REINFECTION IN SYPHILIS.
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INTRODUCTION.
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For 2 years, while on active service in France, it was my duty to inspect and clinically diagnose cases admitted to the syphilis divisions of certain Military Hospitals established for the treatment of venereal diseases. Men with genital sores, of recent origin and little else to aid in the diagnosis, formed a large percentage of the cases. The important question was, in the first instance, "Are these men suffering from syphilis?" To answer this definitely was in many cases very difficult.

Free use was made of the Dark Ground substage condenser to search for the Treponema Pallidum, and the Wassermann reaction was done in nearly all cases.

Whenever the Dark Ground examination was positive, treatment with one of the salvarsan preparations was at once commenced.

Cases with negative Dark Ground findings and Wassermann reactions were reconsidered.
Some were clinically certain syphilis. In these the negative findings were neglected and treatment commenced, without further waste of time, so that these men should not pass that early stage of syphilis when our therapeutic remedies attain their maximum value. In these the clinical signs easily discounted the negative pathological findings, which were no doubt fully accounted for by some small technical error in film preparation or search, or by the use of antiseptics in the early treatment adopted by the soldier before his admission to hospital. There were still many cases remaining. These I kept under constant observation, and it was from this number that I collected the material for this paper.

I believe that a reconsideration of prevailing opinions regarding reinfection in syphilis and the value of the Wassermann reaction helped to throw light on many difficult cases.

It certainly persuaded me to give some of them a trial of Salvarsan treatment, which would otherwise have been withheld. The almost uniformly good therapeutic results obtained in the selected cases fully justified this proceeding. I will endeavour to set forth and support some of the theories upon
which this selection was founded.

The classical appearance of a Primary Syphilitic Chancre on the male genitals is comparatively well known, and a typical one is easily diagnosed.

In dealing with many thousands of cases of "sores on the penis," I have been much impressed by the fact that only a comparatively small proportion of them presented characters which were strictly those of the classical primary syphilitic lesion. Of the remainder some were primary chancrecs only slightly atypical, and the Dark Ground examination or the characteristic enlargement of the neighbouring glands in the groins soon cleared up any doubts regarding them. The occurrence of secondary lesions on the penis, especially if unaccompanied by other signs of generalised syphilis, was a slightly more difficult problem. Here the diagnosis was usually soon made certain by a combined Dark Ground examination and Wassermann test. Both were usually strongly positive. The gumma, single or multiple, was much commoner on the penis than text books had led me to expect. It was unaccompanied by marked glandular en-
largement in the groins. A positive Wassermann reaction was usually to be obtained, but was not invariable. Other signs of "syphilis in the past" were often so indefinite as to afford little help. Lesions due to trauma, scabies, herpes genitalia, so-called venereal warts, epithelioma, and some other non-venereal skin conditions such as psoriasis, lichen planus and pemphigus vegetans, I will merely mention as possibilities which had to be considered in the diagnosis, as they often assume an ulcerative condition on the penis.

Lesions, due to the many organisms capable of setting up a simple balanitis under a phimosed prepuce, disappear rapidly when freely exposed and subjected to simple cleanliness.

The soft chancre or uncus molle was not so easily differentiated, and, as I will attempt to show, syphilitic lesions, modified by influences that I will indicate, can so closely resemble the uncus molle as to be clinically almost indistinguishable. I am convinced that any chronic lesion on the penis may secondarily assume the characters of a gumma in a patient the subject of active tertiary syphilis.
hilis. I have seen this change particularly in chronic soft sores and in neglected ulcerating scabetic impetigo.

Since the introduction of Salvarsan treatment another ulcer has been added to increase our difficulties. Thibierge (1) has called this the "salvarsan sore." With Thibierge I agree that it is a definite new clinical entity. It may be of the nature of confluent and ulcerating herpes, which is very common on the penis during or immediately after the completion of a course of Salvarsan. I must own that I have never seen any characteristic lesions of herpes in its neighbourhood, and therefore this explanation of the condition has little to support it.

What have been variously described as Redux and Recurrent Chancre are, I believe, gummatous in nature, and I will attempt to explain why these conditions have become much commoner since salvarsan has been extensively used in the treatment of syphilis.

A tough, non-pitting oedema of the skin of the penis, like that seen in elephantiasis of the limbs, was occasionally seen as a tertiary syphilitic condition, and no solution of skin could usually be found in these cases.
A similar but less tough oedema often accompanied a hidden primary chancre. It is said that here the oedema may in itself be the primary lesion and no ulcer need exist. I believe a chancre of some sort always existed, though it may have healed by the time its site could be exposed.

Lastly, mixed Ducrey and Syphilitic infections were fairly common, and if the soft sore remained unhealed throughout the syphilis incubation period, it then assumed some of the characters of a primary syphilitic sore, but was never quite typical of the latter. In these cases a correct diagnosis could sometimes be made if the patient had been under constant observation during the transition period.

The Treponema Pallidum was always extremely difficult to find in these cases, and usually repeated searches were unsuccessful, though the patient subsequently developed a positive Wassermann reaction and signs of secondary syphilis.

Grouped under the above headings, I considered the percentage of soft sores abnormally high. This number really included all cases which clinically did not fall under any other heading, and repeated searches for the Treponema Pallidum had produced negative results. Ducrey's bacillus was re-
gularly searched for, but was rarely found. In spite of this the cases were still treated as soft sores being merely not typical of anything else.

I carefully reviewed my clinical records of these cases, and as a result one point particularly impressed me. The incubation periods in these cases varied from 3 to 15 days.

At first I thought that the supposed existence of several varieties of soft chancre was a sufficient explanation for this. I further analysed those cases in which the incubation period had been longest. Here I found mention of previous venereal disease extremely frequent either in the history or in the clinical signs. Previous syphilis was clearly indicated in some cases, while in others there were doubtful signs recorded.

On account of these a Wassermann reaction had almost always been done, and this was invariably negative. It occurred to me that many of these might be cases of infection with the Treponema Pallidum, and the resulting lesion so modified under the influence of a previous syphilitic infection as to be clinically unrecognisable. In other words, the question amounted to this: If a man has once had syp-
hilis, congenital or acquired, and he exposes himself to infection again, may he not get a second inoculation as the result?

In reviewing the literature of reinfections I found that, in the past, cases have been recorded by clinicians of such high standing that their observations must be accepted. (2). Since the introduction of salvarsan treatment many more cases have been classified as reinfections.

A series of cases was published by Major C. F. White, R.A.M.C., in the British Medical Journal of October 20th, 1917 (3). He considered that the following conditions must be fulfilled before a claim to reinfection is established:

1. There must be definite pathological proof that the first infection was syphilis. If the case was seen in the primary stage, there must be a record that Treponema Pallidum had been found. If seen in the secondary stage, either the Treponema Pallidum must have been found, or the serum tested and a positive Wassermann reaction recorded.

2. The second primary sore must occupy a site sufficiently removed from the original scar to eliminate redux and recurrent chancres.
3. The Treponema Pallidum must be found in the lesion of the second infection, and

4. The Wassermann reaction must, on this occasion, be negative.

This series of cases had their value further enhanced by the fact that they were, on both occasions, treated by the same observer.

The above conditions would seem to have been sufficiently rigid, but some workers in this subject still doubted and in their criticism suggested that they were all cases of recurrent chancre. In this latter condition they contended the Treponema Pallidum may or may not be found, and the Wassermann reaction is often negative.

The chief point of interest in Major White's cases was the short time that elapsed between the 2 infections. In the earlier cases recorded by Sir Jonathan Hutchinson the intervening period was in most cases several years. In this series the time was measured in months.

This, I think, more than any other feature, gave weight to the contention that the lesions signified a relapsing condition rather than a fresh infection. Many of the most en-
thusiastic supporters of Salvarsan treatment hold that one of the most promising features seen, when this remedy is used, is that cases relapsing show lesions corresponding to the stage when treatment was discontinued, and irrespective of the time elapsing since the original infection.

Harrison in his teaching uses the picturesque expression, "606 stops the clock." Infrequent as relapses are, with the large amount of clinical material that I have been privileged to handle, I have seen a considerable number following salvarsan treatment. Amongst these I have seen patients exhibiting well-marked secondary signs 2 years after infection, but the proportion constituted by these is quite insufficient to prove that "606 stops the clock." These cases are the few in which 606 has failed most lamentably. Its only effect has been to delay the onset of generalised signs. That the fault rests with the patient or his particularly virulent disease, and not with the drug, is the most likely explanation. Several relapses are the rule rather than the exception in these cases.

Clinically it is impossible to divide syphilis into the
3 classical stages. Many cases show lesions with characters belonging to more than one stage. Hence such expressions as "late secondary" and "early tertiary" have arisen to aid us in classification, but the division is nevertheless sufficiently accurate to be of use and its convenience justifies its retention. The fact remains that Syphilis as a disease exhibits a constant variation in the characters of the lesions it produces. The acute condyloma as seen in the anal fold, say 6 months after infection, disappears, and a year later appears again, this time much more "warty" in appearance, and the Treponema Pallidum, easily found a year ago, is now difficult, if not impossible, to demonstrate. The "warty" lesion disappears, and in a year, or may be 2 or 3 years, appears again. This time much more chronic in progress, not so warty, showing more tendency to ulcerate in the middle and spread in a nodular fashion at the margins. We now call it a subcutaneous gumma.

Again, 3 months after infection maculo-squamous spots appear on a scrotum usually as part of a generalised rash. These disappear, and 6 months or 9 months later on the same site some more scaly lesions occur. Now these have taken on
a circular outline and are said to be circinate and indicative of "late secondary" syphilis. Four years later another type of scaly lesion occurs. It is now serpigenous, and as was the case with the gumma in the anal fold, there may be a tendency to ulceration and nodular spread.

Examples could be multiplied indefinitely. Does the variation seen in the lesion depend on a cycle through which the Treponema Pallidum passes. It doesn't change its form, or at least not sufficiently for us to be able to see the change under the microscope, but that is not necessary. McDonagh (4) describes a cycle in which there is a very obvious change in form, but the Treponema found in sections of gummata, and those found between the fibres of myocardium in old-standing syphilis, are indistinguishable from those found in a primary Hunterian chancre. Does the host or his means of resistance undergo a change and the Treponema remain constant.

The fact remains that there is a "cycle." We are in the habit of talking about stages in the progress of the disease. Why not stages representing nature's progress in the cure of the disease. Nature alone does in many cases
cure syphilis after passing through these apparent stages.

It appears to me that, amongst diseases, we have, in the past, placed syphilis in a class by itself; a disease curable if the patient will submit to a prolonged mercury treatment or shorter but more drastic salvarsan treatment, but incurable by Nature unaided. It is a chronic disease, but the patient's resistance unaided by drugs may in a longer or shorter time completely eradicate it. In the majority of cases treated with salvarsan, the cure is comparatively rapid. In untreated cases a cure is eventually established in many. The remainder are the unfortunate minority in whom the disease attacks directly or indirectly some vital part, thereby causing the patient's death.

The death-roll from syphilis is deplorably high, but if a large proportion of syphilitics were not eventually cured of their diseases, it would be higher still.

Now it is probable that in the cure of syphilis quickly by salvarsan, slower by mercury, or slower still by Nature unaided, all these stages are gone through. It is not necessary that the patient should exhibit lesions corresponding to each stage, and if under active treatment it is unlikely that he will.
Far from always "stopping the clock," salvarsan in most cases "hastens the clock" in a most remarkable way. This accounts for the previously rare conditions one hears so frequently discussed nowadays. "Early nervous relapses," lesions clinically resembling gummata within a year of infection, etc., etc. It likewise accounts for some of the clinical phenomena I am to describe later in this paper.

I think it also explains the short time that elapsed between the 2 syphilitic infections in Major White's series of cases to which I have already referred. All these cases were treated with salvarsan remedies, and they were thereby rendered capable of being infected a second time within a much shorter interval than would have been the case had mercury been used. Now these cases of reinfection, either in the few following mercury treatment, or in the many following salvarsan, all showed typical primary lesions and accompanying glandular enlargement when they appeared with the second infection.

The class of case to which I wish specially to refer is one that does not show a typical primary lesion and accompanying adenitis. They are almost always, therefore, diag-
nosed as soft sores. I did this myself until I formed the opinion that the varying incubation period, to which I have already referred, was worthy of further consideration. As I have said, their incubation periods varied from 3 to 15 days. I am by no means unaware of the lying propensities of the venereal patient, and I am prepared to make liberal allowance for it. I went to considerable trouble to, as far as was possible, verify patients' statements regarding this point in their histories. I still remained convinced that incubation periods did vary within the limits I have stated.

My practice was to have these lesions examined for both the Treponema Pallidum and Ducrey's bacillus. Both examinations invariably proved negative. Neither syphilis nor soft sore was thereby definitely excluded, but the lesions failed to respond to all forms of local antiseptic treatment. Were these all cases of resistant Soft Chancre? If so, this condition is not nearly so amendable to treatment as we have believed.

In many of these a Wassermann reaction had been done and found to be negative, and the subject of past syphilis dis-
I suggested the following theory. A man who has once had syphilis, congenital or acquired, is capable of being, and often is, infected a second time by sexual contact with a woman who has active and infective syphilitic lesions. The character of the lesion varies within fairly wide limits.

Occasionally a second typical primary lesion presents itself and is accompanied by characteristic enlargement of the glands in the groins. These are the cases recorded as second infections, and only these. The atypical sores, in which the Treponema Pallidum is not found and the glands do not become classically enlarged, are not. They are not suspected as being syphilitic at all. Exclusion of syphilis seems to be supported by the subsequent observation; Treponema Pallidum are constantly absent; the Wassermann reaction does not become positive, and no secondary signs appear when they might be expected. Now is this sufficient evidence on which to claim that the causative virus is not the Treponema of syphilis? I do not think it is. As to the lesions themselves, they certainly do not conform to the classical description of a primary sore. Some resemble gummata, and others very closely simulate the soft or follicular sore. Many
transitional forms between these two end types are also seen.

Even with much clinical experience it would be very difficult to indicate the type of lesion that one would expect to find in any particular case as the result of a second successful inoculation. It would be necessary to take into consideration the age of the first infection and the treatment received, and to make allowances for the varying resistance of different individuals against the virus, the varying virulence of the virus itself and the individual variation in response to the particular form of treatment that had been employed. There is not, however, an entire lack of uniformity, and the following are average examples:

1. If a patient recently treated for primary syphilis with salvarsan remedies again exposes himself to infection with a contagious woman, and is successfully inoculated, he may exhibit

(a) A typical primary syphilic sore with spirochaetes demonstrable by the usual methods employed in Dark Ground examinations and typical enlargement of the corresponding glands in the groins, incubation period about 25 days, Wassermann reaction at first negative and later becoming positive. Second-
ary and tertiary signs may develop in due course.

If the above conditions are fulfilled, then this patient was cured of his first infection by the treatment employed, and his case would form an addition to the records of reinfection already recognised as such.

But he may present a sore resembling an Uncus Molle acute and apparently inflamed. Here no spirochaetes can be demonstrated by the usual Dark Ground methods employed, and the corresponding glands in the groins are only slightly enlarged, if at all. The incubation period is 9 to 12 days, or may even be as short as 6 days. The shorter the incubation period the more active the sore appears to be. The Wassermann reaction is negative and remains negative. No secondary signs will follow as the result of this infection. The lesion is particularly resistant to all ordinary local antiseptic treatment. In spite of its clinical appearance it responds readily to Salvarsan and can usually be healed with one injection. This man was not cured by his previous treatment.

I have taken the 2 extremes. First the case in which the patient was definitely cured, and secondly the case in which he was just sufficiently sterilised to be rendered capa-
ble of reinfection. Between these two would come many other variations in the type of chancre produced. Depending on the factors I have already indicated, we may find any gradation from the acute lesion resembling the soft sore to a chronic ulcer, an almost typical gumma. Although, clinically, I have never seen such a case, there seems to me to be no reason why the patient described as "not cured" may not later develop signs indicative of some tertiary syphilitic condition and then show a positive Wassermann reaction. I would conclude this to be the result of his first infection, though admitted ly it would be difficult to prove that it was unconnected with the second.

If now we take the case of a patient who remains uncured after a lapse of, say, 2 years following his original infection, and is then successfully reinfected, the incubation period tends to be longer, about 10-15 days. The lesion resembles a gummatous ulcer and appears chronic and inactive. The glands in the groins are again not appreciably enlarged. The Wassermann and Dark Ground examinations are again negative. This lesion, too, is very resistant to all ordinary local antiseptic treatment. No secondary signs will follow, but as
before he may become the subject of tertiary syphilis due to his first infection. If we go on taking examples, allowing more and more time to elapse, we will find that the lesion approaches the gumma more and more closely, and resembles less and less the soft sore. As long as the patient remains syphilitic in virtue of his first infection, the glands in the groins fail to enlarge and no secondary signs follow. The incubation period gets longer and longer, but rarely exceeds 15 days. This goes on until nature and time have completed the cure of the first attack, and now the patient is again a candidate for a second typical primary sore with classical incubation period, characteristic enlargement of glands in groins, and to be followed in due course by secondary manifestations. Treponema Pallidum are now to be found, and the Wassermann reaction, at first negative, becomes positive, with the development of secondary signs.

The case of patients treated inefficiently with local treatment only, or with insufficient quantities of mercury, is only a little different. We find that a much longer period must elapse after the first injection before the patient is in a condition to be infected again. Allowing this, the condi-
tions noticed are similar. It is not an essential condition that the serum reaction should be negative in these atypical reinfections. I have found it positive, but it is usually negative, and it would therefore appear most likely to occur amongst that 60 per cent of latent cases whose sera are negative.

If, now, it is accepted that a man who has once suffered from syphilis may be, and often is, infected a second time, and that these atypical lesions are the result of such a second infection, then we must qualify the old axiom that the only proof of a perfect cure of syphilis is that the patient becomes infected again.

In these cases I have described the patient is not cured of his first infection. That factor, whatever it is, that determines the Wassermann reaction is sufficiently weak to render the test negative and to make the patient capable of being infected again, but is sufficiently strong to at least influence the type of lesion which results from the inoculation.

It is also sufficient to prevent the Treponema Pallidum thriving to such an extent that it is easily demonstrable in
the lesion, and to inhibit the onset of secondary signs. We might also suggest that the second infection, acting in a way analogous to a dose of vaccine, may even exert a beneficial influence and so sufficiently stimulate a further output of antibody to finish the cure of the original syphilis, which according to this theory is almost worn down.

The axiom must then be corrected to read: "The only sure proof of a certain cure of syphilis is that the patient becomes infected a second time and develops a typical primary sore with classical incubation period, corresponding enlargement of glands in groins, and followed by secondary signs and a positive Wassermann reaction."

Two points would appear to require immediate explanation. Firstly, the negative Dark Ground findings, and, secondly, the negative Wassermann reactions.

Regarding the Dark Ground examinations, I have purposely added "by the ordinary Dark Ground methods employed."

This consists in scraping the margins of the sore, removing some serum on a cover-slip, adding a drop of normal saline, mixing, pressing the cover-slip down on the slide and painting vaseline round the margin to prevent drying or escape of con-
tagious fluid. By this method it is practically never possible to demonstrate the presence of the Treponema Pallidum in a gumma, yet they are usually there, and if the lesion were excised and sectioned they would more often be found. A resistance to syphilis acquired by a previous infection is sufficient to reduce the number of organisms present in a lesion. Hence they are absent in a gumma and would be likely to be absent, also, in the lesions under discussion. Not only have these patients had syphilis — they are still syphilitic. In the acute sore described, too, we have the additional factor, namely, inflammation. This may have been due in some cases to superadded septic infection, but was in most cases, I believe, due to a marked reaction against the spirochaeté on the part of the tissues.

It is well known that positive Dark Ground findings are difficult to obtain from inflamed lesions, and even in dealing with typical primary sores it is often necessary to allow a superadded inflammatory condition to subside before the presence of the spirochaeté can be demonstrated.

Regarding the condition of the glands in the groins in these cases. As the living organisms are few, there is
little reaction called for on the part of the lymphatic glands. They are therefore only slightly enlarged. This, too, is seen where an undoubted gummatous ulcer is present on the penis.

The second point, the negative Wassermann reaction, again opens up the question about which so much has been written in recent medical literature. After a wide experience with this reaction I have come to the following conclusions, and I venture to suggest that they express the view of a large section of workers in this subject. If the few rare conditions such as Yaws and tuberous leprosy can be excluded, then a Positive Wassermann reaction means that the patient from whom the serum has been taken is syphilitic or has had syphilis. To be conclusive, the test should be done on more than one occasion, preferably by two different pathologists. Two separate specimens of serum should be taken at an interval of at least a week. They should be drawn off at times such that the relation to the taking of food would be different in the 2 cases. Two different guinea-pigs should be used to supply the complement for the two tests. Both results should be frankly
positive. Even this would not necessarily prove that the patient's syphilis was active. It would not even justify a certain prognosis that it ever would become active. It therefore does not follow that every patient whose blood gives a positive Wassermann reaction should at once be put on active anti-syphilitic treatment.

On the other hand, a negative Wassermann reaction does not prove that the patient from whom the serum was taken had never had syphilis. Boas (5) in an analysis of 6,043 sera, showed that in cases of latent syphilis of over 3 years' standing, about 47 per cent gave a positive Wassermann reaction, and where less than 3 years had elapsed, the percentage of positives was less than 40. We cannot prove that the prognosis, as regards further active syphilitic manifestations, is any worse in the positive than in the negative cases.

Most patients showing active lesions of syphilis give a positive Wassermann reaction, but this is by no means invariable. With few exceptions a positive result is obtained in active secondary cases. All cases of primary syphilis, if left untreated, will eventually show a pos-
itive serum reaction, but the period that must elapse after the appearance of the initial lesion varies widely. Taking the time from the first appearance of the primary lesion, a few cases become positive in 18 days. Thereafter the proportion increases until the 28th day, by which time most cases are returned positive. A few take much longer - 6 weeks is fairly common - and I have seen a few cases where 3 months was required.

Tertiary cases, when showing active signs, usually give a positive reaction, but the test is much less reliable here than in secondary cases. Notable, but by no means constant exceptions, are tertiary lesions of the tongue or oral cavity and syphilis of the central nervous system.

Modern treatment with Salvarsan greatly diminishes the value of the Wassermann test if it should be required later to confirm a supposed relapse, and this is especially the case if the patient was originally treated for primary syphilis while his blood was still negative.

Patients who have received large quantities of salvarsan not infrequently appear showing most marked active
signs of generalised syphilis constituting a severe relapse, and spirochaetes may be obtained from the lesions, yet the serum, while never giving a frank negative reaction, may only show a trace.

This is, I think, undoubtedly due either to the drug still stored in the tissues, or serum, or much more likely to some tissue or serum derivative of it. It certainly handicaps one considerably in the diagnosis of some of the clinically less severe relapses.

Immediately following a course of 606 treatment, a negative Wassermann reaction means very little. We know that cases finishing with this popularly desired result do frequently relapse with a positive reaction. We have no certain evidence that if a patient finishes a reasonable course of salvarsan (say 6, 7 or 8 injections amounting to about 3.5 gms), with his serum still positive, he is in immediate need of further treatment. Partial positives are never to be taken as, in themselves, conclusive, but as adding to the weight of clinical evidence they are a great help in diagnosis. I have already indicated the influence of previous salvarsan treatment in producing some of these
partially positive results.

It has never yet been shown upon what constituent in the serum the Wassermann reaction is dependent. It is customary to assume that it is dependent on the syphilitic antibody, whatever that may be. This is extremely unlikely, and if it were so, then our deductions from this test would need considerable revision.

It would certainly be necessary to conclude that a person with a positive Wassermann reaction and no clinical signs, is no worse off than a person who once had enteric and still has a positive Widal. It would likewise seem fair to suppose that a positive Wassermann was to some extent a desirable condition.

That the Salvarsan remedies do influence the Wassermann reaction, apart altogether from their influence on the disease, seems extremely likely. I have indicated certain points in this connection. Two more I should like to mention. The first is what is known as the "Prevocative dose of 606." An intravenous injection of 606 given 4 to 7 days before a serum is drawn will often render a partially positive blood strongly positive. This is probably due to the
direct action of the drug. Later, when more injections have been administered, the body gradually acquires the habit of manufacturing an antibody to this foreign substance, and the reaction now, in virtue of this chemical antibody, becomes more and more negative, until finally no haemolysis takes place, and the result is declared negative.

One would at least think that if a syphilitic had received so much salvarsan, that he exhibits clinical signs of poisoning, e.g., "606 jaundice" or dermatitis, he would be cured of his syphilis. Yet I have seen relapses in cases where treatment with 606 had caused these undesirable complications. I have now seen quite a few cases of both these complications. I have always taken the opportunity to have the serum tested while the patient is actually suffering from the jaundice or dermatitis, and without exception the Wassermann reaction has been negative irrespective of the number of injections and actual amount of 606 administered.

Now this would appear to disprove the theory that the negative reaction in the Wassermann test depended
on the chemical antibody to salvarsan. If the patient had sufficient antibody to salvarsan to produce a negative Wassermann reaction, why should he show signs of being poisoned by the drug? My answer to this is that both the dermatitis and the jaundice are just as likely due to the chemical antibody as to the salvarsan.

I am not condemning the use of 606 in the treatment of syphilis. On the contrary, after a wide experience in the use of this drug, I am convinced that it clears up active lesions quicker than any drug previously used, that in many cases it actually cures syphilis. It renders infective lesions non-contagious in a very short time, and so prevents much spread of the disease. When compared with its therapeutic value, the dangers resulting from its administration, if due care be taken, are negligible.

All I wish to emphasise is this:— After a course of salvarsan remedies we have at present no certain indication as to whether the patient is cured or not. The Wassermann reaction is of no value whatever, and after a course of 6 or 7 injections, amounting say to 3.9 grms. of 914 or 2.7 grms. of 606, I should certainly discontinue
treatment for 3 months, provided there are no clinically active signs, whether the blood reaction was positive or negative. Any further administration I consider is submitting the patient to some risk of jaundice or dermatitis, and in the light of the above argument is in my opinion unjustifiable.

I think this view of the Wassermann reaction, if accepted, explains some of the apparent anomalies.

To return to the incubation period in reinfections. This shortening for second inoculations has been noted in other diseases when the influence of a first inoculation still exists.

With our modern vaccination against smallpox, we actually give the patient a definite disease, cowpox. If the influence of a previous vaccination is sufficiently strong, no lesion develops from a second attempt at vaccination. If the influence is still there, but is not sufficient to prevent the "vaccine taking," we merely get a shortening of the incubation period. Further, it is well-known that a patient with a primary syphilitic lesion can reinfect himself within 7 days of the first appearance of
the sore. Lesions thus produced have a shortened incubation period, 10-15 days.

Regarding the character of the lesions resulting from reinfection. In those few experiments where primary syphilitic material has been experimentally inoculated with known tertiary syphilitics, the ulcers produced resembled gummata, and were not in the least like primary syphilitic chancre. The incubation period was shorter than for primary syphilis. It is argued that in these experiments gross amounts of material were used, and unless the inoculation was deep and very thorough, no lesions were produced. It is claimed that such an inoculation could hardly be produced during sexual contact. This is not a very weighty objection. The infective agent of syphilis seems to have a selective choice for the genitals, and also seems to be better capable of survival if the contagion results from coitus. Possibly certain pabulum present at this time aids its survival, and these conditions are not easily imitated experimentally.

In practice the therapeutic test provided the most convincing argument. I kept my selected cases under observa-
tion for varying times during which I experimented with all forms of local treatment.

With few exceptions they failed to heal. Finally I administered salvarsan. Although Treponema Pallidum had not been found and their sera still gave a negative Wassermann reaction, they healed with remarkable rapidity. I had tried salvarsan in cases of clinically typical soft sores, and had never found it to be of the slightest value. One explanation offered is that these were chancroids, modified in their appearance and made more resistant to treatment by the influence of previous syphilis. As I have already mentioned, this influence can cause a chancroid to take on gummatous characters. In the cases I have observed the syphilis was active and the sera gave positive Wassermann reactions. The incubation period in these cases was unaffected.

There is another point of view from which this whole problem may be approached. Are the varieties found in the lesions dependent not on any previous syphilis in the person who contracts, but on the age, and perhaps stage in the life cycle (if such exists) of the
Treponema Pallidum contained in the lesions of the woman imparting the infection. Are these lesions the result of contact with late secondary or tertiary lesions in the woman? I do not think there is anything to support this view.

Some of the ulcers that I am trying to claim as syphilitic in origin might have failed to satisfy some clinicians because they did not exhibit well-marked induration which by many is considered essential to establish a diagnosis of syphilis.

I think perhaps too much prominence has been given to this sign. It is rarely found in the early stages of many primary syphilitic sores. In at least one variety, the primary granulating sore, it is conspicuous by its absence. Induration would appear to be primarily dependent on the site of inoculation of the virus. In its acme of development it is seen in the primary Hunterian chancre which invariably occurs on the inner surface of the prepuce and here produces the characteristic "elastic button." It is almost as well shown in the urethral chancre and to a slightly less extent in the meatal chancre. Around the papulo-
erosive sore in the coronal sulcus a "half button" of marked induration may be found in the adjacent part of the inner surface of the prepuce.

The primary granulating sore already mentioned as failing to exhibit induration is, in spite of this, perhaps the least variable of all primary lesions. It may occur on any skin surface, but is usually found on the skin of the body of the penis. It is always regularly oval in shape, its surface is smooth, red and glistening, and neither raised nor depressed in relation to the surrounding skin surface. From this surface there is an abrupt transition to healthy skin, which shows neither redness nor induration. When in its commonest situation, the body of the penis, the long axis of the oval is at right angles to the long axis of the penis. It heals leaving a most characteristic oval, deeply pigmented area, permanently to mark its site and to brand the patient as an undoubted victim of syphilis.

Another variety that rarely shows any induration is the syphilitic abrasion which occurs on the glans penis.

The second factor upon which induration would appear
to be dependent is superadded septic infection, and a third factor is the use or misuse of caustics or other irritating applications. Induration under these circumstances cannot be said to be characteristic of syphilis. Lesions resulting from almost every cause may under these influences become the site of cellular accumulation. When a soft sore has existed for some considerable time, as it occasionally will do, and treatment has been active or septic infection marked, pronounced induration results. This, of course, at once leads to the suspicion that syphilis has supervened, but observation and tests over a long period have failed to support this contention. In my experience in the army, the want of induration in the primary granulating sore was the commonest cause of errors in diagnosis. One could almost predict this as the mis-diagnosed lesion when a soldier presented himself with secondary signs of syphilis and stated that he had been treated by his Regimental Medical Officer for a soft chancre until these showed themselves. Syphilis therefore does not necessarily constitute induration, though induration frequently means syphilis.
SUMMARY.

In this paper I have endeavoured to show that syphilitic reinfection is possible before the individual has entirely recovered from the effects of his previous syphilis. I have tried to show that this occurs in other diseases. I have dealt with such objections as have suggested themselves to me.

I am aware that my contention is based chiefly on clinical observation, but as the result of this I have been fully convinced.

Further investigation might throw more positive light on this subject and clear up many of the difficulties which I feel other clinicians must have shared with me.
REFERENCES.

(1) Syphilis and the Army, G. Thibierge, Chapter IV, Military Medical Manuals.

(2) Syphilis. Sir Jonathan Hutchinson, Chapter VIII.


(4) Biology and Treatment of Venereal Diseases. McDonagh.


I hereby declare that the above is an entirely original commentary only where indicated is the work of others embodied.