficult to arrive at any conclusion as to what the dose should be; however, grs. 10 given every alternate day until a total

benzene it is called an 'aryl' group, and the arsonic acid would be an 'aryl-arsonic acid'. In the case of 'atoxyl' and 'soamin' the aryl radicle is aniline. Briefly, the prefix 'aryl' to arsonates indicates a radicle belonging to the aromatic series.

of grs. 100 is administered has been arrived at as the correct and safe dose. The drug is given by intramuscular injection, care being taken that the solution is made up fresh each day, and that the syringes used are sterilized in boiling oil, since acids decompose the drug.

It can be recorded that of the 70 cases treated, not one has shown the least toxicity or any bad effect ; on the contrary, they have all done remarkably well.

Conclusions. It is far too soon to express an opinion as to whether arylarsonates are likely to prove of permanent benefit in syphilis, or whether they are ever likely to take the place of mercury in the treatment of the disease ; at the same time, it can, at any rate, be said that the results are encouraging. With regard to the question as to whether they have any prophylactic or abortive effect on the future development of syphilis after inoculation, I am unable to speak, except to note that when given at an early stage they delay and modify considerably the secondary signs of the disease.

It appears to have very beneficial effects on all syphilitic mucous ulceration.

It is apt to exaggerate the appearance of all syphilitic rashes and eruptions, and very often produces a peculiar papular scaly eruption of its own.

The main point which, to my mind, is now well established, is that in the arylarsonates we have a second specific for syphilis, the importance of which cannot well be exaggerated.

CHAPTER XXI

COMPARISON OF THE DIFFERENT METHODS

In describing the different methods of administering mercury, we have discussed the advantages and disadvantages of each in turn, so that there is no need to recapitulate these. It is very plain that the preponderance of the advantages possessed by intramuscular injection of the insoluble salts of mercury over that possessed by any of the other methods of giving mercury is overwhelming, whilst its disadvantages are very few—in fact, that none of the other methods will bear comparison with this.

Up to recent times the external or inunction method held its own in the treatment of certain cases of syphilis—that is, urgent cases where intense therapeutic effects were necessary. Now, however, that we can use calomel with impunity, this salt has entirely taken the place of metallic mercury, as its therapeutic intensity is far more marked. Finally, without taking into consideration other advantages of the intramuscular method—absence of gastro-intestinal troubles, more certainty as to absorption, more accurate dosage, &c.—it possesses one supreme advantage which is quite sufficient to make this method all-important in the treatment of syphilis over all other known methods, i.e. that it is absolutely the only method by which the patient can be sure of receiving his treatment with certainty and regularity, and which will enable us to carry out that prolonged treatment which we know to be necessary for the cure of syphilis, with the view of preventing the future dangers of the disease.

Summary

Having discussed the subject of the specific treatment of syphilis, I may now attempt to summarize the conclusions arrived at.

1. Specific treatment is necessary for the cure of syphilis, as well as for preventing its further dangers. For in spite of the fact that some few cases do recover without further trouble, syphilis, when left to itself, almost invariably leads to tertiary manifestations.

2. Experience shows that the virus of syphilis can be so attenuated by specific treatment, that the dangers of the disease may not only be prevented, but that the disease may be cured.

3. That syphilis must be treated not only from a curative point of view, but also from a preventive, having regard to its future dangers to the individual patient, and also to the offspring.

4. That treatment must be both prolonged and intermittent.

5. That each and every case of syphilis must be thoroughly treated.

6. That from the point of view of treatment we should ignore the existence of *mild* or *benign* syphilis.

7. That experience teaches us that by far the greater number of cases of tertiary manifestations follow on what is termed 'benign secondary syphilis', being the result of inefficient or insufficient treatment, this again being due to negligence owing to the apparent mildness of the case.

8. That abortive measures for preventing the further development of the disease have generally failed and are not to be depended on; at the same time Metchnikoff's suggestion as to the application of a mercurial preparation, with the same end in view, ought, if possible, to be carried out.

9. That mercury is a 'specific' in the truest sense of the word for syphilis, and that it has a bactericidal effect on the *Spirochaete pallida*.

10. That the secret of the success of mercurial treatment depends to a great extent on obtaining the proper degree of its intensity during the whole course of treatment—the smaller the dose which will effect this, the better would appear to be the result.

11. That by far the best method of administering mercury is the intramuscular injection of the insoluble salts of mercury, which are much to be preferred to the soluble.

12. That calomel holds first place among all the salts as regards therapeutical intensity, but that metallic mercury itself is much more lasting in its effects, for the reason that it is more slowly absorbed, and just as slowly eliminated.

13. That whilst it is well to commence treatment with injections of calomel, owing to the manifest advantage of beginning treatment energetically, resource should be had very soon to metallic mercury, which is far preferable in carrying on treatment over that prolonged time which we know to be necessary in order to effect a cure, or prevent the future ravages of the disease.

14. Although, as already shown, specific treatment is necessary for dealing successfully with syphilis, yet the treatment of the disease does not consist merely in the administration of mercury, but, on the other hand, embraces all the other therapeutical indications which are necessary to relieve and cure the patient.

15. It is possible that most of the cases met with are suffering exclusively from syphilis, and present only symptoms directly due to it; in such cases mercury alone might be sufficient to cure the disease, but on the other hand a great number suffer from some idiosyncrasy which in many instances influences the course by creating morbid opportunities for the disease; in other words, by rendering the disease different from what it would be alone, or by complicating it and making it more intense and baneful. These cases will require to be dealt with by other means than the mere administration of mercury.

16. The hereditary or acquired tendencies and constitution of each individual should be studied, since every depressing influence, by lessening resistance, may lead to increased virulence of the disease; i.e. the presence of malaria, for instance, will probably influence materially the progress of the disease. In such cases, quinine will need to be vigorously pushed before any other treatment is attempted, and should be continued during the specific treatment.

A tubercular family history should be regarded as a special indication for hygienic precautions. The diet in such cases should be rich in digestible fats and carbohydrates, and to specific treat-

ment may be added, with advantage, cod-liver oil with iron or the hypophosphites.

Gout and Rheumatism exert a distinctly unfavourable influence over syphilis, as they predispose to cerebral disease, to endarteritis, to troublesome squamous syphilides, to iritis, to periosteal nodes, &c. Here the diet must be carefully regulated; the patient should be told to eat sparingly of red meat and sugar, to drink freely of potash water, and to eschew altogether wines and spirits. Salicylates may well be given in combination with specific treatment.

Neurotic Patients seem to be especially predisposed to affections of the brain and spinal cord. Now the most common and at the same time the most grave dangers of syphilis are connected with nervous manifestations. Again, the nervous manifestations attack, by preference, subjects who are predisposed to them by hereditary or acquired influences.

It is a fact that, as regards tertiary syphilis, the nervous system is attacked much more often than any other part of the body. Fournier's figures show that, out of a total of 4,700 cases of tertiary syphilis, in 2,000 the nervous system was affected in different ways—cerebral, spinal, tabes, or general paralysis—the remainder, i.e. 2,700, consisted of affections of other parts of the body (Fournier).

Hereditary or acquired neurasthenia is undoubtedly one of the chief localising causes of syphilis, and is one reason why it attacks the brain and spinal cord.

It is manifest, then, that such patients require special hygienic measures from the beginning of the disease; they should avoid, as much as possible, all likely causes of morbid stimulation of the nervous system, such as intellectual work requiring much mental strain, excesses of all kinds, i.e. alcoholic or venereal, excessive emotion or business worry, fatigue of all sorts, and late hours. Bromide of potassium and such-like agents may be found useful in these cases, and above all, hydrotherapy is here strongly indicated.

Increase and Maintenance of Tissue Metabolism. For this purpose, and as an adjunct to the specific treatment of syphilis, the

value of hot baths is beyond dispute. Through them the elimination of mercury is facilitated, large quantities are tolerated, and in certain cases, where, without the baths, doses of mercury, far too small to influence materially the lesions of syphilis, produce early symptoms of ptyalism, efficient doses can be given without untoward symptoms.

Baths may be given of hot water, 100° F. to 105° F., or hot air 180° F. to 200° F.

Heat thus applied increases the systemic metabolism, and by these means facilitates the elimination of mercury. Hot-air baths are particularly serviceable, since they occasion free diaphoresis and elimination through the sweat glands, and in consequence of the thirst they cause, large quantities of bland fluids are drunk, which, being taken up into the circulation, tend to increase metabolism.

The conclusions as regards hot baths in the treatment of syphilis are as follows :—

1. Both tepid, hot-water, and hot-air baths invariably increase the elimination of mercury by the urine.

2. The higher the temperature, the more energetic the elimination.

3. The cause of such intensified excretion of mercury is the increase of systemic metabolism, and the disintegration of mercurial albuminates.

4. In cases of mercurialism, when the elimination of mercury ceases spontaneously, the drug can be made to reappear in the excretions by the use of hot baths.

5. Hot-air baths, by producing free perspiration, promote the elimination of mercury also through the sweat glands (hence, as a means of freeing the system from mercury, hot-air baths ought to be preferred to other baths).

6. The appearance of mercury in the sweat suggests that diaphoretics generally are useful in the treatment of mercurial salivation.

7. Hot-air baths, by inducing thirst, lead to an increase of bodily metabolism.

8. Hot-air baths are better borne than hot-water baths.

As to the necessity of increasing and maintaining tissue metabolism, the conclusions come to are :—

1. That in importance it is second only to the administration of mercury, and that, whilst in most cases it is always beneficial, in some it is almost a necessity.

2. That it is still more indicated during the administration of mercury, for with its assistance the latter can be given with far greater freedom and safety.

3. That through it alone certain virulent forms of syphilis can be much relieved.

4. That it can be carried out by means of Turkish baths, radiant heat, or hot-water baths, and that dry-air baths are much to be preferred.

CHAPTER XXII

IODIDE OF POTASSIUM

IODIDE of potassium was first introduced as a treatment for syphilis by Wallace, of Dublin, in 1836. Since then it has been employed in the treatment of the disease with varying fortune. At one time it began to be looked upon as an absolute specific, destined to take the place of mercury; but time has not justified these hopes, and to-day it is regarded by most syphilographers, not as a specific in itself, but as a most valuable adjunct to mercury, the reasons for these conclusions being :—

1. That it has very little action (sometimes none at all) on secondary lesions.

2. Because it allows the secondary lesions to persist for a long time.

3. Because it does not constitute a safeguard for the future by removing the tendency to tertiary manifestations.

In the early stages of syphilis it is of little value, its therapeutic efficiency increasing in direct ratio with the age of the disease.

It appears to act by promoting fatty degeneration and absorption of the imperfectly organized exudates, hence its marked action on lesions of the late tertiary period which are made up of imperfectly organized tissue and excessive cell-growth.

As a rule, iodide of potassium is unnecessary in the early stages of syphilis, except in certain cases, i.e. to relieve nocturnal headache, and periosteal pains generally, and again in those cases which have been termed 'precocious', that is, where the early symptoms resemble in character those of the tertiary period, affecting the fibrous or connective tissues, the bones, the nerve-centres, and important viscera, or when they appear in the form of deep ulcers or infiltrations of the skin.

It is in the later stages of syphilis that iodide of potash is so

useful; then it is that its action in combination with mercury is so marked that the results of its administration appear to be marvellous; it is at this stage that we see under its influence swollen testicles, periosteal nodes, and bony lippings melt away, gummata subside, and rupial ulceration clear up. When pushed, the iodides frequently cause the disappearance of motor and sensory paralysis, and even at times the re-establishment of the mental faculties after they have been to all appearances hopelessly disorganized.

On the other hand, when given in an unscientific manner, iodides lead to grave results. In the first place, 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 they produce the well-known signs of iodism as represented by gastro-intestinal irritation, coryza, pustular and other forms of skin eruptions, lachrymation, tinnitus aurium, mental depression, various forms of neuritis and neurasthenia, and acute oedema of the larynx.

The skin lesions of iodism may simulate almost any of the recognized forms of acute cutaneous eruptions, acne, erythema, eczema, and herpes; purpura is often seen, whilst a form of psoriasis of an ulcerating, and still more rarely of a sloughing, variety sometimes occurs. As a rule, these eruptions as well as the other signs of iodism are due to an idiosyncrasy, and bear no definite relation to the dose employed; on the other hand, they occur very often as the result of long-continued overdosing with iodides.

In the doses ordinarily employed, a large number of patients will exhibit no symptoms whatever from the use of iodides, a smaller proportion will be troubled by a coppery taste in the mouth, acneiform eruption, coryza, lachrymation, and gastro-intestinal catarrh. A very small number of cases are entirely intolerant to iodide of potassium, and will suffer from swelling of the mucous membranes, especially of the larynx and pharynx, this swelling, in the case of the larynx, being sometimes so great as to produce acute oedema in a few hours, which may rapidly end fatally. It may be added that in many cases the skin eruptions are very severe in character.

Methods of giving Iodides. 1. The most important practical point in securing the fullest and best effects of iodide of potash, with the least harmful results, is to give it in dilute solution.

2. Excipients facilitate the proper absorption of iodides.

3. Iodides should be given about an hour after meals.

4. Iodide of potassium should be given in *intermittent* courses of increasing doses, and never, under any circumstances, should it be given *continuously*. Given intermittently its full therapeutic intensity is secured, whereas if it be given in a *continuous* manner it acts as a veritable poison to the system, lowering it in every possible way, leaving it, as already described, an easy prey to further developments of the disease.

It should never be given for longer than fourteen days at a time, after which there should be an interval of at least a week.

Dosage. When given in the early secondary stage, iodides should be ordered in five-grain doses three times a day ; this may be increased every third day by five grains, until the symptoms for which the drug has been administered have disappeared, which they will probably do in this early stage in two or three days, as the drug when given for these symptoms generally acts like magic.

When given in the later stages of the disease, iodides will have to be exhibited in much larger doses—10 grs. three times a day, gradually increasing up to 30 grains three times a day, so that by the end of a course of ten or fourteen days the patient will be taking ʒij per day. As a rule, this dose will be found sufficient, but cases are met with which may require much larger doses, and then as much as ʒj and more three times a day may be found necessary.

Manner of giving Iodides. Iodides may be given in an ordinary mixture with bark to conceal the taste, and when patients object to take the drug in a mixture, it can be given in the form of a saturated solution, one drop of which represents approximately one grain of potassium iodide :—

℞

Potassii iodidi	ʒv
Aquam q.s. ad	ʒj

5 to 10 ♏. as the case may be, in half a glass of milk or

water three times a day, increasing the number of drops as required.

When the above disagrees with the stomach, 5 to 10 grs. of pepsin may be added; this forms a kind of junket which completely masks the taste of the iodide, and the stomach is soon rendered tolerant. Should the iodide cause griping pains, tannic acid added to each dose will be found most beneficial.

The great thing to remember in giving iodide internally is to give it well diluted, and as a vehicle for this purpose nothing is better than milk, but iodides may also be given in wine or beer, or in any liquid which diminishes the disgust which many patients have for their saline taste.

In certain cases it may be necessary to administer iodides otherwise than by the mouth, when recourse may be had to enemas. Such cases may be due to inability on the part of the patient to swallow, owing to deep ulceration of the throat, oesophagus, or to some form of paralysis. When given by enema, the intestine must first be evacuated by a simple enema; when the intestine is emptied an enema of iodide of potash, 30 or 40 grs. dissolved in ℥ij of water with a few drops of laudanum may be given.

This method I have found most useful in many cases, and have had to have recourse to many times.

Some patients, in spite of all precautions, are found to be quite unable to take iodides at all; again, in certain cases of syphilis, such as cerebral with loss of consciousness and relaxation of the sphincters, other methods of giving iodides must be sought for.

Hypodermic injection of iodide of potassium is resorted to in some cases like these, but is not to be recommended with our present knowledge, as the injections are very frequently followed by abscesses and sloughing.

Iodipin. A better substitute is iodipin or iodoglycerine. Iodipin is a combination of iodine and sesame oil. It is prepared in two strengths, i.e. 10 and 25 per cent. Until recently only the weaker solution has been given internally, but now I give the 25 per cent. solution in gelatine capsules or in milk; its dose is

min. xxx three times in the day. As a rule, although I have found its therapeutic effects well marked when given in this way, still it is very apt to disagree and bring on dyspepsia. I prefer to give it by hypodermic injection, and my custom is, to administer it in doses of from 15 to 20 c.c. for ten consecutive days. The syringe used for these injections should be large enough to hold at least 10 c.c. and the needle fairly long ($2\frac{1}{2}$ inches), with a large bore. The seat of injection is best in the loose tissues of the loins. Iodipin is a viscid fluid, and requires heating to at least body temperature to render it thin enough to inject. The advantages claimed for iodipin over iodide of potash are, that it is more slowly absorbed and much more slowly excreted, that it is non-depressant, and does not interfere with the digestion. The injections are non-toxic and quite painless. Three months after a course of ten injections of iodipin it can still be found in the urine. It can be strongly recommended as a substitute for iodide of potash in all cases where the latter is inadmissible. Iodo-gelatine is a similar combination of iodine and gelatine, and is used in Milan with very good results.

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 continued or its dose even slightly increased, since in most cases tolerance is established and the coryza and eruption soon disappear. When severe, the drug must be discontinued at once, and the symptoms will then generally show immediate improvement.

Before leaving the subject of iodide of potassium, it is well to remember that iodide eruptions often simulate the cutaneous eruptions of syphilis so closely as to lead to serious mistakes; this is a fact which should always be kept in mind. However, there are certain signs which will generally enable us to distinguish an iodide rash :—

1. The rapidity of invasion. An iodide rash always appears suddenly, whilst one due to syphilis takes much longer to develop.

2. The initial form of eruption. The iodide eruption generally begins as a vesicle and runs rapidly through the pustular to the crustaceous stage.

3. The inflammatory character of the margins. The areola of an iodide eruption is generally bright red and inflamed; the syphilitic, brown, ham-coloured and indolent.

4. The base of an iodide eruption is soft, never hard like that of the syphilide.

5. The suppression of the drug will at once remove any doubt, as the rash will invariably clear up on the discontinuance of the iodide

CHAPTER XXIII

LOCAL TREATMENT

ALTHOUGH the local treatment of syphilitic lesions has already been described by the author in Vol. I (pp. 217–18) of this work, it may be well to allude again to it here under the subject of the general treatment of syphilis.

As a rule, a *chancre* requires little if any local treatment other than the application of antiseptic washes such as boric acid, lotio nigra, &c., but when there is a tendency to the formation of crusts, ointments are best, as for example :—

Iodoform	℥ij
Bals. Peru	℥j
Ung. lanolin q.s. ad	℥j

When covered by a tough pseudo-membrane beneath which ulceration is going on, the covering must be removed and the ulcerating surface cauterized with acid nitrate of mercury or strong nitric acid.

In the case of a phagedaenic chancre the best application is crude chromic acid, for which purpose the patient should be placed under an anaesthetic and the acid thoroughly applied; a black slough follows, which can be removed by the application of antiseptic fomentations. Iodoform is the best of all the dry powders; it can be applied pure or mixed with boric acid and starch. Calomel dusted on pure, or mixed with lycopodium, is also an excellent remedy.

For urethral and rectal chancres iodoform in the shape of suppositories may be applied after irrigating with mercuric chloride solution (1 in 5,000). The suppositories of appropriate size and shape may contain up to 5 grs. of iodoform each.

Chancres of the tongue, mouth, and tonsil are best treated with frequent washing and gargling of corrosive sublimate (1 in 6,000).

Syphilis of the skin. Erythematous syphilides require no local treatment. Papular syphilides are benefited by vapour baths containing mercury or an ointment such as :—

℞
Ung. hydrarg. nit.
Ung. lanolin carbol. . . . . āā ℥j

This ointment is especially useful in papulo-squamous eruptions.

Mucous patches can generally be prevented from appearing in the mouth by scrupulous attention to the teeth, gums and mucous membrane, and above all by the limitation of smoking and by the frequent use of astringent antiseptic mouth-washes. When they do appear they should be touched two or three times a day with a weak solution of nitrate of silver or of one containing boric acid or better still peroxide of hydrogen. Scaly patches are best treated with a daily application of chromic acid (10 per cent.) whereas ulcerated patches will require a stronger solution of chromic acid (20 per cent.) and nitrate of silver, the ulcer being first dried with a piece of cotton wool; the chromic acid solution is then applied, and after this a solid stick of nitrate of silver is rubbed over it; this forms chromate of silver.

In some cases acid nitrate of mercury succeeds best, and another application which has lately given me much satisfaction is perhydrol. This is a 50 per cent. solution of peroxide of hydrogen manufactured by Merck of Darmstadt; it is quite unirritating and can be used in any strength. Some ulcerations of the throat and pharynx will resist all applications; these should be scraped with a Volkmann's scoop and the surface touched with a 10 per cent. solution of chromic acid. This scraping should not be delayed too long.

For *condylomata* strong nitric acid is by far the best application. It may be necessary to apply it more than once, and after each application iodoform ought to be dusted over the surface.

At other times they can be best treated by the following :—

℞

Acidi salicylici
Ext. cannabis indicae . . āā gr. xxx
Collodion flexile . . . . . ℥j

This dries them up and they peel off in a few days.

Pustular syphilides are best treated by mercurial vapour baths. When occurring on the face active treatment ought to be begun at once and local mercurial fumigation is best; this can be carried out by generating the vapour in a box by means of a spirit lamp placed beneath a metal dish containing calomel; the patient's face should be held over the box for a short time every evening. As a local application for the same condition we may use :—

℞

Hydrarg. oxidi rubr. . . . . ℥ij
Ung. zinci oxidi . . . . . ℥ij

Treatment of Hereditary Syphilis.

The treatment of hereditary syphilis consists of prophylactic measures as regards the parents as well as the curative treatment of the offspring. Where there is reason to believe that the pregnant woman is syphilitic, or that she is the wife of a husband who, being infected with syphilis, may have married before he has had sufficient treatment or who may have developed symptoms of syphilis after marriage, then it becomes essential that the woman be placed under treatment at the earliest possible opportunity, as it is believed that treatment has little chance of being successful after the fifth month of pregnancy. (See also vol. ii, pp. 375–6.)

In dealing with a case such as this, my custom is as early as possible to put the patient under a full course of intramuscular injections of metallic mercury. I give one injection containing gr. 1 of mercury once a fortnight for two months; this is followed by one month's period of rest from all treatment, then the two months' treatment is repeated, with another month's rest, two

months' further treatment, and then all treatment is stopped to the end of pregnancy. When I say all treatment I mean mercurial treatment, as in some cases, especially of long standing, I give one course of iodide of potassium during the periods of rest. In tabular form this reads—

2 months' treatment (4 mercurial injections).
1 month's rest (perhaps a 10 days' course of potassium iodide) or of iodipin,
2 months' treatment (4 mercurial injections).
1 month's rest.
1 month's treatment (2 mercurial injections).

Of course this is open to variation and a good deal will depend on the class of case we may have to deal with, as well as the time of the pregnancy at which one is enabled to begin treatment. However, this line of treatment or one as closely following it as circumstances will permit, has proved wonderfully successful in the author's hands.

It is needless to point out the advantage of being able to give mercury by the intramuscular method in cases of pregnancy instead of being obliged to resort to one of the other methods, such as internal administration, remembering the state of the gastric system at that time. The father should also be placed under treatment and ought to have an energetic course of mercurial injections.

The child of syphilitic parents, although born apparently healthy, may develop hereditary syphilis later; thus it will require to be watched very closely with a view to determine whether it should have specific treatment or not. My own opinion is, that when either of the parents has recently suffered from secondary syphilis the child should be put on specific treatment from birth. If it be the offspring of parents whose disease is of old standing, and it has been born apparently healthy, we should watch the child carefully and await further developments before submitting it to treatment. At the same time in such cases as this it will be well to remember that syphilis may exist but may be exclusively visceral without showing any external signs. (See vol. i, p. 65.)

By far the best and most satisfactory way of administering mercury to the infant is by inunction. This can best be carried out by rubbing about ʒj of ung. hydrarg. into the child's binder; the movements of the child soon cause absorption of the ointment, or else a small quantity of oleate of mercury may be substituted. This method of giving mercury is a very old one, but it cannot be improved upon and is far better than the way in which it is sometimes administered, i.e. grey powder $\frac{1}{3}$ gr. or $\frac{1}{2}$ gr. given internally three times a day.

The physiological effects of mercury are far more easily established in the child than in the adult, and it is wonderful to see how rapidly even the most pronounced lesion of syphilis disappears under it in the case of children.

The intramuscular method is not suitable for infants and young children except when therapeutic intensity is a matter of time, when it may become necessary to administer calomel by injection. The infant will require, as in the case of the adult, prolonged and intermittent treatment. In the first instance it ought to be continued, counting periods of treatment and of rest, up to 18 months. After this the growing child will require strict observation. I think that it ought to be laid down as a rule, that all children who required specific treatment in infancy and early childhood ought to undergo a full course at about the tenth year of life, as we know that this is a precarious time in such cases because it is the time syphilis generally selects for its further ravages. (For Treatment of Congenital Syphilis, see also vol. i, pp. 361–7.)

CHAPTER XXIV

TREATMENT OF VIRULENT OR MALIGNANT SYPHILIS

VIRULENT or malignant syphilis is a form of the disease over which as regards treatment much discussion has taken place; certain it is that here treatment will have to be much modified as compared with that of ordinary syphilis. Until a comparatively recent time such cases were looked upon as more or less hopeless so far as any specific line of treatment was concerned, and some of the greatest authorities on the disease, notably Carmichael of Dublin, whose work on the whole subject of syphilis is classic, taught that the giving of mercury in these cases was both contra-indicated and actually harmful. I have not the slightest doubt that, restricted as were the means at that time of introducing mercury into the system, this teaching was correct, and I can well recall more than one case in my earlier practice which not only resisted specific treatment but went from bad to worse while it was being used; it must be remembered that in those days the only really practical way we had of giving mercury was by the 'internal method'. Since that time we have learnt 'that mercury given internally over any lengthened period sooner or later brings about depletion of the system generally'; how much sooner and with what more serious effects will it act when given thus in malignant cases? However, the introduction of the modern means of giving mercury, notably that by intramuscular injection, places us in a much stronger position to deal not only with the ordinary cases of syphilis but also with those of a virulent type. Given by this method mercury will prove itself as beneficial even in these

virulent cases as it has already done in all others, that is, provided due care be exercised in regard to its dosage and by paying strict attention to what I venture to call its essential adjuncts. If these be adhered to, mercury can be given with the greatest safety and benefit in all cases of syphilis, and I have not the slightest hesitation in saying that, if carried out properly, we would see but little of the deplorable effects of these virulent cases. I would add that in my opinion one of the main causes of the latter is the reprehensible practice which exists among a great many practitioners of giving mercury internally combined with potassium iodide for lengthened periods, irrespective of their syphilitic patient's condition or of his symptoms.

In discussing the treatment of these cases of so-called virulent syphilis it will be necessary to take into consideration certain points in connexion with them, points which may have the most important bearing on the question. First and foremost comes the question as to what may be the factor in causing the disease both to assume its virulence and continue in the same groove. This may have been due to some organic disease: if so, our attention in the first instance must be riveted on it, and if possible we must endeavour to palliate it before active specific treatment is begun. Again, the state of the general health must be looked to; should it have been broken down by climatic or other depressing influences, it must be carefully considered and dealt with accordingly. The patient ought to be removed from any lowering conditions of mind and body, and his mind diverted as much as possible from his condition. This is of the utmost importance and, although very often it may be hard to attain, it is well to bear it always in mind. As to the physical condition, nine out of ten of these cases will require feeding up with a nourishing and wholesome diet. Some cases are only able to assimilate very little nourishment; in these cases milk may be given mixed with plasmon, pure beef juice and concentrated beef jellies, sanatogen also I have found most beneficial. Stimulants are generally called for in these cases, and I must say that I have seen some of the worst

cases apparently derive the greatest benefit from a fairly liberal allowance of champagne; next to this comes Guinness's stout. As soon as the patient can be moved he ought to be brought into the open air, and kept in it as much as possible. This precaution can hardly be sufficiently insisted on. With regard to drugs, irrespective of specifics, tonics of all sorts will be required, both mineral and vegetable, and first among them comes sarsaparilla, which should be given in large doses in nearly all cases of virulent syphilis; cod-liver oil with syrup of the iodide of iron is also very useful. In these cases there is often a tendency to haemorrhage, owing probably to the want of coagulability of the blood; to improve this nothing is better than chloride of calcium, given in from 10 to 30 gr. doses thrice daily.

Should malaria be suspected to be in any way connected with such cases, quinine should be at once given, and its use continued both before and during specific treatment.

Specific treatment is, of course, the most important question to be considered in connexion with these cases, and the points that arise are, when to begin it, how long to persist, and lastly —when to desist. As regards the first, a great deal will depend on the particular kind of case we have to deal with, and as to whether mercury has been given beforehand in the same case. For instance, the disease may have begun in the ordinary way—i.e., a hard sore followed by one of the milder rashes &c.—the course of treatment may have been supposed to be going on well, when a sudden outbreak of alarming symptoms takes place—rupial ulcers appear on various parts of the body, the throat becomes deeply ulcerated and the bones of the skull, perhaps, are involved in caries. These are always urgent cases, and unless they are dealt with at once will rapidly go from bad to worse. At the same time their specific treatment calls for the greatest circumspection, and a good deal will depend on whether they have had mercury already as well as upon the duration of the previous treatment. Should these symptoms appear whilst the patient is under the effects of the drug it will

be necessary to stop it for a time and trust to general treatment with *mild sweating in hot air daily*. Other cases may require the mercury to be increased, while a third class of case in which mercury has not been previously given at all will require the drug to be rapidly introduced into the system. Generally speaking, most cases will require mercury, and will very often do well by being given it at once in mild courses. As to dosage, the majority of cases will do best with small, I might even say minute, doses. For this purpose I give a weekly intramuscular injection of half a grain of metallic mercury as a maximum, never exceeding this, but am very often satisfied with one-quarter or one-eighth grain per week.

Intramuscular injections of calomel will be necessary for those cases which require to be dealt with rapidly, such as phagedaenic syphilitic chancre, but extra caution must be taken with these, and the dose should not be greater than half a grain once a week until its physiological effects are apparent; when these occur metallic mercury must be substituted for calomel; personally I think that calomel ought in no case to be persisted in for more than four weeks running.

How long to persist in specific treatment. My custom in treating these cases is, if all goes well, to give an injection, once a week for a month at a time, then to desist from all specific treatment for the next month. This system of a month's active treatment alternating with one of rest can be continued for a considerable time, and seems particularly suited to this class of case; I am of course speaking generally, as every case must be treated on its merits.

During the period of active treatment, should symptoms, as they often do, show signs of exacerbation, the mercury must be stopped for a time, when they will probably improve; one can then resume specific treatment. These exacerbations must be carefully watched for; their occurrence is no indication that specific treatment should be abandoned altogether, on the contrary it should be persevered in.

Next in importance to specific treatment comes the question

of the increase and maintenance of tissue metabolism. In the class of case under consideration this is an absolute necessity if one is to look for favourable results, and one cannot lay too much stress on it, for, beneficial as it is in an ordinary case of syphilis, it is usually ten times more so in the virulent cases we are now considering. It is the recognition of this fact which has doubtless been at the bottom of the success which has attended the treatment at Aix for so many years, for there metabolism is insured by the use of the natural waters of the place, which are both slightly diuretic and aperient, also by prolonged immersion daily in hot baths. Again, we may see the surprising improvement which sometimes follows a course of Zittmann's treatment, which consists of sweating, purging, and the administration of mercury, in a more or less drastic manner, for a limited number of days, and although this improvement may too often be only of a transient nature, it nevertheless shows the value of bringing about and maintaining tissue change.

The various means of effecting and keeping up this tissue change have already been described; of these, *hot-air baths*, whether effected by means of radiant heat or otherwise, are far the best, especially for cases of malignant syphilis. As a rule a case of this kind should have a hot-air bath at least every second day, being exposed to a temperature of from 180° F. to 200° F. for about five minutes, and this time can be gradually increased. Whilst writing on the subject of hydrotherapy in syphilis I would remark, that it is sometimes surprising what remarkable results the hot-air baths bring about in these virulent cases even unaided by any specific treatment, and in those cases of old standing, which have been saturated with mercury and potassium iodide, this method of treatment is absolutely invaluable even by itself.

Iodide of potassium. As in the ordinary cases of syphilis at the outset of these virulent cases, iodide of potassium is of little avail and does more harm than good, but as the case progresses its efficacy is far more marked than in more benign varieties.

At the same time, it will require to be given with much circumspection and care, and the rule of giving it in *intermittent courses* of increasing doses, each course not exceeding fourteen consecutive days, should never be departed from, ever bearing in mind, that if continued beyond this time the drug appears to lose its beneficial effects, and then only acts as a constitutional depressant, which is the very last thing to be desired. Given in the way described, iodide of potassium is most valuable in these virulent cases of syphilis, and mitigates in a very marvellous way the various bone and skin lesions, to say nothing of the later syphilitic affections.

Iodipin. It is in these cases that I have derived the best results from iodipin, which, from the slowness both of its absorption and elimination, has the very best effects. I have seen very many cases which, although they had shown no change for the better under iodide of potassium, have responded almost at once to subcutaneous injections of iodipin, given as already described by this method in 15 c.c. doses every day for ten consecutive days, the courses to be repeated every three months if necessary. As I have already said (p. 321), I am in the habit of giving in addition the 25 per cent. solution in 30 gr. doses thrice daily, either in milk or made up in gelatine capsules.

Local lesions. The local treatment of these is of course very important in virulent syphilis. For chronic affections of the mucous membrane nothing is better than touching with either chromic acid 10 to 20 per cent., either alone or followed by the application of the solid stick of nitrate of silver, which forms chromate of silver. In the more severe forms of ulceration the curette should be employed at once, and it should be freely used after applying the chromic acid.

For phagedaenic sores in all situations I find the application of crude chromic acid best; this may require to be done more than once; after the sloughs have separated iodoform should be dusted over the surface. Some sores do best by continually bathing in hot boric or sublimate solutions, but all large chronic ulcers should be treated on general surgical principles, i.e. rest, cleansing,

opening-up of gummata and sinuses, and securing good drainage. In the first instance gummata should be treated with soothing applications, afterwards with stimulating. The early removal of all sequestra should always be attempted.