REMARKS ON THE TREATMENT OF SYPHILIS
BY INTRAMUSCULAR INJECTIONS.*

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THE treatment of syphilis by intramuscular injections of mercury is a plan which in certain phases of the disease may be adopted with advantage, and is a useful addition to the therapeutic measures at our disposal; but it is one which hardly commends itself as a routine, and is unlikely ever to supplant the simpler and more familiar method of administration by the mouth. As a general rule, syphilis in its early stages is a disease which is most amenable to the ordinary mercurial treatment, and one in which a favourable prognosis may usually be given; but there are cases which do not respond to such treatment, and in which recourse must be had to more drastic measures. Ingestion of some mercurial preparation by the mouth is at once simple, convenient, painless, and efficacious, and will usually ensure a rapid disappearance of the symptoms; but a certain proportion of patients will be encountered who are intolerant to mercury so introduced into the system. For instance, in some it induces dyspepsia, colic, diarrhoea, loss of weight, anaemia, and cachexia, and the discomfort attending this plan of mercurial treatment is in no way counteracted or affected by the addition of opium. In the case of patients who are intolerant to mercury administered by the mouth, the usual alternative has been the introduction of the drug through the skin by means ofunction with mercurial ointment. But this plan possesses many drawbacks and disadvantages, such as its uncertainty, its uncleanness, its inconvenience, and the fact that it is contraindicated in cases in which the skin is tender and irritable, and in the presence of a general pustular syphilide.

In addition to these cases in which the ingestion of mercury by the mouth, or its introduction by way of the skin presents these inconveniences and disadvantages, there are others in which a more rapid action of the drug is essential, and in which the future prospects, and even the life of the patient, are endangered unless more urgent measures are adopted. For instance, cases of malignant syphilis attended by severe ulcerative lesions, and possibly entailing disfigurement or mutilation; syphilitic iritis threatening destruction or impairment of vision; cerebral or spinal syphilis; tertiary syphilitic laryngitis and pharyngitis; chronic and inveterate syphilides, resisting the ordinary methods of treatment; ulcerating tuberculous and spreading serpiginous lesions; chronic glossitis and the so-called palmar and plantar psoriasis. Chronic glossitis and syphilitic leukoplakia are conditions which particularly call for strenuous measures, since, if they are allowed to continue unchecked, they are liable to proceed on to carcinoma linguae. In cases such as these it is absolutely necessary that the patient should be brought under the influence of mercury as rapidly as possible, and no more efficient plan is at present at our disposal than that of intramuscular injections.

There is no glamour of novelty about this method, for it was introduced by Scarenzio in Italy more than forty years ago, but owing to the many drawbacks and accidents by which it was attended, it was only practised sporadically, and was not held in high repute. One of the almost inevitable sequelae of the injections as at first employed was acute inflammatory reaction proceeding to suppuration, and abscess was the rule rather than the exception. The large doses at first introduced were to some extent responsible for this complication, but the ignorance of the principles of antiseptics and aseptics was another more important factor. The usual locality selected for the introduction of these injections was the buttock, but very little regard was paid to the anatomical disposition of the blood vessels and nerves of that region, with the consequence that severe and even fatal complications occasionally ensued. The needle thrust in indiscriminately might happen on the great sciatic nerve, with the result of an acute attack of sciatica, and possibly localized paralysis; or it might penetrate into one of the large tributaries of the gluteal veins, and

the injection be conveyed to the lungs, giving rise to pulmonary embolism. Moreover, acute stomatitis and profuse salivation usually followed the injections, and occasionally enteritis with severe colic and diarrhoea, and more rarely ulceration and perforation of the intestine.

These many disadvantages and dangers were sufficient to damp the enthusiasm of many of the early supporters of the injection treatment, though they do not appear to have discouraged its principal advocate, Scarenzio. Still, though at first this treatment resulted practically in failure, there is no doubt that the labour of its author was not in vain, and, with certain modifications and restrictions, this method is now becoming well recognized, and in appropriate cases is adopted in all the clinics of dermatology and syphilography.

The substances at present employed for these injections are too numerous for me to mention, but they may be primarily divided into the soluble and insoluble preparations of mercury—the soluble salts being dissolved in sterilized water, and the insoluble suspended in sterilized oil, vaseline, and some similar vehicle. The soluble salts are introduced daily, or on alternate days, twenty to thirty injections constituting a course; the insoluble preparations are given once a week, or once a fortnight, the course in this instance consisting of from ten to twelve injections. Whichever preparation is made use of, every precaution must be taken to avoid any of the accidents and disasters previously alluded to. The locality almost universally selected for the injections is the buttock, and a part of that region devoid of any large vessels or nerves, and consequently above and to the outer side of the great sacro-sciatic foramen; the centre of a line drawn between the anterior superior spine of the ilium, and the summit of the intergluteal fold is one of almost perfect safety; I say almost, because here occasionally one of the tributaries of the gluteal vein may be encountered. To guard against introducing the injection directly into the arterial or venous circulation, it may be performed in two stages. In the first the needle is thrust into the buttock, and if no blood escapes the syringe is attached to the needle and the injection introduced; should there be any flow of blood through the needle, it should be removed and inserted into some spot adjacent until a point free from any blood vessels is met with. Having determined the locality, the next important step is the surgical cleansing of the skin; this can best be effected by ether soap, followed by the application of a solution of mercury biniodide in rectified spirit, 1 to 500. The syringe made use of should be one capable of being easily sterilized, the best form being known as Luer's, made entirely of glass. The needle should be made of platino-iridium, as this will withstand the chemical action of the mercurial salts and also sterilization by heat; it should be about 2 in. in length, and for the insoluble injections of somewhat larger calibre than the ordinary hypodermic needles. Both needle and syringe should be sterilized by immersion in boiling water. The patient should be placed in the prone position, and the needle, directed perpendicularly, should be sharply plunged into the buttock in the spot already indicated to its full extent; the contents of the syringe should then be introduced slowly, as thereby less pain ensues than if the injection is made rapidly; gentle massage of the buttock should then be employed, as thereby the pain is to some extent lessened and the material injected is more widely diffused; over the seat of the puncture a small piece of antiseptic gauze should be affixed by means of collodion.

The soluble salts have the advantage over the insoluble in that they are more rapidly absorbed, and consequently their effect on the syphilitic manifestation is more quickly observed; they are in addition comparatively painless. On the other hand, the necessity for their daily introduction is an almost insuperable objection, at any rate in private practice, since very few patients are able or willing to visit their attendant so frequently; further, each visit is followed by a certain amount of discomfort, and several courses of injections have to be given annually. With the insoluble salts, the absorption is hardly so rapid, but the therapeutic action of the drug is most energetic, and is usually successful in cutting short any urgent symptoms. The object of this method of treatment is to introduce a larger quantity of mercury into the system at a time; here it remains as a reservoir from which absorption may subsequently take place. The insoluble have

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the advantage over the soluble salts in that they are given at longer intervals, and a much smaller number of injections is required to constitute an efficient course; their principal disadvantage is the pain by which they are almost always attended, which is occasionally so intense as to necessitate the abandonment of the treatment. It is also impossible to regulate or to foresee how much of the drug will be absorbed after each injection, and certainly in some cases the injection becomes encysted in the gluteal muscles, so that the material employed does not enter at once into the circulation, but possibly at the time when the effect of the drug is no longer required. Occasionally the absorption of the drug is so rapid that the injection is shortly followed by signs of mercurial poisoning, such as severe stomatitis or enteritis. The disadvantages have, I think, been somewhat exaggerated, and are quite outweighed by the beneficial effects which, as a rule, accrue from the treatment.

With a view of making myself thoroughly cognizant with this treatment, I have carried it out as a routine amongst my patients at the Female Lock Hospital for the past three years, and I must say that I consider the results in every respect satisfactory, and sufficient to justify me in continuing with this practice, at any rate when the patients are under constant supervision. The number of hospital cases treated in this manner was 375, and the number of injections given was 4,516. At the commencement I employed the soluble preparations, and was quite satisfied with them as a rule, though I found that in some of the graver lesions their action left something to be desired; later, however, I utilized the insoluble preparations almost entirely, and relied mainly upon the most powerful vehicle for the introduction of mercury into the system—namely, calomel.

The salt I first utilized was mercury socalodolate combined with sodium iodide, in the proportion of $\frac{1}{2}$ grain of the former to 1 grain of the latter; 46 patients were treated in this manner, the number of injections being 759. I then gave a prolonged trial to mercury succinimide in doses of $\frac{1}{2}$ grain, utilizing it on 91 patients, and introducing 1,940 injections. After a trial of the soluble salts extending over fifteen months I abandoned them for the insoluble preparations, using almost exclusively calomel, and continued that treatment until the end of last year, at which time I was transferred to the male department of the Lock Hospital, where I am employing similar treatment. The dosage of calomel is $\frac{3}{8}$ grain of the sublimed powder suspended in 17 minims of sterilized olive oil; for hospital patients this preparation is kept in a glass bottle, from which the required quantity is taken, but probably a safer method, and the one always employed by me in private practice, is to have each injection prepared separately and introduced into minute flasks hermetically sealed. The deposit of calomel seen in the small flasks at once disappears on heating them over a spirit lamp, when the contents assume a milky appearance, and the powder is in a state of perfect suspension. The number of patients injected with calomel was 166 and the number of injections 1,241.

Another variety of the insoluble preparations I also employed, though not nearly to the same extent, was grey oil. Grey oil is a term applied to a large number of preparations of different strengths and compositions, but consisting essentially of metallic mercury suspended in some fatty vehicle. The formula of one variety of grey oil, which is much employed by our Army Medical Staff, is:

R Hydrargyri $\frac{3}{4}$
 Adipis lanae $\frac{3}{4}$ iv
 Paraffini liquid (carbolic acid 2 per cent.), ad $\frac{3}{4}$ x.

One grain of metallic mercury is contained in 10 minims, and a suitable weekly dose for an adult male is from 10 to 15 minims. I employed this in 15 patients, the number of injections being 125.

Another insoluble preparation made use of was the basic salicylate of mercury suspended in vaseline, of which 1 grain was injected weekly. The number of patients treated by this salt was 14, and the number of injections 157.

Of the 375 patients alluded to, 311 were discharged relieved, that is to say, they were free from all active signs of disease; 64 patients were discharged at their own request, for the most part greatly improved in health, but still showing some syphilitic manifestations. As regards

the pain resulting from this treatment, 8 of the patients on soluble injections complained, and 15 of those on insoluble, and 10 of the latter declined to continue the injections, and were consequently treated by the simpler methods. In 2 cases of soluble injections there is a note of enteritis and melaena, necessitating a modification in the treatment. In 2 cases of soluble injections and in 5 of the insoluble, there occurred an abscess in the buttock, or what was described as such; but in only 1 case was there any collection of pus that required evacuation, and that was quite subcutaneous, and due to some infection from the skin. In the other 6 cases the patients complained of deep-seated pain and swelling in the buttock; on aspiration of the swelling in each of these cases a chocolate-coloured fluid of thick consistence was drawn off, and on injecting the swellings with some boric acid lotion they subsided without any further treatment. In a considerable number of cases, especially those treated with insoluble injections, some nodosities in the buttock were to be felt, but I have no accurate record of the exact number of patients so affected, since the pain resulting therefrom was not sufficient to induce any comment. The majority of the patients were affected with gingivitis to a greater or lesser extent, but in any vigorous form of antisyphilitic treatment this is to be expected, and almost welcomed, since it indicates that the drug is having the desired effect. The hygiene of the mouth requires the same, if not more, careful supervision during the treatment by injections, as in other methods, and one of the essential concomitants is the frequent use of an astringent mouth wash and tooth powder.

I do not advocate intramuscular injections as a routine treatment, though I do strongly recommend them in the exceptional circumstances and conditions previously mentioned, and also in the case of patients detained in hospital and under constant observation. The shorter the stay of a patient in hospital, especially in a Lock Hospital, the better it is for the patient, so any treatment that will lessen the duration of the symptoms of the disease is to be commended. The disasters which have been reported with the view of discouraging and discountenancing this treatment have been somewhat magnified, and are rather a memory of the past, and under the present more careful supervision and improved technique they do not occur. For instance, in the 4,500 injections I have alluded to, neither I nor the house-surgeon working under my directions have ever seen any of the alarming symptoms to which I have drawn attention; the worst that has occurred has been severe diarrhoea, in two cases complicated by melaena, symptoms which immediately disappeared on the cessation of the treatment.

So far, I have only alluded to my hospital practice, from which the statistics I have given have been drawn, but my experience in hospital patients led me to introduce it into private practice in appropriate cases, and with the most gratifying results. I have here only utilized it in very severe cases, or in those which had resisted the more ordinary measures, but my results have been most satisfactory and encouraging. In the latest work on the treatment of syphilis by the great French authority, Fournier, he states, apropos of intramuscular injections and alluding to calomel injections in particular, that it constitutes the best method for preventing patients continuing treatment, but neither in hospital or in private work have I found this the case. Furthermore, the pain gradually diminishes from the first injection, so that one is in a position to assure one's patients that they will ultimately suffer very little, if any, inconvenience therefrom.

As regards the particular indications for the different forms of injection, the energy of the treatment should be in proportion to the severity of the disease, and since the insoluble preparations are far more powerful than the others, they are specially called for in the severe and malignant cases where it is desirable to get the patient under the influence of mercury in the shortest possible time. Of the insoluble preparations calomel is by far the most powerful, and should in these cases be utilized in preference to any of the other insoluble salts. It is especially indicated in destructive and progressive ulcerative lesions, in syphilitic iritis, and in syphilis attacking the brain or spinal cord.

The soluble salts, though decidedly inferior to the others, are in some cases of the greatest service, and are

specially indicated in cases requiring the exhibition of small doses of mercury frequently repeated, in cases in which the patient is also tuberculous, in which the functions of the liver and kidneys are not being carried out satisfactorily, in nervous women, in the milder forms of ocular lesions, and in those whose digestion is impaired, and who are consequently intolerant of the drug when administered by the mouth.

There are certain subjects who are not amenable to injections in any form; those suffering from Bright's disease particularly, and in a lesser degree patients with any hepatic disease; the alcoholic subject is rebellious to this, as he probably is to any other form of treatment, and in those whose mouths are in a septic condition and who are suffering from carious teeth, it should not be attempted until the mouth has been restored to a state of comparative asepsis.

It must be confessed that recurrences are just as frequent after this as after any other form of treatment, and here as in the other methods the chronic intermittent form of treatment has to be pursued over a period of at least five years. But there are few patients who would be able or willing to submit to two or possibly three courses of injections annually, and consequently it is not a treatment to be pursued throughout the course of the disease unless possibly in a few quite exceptional cases. It is of the greatest use in suppressing the disease in its most active stage, and in eliminating the syphilis toxin at the period of its greatest virulence. If resorted to at the commencement of the disease, and carried on until symptoms of mild mercurialism are present, its place may be taken later by one of the milder and simpler measures, such as ingestion by the mouth. In cases which have been inadequately treated at the outset, and in which constant recurrences of the symptoms occur, it will usually so attenuate the disease as to render it subsequently more amenable to ordinary remedies. Finally, in cases of destructive tertiary lesions, it is one of the principal mainstays of treatment, for not only does it succeed here when other remedies have failed, but it tends to alter the character of any lesions which may crop up later, and causes them to assume a more benign character.

A CASE OF SYPHILIS, PHTHISIS, AND LOCOMOTOR ATAXIA.

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THE following case is of interest, not only as a clinical history of the sequence of three diseases, but also for its bearing on the much disputed clinical problem of the influence of syphilis on phthisis, and on the relation of locomotor ataxia to syphilis.

A. H., aged 46, a native of Finland, and an officer in the mercantile marine, was seen by me on January 1st, 1908, complaining of cough, headache, loss of appetite, and pains in the legs.

Family History.

His mother died of phthisis, aged 47, when he was 11 years old, and some years later his father died of heart failure. He has one younger brother, who has always enjoyed good health.

Patient's History.

When 16 years of age A. H. went to sea, and has followed this profession ever since, having risen to hold a master's certificate. At the age of 22 he contracted syphilis, and was treated by inunction, being given fifteen frictions with mercuric ointment, under which the primary lesion disappeared, and the patient believed himself to be cured. Five years later, however, at the age of 27, his skin became covered with blotches and papules, about which he consulted an English doctor in the United States, who put him on mercury pills for three months. The skin lesions disappeared, and he has not seen any manifestations of syphilis since.

At the age of 42, twenty years after contracting syphilis, he began to feel generally weak, was easily tired, and the appetite was diminishing. He continued in this state off and on for some time, and two years later, when 44 years of age, he further noticed a difficulty of walking in the dark, which he describes "as if I was putting my foot on a step which wasn't there"; and at this time he also commenced to suffer from pains in the legs, and from slight cough in the morning. Being in Finland at this time, he consulted a physician in Helsingfors, who told him that he was suffering from a nervous disease, and advised a course of mercury. Two days later, with regard to

the loss of appetite, which had now increased to nausea and vomiting after breakfast, he saw another physician, who found tubercle bacilli in the sputum, and prescribed residence in a sanatorium. He was extremely surprised to find himself phthisical, and the same day consulted a professor of the University of Helsingfors, who confirmed both diagnoses. At this time the patient felt very weak, and entered Nummela Sanatorium, where he received ten injections of mercury, on the instructions of his physicians. He resided at Nummela for four months; on leaving, his weight had increased from 59 kilos to 75 kilos, the nausea, sickness, and cough having entirely disappeared. Five months later his weight rose to 84 kilos.

Six months ago the patient noticed that the cough, which at the commencement of his illness had attracted little attention, was now returning with increased frequency, and for this he saw a doctor in Germany, who prescribed the iodides of sodium and calcium, from which, however, no benefit was derived.

Present Condition.

The patient is a well-developed man of 48, weighing 76 kilos. He complains of cough, headache, loss of appetite, and pains in the legs. Temperature is normal.

The cough is most frequent in the morning, and his sleep is undisturbed by this. During the whole course of his illness he has never suffered from night sweats nor from fever. The chest is well developed, and there is no diminution of "tidal breathing" on either side. Percussion and vocal fremitus were normal throughout. On auscultation wheezing rhonchi were heard during expiration over both lungs, but in only one spot could any alteration in the breath sounds be detected, and this in the upper lobe of the left lung over an area corresponding to a dollar, situated in the middle of the anterior maxillary fold. Over this very limited area the breathing was bronchial, vocal resonance was increased, but no accompaniments could be heard. The sputum has been white and frothy for the past week, but prior to this was greyish-white. A small piece of solid substance when examined contained large quantities of tubercle bacilli.

The appetite is poor, he has nausea after food, and is constipated. The liver is not enlarged.

The heart is normal in size and function. The radial arteries appear thickened and fibrous. The pulse is regular, frequency 70, the wave is full and well sustained, but the arterial tension is high. The urine contains no abnormal constituents. The spleen is not enlarged, but the inguinal and posterior occipital glands show adenopathy.

The patient is an intelligent man, takes considerable interest in his case, and has the nervous temperament. He has now suffered from pains in the legs for two years intermittently, and describes the sensation as a dull pain, with now and then sharp twitches running from the hip to the knee, sometimes in the reverse direction. He has still the uncomfortable sensation when walking in the dark of being uncertain of feeling the ground, and his feet are often numb and cold. Both knee-jerks are absent, but neither paraesthesia, alchoelia, nor Romberg's sign is present. The gait is not ataxic, the legs are well developed, and hypotonia cannot be elicited. The left pupil is smaller than the right, and both eyes show the Argyll-Robertson pupil.

There is little doubt but that this patient has suffered from chronic phthisis for four years, and it appears that the pulmonary lesion, of which a small part is now apparent in the left upper lobe, has its centre at the root of the left lung, possibly in enlarged bronchial glands, which by irritation of the sympathetic chain have brought about the contraction of the left pupil. Recently the patient has had chronic bronchitis which, from the absence of fever, may have been a superadded non-tuberculous infection. In any case this cleared up in a few days. One may here touch for a moment on the purely theoretical possibility of the phthisis having supervened on a tertiary lesion in the lung. In a patient who has had syphilis, and who in after-years becomes phthisical, there is always the possibility of a dual infection, although diagnostic certitude is impossible. On this chance Sergeant¹ advises that such patients be put on mercury, and this practice seems worthy of trial. In this case, however, it is improbable that a tertiary lesion existed, as there were no pulmonary symptoms prior to the onset of phthisis, and as the presence of locomotor ataxia apparently precludes the formation of gummata. At the same time, if there still be syphilis in the system, such treatment would be beneficial.

The patient has all his life been a great milk drinker. He states that in no other country he has visited does milk enter so largely into the general diet as in Finland, which is chiefly a pastoral country and ships seven thousand casks of butter every week to Britain. He informs me that up to a few years ago tuberculosis was rife among the cattle, but that now there is an efficient inspection of milk and butter by Government chemists