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AN IMPROVED PREPARATION FOR INTRAMUSCULAR
INJECTIONS OF INSOLUBLE SALTS OF MERCURY
IN THE TREATMENT OF SYPHILIS.

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SINCE Scarenzio, in 1864, first suggested injections of insoluble salts of mercury in the treatment of syphilis, certain obstacles have always existed in connection with it which have undoubtedly militated against its being universally adopted as the best and by far the most convenient way of treating the disease, *i.e.*, pain at the site of injection, painful nodosities, abscesses and embolism. Although with the progress of knowledge and improved technique the first (as regards metallic mercury) has been reduced to a minimum, and the three last practically caused to disappear, still, that they do exist even now, if to a limited extent, there can be no doubt, and this is the chief cause, and indeed, in a great many cases, the only one, why some of the best known syphilologists of the day hesitate in recommending the intramuscular method before all others in the treatment of syphilis.

Fournier, in his "Traité de la Syphilis," says: "Lastly, a weighty argument (which I have already developed in the previous remarks) which condemns the method, is that by its inconvenience, and especially by the pain it inflicts on patients, it constitutes the best method for preventing patients continuing treatment."

In the early days of treatment by this method the main causes

2 *Insoluble Salts of Mercury in the Treatment of Syphilis*

of the difficulties alluded to were undoubtedly due in the first instance to the ignorance existing at this epoch as regards the necessity for employing antiseptic precautions in carrying out injections, and, secondly, to the unsuitability of the substances which had to be employed as vehicles for the suspension of mercury in the preparation used for injection purposes. The former has, of course, been long since remedied, and pain (at any rate where metallic mercury is concerned) has, as previously stated, been reduced to a minimum, but the other objection has existed more or less up to this day.

The substances which have been employed to hold the mercury in suspension are as follows: Glycerine, gum water, olive oil, vaseline, oil of vaseline and lanolin. Each of these has had its day, one being introduced from time to time as an improvement on the other, and in some respects they may have succeeded in this. Personally, I could never get away from one objection which was common to all. "Being insoluble in the organism they entered the circulation as foreign bodies, and as such might possibly have produced nodosities, abscesses, and embolism." This, of course, is a most grave objection and has always been a source of anxiety to me; however, perhaps I ought not to grumble at the substances (lanolin and liquid paraffin) which I have been in the habit of using, as I have personally never seen any of these accidents follow their use; at the same time, there can be little doubt but that some of those grave accidents which have been recorded in connection with intramuscular injections of mercury must be put down to the use of these insoluble substances. Besides this main objection some of the above have others which are much against them. Glycerine and gum water are very irritating and painful, whilst olive oil, vaseline, and oil of vaseline are apt to go rancid.

Some eighteen months ago, in discussing this matter with M. Duret, a well-known French chemist, he suggested *palmitin* as a substitute for any of the above substances 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 glycerine of palmitic acid, is therefore easily saponified in the fluids of the organism, being converted into a soluble alkaline palmitate and glycerine, and thus it enters the circulation not as a foreign body, like all substances hitherto used as vehicles. For close on eighteen months I have been experimenting with palmitin as a vehicle and have practically adopted it as such at the Military Hospital, Rochester Row, and with the greatest success.

It is unnecessary for me to point out the preponderance of the advantages which I claim for palmitin over all other known substances as vehicles for the suspension of mercury in any form. (1) It is non-irritant and non-toxic; (2) is not so easily oxidised as the other compounds of human fat;¹ (3) being already a normal constituent of the human organism, is easily saponified and soluble therein, and *does not* enter the circulation as a foreign body; (4) as a vehicle it makes a more homogeneous preparation for injection purposes than any other; (5) its melting point can be raised and lowered with the greatest facility.

I may here state that pure palmitin (which is the only preparation used) is a snowy-white flocculent powder, and great care is necessary to get it *pure*.

ANALGESIA.

As regards Pain.—Although (as far as metallic mercury is concerned) this has been reduced to a minimum, still there is no doubt that it constitutes a grave objection in the practice of intramuscular injections, especially when calomel has to be employed.

With a view to, if possible, abolishing pain altogether after injections, various substances have from time to time been introduced into the mercurial preparations used for that purpose, *i.e.*, morphia, cocaine, beta-eucaine, &c.; these, acting as they do almost at once, will assuage any pain which may follow immediately after inoculation, but unfortunately, this is not the kind of trouble we have as a rule to deal with, as the pain which bothers us is one which comes on two or three days after the injection, when the above local anæsthetics are fruitless. This is a very serious matter in any case, but especially as regards injections of calomel, for it is here that pain is most marked and severe; the consequence is that being hitherto unable to cope with it, we have been forced to more or less abandon injections of calomel as anything like a routine method of treating syphilis, and have only employed it under exceptional circumstances when pain was of no consideration. Hence was lost to us our keenest weapon for dealing with syphilis. It has always been my endeavour to overcome this drawback.

¹ *Palmitin.*—In Stirling's work on "Physiology," page 29, it is stated that neutral fats of adipose tissues of the body generally consist of a mixture of stearine, palmitin, and olein.

Professor Halliburton, in "Essentials of Chemical Physiology," page 15, states that the fat cells are composed of three different fats called palmitin, stearine, and olein. Charles, "Physiology and Pathology," page 84, says, palmitin is more abundant than stearine in human fats and *is the chief component* of most animal fats.

4 *Insoluble Salts of Mercury in the Treatment of Syphilis*

Being cognisant of the analgesic powers of creosote, it struck me that some combination between it and camphor might possibly meet with success. With this in view I consulted the well-known chemists, Messrs. Oppenheimer and Co., London, who informed me that they manufactured *absolute creosote* from the ordinary product, which is obtained from beechwood; that there is a very great difference between what is known as guaiacol and this purified creosote, the former constituting only about 20 per cent. of the bulk of beechwood creosote; the purified creosote is an intimate chemical substance, consisting roughly of 20 per cent. guaiacol, 40 per cent. creosote, and 40 per cent. monatomic phenyl; it is methyl-catechol, and has the empirical formula of $C_6N_4C_{10}H_{16}$; it possesses double the bactericidal effects of pure carbolic acid when tested by the Rideal-Walker process.

With this substance, in combination with camphoric acid, I have been experimenting for some little time now, and I may say at once that it has proved a thorough success as an analgesic in not only combating any pain which may immediately follow on an injection, but, what is much more to the point, it apparently succeeds admirably in preventing the occurrence of that after-pain which comes on on the second or third day, especially after calomel.

The abolition of pain after injections, I need not point out, is one of the very greatest, if not of vital, importance to us syphilologists, not so much as regards metallic mercury (which never caused much), but in the case of calomel it is of prime interest. Syphilologists 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 when called upon in acute cases, whilst 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 has been more or less unanimously abandoned owing to one great drawback, *i.e.*, the intense pain which was liable to follow its use as an injection, this latter usually coming on about the second or third day after inoculation, and lasting with more or less severity for three or four days. As regards this pain Fournier gives statistics, collected by himself and Portalier, of 473 cases of syphilis treated by injections of calomel; in 34 per cent. pain was slight, in 34 per cent. it was moderate, in 29 per cent. it was acute, and in 3 per cent. it was intolerable.

This estimate coincides with my own experience, and rather understates the actual amount of pain than otherwise. I have seen so many cases where this has been almost intolerable, that as years went on I approached the giving of intramuscular injections by calomel with more or less dread, and only employed them when absolutely obliged to from the nature of the case. Since I began to use this substance, absolute creosote and camphor, as an analgesic, I have been giving intramuscular injections of calomel with impunity; in fact, during the last few months at the Military Hospital, Rochester Row, I have to a certain extent modified my method of treating syphilis, for whereas previously patients undergoing injection-treatment were put first on metallic mercury, latterly to begin with they are put on weekly injections of calomel; this rapidly causes the disappearance of signs and symptoms, and then they are put on intramuscular injections of metallic mercury.

With reference to this latter it may be well to remark here a fact which has been long since noticed by myself as well as by others, *i.e.*, that although the action of calomel on syphilis is so markedly energetic and rapid, that it is short-lived when compared with that of metallic mercury, hence the necessity of reverting to the latter at an early date.

This combination between pure creosote and camphor possesses other advantages besides its analgesic powers, *i.e.*, it is in the first place non-toxic (which cannot be entirely said of other suggested local anæsthetics), and is strongly antiseptic, being twice as much so as pure carbolic acid, besides which, being a viscous body, it lends valuable aid to the palmitin in making up a vehicle which will hold metallic mercury or calomel in suspension; in fact, the combination goes on to form a most homogeneous preparation, much better in this respect than any I have ever seen before; its consistence at a melting point of 37° C. (which is what I am at present using) could hardly be improved upon.

The following are the formulæ for the two mercurial creams:—

	Hydrargyrum pur.	10 grammes
Equal parts of absolute creosote and camphoric acid	} Creo-camph.	20 cc.
		Palmitin basis to 100 cc.
	10 m equals metallic mercury	1 grain.	
	Calomel	5 grammes
Equal parts of absolute creosote and camphoric acid	} Creo-camph.	20 cc.
		Palmitin basis to 100 cc.
	10 m equals calomel	$\frac{1}{2}$ grain.	
	Melting point,	37° C.	

6 Insoluble Salts of Mercury in the Treatment of Syphilis

Lieutenant-Colonel Leishman, R.A.M.C., has examined both of the above creams and found them to be "sterile, and that bacteria would not grow in either."

Creo-camph. (otherwise camphorated creosote) is absolute creosote in combination with camphoric acid, and is isolated as such from creosote obtained from beechwood by fractional distillation as methyl-catechol. As before stated, both these preparations form creams of almost perfect consistence and homogeneousness. Both the metallic mercury and calomel are triturated with the other constituents by a special process which has been highly developed by Messrs. Oppenheimer. Both are very finely divided. Messrs. Oppenheimer, to prevent any chance of overdosing, supply these creams in aseptic vials, each graduated to hold a maximum dose of 15 m.

To sum up, I would briefly remark that, in my opinion, the substitution of palmitin, which is a soluble constituent of the organism, as a vehicle for the suspension of mercury, in place of the insoluble substances hitherto in use, and the success which has followed the adoption of camphorated creosote as an analgesic, begins a new era in the treatment of syphilis by intramuscular injections of insoluble salts of mercury, for, in the first instance, one great objection to the treatment, *i.e.*, the introduction of insoluble foreign bodies into the circulation, is done away with, and in the second, pain has been practically abolished even in the case of calomel; needless for me to point out what abolition of pain means to most patients, be it ever so slight, but in this case it means much more from the surgeon's point of view, in that it places at his disposal the best and most energetic mode of dealing with syphilis without let or hindrance, *i.e.*, injections of calomel.