THE TREATMENT OF GONORRHŒA WITH INTRAMUSCULAR INJECTIONS OF MERCURY SUCCINIMIDE AND WITH SOME OTHER MERCURIAL COMPOUNDS.

By Lieutenant-Colonel L. W. Harrison, D.S.O.

Royal Army Medical Corps.

Nobody with experience of it will deny that gonorrhœa is a tantalizing and unsatisfactory disease to treat. The remedies which have been suggested for it are innumerable. Many of these have been vaunted as certain cures in a minimum time, yet most of us find irrigation with potassium permanganate as good as anything and better than most for routine work, and this is our best commentary on them.

Looking at the question from another point of view, the injunction to the patient to go quietly for months, not to drink beer or similar beverages, nor to indulge in sexual intercourse, are tacit admissions that we do not believe we have defeated the gonococcus when the patient leaves our care. For if we had eradicated the causal micro-organism, what need would there be for these precautions? The urethra would recover quickly enough if it were sterilized. The fact is that in the few weeks during which we are allowed to treat the average case of gonorrhœa we succeed only in calming the urethra down to a toleration of the gonococcus.

The explanation of this unsatisfactory state of affairs is easy when we consider the pathology of gonorrhœa. It lies in two factors—the tendency of the gonococcus to penetrate deeply into the mucous membrane and bury itself in the innumerable gland follicles opening thereon, where it is safe from attack by injection and irrigation, and the fact that the urethral membrane is so sensitive that antiseptics of sufficient strength and penetrating power to reach and destroy the gonococcus cannot be used. The extraordinary persistence of gonococci in the secretions of the eye after an attack of gonorrheal ophthalmia, in spite of the fact that in this situation the mucous membrane is considerably less sensitive and local conditions infinitely more favourable to the success of local treatment, shows the difficulty in the case of the urethra.

To the writer it has been clear for a long time that we must seek for a remedy for gonorrhœa amongst compounds which will reach the gonococcus directly from the blood. One is the more certain of this from the conviction that gonorrhœa is far more often
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a septicæmia than is commonly supposed. The frequent instances which one meets of the gonococcus setting up trouble exclusively in a damaged part of the body—a sprained ankle, a damaged finger, or some other odd spot where there is a history of former injury or stress—where one is convinced that but for that local damage the gonorrhœal manifestations would have been confined to the urethra, compel the belief that the gonococcus circulates in the blood of most apparently uncomplicated cases.

Remedies such as sandal-wood oil, copaiba, and the like are probably only other means of applying local treatment. At any rate, without contesting their virtues as adjuncts to the treatment, it is safe to say that none of them is a specific for gonorrhœa.

Specific antibodies induced by the injection of vaccine, though helpful, are uncertain in their action. Possibly this is because the antibody production is inadequate; possibly, also, human beings, like animals, vary greatly in their response to some antigens.

Searching for a specific for gonorrhœa, my attention was recently attracted by the paper of B. L. Wright on "The Treatment of Vegetable Parasitic Origin by Deep Injections of Mercury" (New York Medical Record, February 22, 1913), in which excellent results were claimed from intramuscular injections of mercury succinimide.

I had frequently noticed in cases of combined gonorrhœa and syphilis that by the time the first course of mercury and salvarsan treatment had finished (at that time in about a month) the patient was apparently cured of his gonorrhœa. Thinking that salvarsan might possibly have been the determining factor in the cure of these cases, I had, in fact, treated a number of intractable cases of gonorrhœa with this remedy, but without success. The cases so treated were certainly very persistent ones, however, and of the type which subsequently proved resistant to mercury succinimide, so that it would not be fair to assume from this failure that salvarsan has no beneficial effect on gonorrhœa.

The observation referred to made one ripe for acceptance of the claims put forward by Wright for mercury succinimide, and after a preliminary trial which proved promising an extensive test of this remedy was instituted in a venereal hospital where I happened to supervise the treatment. For the results detailed below I am indebted to the medical officers under whose immediate care the patients were, and who administered the treatment. My own part in the investigation was simply that of instigator and adviser.

The mercury succinimide was administered in a five per cent solution either in three doses of fifty milligrammes or two of
seventy-five milligrammes at intervals of three days. In certain cases a second course of three injections was given after about ten days. Local treatment by irrigations or injections, and all other routine measures for the treatment of gonorrhoea, were continued as before.

In a substantial proportion of the cases the immediate effects were so striking as to produce a marked impression in favour of the remedy, which very quickly became popular with medical officers and patients alike. Since each medical officer was treating from 250 to 400 patients, it may be assumed that any impressions gathered from the effects of a change of treatment would be well founded. In the cases which responded well the change from acute and profuse purulent discharge to no discharge at all in considerably less time than the average was very marked. In other cases the discharge became quickly scanty and mucopurulent, but remained in this condition for a long time, while in a small minority the treatment appeared to have no effect whatever. In a certain number of these cases a second course of injections was given, but these did not prove a great success.

A sufficient number of bacteriological examinations of the urethral secretion had not been made up to the time of writing to justify any opinion as to the bactericidal properties of mercury succinimide when administered in this way. In a small series of examinations the gonococci seemed to disappear from microscopical view, apparently pari passu with the improvement clinically, but inability to find gonococci in a few series of urethral smears from the same cases by no means indicates their total disappearance from the urethras concerned, and further work on this point is necessary before any judgment can be given.

The urethral discharge (taken under precautions to exclude urine) was found to contain mercury by Pte. L. Hulls, to whom I am greatly indebted for valuable work in this and other chemical investigations.

The side-effects of mercury succinimide are, on the whole, mild. Most cases suffer no more inconvenience than a little temporary soreness at the site of the injection, which does not interfere with their getting about. In one of the 3,467 cases treated a small abscess developed at the site of injection, and in another a small superficial slough resulted. Both of these were probably due to a little of the solution having been injected into the skin or subcutaneous tissues, not intramuscularly. In a small proportion of cases the injections were followed by diarrhoea, and some of these
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suffered from mild colitis, with blood and mucus in the stools, but these symptoms yielded to treatment in a few days. Mild stomatitis occurred in a fairly substantial number of the cases treated, especially in those with carious teeth, which were very common amongst the patients treated. Haematuria and albuminuria occurred in six of the cases, but in a mild degree, and yielded quickly to treatment. Altogether, side-effects gave rise to no anxiety.

Before detailing the total results obtained so far, it is necessary to explain that the conditions were considerably more adverse to rapid cure and discharge from hospital than obtain in peace time. Practically all the cases came under treatment for the first time more than a week from the commencement of symptoms, and in the meantime had been exposed to active service conditions of fatigue and exposure, which assisted the disease to obtain a good foothold. Quite ten per cent of the cases were admitted with such complications as epididymitis, arthritis and prostatic abscess, all of them conditions which tend to raise the general average duration under treatment. Before discharge to duty the patients were left for some days without treatment. On discharge to convalescent camp they were examined by a senior officer other than their own, and this examination was repeated on final discharge to duty, while at their base depots they were again examined by a medical officer, who did not hesitate to return them on the least suspicion of a urethral discharge being apparent.

On return to duty they were exposed to conditions favourable to a return of their disease unless this had been thoroughly quieted down—cold, exposure and fatigue (with the help, perhaps, of such distractions as beer and sexual intercourse), and it was necessary to be reasonably sure of the cases not relapsing quickly before returning them to duty. For these reasons patients had to be kept under treatment and observation much longer than is considered necessary in peace time, when patients report much earlier, subsequent conditions are not so adverse, and a relapse means simply a return from barracks to hospital in the same station. It is necessary to explain these details as otherwise an unjust impression of the results detailed below would be derived from the fact that the duration of treatment and observation has all round been longer than in peace time.

The results were as follows: Out of 3,467 cases of gonorrhoea treated with succinimide of mercury, 2,026 were returned to duty in an average of 30.38 days from the date of the first injection; of those returned to duty 829 went in less than 25 days and 1,197 in more than this time.
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Of the cases returned to duty 138, or 6.8 per cent, were re-admitted for relapse. This compares with 10.08 per cent of relapses in 9,762 cases treated under practically identical conditions, but without succinimide. It is not sufficiently below it (considering that it relates to only a quarter of the time) to warrant a claim to any advantage on this score.

Out of the balance of 1,441 still under treatment at the time of writing, 633 had been less than twenty days, 251 from twenty to thirty days, and 557 more than thirty days under treatment.

The average time spent under treatment and observation from date of admission to that of discharge to full duty by the 2,026 cases was 41.15 days, which compares with an average of 49.88 days for the non-succinimide cases referred to above.

The gain from the use of mercury succinimide (8.73 days) does not appear very striking, and it is necessary to explain that included in the succinimide results are practically all the chronic old complicated cases which had been in hospital a considerable time before being treated with the succinimide. This is shown by the fact that although it quickly became routine to commence injections on the day after admission, yet the average time spent in hospital by all the above-mentioned cases from admission to date of first injection was 10.77 days. In an earlier series, included in the above, which contained a rather larger proportion of fresh cases (the average from day of admission to first injection being 9.45 days), out of 2,366 cases which had received the treatment, 869 were returned to duty in an average of 25.26 days from the first injection, or 34.71 days from first admission, 249 of the balance still under treatment at the time of collecting the results having by then been more than twenty-eight days under treatment since the date of the first injection.

On the whole, the results indicate that intramuscular injections of mercury succinimide are a useful means of shortening the duration of gonorrhoea cases under treatment and have effected a fairly substantial reduction of total wastage from this disease. As stated, the best results appear to follow injection in early acute cases, and for the reasons already given an improvement may be anticipated when a larger proportion of cases is treated immediately after admission to hospital.

At the same time it must be said that mercury succinimide does not fulfil one's ideal of a specific for gonorrhoea, and my object in writing this paper has been simply to suggest that this compound may be one end of a thread leading to the discovery of such a specific.
Other mercurial compounds have been tried in the hope of finding one which is better than succinimide, but so far without success. The preparations tried were mercury perchloride, calomel, mercury salicylate, "énésol," "anogon," "argulan," and colloid mercury (Dausse). Those at present under trial are, bibromide and benzoate, both of which are promising better than the ones just mentioned.

I am greatly indebted to the Medical Research Committee, who very kindly supplied me with a substantial amount of mercury succinimide when it seemed impossible to obtain any; to the medical officers of the hospital where this work was carried out for their very valuable co-operation; and to Serjt. Andre, R.A.M.C., who spent many hours' overtime in collecting and compiling the results.