SYPHILIS TREATMENT DURING WWI

In 1906 Paul Ehrlich, the famous German physician, who died in 1915, discovered Salvarsan 606 and Neosalvarsan 614, the world's first chemotherapeutic agents for systemic treatment of a micro-organism. These were to revolutionise the treatment of syphilis. For centuries before Salvarsan, treatment was by the use of mercury and iodides but these medications usually failed to prevent the disease progressing over the years to the incurable tertiary stages. It is of interest that in 1915, nine years after the discovery of Salvarsan, mercury was still prescribed by injection and inunction.

Despite the availability of a specific cure, and the use of the Wassermann test for diagnosis, syphilis was a major problem affecting the health of soldiers on the Western Front; I recall treating an aged lady in 1986 who had developed a manifestation of tertiary syphilis. Her primary infection, in 1919, of which she was unaware, was from her husband who had returned to Australia from the Western Front.

The following account of the treatment of syphilis is taken from the "Practitioner's Encyclopaedia of Medical Treatment" published in 1915 by Oxford Medical Publications. Intravenous injections are commonplace today but they were rarely used at the beginning of the century and Mr McDonough, FRCS., the author of the article quoted below, obviously considered it to be important to describe in detail how they should be given.

Dr M. G. Miller

THE TREATMENT OF SYPHILIS IN 1915.

By J. E. R. McDonough FRCS.

Surgeon to Outpatients, London Lock Hospitals.

The present-day treatment of syphilis can be divided into two heads:

(1) Local; (2) General.

Local Treatment.—A chancre should be excised when possible; if in a position which contra-indicates excision the sore should be cauterised, or frequently bathed with Lotio. Nigra and Unguentum Hydrarg. well rubbed in until every trace of the induration has disappeared. Ung. Hydrarg. should also be rubbed in the skin over any enlarged lymph glands. Condylomata should be frequently bathed with antiseptic lotions, then kept dry with a powder which contains calomel.

- Hydrarg. Subchlor. gr. x
- Magnes. Carb gr. xx
- Zinci Oxidi Xeroformi gr. x
- Pulv. Amyli ad. 1 oz.
M. f. Pulv

Rubbing in a mercurial ointment will hasten the disappearance of any syphilitic skin lesion.

The local application of Iodipin with or without Tinct. Bellad., according to the severity of pain, will assist in bringing about the resolution of a periostitis. For joint affections Scott's dressing is the best application. For chronic ulcers is the chief point to attend to, and when the ulcer is clean, either the use of a mercurial ointment or the judicious employment of Scarlet Red will assist in the general treatment. It must not be forgotten that any scabs should invariably be removed because their proteolytic action on the tissues underneath may increase the ulceration, although the primary cause has been got rid of. The local application of salvarsan to chronic ulcers on the leg or to the tongue, in chronic glossitis, often affords great relief. A 0.1 gm. ampoule dissolved in 1/2 oz. water or glycerine should be applied two or three times a day for a few days.

General Treatment.--Three drugs only need be considered, mercury, iodine and arsenic.

1. Mercury.--The best method of prescribing mercury is in the form of inunctions, but these are useless, except in congenital syphilis, unless carried out by a trained rubber. Mercurial inunctions are messy, and cause the patient some inconvenience, owing to the time they take up. More convenient are mercurial injections. The insoluble preparations are more efficacious than the soluble. The strongest compound is the subchloride, but unfortunately its use is so frequently accompanied by pain and occasional abscess formation that some preparation of metallic mercury is better. The best painless Grey Oil is the following (Captain Adam's formula)--

- Hydrarg. 20 parts
- Anhydrous Lanoline 30 parts
- Chlorbutol 2 parts aa by Weight
- Liq. Paraffin to 100 by measure, 5 minims = 1 gr. Hg.

Sig. Inject. 5-10 minims weekly. Injections can be made either into the buttocks or scapular muscles.

The insoluble preparations, of which Asurol is the best, are now seldom called for owing to the rapid action of salvarsan, but if this is contra-indicated and the symptoms are such that the patient should be got under the influence of mercury as soon as possible, daily injections of 1 cc. 5 per cent. Asurol sol. (= 0.02 gm. Hg.) or Énesol (salicylarsenate of mercury) should be given. Injections every other day of 0.025 - 0.10 gm. of Antiluetin, an antimony salt, can be prescribed as an alternative if required.

When a patient cannot get regular medical attendance, mercury should be taken internally in some form; if this method causes depression or sets up gastro-enteritis or diarrhoea, a suppository of 1 gr. of mercury salicylate in Oleum Theobromi 1/2 gr. inserted every night just before going to bed will often meet the difficulty.

For use in the tropics suppositories will require to be made up with an extra amount of wax.
Iodine.--No preparation has yet been discovered which is so potent as potassium iodide, but unfortunately there are so many people who cannot take it. A mixture of the sodium and ammonium salts is better tolerated, but an idiosyncrasy may be shown to every inorganic salt, in which case an organic salt should be tried, for preference iodoglidine. The non-staining iodex ointment is an excellent local application.

Arsenic.--Fowler's and Donovan's solutions are useful alternatives, but the powerful specificc is salvarsan, and its derivative neosalvarsan. Neosalvarsan is possibly not quite so strong as salvarsan, but it is easier to use, and causes fewer toxic symptoms. Moreover, intravenous injections can be given in the consulting room, and the patient allowed to go home immediately afterwards. Both can be used for intramuscular injections, but the necessary bulk is so great, that much pain and induration may follow. Another great disadvantage of the intramuscular route, which necessitates several injections, is that, as there is no guide as to the amount of the drug that has been absorbed, there is no indication when it is safe to repeat the injection.

"Ioha" is the best preparation of salvarsan for intramuscular use, and for neosalvarsan the proportion of 1 gm. dissolved in 22 cc. of pure distilled water.

Intravenous Injections.--Before submitting a patient to this treatment he should be thoroughly examined and prepared as for an anaesthetic, in the matter of aperients and diet.

Salvarsan

- Dose for man, 0.4 - 0.6 gm.
- Dose for woman, 0.3 - 0.45 gm.
- Dose for child, 0.001 gm. per pound weight.

The glass tube containing the powder should be thoroughly examined before the contents are dissolved, to see that there has been no air inlet.

The contents of one tube of salvarsan should be slowly dissolved in three or four ounces of warm physiological 0.9 per cent. saline which has been prepared with freshly distilled water, in a ten-ounce graduated glass measure.

When the powder has completely dissolved after sufficient stirring with a glass rod, 10 cc. of double decinormal sodium hydrate solution should be added, with the result that a precipitate forms; this precipitate is dissolved by a further addition of sodium hydrate, usually about 10cc.--this may be either more or less, according the actual acidity of the powder. The 10 cc. should be added slowly, and the mixture stirred thoroughly. By using a weak solution of sodium hydrate we avoid the risk of making the solution too alkaline, and the exact quantity required is more easily estimated. When the solution is quite cleared by adding the sodium hydrate, the measure should be filled with saline up to ten ounces, and once or twice filtered through muslin or several layers of plain gauze, so as absolutely to exclude even the smallest solid particle from getting into the vein, where it might cause either a pulmonary embolism or hemiplegia. Ten ounces must be considered the maximum dose.
Two points must be observed concerning the saline. In the first place, the sodium chloride must be chemically pure; secondly, the solution must not be less than 0.8 per cent. or more than 10 per cent. A hypotonic solution is more dangerous than a hypertonic, because the former causes haemolysis -- setting free the haemoglobin from the red-blood corpuscles. Should this happen the patient may collapse after the injection, and there may be haemoglobinuria. Needless to say, every vessel used should be sterile and the sodium hydrate solution should be boiled before use.

To warm the solution, a hot jacket should be placed around the measure and the whole placed in a water-bath; the jacket of gauze prevents the glass vessel from cracking. When injected the fluid should be at exactly body temperature, as the reaction following is considerably greater when it is too hot.

Another vessel filled with saline is placed by the side of the one containing the "606". The patient comes to the side of the bed and hangs his arm over, then a tourniquet is placed on the arm, and the limb made to rest on a table in as comfortable a position as possible. (The simplest and best tourniquet is some rubber tubing, which should be wound tightly around the arm and the two ends fixed with pressure forceps, which can be removed without disturbing the limb.) The bend of the elbow is then sterilised by first rubbing with acetone and then with ordinary, tincture of iodine.

When a vein cannot be seen it can often be felt, and should be marked out with a blue pencil to indicate its course. If this cannot be done, a vein should be exposed by an incision, either under a local or a general anaesthetic. There is no danger in a general anaesthetic, for the subsequent reaction is not in any way influenced. Hitting the bend of the elbow, or warming the arm with hot towels, will often make a vein prominent. An intravenous injection may be the simplest or one of the most difficult operations possible. A common trouble is due to the vein slipping about when the needle tries to pierce it; extending the arm as much as possible, or pulling the skin taut to fix the vein may prevent this.

The solution can either be injected or infused, injection being far preferable, as--

1. The needle is not so easily dislodged. If this should occur while the solution is flowing in, by infusion some must escape into the tissues before the flow can be stopped; with the syringe merely a few drops need escape, as the tap can be turned off at once.

2. The operator has more control over the proceedings.

3. There is less danger of air or a solid particle gaining access to the vein. Air is easily seen in the syringe and remains at the top, never coming over the centre of the outlet unless the piston is pushed right home. A solid particle is also seen; it falls to the bottom of the syringe and is not disturbed, provided that the solution is injected slowly and steadily and the piston not rammed home.

4. The operation is pleasanter from the patient's point of view because it is so much quicker.
5. The risks which are alleged to follow injection, and not infusion, do not exist in actual practice.

6. The operation can be performed without an assistant, and there is practically no apparatus to carry about.

A good syringe is one invented by Schreiber, and made by the firm B. B. Cassell, Frankfurt a. M. The cannula is bayonet-shaped, bent, and fixed to a three-way metal stop-cock, so that the fluid can be sucked up from the vessel and injected directly into the vein. The needle has also a plate at its base upon which a finger can rest to keep it steady. The one disadvantage of this syringe is that the whole apparatus is rigid; therefore the slightest movement of the syringe may be sufficient to dislodge the needle.

To overcome this difficulty, Allen and Hanburys have constructed for me a needle, which is 1 1/4 in length, behind which is a slightly concave metal plate which rests on the arm and is fixed by a piece of tape which runs under a metal bridge and is tied under the arm. This needle is fixed by means of a bayonet-catch to the three-way stop-cock; but the connection between the needle and the bayonet-catch is made by a piece of thick rubber tubing, so that every movement of the stop-cook or syringe behind is broken by this flexible connection and does not affect the needle.

The all-glass syringe, which should hold 20 cc., fits on to the stop-cock by means of a piece of stout rubber tubing, instead of being inserted into a metal tube, which may not fit every syringe.

The syringe is first filled with saline solution and all air expressed both through the tubing and the needle, then the needle is inserted into the vein, and fixed with the stop-cock open. If the vein has been pierced, which can at once be told by the touch, or by blood flowing back into the syringe, the tourniquet should be removed and some saline injected. If the cannula is not completely in the vein, the saline will produce infiltration; this being the case, the needle should be withdrawn and another vein chosen, as it is most important to prevent any of the '606' solution getting under the skin, as considerable pain is caused thereby. If much escapes there will be painful induration and oedema of the arm, which takes weeks to disappear. When the solution has all been injected, some saline should finally be used to avoid leakage of a drop or two of "606", which is done by transferring the tubing from the "606" vessel to the one containing saline. If, during the injection, the needle slips and some of the solution escapes--the patient complaining at the same moment of a burning sensation one should immediately take the needle out, apply a tourniquet to the arm, and allow the vein to bleed, which will often prevent infiltration forming. If the injection is skilfully done, the patient has no pain. In no circumstances must the preparation be injected in a concentrated form, and great care should be taken not to inject it too quickly.

**Neosalvarsan**.--1.5 gm. neosalvarsan equals 1.0 gm. salvarsan. Neosalvarsan oxidises quickly, and the oxidised product is toxic, therefore the solution must be prepared immediately before use and not shaken or stirred more than is absolutely necessary. The water in which the powder is to be dissolved must be warm enough to inject, and not above 30° C., and should be warmed before the powder is dissolved. Apyrogenetic water must be employed, without the addition of
NaCl or NaOH 35 cc. to 0.1 gm. of powder. The average dose can vary between 0.45 and 0.9 gm. Both Salvarsan and Neosalvarsan can be injected intravenously at weekly intervals.

The best procedure of treating syphilis in its various stages is, **in the primary and secondary stages** to give as many weekly injections of salvarsan or neosalvarsan as are necessary to procure a negative Wasserman's reaction in the blood withdrawn the day of the last injection. By this means the patient gets one injection after his blood becomes negative. In the primary stage between three and five injections will be required and in the secondary of between five and nine. In the primary stage an examination of the blood should be made before treatment is begun. In both cases four courses of eight weekly intramuscular injections of mercury should also be given and iodides prescribed for three weeks after each course, then six months, and a year later the Wassermann's reaction should be tested and a provocative injection of salvarsan given before a cure can be pronounced.

**In the latent stage**, diagnosed by giving a provocative injection of salvarsan, the treatment should be the same as above described. It is no use giving a provocative injection unless at least six months have elapsed since the patient last had an injection.

**In the tertiary stage**, when a cure in the strict sense of the word is practically unattainable, it is best to prescribe two injections of salvarsan to get rid of the symptoms, with a subsequent course or two of mercury and iodides.

**In syphilis of the nervous system** salvarsan should only be urged in cases of cerebro-spinal meningitis. In tabes it may occasionally do good when mercury has failed, but an aggravation of symptoms may occur. In **General Paralysis of the Insane** salvarsan should never be prescribed.

In **congenital syphilis** salvarsan should only be given when mercury fails to cure the symptoms, and mercurial treatment should be continued for at least three years. The treatment should be intermittent and alternating, i.e. one course should consist of inunctions, another of Hydr. cum Cret. given internally, and another of wearing clothing next to the skin which has been impregnated with mercury.

**Pregnant syphilitic women** should be given four or five injections of salvarsan as soon as conception is known to have occurred, and mercury continued throughout pregnancy.

Last but not least, oral hygiene should never be omitted when a patient is taking mercury; cleaning the teeth with pebeco and washing out the mouth and gargling with potassium chlorate or a 1 in 20 solution of perhydrol after each and every meal should be considered imperative. A lotion containing some formalin, tincture of myrrh and rhatany for hardening the gums is often useful.